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Silver-catalyzed three-component reaction of uracils, arylboronic acids, and selenium: synthesis of 5-arylselanyluracils†

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Herein, we describe a simple and general multi-component synthesis of 5-arylselanyluracils by the regioselective C–H selenation of uracils. Reactions of uracils with arylboronic acid and Se powder in the presence of $AgNO_3$ (10 mol%) at 120 °C under aerobic conditions afforded various 5-arylselanyluracils. The source of the introduced selanyl group was prepared from a commercially available arylboronic acid and Se powder in the reaction system, thereby ensuring a simple and efficient protocol. This reaction represents the first example of the synthesis of a 5-arylselanyluracil in a multi-component system.

Introduction

5-Substituted uracils have played very important roles in a wide range of fields, including organic synthesis, medicinal chemistry, and drug discovery.[1] Among these, 5-selanyluracils have attracted significant interest due to their potential as biological and pharmaceutical therapeutic agents (Fig. 1). For instance, 5-phenylselanyluracil **I** is a potent inhibitor of DHUDase and UedPase,[2] selenoimidazole nucleoside **II** potently inhibits human and malarial orotate phosphoribosyltransferase,[3] and selenocyanic acid **III** acts as a hypoxic radiosensitizer and genomic DNA molecular probe.[4] Owing to the importance of 5-selanyluracils, as mentioned above, a number of synthetic strategies have been developed to prepare 5-arylselanyluracils from uracils. Conversions from 5-halouracil include nucleophilic substitution reaction with phenylselenol promoted by microwave irradiation[5] and Cu-mediated cross-coupling reaction with a diaryl diselenide.[6] A more versatile method involves the reaction of 5-unsubstituted uracils with phenylselanyl chloride or a diaryl diselenide. Anzai reported the first synthesis of 5-phenylselanyluracil by reacting uracil with phenylselanyl chloride,[7] while Kim *et al.* developed the reaction of a 5-unsubstituted uracil with phenylselanyl chloride in the presence of a silver reagent, such as Ag_2O, $AgBF_4$, or $AgOCOCF_3$.[8] These authors also reported the reactions of uracils with diphenyl diselenide using $Mn(OAc)_2$ and hypervalent iodine reagents, such as (diacetoxyiodo)benzene.[9,10] On the other hand, Yotphan *et al.* reported the Cu-catalyzed C–H selenation of a uracil with diphenyl diselenide, and iodine-persulfate-promoted selenation,[11,12] while Cheng *et al.* developed the oxidative coupling of a uracil with a diaryl diselenide using a NaI–H_2O_2 system.[13] Ma *et al.* and He *et al.* performed reactions of uracils with diaryl diselenides in electrolytic syntheses in the presence of NH_4I[14] and KI,[15] respectively. Furthermore, Choudhury *et al.* recently reported photoreaction under irradiation of visible light using Rose Bengal as a photocatalyst.[16] However, selenium source, such as the diaryl diselenides, arylselanyl chlorides, and arylselenols used in these reactions, is poorly commercially available and/or require complicated synthetic procedures. Moreover, these reactions are limited to two-components, and the efficient syntheses of 5-selanyluracils using multi-component reactions and readily available selenium sources have, to the best of our knowledge, not been reported to date.

Ag-catalyzed reactions are powerful tools for the formation of carbon–carbon and carbon–heteroatom bonds and are attracting increasing attention in modern organic chemistry.[17] Among these, Liu and co-workers developed Ag-catalyzed three-component reactions for C–Se bond formation using an arylboronic acid, Se powder, and an epoxide or acetylene derivative;[18–21] the reactions with epoxides catalyzed by $AgNO_3$ afford β-hydroxyselenides through epoxide ring-opening and

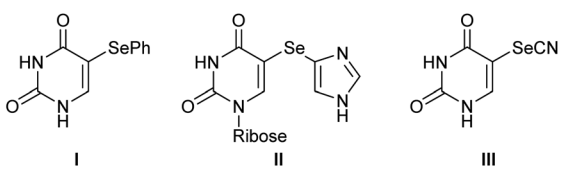

Fig. 1 Biologically active 5-selanyluracils.

