Synthesis of Novel 5-Phenylselenenyl-2,4-Disubstituted Pyrimidine Analogs

ISMAIL, UPENDAR REDDY CH and THALARI GANGADHAR

Department of Chemistry, Nizam College, Bhasheerbhagh, Hyderabad-500001, Andhra Pradesh, India

gangadhar.thalari@gmail.com

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Abstract: 5-Phenylselenenyl-2,4-disubstituted pyrimidine analogs were prepared efficiently in four steps. Thiol group of 2-thiouracil was protected with various alkylating agents in presence of base furnishes 2-alkylthiouracils (2a-c), these on reaction with phenylselenenyl chloride in pyridine under anhydrous conditions yielded 5-phenylselenenyl-2-alkylthiouracils (3a-c). Chlorination of 5-phenyl-selenenyl-2-alkylthiouracils with excess POCl₃ under reflux furnishes 5-phenylselenenyl-4-chloro-2-alkylthiopyrimidines (4a-c). Aromatic nucleophilic substitution reaction of 5-phenyl-selenenyl-4-chloro-2-alkylthiopyrimidines with oxygen nucleophiles like sodium phenoxides furnished the target compounds (5a-o) in 60-75% yield. All the synthesized compounds were evaluated for antimicrobial activities.

Keywords: Pyrimidine analogs, 2-Alkylthiouracils, 5-Phenylselenenylpyrimidines, 2,4,5-Trisubstituted pyrimidines

Introduction

Selenium, an essential trace mineral is a vital component of the selenoproteins specifically glutathione peroxidase mainly required for normal health and reproduction. Selenium was discovered in 1818 by Swedish chemist Berzelius. It was considered as a poison until it was identified as a micronutrient for bacteria, mammals and birds. Selenium is essential for the efficient and effective operation of the immune system in both animals and humans. Organoselenium compounds have substantially greater bioavailability than that of inorganic selenium. More importantly, organic selenium is usually found to be less toxic than inorganic forms. Organoselenium compounds have been tested as antibacterial, antiviral, antifungal, antiparasitic, antihistamine and anticancer agents. During the last few years, tremendous effort has been directed towards the synthesis of stable organoselenium compounds that could be used as antioxidants, enzyme modulators, antitumors, antivirals, antimicrobials, antihypertensive agents and cytokine inducers. Though several organoselenium compounds are known, they are less explored for their antibacterial properties. Phenylselenenyl substituted pyrimidines were synthesized and evaluated for the inhibition of enzymes involved in pyrimidine metabolism such as dihydrouracil dehydrogenase (DHUDase), orotate phosphoribosyl transferase (OPRTase), Thymidine phosphorylase (Thdpase) and uridine phosphorylase (Urdpase). Herein, we report a facile methodology for the synthesis of various 5-phenylselenenyl-4-phenoxy-2-alkylthiopyrimidines starting from 2-thiouracil.
Experimental

2-Thiouracil was purchased from Hi-Media Laboratories Pvt. Ltd., Mumbai (India), methyl iodide, ethyl iodide, benzyl chloride, POCl₃ and phenols were purchased from SISCO Research Laboratories Pvt. Ltd., Mumbai (India). All the solvents used were laboratory grade or were purified according to standard procedures. Melting points were determined by using a Thomas-Hoover melting point apparatus and were uncorrected. IR spectra in KBr disc were recorded on Perkin-Elmer-Spectrum-one FTIR spectrophotometer (ν max in cm⁻¹) and ¹H NMR spectra in DMSO-d₆ and/or CDCl₃ on amx 400, 400 MHz spectrophotometer using TMS as internal standard (chemical shift in δ or ppm). Mass spectra were recorded on a JEOL SX 102 Mass spectrometer using Argon/Xenon (6kv, 10 mA) as the FAB gas. Purity of the compounds was checked by TLC using silica gel ‘G’ plates obtained from Whatman Inc and a fluorescent indicator. 2-alkylthiouracils 2a-c were prepared by following the literature method₁₈a-d.

