Microwave-Assisted Synthesis and Functionalization of Selenolopyrimidines

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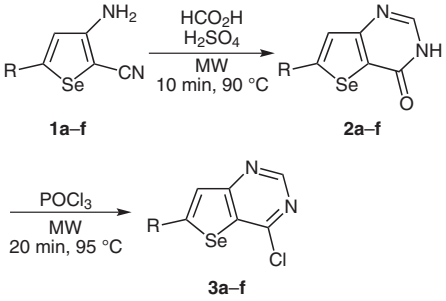
Abstract: Microwave-assisted synthesis allowed efficient access to 4-chloroselenolo[3,2-*d*]pyrimidines in short times and very good yields. Some functionalizations by S_NAr and palladium-catalyzed reactions are also reported.

Key words: selenium, pyrimidines, heterocycles, cyclizations, microwave-assisted reactions

Heterocyclic condensed pyrimidines have attracted considerable attention due to their interesting biological properties. For example, pyrrolo[2,3-*d*]pyrimidines[1] and pyrazolo[3,4-*d*]pyrimidines[2] have been described as anti-angiogenic agents, thieno[3,2-*d*]pyrimidines[3] as antagonists of human adenosine A2 receptors, and furo[2,3-*d*]pyrimidines[4] as inhibitors of Lck. In contrast, studies of selenolopyrimidines have been scarce.[5]

Our laboratory has been interested in the synthesis of selenophenes and selenolocondensed systems for many years.[6] We recently described the synthesis of selenophene analogues of tacrine, starting from 3-aminoselenophene-2-carbonitriles,[7] and thought that those starting materials would also allow easy access to selenolopyrimidines, as we have previously done the same in the thiophene series.[8] This moiety is of interest, as 4-(alkylamino)pyrimido[4′,5′:4,5]selenolo[2,3-*b*]quinolines were reported to be antitumor agents[9] and pyrimido[4′,5′:4,5]selenolo[2,3-*c*]pyridazines were tested for anti-inflammatory activity.[10]

3-Aminoselenophene-2-carbonitriles **1a–f** were reacted with formic acid in the presence of catalytic amounts of sulfuric acid under microwave irradiation (Scheme 1). Selenolo[3,2-*d*]pyrimidin-4-ones **2a–f** were obtained in good yields after only ten minutes of irradiation. Compounds **2a**, **2b**, and **2f** were also synthesized under classical heating (110 °C, 4 h) in yields of 77, 86, and 53%, respectively. Compounds **2a–f** were converted into 4-chloroselenolo[3,2-*d*]pyrimidines **3a–f** by reaction with phosphoryl chloride. Reactions were also performed under microwave irradiation for only 20 minutes at 95 °C (Scheme 1, Table 1). Compound **3b** was also prepared under classical heating (90 °C, 18 h) in 71% yield. In both cases, namely the syntheses of compounds **2** and **3**, the use of microwave irradiation allowed shorter reaction times and higher yields.

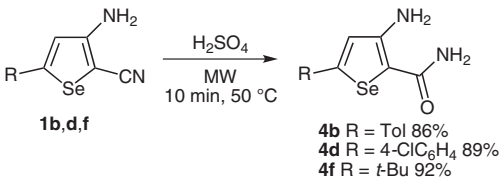


Scheme 1

Table 1 Microwave-Assisted Synthesis of Chloroselenolopyrimidines

R	Product **2**	Yield (%)	Product **3**	Yield (%)
Ph	**2a**	83	**3a**	98
Tol	**2b**	88	**3b**	93
PMP	**2c**	91	**3c**	95
4-ClC_6H_4	**2d**	92	**3d**	98
4-$O_2NC_6H_4$	**2e**	87	**3e**	83
t-Bu	**2f**	65	**3f**	67

Inspired by literature procedures,[11] we also tested another preparation of selenolo[3,2-*d*]pyrimidin-4-ones by the reaction of 3-aminoselenophene-2-carboxamides with ethyl oxalate. First, the cyano groups of compounds **1b**, **1d**, and **1f** were converted into amides after ten minutes of microwave irradiation in concentrated sulfuric acid (Scheme 2). Compound **4b** was also obtained under classical conditions (20 °C, 15 h) in 75% yield.