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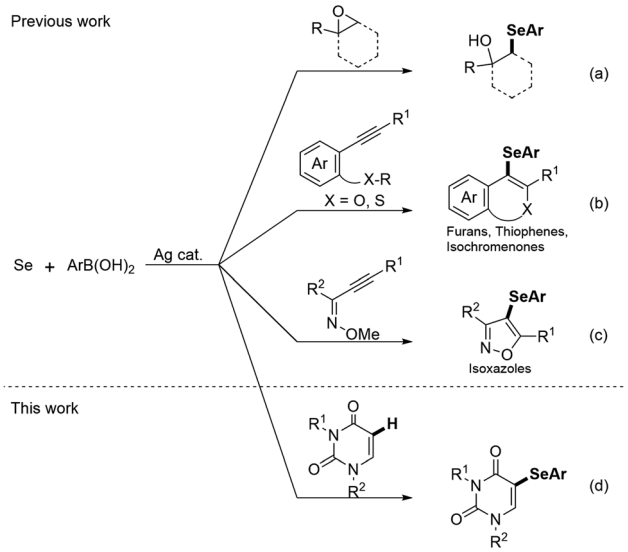


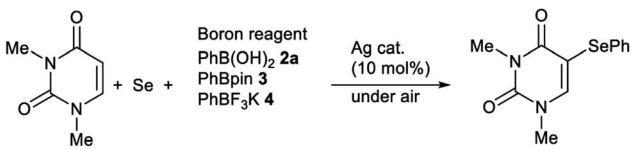
Scheme 1 Diverse Ag catalyzed reaction using selenium powder and boronic acid.

selenation (Scheme 1a).[18] Reactions with 2-alkynyl-anisoles, -thioanisoles, -aryl esters, and alkynone *O*-methyloximes catalyzed by $AgNO_3$ and $AgNO_2$ gave furan and thiophene derivatives, isochromenones, and isoxazoles through the tandem cyclization and selenation (Scheme 1b and c).[19–21] Clearly, the use of Se powder, which is commercially available, stable, and easy-to-handle, as a reagent for the construction of C–Se bonds provides a more straightforward and attractive alternative. However, the previous methods used either for ring-opening reactions of epoxides or for electrophilic annulation reactions to form heterocycles. Inspired by the aforementioned reports, in this paper we present the simple and efficient C–H selenation of uracils (Scheme 1d). The developed protocol involves the Ag-catalyzed regioselective three-component reaction of uracils, selenium, and arylboronic acids under aerobic conditions, and are first examples of using for C–H selenation.

Results and discussion

Initially, we focused on identifying the optimal experimental conditions for the synthesis of 5-phenylselanyluracil **5a** using a Ag-catalyzed three-component reaction involving *N*,*N*-dimethyluracil **1a**, Se powder and phenylboron reagents **2a–4**, the results of which, including screening for suitable Ag catalysts, solvents, and aryl donors, are summarized in Table 1. We first reacted **1a** (0.5 mmol) with Se powder (0.5 mmol) and phenylboronic acid **2a** (0.5 mmol) using a variety of available Ag

Table 1 Optimization of the reaction conditions[a]



1a **5a**

Entry	Boron reagent	Ag cat.	Temp. (°C)	Solvent	Time (h)	Yield[b] (%)
1	**2a**	$AgNO_3$	120	DMSO	4	97 (96)[c]
2	**2a**	$AgNO_2$	120	DMSO	4	75
3	**2a**	AgOAc	120	DMSO	24	—
4	**2a**	AgOTf	120	DMSO	24	—
5	**2a**	$AgBF_4$	120	DMSO	24	—
6	**2a**	$AgSbF_6$	120	DMSO	24	—
7	**2a**	Ag_2CO_3	120	DMSO	24	—
8	**2a**	Ag_2O	120	DMSO	24	—
9	**2a**	—	120	DMSO	24	—
10	**2a**	$AgNO_3$	100	1,4-Dioxane	24	22
11	**2a**	$AgNO_3$	80	MeCN	24	18
12	**2a**	$AgNO_3$	120	NMP	24	7
13	**2a**	$AgNO_3$	100	Toluene	24	7
14	**2a**	$AgNO_3$	80	1,2-DCE	24	3
15	**2a**	$AgNO_3$	120	DMF	24	—
16[d]	**2a**	$AgNO_3$	120	DMSO	4	89
17[e]	**2a**	$AgNO_3$	120	DMSO	24	8
18	**2a**	$AgNO_3$	100	DMSO	24	52
19[f]	**2a**	$AgNO_3$	120	DMSO	24	87
20[g]	**2a**	$AgNO_3$	120	DMSO	24	11
21	**3**	$AgNO_3$	120	DMSO	6	64
22	**4**	$AgNO_3$	120	DMSO	24	—

[a] Reaction conditions: **1a** (0.5 mmol), **2a–4** (0.5 mmol), Se powder (0.5 mmol), Solvent (3 mL). [b] GC yield using biphenyl as internal standard. [c] Isolated yield. [d] Under O_2 (1 atm). [e] Under Ar. [f] Ag cat. (5 mol%). [g] Ag cat. (1 mol%).