General procedure for the preparation of 5-phenylselenenyl-2-alkylthiouracil (3a-c)

Phenylselenenyl chloride (0.006 mol) was dissolved in dry pyridine (30 mL) and then 2-alkylthiouracil (0.006 mol) was added. The reaction mixture was stirred at 60–65 °C for 24 h under nitrogen atmosphere (monitored by TLC). The reaction mixture was allowed to cool to room temperature and then concentrated under vacuum to remove pyridine. The residue was co-evaporated with benzene and EtOH (20:10 mL). The residue was loaded on silica gel column and eluted with CHCl₃ to remove diphenyldiselenide. The product was then obtained on elution with CHCl₃: MeOH (95:5) and TLC pure fractions were pooled and concentrated.

2-Methylthio-5-phenylselenenyl pyrimidin-4(3H)-one (3a)

Anal. Calcd. for C₁₁H₁₀N₂OSSe: C, 44.45; N, 9.42. Found: C, 44.47; N, 9.45; IR (KBr, cm⁻¹): 3200 (NH), 1630 (C=O), 1595 (C=N); ¹H NMR (400 MHz, CDCl₃, δ / ppm): 2.50 (s, 3H, SCH₃), 7.50-7.30 (m, 5H, C₆H₅), 7.65 (s, 1H, C₆H), 12.2 (s, 1H, NH); ¹³C NMR (100 MHz, CDCl₃, δ / ppm): 170, 165, 139, 133 (2C), 130, 128, 127 (3C), 15; MS (m/z, (relative abundance, %)): 298 (M⁺, 100%).

2-Ethylthio-5-phenylselenenyl pyrimidin-4(3H)-one (3b)

Anal. Calcd. for C₁₃H₁₂N₂OSSe: C, 46.30; N, 9.00. Found: C, 44.32; N, 9.02; IR (KBr, cm⁻¹): 3190 (NH), 1620 (C=O), 1585 (C=N); ¹H NMR (400 MHz, CDCl₃, δ / ppm): 1.30 (t, 3H, SCH₂CH₃), 3.20 (q, 2H, SCH₂CH₃), 7.55-7.35 (m, 5H, C₆H₅), 7.68 (s, 1H, C₆H), 12.5 (s, 1H, NH); ¹³C NMR (100 MHz, CDCl₃, δ / ppm): 172, 163, 139, 133 (2C), 130, 128, 127 (3C), 26, 16; MS (m/z, (relative abundance, %)): 312 (M⁺, 100%).

2-Benzylthio-5-phenylselenenyl pyrimidin-4(3H)-one (3c)

Anal. Calcd. for C₁₇H₁₄N₂OSSe: C, 54.69; N, 7.50. Found: C, 54.67; N, 7.51; IR (KBr): NH 3180, C=O 1636, C=N- 1591 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, δ / ppm): 7.53-7.26 (m, 10H, C₆H₅), 7.79 (s, 1H, C₆H), 12.4 (s, 1H, NH); ¹³C NMR (100 MHz, CDCl₃, δ / ppm): 175, 162, 140, 136, 132 (2C), 130 (2C), 127 (5C), 125 (3C), 37; MS (m/z, (relative abundance, %)): 374 (M⁺, 100%).

General procedure for the preparation of 5-phenylselenenyl-4-chloro-2-alkylthio-pyrimidines (4a-c)

A mixture of 5-phenylselenenyl-2-alkylthio uracils (3a-c) (0.01 mol) and POCl₃ (0.1 mole) was refluxed for 3 hrs (monitored by TLC). Excess POCl₃ was removed under reduced pressure and the mixture was treated with ice-cold water. The separated solid was extracted
with ether and washed with aq. NaHCO₃ (5%) solution. Ether layer was collected and dried over anhydrous sodium sulphate and after solvent evaporation yielded the title compounds 4a-c and were recrystallized from EtOH.

4-Chloro-2-methylthio-5-phenylselenenyl pyrimidine (4a)
Anal. Calcd. for C₁₁H₉ClN₂SSe: C, 41.85; N, 8.87. Found: C, 41.87; N, 8.89; ¹H NMR (400 MHz, CDCl₃, δ / ppm): 2.53 (s, 3H, SCH₃), 7.25-7.40 (m, 5H, C₆H₅), 7.70 (s, 1H, C₆H); ¹³C NMR (100 MHz, CDCl₃, δ / ppm): 173, 160, 155, 138 (2C), 130, 127 (3C), 120, 15; MS (m/z, (relative abundance, %)): 316 (M⁺, 100%).