Scheme 2

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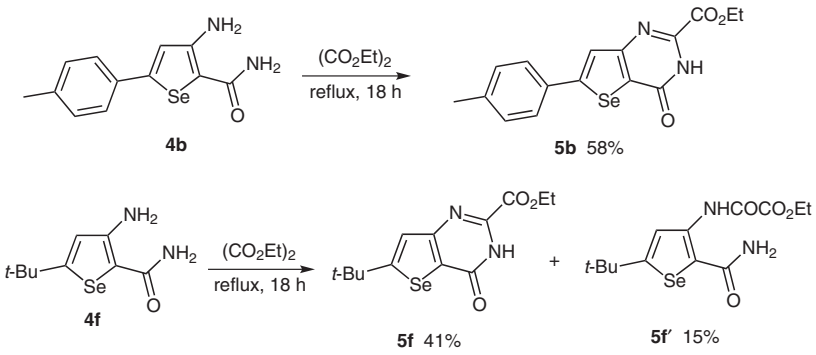
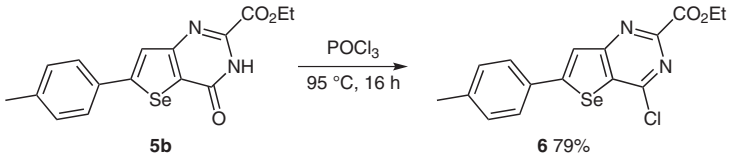
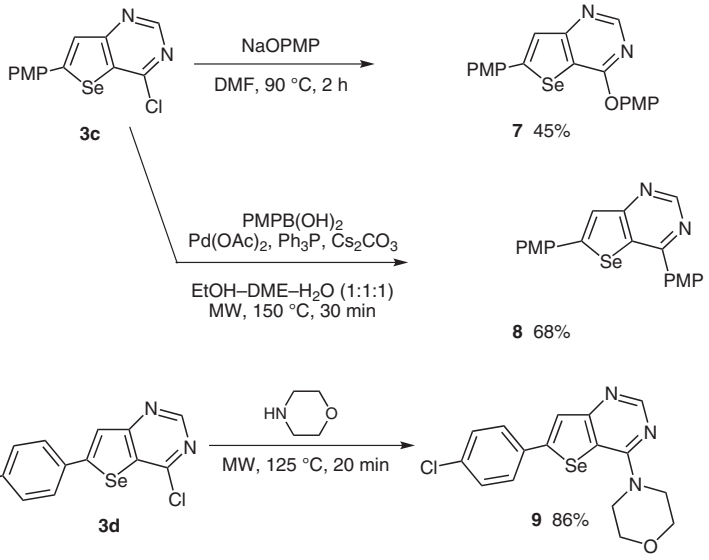


Scheme 3



Scheme 4



Scheme 5

Subsequent reaction of compound **4b** with ethyl oxalate led to selenolo[3,2-*d*]pyrimidin-4-one **5b** in 58% yield after 18 hours of reflux (Scheme 3). The reaction mixture was cooled to room temperature and diluted with cyclohexane; compound **5b** precipitated and was isolated by filtration. The same reaction was performed with compound **4f** (Scheme 3). After similar treatment, the non-cyclized intermediate **5f′** was isolated by filtration in 15% yield. Hydrolysis and extraction of the reaction mixture gave the expected product **5f** in 41% yield. Attempts were made to transpose this reaction under microwave irradiation, but it was difficult to find the right conditions. Compound **5b** was then submitted to chlorination, and product **6** was obtained in 79% yield (Scheme 4).

We next studied the reactivity of the chlorine atom of some 4-chloroselenolopyrimidines in S_NAr and palladium-catalyzed reactions. Compound **3c** was reacted with sodium 4-methoxyphenoxide in *N*,*N*-dimethylformamide, and gave compound **7** in 45% yield (Scheme 5). Suzuki coupling was performed under microwave irradiation and gave compound **8** in good yield. Substitution by a secondary aliphatic amine was also easy under microwave irradiation, as compound **3d** readily reacted with morpholine to give compound **9** in 86% yield.

In conclusion, 3-aminoselenophene-2-carbonitriles are interesting scaffolds and have allowed the synthesis of 18 new selenolo[3,2-*d*]pyrimidines with diverse substituents. The syntheses we described here were achieved in very short times thanks to the use of microwave irradiation.

Moreover, this procedure is also attractive due to easy workup (simple filtrations) and easy purification when necessary (only recrystallization and no column chromatography on silica gel).