4-Chloro-2-ethylthio-5-phenylselenenyl pyrimidine (4b)
Anal. Calcd. for C₁₂H₁₁ClN₂SSe: C, 43.71; N, 8.50. Found: C, 43.72; N, 8.51; ¹H NMR (400 MHz, CDCl₃, δ / ppm): 1.27 (t, 3H, SCH₂CH₃), 3.00 (q, 2H, SCH₂CH₃), 7.30-7.45 (m, 5H, C₆H₅), 7.86 (s, 1H, C₆H); ¹³C NMR (100 MHz, CDCl₃, δ / ppm): 172, 160, 156, 137 (2C), 131, 128 (3C), 121, 30, 16; MS (m/z, (relative abundance, %)): 330 (M⁺, 100%).

4-Chloro-2-benzylthio-5-phenylselenenyl pyrimidine (4c)
Anal. Calcd. for C₁₇H₁₃N₂SSeCl: C, 52.12; N, 7.15. Found: C, 52.14; N, 7.16; ¹H NMR (400 MHz, CDCl₃, δ / ppm): 4.3 (s, 2H, SCH₂Ph), 7.6-7.1 (m, 10H, C₆H₅), 8.0 (s, 1H, C₆H); ¹³C NMR (100 MHz, CDCl₃, δ / ppm): 172, 160, 156, 137 (3C), 130, 128 (5C), 127 (3C), 120, 35; MS (m/z, (relative abundance, %)): 392 (M⁺, 100%).

General procedure for the preparation of 5-phenylselenenyl-4-phenoxy-2-alkylthiopyrimidines (5a-o)
To a solution of appropriate phenol (0.004 mole) in dry toluene (10 mL) was treated with 60% w/v sodium hydride (0.004 mole) in oil under an inert atmosphere. The mixture was warmed to 50-60 °C for 30 min to facilitate the formation of sodium salt. After all the sodium hydride had reacted, the suspension was cooled and a solution of 5-phenylselenenyl-4-chloro-2-alkylthiopyrimidines (4a-c) (0.001 mole) in toluene (10 mL) was added slowly at room temperature. After stirring the reaction mixture at 75-80 °C overnight (monitored by TLC), it was allowed to cool to room temperature and the mixture was treated with water (25 mL). The separated solid was extracted with ether (3x25 mL) and washed with 10% aq sodium hydroxide (3x25 mL). Ether layer was collected, dried over anhydrous sodium sulphate and evaporation of the solvent furnished the crude compounds, which were recrystallized from EtOH yielded the title compounds 5a-o.

2-Methylthio-4-phenoxy-5-phenylselenenyl pyrimidine (5a)
Anal. Calcd. for C₁₃H₁₄N₂OSSe: C, 54.69; N, 7.50. Found: C, 54.70; N, 7.52; ¹H NMR (400 MHz, CDCl₃, δ / ppm): 2.50 (s, 3H, SCH₃), 6.95-7.35 (m, 10H, C₆H₅), 8.70 (s, 1H, C₆H); ¹³C NMR (100 MHz, CDCl₃, δ / ppm): 180, 170, 160, 155, 138 (2C), 130 (3C), 128 (3C), 125, 122 (2C), 106, 15; MS (m/z, (relative abundance, %)): 374 (M⁺, 100%).

2-Methylthio-4-(o-tolyloxy)-5-phenylselenenyl pyrimidine (5b)
Anal. Calcd. for C₁₅H₁₅N₂OSSe: C, 55.81; H, 4.16; N, 7.23. Found: C, 55.83; H, 4.15; N, 7.25; ¹H NMR (400 MHz, CDCl₃, δ / ppm): 2.15 (s, 3H, CH₃), 2.51 (s, 3H, SCH₃), 7.05-7.30 (m, 9H, C₆H₅), 8.65 (s, 1H, C₆H); ¹³C NMR (100 MHz, CDCl₃, δ / ppm): 180, 170, 160, 150, 138 (2C), 135, 130, 128 (4C), 126, 124, 119, 106, 17, 15; MS (m/z, (relative abundance, %)): 388 (M⁺, 100%).
2-Methylthio-4-(m-tolyloxy)-5-phenylselenenyl pyrimidine (5c)
Anal. Calcd. for C$_{18}$H$_{16}$N$_2$OSSe: C, 55.81; N, 7.23. Found: C, 55.82; N, 7.24; $^1$H NMR (400 MHz, CDCl$_3$, δ / ppm): 2.13 (s, 3H, CH$_3$), 2.49 (s, 3H, SCH$_3$), 7.06-7.35 (m, 9H, C$_6$H$_5$), 8.62 (s, 1H, C$_6$H); MS (m/z, (relative abundance, %)): 388 (M$^+$, 100%).

2-Methylthio-4-(p-tolyloxy)-5-phenylselenenyl pyrimidine (5d)
Anal. Calcd. for C$_{18}$H$_{16}$N$_2$OSSe: C, 55.81; N, 7.23. Found: C, 55.80; N, 7.23; $^1$H NMR (400 MHz, CDCl$_3$, δ / ppm): 2.35 (s, 3H, CH$_3$), 2.50 (s, 3H, SCH$_3$), 7.06 (d, 2H, ArH), 7.12 (d, 2H, ArH), 7.30-7.45 (m, 5H, C$_6$H$_5$), 8.71 (s, 1H, C$_6$H); MS (m/z, (relative abundance, %)): 388 (M$^+$, 100%).

2-Methylthio-4-(p-chlorophenoxy)-5-phenylselenenyl pyrimidine (5e)
Anal. Calcd. for C$_{17}$H$_{13}$ClN$_2$OSSe: C, 50.07; N, 6.87. Found: C, 50.08; N, 6.89; $^1$H NMR (400 MHz, CDCl$_3$, δ / ppm): 2.50 (s, 3H, SCH$_3$), 7.08 (d, 2H, ArH), 7.12 (d, 2H, ArH), 7.30-7.48 (m, 5H, C$_6$H$_5$), 8.70 (s, 1H, C$_6$H); MS (m/z, (relative abundance, %)): 408 (M$^+$, 100%).

2-Ethylthio-4-phenoxy-5-phenylselenenyl pyrimidine (5f)
Anal. Calcd. for C$_{18}$H$_{16}$N$_2$OSSe: C, 55.81; N, 7.23. Found: C, 55.82; N, 7.25; $^1$H NMR (400 MHz, CDCl$_3$, δ / ppm): 1.30 (t, 3H, CH$_3$), 3.2 (q, 2H, SCH$_2$), 6.95-7.45 (m, 10H, C$_6$H$_5$), 8.68 (s, 1H, C$_6$H); 13C NMR (100 MHz, CDCl$_3$, δ / ppm): 170, 168, 160, 155, 137 (2C), 129 (3C), 128 (3C), 124, 122 (2C), 105, 15, 17; MS (m/z, (relative abundance, %)): 388 (M$^+$, 100%).

2-Ethylthio-4-(o-tolyloxy)-5-phenylselenenyl pyrimidine (5g)
Anal. Calcd. for C$_{19}$H$_{18}$N$_2$OSSe: C, 56.85; N, 6.98. Found: C, 56.86; N, 6.99; $^1$H NMR (400 MHz, CDCl$_3$, δ / ppm): 1.30 (t, 3H, CH$_3$), 2.15 (s, 3H, CH$_3$), 3.2 (q, 2H, SCH$_2$), 7.05-7.30 (m, 9H, C$_6$H$_5$), 8.70 (s, 1H, C$_6$H); 13C NMR (100 MHz, CDCl$_3$, δ / ppm): 171, 165, 158, 154, 135 (2C), 130 (3C), 129 (3C), 125, 121 (2C), 106, 32, 17, 15; MS (m/z, (relative abundance, %)): 402 (M$^+$, 100%).

2-Ethylthio-4-(m-tolyloxy)-5-phenylselenenyl pyrimidine (5h)
Anal. Calcd. for C$_{19}$H$_{18}$N$_2$OSSe: C, 56.85; N, 6.98. Found: C, 56.84; N, 6.97; $^1$H NMR (400 MHz, CDCl$_3$, δ / ppm): 1.30 (t, 3H, CH$_3$), 2.13 (s, 3H, CH$_3$), 3.2 (q, 2H, SCH$_2$), 7.06-7.35 (m, 9H, C$_6$H$_5$), 8.62 (s, 1H, C$_6$H); MS (m/z, (relative abundance, %)): 402 (M$^+$, 100%).