Melting points were determined on a Stuart SMP3 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on an AC Bruker 250-MHz spectrometer. HRMS was performed on a Bruker MICROTOF-Q ESI/QqTOF spectrometer. IR spectra were recorded on a Perkin Elmer Spectrum BX spectrometer. A CEM Discover microwave oven was used for the microwave-assisted reactions. 3-Aminoselenophene-2-carbonitriles **1a–f** were synthesized as previously reported.[7]

Selenolopyrimidinones 2a–f; General Procedure
A 50-mL one-necked round-bottomed flask equipped with a stirrer bar was charged with the appropriate 3-aminoselenophene-2-carbonitrile **1** (2 mmol), HCO_2H (99%, 4 mL), and concd H_2SO_4 (0.25 mL). The reaction mixture was placed in a microwave reactor (CEM Discover) and was heated at 90 °C for 10 min. After cooling, the mixture was poured into H_2O and the precipitate was filtered. The crude product was purified by recrystallization from EtOH.

6-Phenylselenolo[3,2-*d*]pyrimidin-4-one (2a)
Brown solid; mp 190 °C (dec).

IR (KBr): 3437, 1639 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 12.50 (br s, 1 H), 8.17 (s, 1 H), 7.99 (s, 1 H), 7.78 (d, *J* = 7.7 Hz, 2 H), 7.45–7.47 (m, 3 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 160.8, 158.0, 155.8, 147.3, 134.4, 129.6, 129.3, 126.4, 125.3, 124.0.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_9N_2OSe$: 276.9875; found: 276.9884.

6-(4-Tolyl)selenolo[3,2-*d*]pyrimidin-4-one (2b)
Brown solid; mp 270 °C (dec).

IR (KBr): 1660 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 12.46 (br s, 1 H), 8.16 (s, 1 H), 7.94 (s, 1 H), 7.69 (d, *J* = 7.9 Hz, 2 H), 7.28 (d, *J* = 7.9 Hz, 2 H), 2.33 (s, 3 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 160.9, 158.0, 156.0, 147.2, 139.5, 131.7, 129.8, 126.3, 124.8, 123.3, 20.8.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{11}N_2OSe$: 291.0031; found: 291.0023.

6-(4-Methoxyphenyl)selenolo[3,2-*d*]pyrimidin-4-one (2c)
Brown solid; mp 260 °C (dec).

IR (KBr): 3436, 1683 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 8.14 (s, 1 H), 7.85 (s, 1 H), 7.74 (d, *J* = 8.8 Hz, 2 H), 7.02 (d, *J* = 8.8 Hz, 2 H), 3.80 (s, 3 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 161.1, 160.4, 158.0, 155.8, 147.2, 128.0, 127.0, 123.5, 122.5, 114.6, 55.4.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{11}N_2O_2Se$: 306.9980; found: 306.9984.

6-(4-Chlorophenyl)selenolo[3,2-*d*]pyrimidin-4-one (2d)
Brown solid; mp 235 °C (dec).

IR (KBr): 3402, 1673 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 12.50 (br s, 1 H), 8.18 (s, 1 H), 8.04 (s, 1 H), 7.83 (d, *J* = 8.6 Hz, 2 H), 7.53 (d, *J* = 8.6 Hz, 2 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 160.7, 158.0, 154.1, 147.4, 134.2, 133.3, 129.2, 128.2, 125.7, 124.8.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_8ClN_2OSe$: 310.9483; found: 310.9465.

6-(4-Nitrophenyl)selenolo[3,2-*d*]pyrimidin-4-one (2e)
Brown solid; mp 272 °C (dec).

IR (KBr): 3436, 1651 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 12.62 (br s, 1 H), 8.24–8.30 (m, 3 H), 8.21 (s, 1 H), 8.10 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 160.5, 158.0, 152.3, 147.6, 147.5, 140.4, 127.6, 127.5, 127.3, 124.4.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_8N_3O_3Se$: 321.9725; found: 321.9727.

6-*tert*-Butylselenolo[3,2-*d*]pyrimidin-4-one (2f)
Brown solid; mp 225 °C (dec).

IR (KBr): 3448, 1644 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 12.36 (br s, 1 H), 8.10 (s, 1 H), 7.34 (s, 1 H), 1.37 (s, 9 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 172.9.5, 160.2, 158.4, 146.8, 123.9, 122.9, 36.8, 32.0.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{13}N_2OSe$: 257.0188; found: 257.0182.