2-Ethylthio-4-(p-tolyloxy)-5-phenylselenenyl pyrimidine (5i)
Anal. Calcd. for C$_{19}$H$_{18}$N$_2$OSSe: C, 56.85; N, 6.98. Found: C, 56.83; N, 6.97; $^1$H NMR (400 MHz, CDCl$_3$, δ / ppm): 1.30 (t, 3H, CH$_3$), 2.35 (s, 3H, CH$_3$), 3.2 (q, 2H, SCH$_2$), 7.06 (d, 2H, ArH), 7.09 (d, 2H, ArH), 7.30-7.45 (m, 5H, C$_6$H$_5$), 8.71 (s, 1H, C$_6$H); MS (m/z, (relative abundance, %)): 402 (M$^+$, 100%).

2-Ethylthio-4-(m-chlorophenoxy)-5-phenylselenenyl pyrimidine (5j)
Anal. Calcd. for C$_{18}$H$_{15}$ClN$_2$OSSe: C, 51.25; N, 6.64. Found: C, 51.27; N, 6.65; $^1$H NMR (400 MHz, CDCl$_3$, δ / ppm): 1.30 (t, 3H, CH$_3$), 3.2 (q, 2H, SCH$_2$), 7.08 (d, 2H, ArH), 7.12 (d, 2H, ArH), 7.30-7.48 (m, 5H, C$_6$H$_5$), 8.70 (s, 1H, C$_6$H); MS (m/z, (relative abundance, %)): 422 (M$^+$, 100%).

2-Benzylthio-4-phenoxy-5-phenylselenenyl pyrimidine (5k)
Anal. Calcd. for C$_{23}$H$_{18}$N$_2$OSSe: C, 61.47; N, 6.23. Found: C, 61.50; N, 6.25; $^1$H NMR (400 MHz, CDCl$_3$, δ / ppm): 4.4 (s, 2H, SCH$_2$), 6.95-7.45 (m, 15H, C$_6$H$_5$), 8.68 (s, 1H, C$_6$H); 13C NMR (100 MHz, CDCl$_3$, δ / ppm): 170 (2C), 160, 155, 137 (3C), 129 (3C), 128 (5C), 127 (3C), 124, 122 (2C), 105, 35; MS (m/z, (relative abundance, %)): 450 (M$^+$, 100%).
2-Benzylthio-4-(o-tolyloxy)-5-phenylselenenyl pyrimidine (5l)
Anal. Calcd. for C_{24}H_{20}N_{2}OSSe: C, 62.20; N, 6.04. Found: C, 62.18; N, 6.02; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, \delta / ppm): 2.10 (s, 3H, CH\textsubscript{3}), 4.40 (s, 2H, SCH\textsubscript{2}), 6.97-7.47 (m, 15H, C\textsubscript{6}H\textsubscript{5}), 8.65 (s, 1H, C\textsubscript{6}H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}, \delta / ppm): 172 (2C), 161, 153, 138 (3C), 130 (3C), 125 (5C), 121, 122 (2C), 103, 36, 16; MS (m/z, relative abundance, %)): 464 (M\textsuperscript{+}, 100%).

2-Benzylthio-4-(m-tolyloxy)-5-phenylselenenyl pyrimidine (5m)
Anal. Calcd. for C_{24}H_{20}N_{2}OSSe: C, 62.20; N, 6.04. Found: C, 62.21; N, 6.06; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, \delta / ppm): 2.13 (s, 3H, CH\textsubscript{3}), 4.41 (s, 2H, SCH\textsubscript{2}), 6.90-7.47 (m, 15H, C\textsubscript{6}H\textsubscript{5}), 8.65 (s, 1H, C\textsubscript{6}H); MS (m/z, relative abundance, %)): 464 (M\textsuperscript{+}, 100%).

2-Benzylthio-4-(p-tolyloxy)-5-phenylselenenyl pyrimidine (5n)
Anal. Calcd. for C_{24}H_{20}N_{2}OSSe: C, 62.20; N, 6.04. Found: C, 62.20; N, 6.04; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, \delta / ppm): 2.17 (s, 3H, CH\textsubscript{3}), 4.45 (s, 2H, SCH\textsubscript{2}), 6.90-7.40 (m, 15H, C\textsubscript{6}H\textsubscript{5}), 8.60 (s, 1H, C\textsubscript{6}H); MS (m/z, relative abundance, %)): 464 (M\textsuperscript{+}, 100%).