Chloroselenolopyrimidines 3a–f; General Procedure
A mixture of the appropriate selenolopyrimidinone **2** (1 mmol) and $POCl_3$ (8 mL) was heated at 95 °C for 20 min in a microwave reactor. The excess $POCl_3$ was removed by distillation under reduced pressure. The residue was triturated with ice and H_2O, and the solid thus obtained was collected and recrystallized from EtOH.

4-Chloro-6-phenylselenolo[3,2-*d*]pyrimidine (3a)
Brown solid; mp 90 °C (dec).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 9.00 (s, 1 H), 8.35 (s, 1 H), 7.90–7.94 (m, 2 H), 7.44–7.53 (m, 3 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 159.6, 157.9, 156.2, 147.5, 134.3, 129.7, 129.3, 126.5, 125.3, 123.4.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_8ClN_2Se$: 294.9533; found: 294.9532.

4-Chloro-6-(4-tolyl)selenolo[3,2-*d*]pyrimidine (3b)
Brown solid; mp 310 °C (dec).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 8.98 (s, 1 H), 8.28 (s, 1 H), 7.81 (d, *J* = 8.1 Hz, 2 H), 7.33 (d, *J* = 8.1 Hz, 2 H), 2.36 (s, 3 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 165.6, 159.5, 155.5, 155.2, 141.0, 131.5, 130.8, 130.0, 127.0, 122.4, 20.9.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{10}ClN_2Se$: 308.9690; found: 308.9681.

4-Chloro-6-(4-methoxyphenyl)selenolo[3,2-*d*]pyrimidine (3c)
Brown solid; mp 160 °C (dec).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 8.96 (s, 1 H), 8.21 (s, 1 H), 7.88 (d, *J* = 8.8 Hz, 2 H), 7.07 (d, *J* = 8.8 Hz, 2 H), 3.83 (s, 3 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 165.8, 161.4, 159.4, 155.3, 155.2, 131.1, 128.8, 126.1, 121.4, 114.8, 55.5.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{10}ClN_2OSe$: 324.9641; found: 324.9650.

4-Chloro-6-(4-chlorophenyl)selenolo[3,2-*d*]pyrimidine (3d)
Brown solid; mp 125 °C (dec).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 9.02 (s, 1 H), 8.40 (s, 1 H), 7.96 (d, *J* = 8.5 Hz, 2 H), 7.59 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 160.3, 158.0, 152.4, 147.6, 147.5, 140.4, 127.6, 127.5, 127.2, 124.4.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_7Cl_2N_2Se$: 328.9146; found: 328.9148.

4-Chloro-6-(4-nitrophenyl)selenolo[3,2-*d*]pyrimidine (3e)
Brown solid; mp 180 °C (dec).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 9.06 (s, 1 H), 8.58 (s, 1 H), 8.17–8.32 (m, 4 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 160.9, 160.4, 158.0, 155.9, 147.2, 127.9, 127.0, 124.2, 122.4, 114.6.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_7ClN_3O_2Se$: 339.9384; found: 339.9381.

6-*tert*-Butyl-4-chloroselenolo[3,2-*d*]pyrimidine (3f)
Compound **3f** was isolated by extraction of the reaction mixture with CH_2Cl_2; the organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure.

Brown solid; mp 68–70 °C.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.88 (s, 1 H), 7.48 (s, 1 H), 1.47 (s, 9 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 176.9, 165.2, 156.5, 154.7, 132.2, 122.2, 37.6, 32.5.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{12}ClN_2Se$: 274.9846; found: 274.9845.

Conversion of Nitriles 1b,d,f into Amides 4b,d,f; General Procedure
The appropriate 3-aminoselenophene-2-carbonitrile **3** was dissolved in H_2SO_4 (1 mL/mmol) and the reaction mixture was irradiated at 50 °C for 10 min in a CEM Discover microwave oven. The reaction mixture was poured onto H_2O and neutralized with sat. aq Na_2CO_3. The precipitate was filtered.

3-Amino-5-(4-tolyl)selenophene-2-carboxamide (4b)
Brown solid; mp 238 °C (dec).

IR (KBr): 3455, 3339, 3298, 3153, 1640 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 7.40 (d, *J* = 7.6 Hz, 2 H), 7.21 (d, *J* = 7.6 Hz, 2 H), 7.14 (s, 1 H), 6.79 (br s, 2 H), 6.63 (br s, 2 H), 2.29 (s, 3 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 167.6, 155.6, 148.6, 138.3, 132.3, 129.7, 125.5, 120.3, 100.3, 20.7.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{13}N_2OSe$: 281.0188; found: 281.0191.

3-Amino-5-(4-chlorophenyl)selenophene-2-carboxamide (4d)
Brown solid; mp 195 °C (dec).

IR (KBr): 3368, 3272, 3165, 1662 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 7.3 (d, *J* = 8.6 Hz, 2 H), 7.46 (d, *J* = 8.6 Hz, 2 H), 7.22 (s, 1 H), 6.85 (br s, 2 H), 6.66 (br s, 2 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 167.5, 155.4, 146.8, 133.9, 133.1, 129.2, 127.3, 121.6, 101.4.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{10}ClN_2OSe$: 300.9641; found: 300.9644.

3-Amino-5-*tert*-butylselenophene-2-carboxamide (4f)
Brown solid; mp 105 °C (dec).

IR (KBr): 3485, 3448, 3327, 1634 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.58 (s, 1 H), 5.77 (br s, 2 H), 5.10 (br s, 2 H), 1.34 (s, 9 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 168.3, 167.3, 155.06, 120.0, 99.3, 36.6, 32.2.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_9H_{15}N_2OSe$: 247.0344; found: 247.0355.

Ethyl Selenolo[3,2-*d*]pyrimidine-2-carboxylates 5; General Procedure
The appropriate 3-amino-selenophene-2-carboxamide **4** was dissolved in diethyl oxalate (3 mL/mmol) and the reaction mixture was refluxed for 18 h. After cooling, the mixture was concentrated under reduced pressure and diluted with cyclohexane. The precipitate was filtered.

Ethyl 6-(4-Tolyl)selenolo[3,2-*d*]-4-oxopyrimidin-2-carboxylate (5b)
Brown solid; mp 205 °C (dec).

IR (KBr): 3427, 1752, 1651 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.96 (br s, 1 H), 7.88 (s, 1 H), 7.52 (d, *J* = 7.6 Hz, 2 H), 7.28 (d, *J* = 7.6 Hz, 2 H), 4.58 (q, *J* = 7.1 Hz, 2 H), 2.41 (s, 3 H), 1.50 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 160.6, 159.8, 159.3, 157.6, 143.8, 140.3, 132.0, 130.0, 129.0, 126.6, 123.5, 64.2, 21.3, 14.2.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{15}N_2O_3Se$: 363.0242; found: 363.0243.

Ethyl 6-*tert*-Butylselenolo[3,2-*d*]-4-oxopyrimidin-2-carboxylate (5f)
Brown solid; mp 130–132 °C (dec).

IR (KBr): 1739, 1651 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 10.50 (br s, 1 H), 7.52 (s, 1 H), 4.56 (q, *J* = 7.2 Hz, 2 H), 1.41–1.51 (m, 12 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.7, 160.6, 159.23, 157.8, 143.5, 128.3, 123.4, 64.1, 37.4, 32.5, 14.2.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{17}N_2O_3Se$: 329.0399; found: 329.0392.

Ethyl {[2-(Aminocarbonyl)-5-*tert*-butylselenophen-3-yl]amino}(oxo)acetate (5f′)
Brown solid; mp 214–215 °C (dec).

IR (KBr): 3390,3336, 3259, 3167, 1727, 1697, 1663 cm^{-1}.

^{1}H NMR (250 MHz, DMSO-d_6): δ = 12.75 (br s, 1 H), 8.11 (s, 1 H), 7.59 (br s, 2 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 1.38–1.26 (m, 12 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 168.2, 166.6, 159.6, 152.8, 142.1, 119.0, 116.2, 62.7, 36.4, 32.1, 13.7.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{19}N_2O_4Se$: 347.0505; found: 347.0528.

Ethyl 4-Chloro-6-(4-Tolyl)selenolo[3,2-*d*]pyrimidin-2-carboxylate (6)
A mixture of selenolopyrimidinone **3c** (1 mmol) and $POCl_3$ (8 mL) was charged in a round-bottom flask and heated at 95 °C for 16 h. The excess $POCl_3$ was removed by distillation under reduced pressure. The residue was triturated with ice and H_2O, and the solid thus obtained was collected by filtration.