2-Benzylthio-4-(p-chlorophenoxy)-5-phenylselenenyl pyrimidine (5o)
Anal. Calcd. for C_{23}H_{17}ClN_{2}OSSe: C, 57.09; N, 5.79. Found: C, 57.10; N, 5.80; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, \delta / ppm): 4.38 (s, 2H, SCH\textsubscript{2}), 7.30-7.45 (m, 14H, C\textsubscript{6}H\textsubscript{5}), 8.67 (s, 1H, C\textsubscript{6}H); MS (m/z, relative abundance, %)): 484 (M\textsuperscript{+}, 100%).

Results and Discussion

2-Thiouracil 1 was reacted with alkylhalides in presence of base furnished 2-alkylthiouracils (2a-c) in 63-90% yield (Scheme 1 and Table 1). The reaction of compounds 2a-c with phenylselenenyl chloride in dry pyridine under anhydrous condition at 60-65 oC for 24 h furnished the expected compound 5-phenylselenenyl-2-alkylthiouracils (3a-c) in 65-70% yield. The IR spectrum of compound 3c shows characteristic absorptions of NH at 3180, C=O 1636 and –C=N 1591 cm\textsuperscript{-1} respectively. Further, the structure of compound 3c was confirmed by the \textsuperscript{1}H NMR spectrum and the characteristic signals are at \delta 12.4 (s, 1H. NH), 7.79 (s, 1H, C\textsubscript{6}H), 7.53-7.26 (m, 10H, C\textsubscript{6}H\textsubscript{5}), 4.36 (s, 2H, SCH\textsubscript{2}Ph). Further the structure of compound 3c was confirmed based on the mass spectral data, the molecular ion peak at m/z = 374 (M\textsuperscript{+1}, 100%). The \textsuperscript{1}H NMR spectrum of the compound 3c indicates the phenylselenenyl group was attached to the C3-position of the pyrimidine ring. A significant deshielding effect of C\textsubscript{6}H was caused by the presence of a selenium substituent at the C5-position of the pyrimidine ring.

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\text{Scheme 1. Synthesis of 5-phenylselenenyl-2,4-disubstituted pyrimidines (5a-o)}
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The title compounds 5c-phenylselenyl-4-chloro-2-benzylthiopyrimidine spectral data, the molecular ion peak at m/z = 450 (M+1, 100%).

Further the structure of compound 5 via the aromatic nucleophilic substitution reaction. for overnight at room temperature, solid. The 1H NMR signals are at δ 8.0 (s, 1H, C6H), 7.65-7.1 (m, 10H, C6H5), 4.35 (s, 2H, SCH2Ph). Additional confirmation is the absence of C=O absorptions at 1636 cm⁻¹ respectively, while it shows the presence of C-Cl absorption at 735 cm⁻¹. Further confirmation of the structure of compound 4c was based on the following spectral data, IR spectrum of compound 4c shows the absence of NH peak at δ 12.4 due to the aromatization of 5-phenylselenenyl-2-benzylthiouracil 3c to 5-phenylselenenyl-4-chloro-2-benzylthiopyrimidine 4c. Further the structure of compound 4c was confirmed based on the mass spectral data, the molecular ion peak at m/z = 392 (M⁺, 100%). The title compounds 5a-o were obtained by the reaction of compounds 4a-c with oxygen nucleophiles such as sodium phenoxides in dry toluene under N₂ atmosphere for overnight at room temperature, via the aromatic nucleophilic substitution reaction. Compound 5k was obtained in 70% yield, having m.p. 67-69 °C as a brown crystalline solid. The 1H NMR signals are at δ 8.22 (s, 1H, C₆H), 7.65-7.15 (m, 15H, C₆H₅), 4.35 (s, 2H, SCH₂Ph). Further the structure of compound 5k was confirmed based on the mass spectral data, the molecular ion peak at m/z = 450 (M⁺, 100%).

Table 1. Synthesis of 5-phenylselenenyl-4-substituted-2-benzylthiopyrimidines (5a-o)

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<th>Yield, %</th>
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*Melting points are uncorrected, Yield refers to purified product*
Conclusion
In conclusion, we have developed novel and efficient synthesis of 2,4,5-trisubstituted pyrimidine analogs bearing four hetero atoms like N, O, S and Se.

References