Brown solid; mp 135–136 °C (dec).

IR (KBr): 1740 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 8.06 (s, 1 H), 7.59 (d, *J* = 7.9 Hz, 2 H), 7.31 (d, *J* = 7.9 Hz, 2 H), 4.59 (q, *J* = 7.1 Hz, 2 H), 2.44 (s, 3 H), 1.49 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 165.8, 163.1, 161.4, 156.9, 153.7, 141.6, 135.0, 133.1, 130.2, 127.1, 122.5, 63.0, 21.5, 14.3.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{14}ClN_2O_2Se$: 380.9902; found: 380.9895.

4-(4-Methoxyphenoxy)-6-(4-methoxyphenyl)selenolo[3,2-*d*]pyrimidine (7)

A 10-mL round-bottom flask was charged with compound **3c** (0.5 mmol), NaOPMP (1 mmol) and DMF (2.5 mL). The reaction mixture was heated at 90 °C for 2 h. After cooling, the mixture was poured onto H_2O and the precipitate was filtered.

Yellow solid; mp 170 °C (dec).

^1H NMR (250 MHz, DMSO-d_6): δ = 8.64 (s, 1 H), 8.10 (s, 1 H), 7.83 (d, *J* = 8.7 Hz, 2 H), 7.27 (d, *J* = 9 Hz, 2 H), 7.06 (d, *J* = 8.7 Hz, 2 H), 7.00 (d, *J* = 9 Hz, 2 H), 3.82 (s, 3 H), 3.78 (s, 3 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 166.8, 165.1, 160.9, 157.2, 157.0, 154.9, 145.1, 128.4, 126.6, 122.9, 121.2, 116.8, 114.8, 114.6, 55.44, 55.42.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{17}N_2O_3Se$: 413.0400; found: 413.0409.

4,6-Bis(4-methoxyphenyl)selenolo[3,2-*d*]pyrimidine (8)

A 50-mL round-bottomed flask was charged with compound **3c** (1 mmol), $PMPB(OH)_2$ (1.5 mmol), Cs_2CO_3 (3.1 mmol), PPh_3 (5 mol%), $Pd(OAc)_2$ (2.5 mol%), and DME–EtOH–H_2O (1:1:1, 30 mL), and flushed with argon. The reaction mixture was placed in a microwave synthesizer. The microwave vial was purged three times with argon and then heated under microwave irradiation (150 °C) for 30 min. The mixture was subsequently allowed to cool to r.t. and was quenched with EtOAc–H_2O (1:1, 20 mL). The aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine and dried ($MgSO_4$). The solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel, EtOAc); this gave product **8**.

Pale yellow solid; mp 169 °C.

^1H NMR (250 MHz, DMSO-d_6): δ = 9.14 (s, 1 H), 8.15–8.08 (m, 3 H), 7.89–7.83 (d, *J* = 8.8 Hz, 2 H), 7.20 (d, *J* = 8.8 Hz, 2 H), 7.07 (d, *J* = 8.8 Hz, 2 H), 3.87 (s, 3 H), 3.83 (s, 3 H).

^{13}C NMR (62.5 MHz, DMSO-d_6): δ = 165.8, 161.5, 161.0, 159.7, 157.6, 155.4, 129.9, 129.4, 128.5, 128.0, 126.4, 121.5, 114.8, 114.6, 55.44, 55.42.

6-(4-Chlorophenyl)-4-morpholinoselenolo[3,2-*d*]pyrimidine (9)

Compound **3d** (0.5 mmol) was dissolved in excess morpholine (4 mL). The reaction mixture was heated at 125 °C for 20 min under microwave irradiation. After cooling, the mixture was poured onto H_2O and the precipitate was filtered.

Brown solid; mp >300 °C.

^1H NMR (250 MHz, acetone-d_6): δ = 8.51 (s, 1 H), 7.92 (s, 1 H), 7.84 (d, *J* = 8.5 Hz, 2 H), 7.54 (d, *J* = 8.5 Hz, 2 H), 3.89–391 (m, 4 H), 3.81–3.83 (m, 4 H).

^{13}C NMR (62.5 MHz, acetone-d_6): δ = 166.5, 160.9, 165.6, 152.9, 135.9, 134.3, 130.3, 129.1, 125.6, 116.4, 67.2, 47.1.

ESI-HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{15}ClN_3OSe$: 380.0061; found: 380.0064.

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