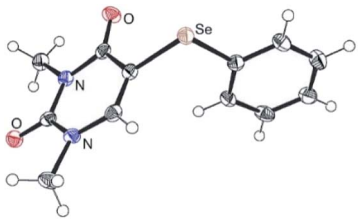
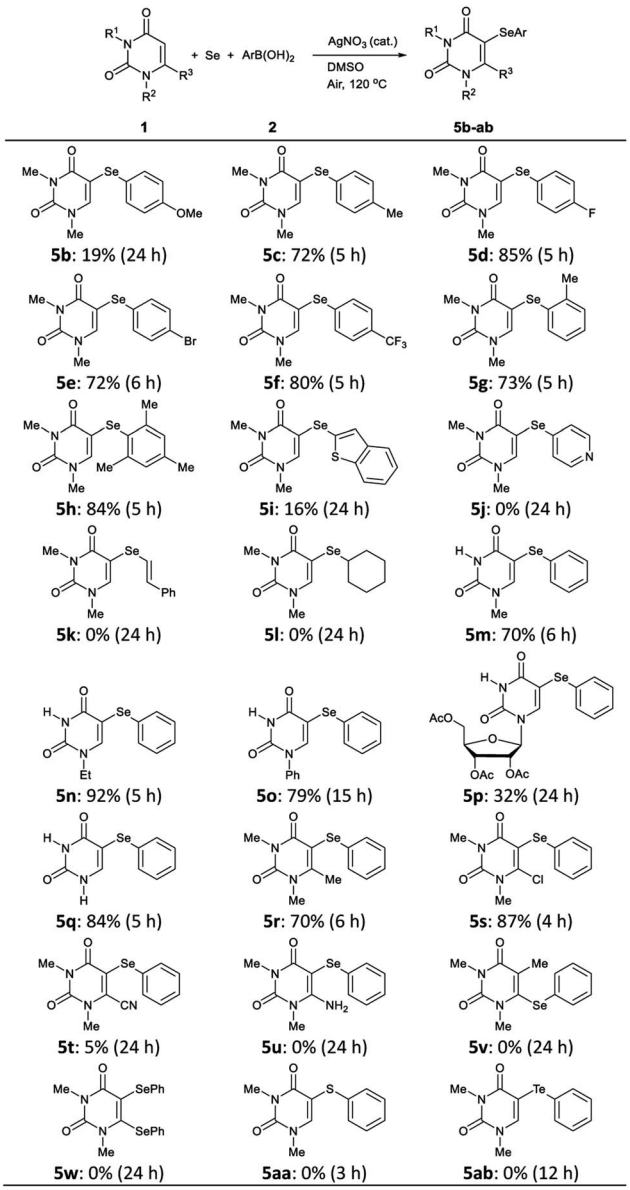


Fig. 2 ORTEP drawing **5a** with 50% probability (CCDC 2093049).

catalysts (0.05 mmol) under aerobic conditions in DMSO at 120 °C (entries 1–8). $AgNO_3$ and $AgNO_2$ gave coupling product **5a** in high yields (97% and 75%, respectively); however, the other silver catalysts examined did not produce **5a**. Therefore, $AgNO_3$ was identified to be the best catalyst for this reaction in terms of the yield of product **5a** (entry 1). The reaction also did not proceed in the absence of the Ag catalyst (entry 9). Solvent screening revealed that the reaction proceeded effectively only in DMSO, whereas NMP, DMF, MeCN, 1,4-dioxane, toluene, and 1,2-DCE were inefficient reaction solvents (entries 1, and 10–15). The reaction under oxygen produced **5a** in a high yield (89%) that was almost the same as that obtained under aerobic conditions, while the reaction yield was suppressed (8%) under argon (entries 16 and 17). This reaction gives the best result under aerobic conditions, which are operationally superior reaction conditions (entry 1). A lower yield was obtained at 100 °C compared to 120 °C (entry 18), and decreasing the $AgNO_3$ loading from 10 to 5 or 1 mol% significantly decreased the yield of **5a** and extended the reaction time (entries 1, 19 and 20). The reaction of **1a** with 2-phenyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **3** gave coupling product **5a** in 64% yield, while no reaction was observed with potassium phenyltrifluoroborate **4** (entries 21 and 22). These results show that boronic acid **2a** is a superior aryl-group donor. The regiochemistry of 5-selanyluracil **5a** was elucidated by ^{1}H NMR spectroscopy and single-crystal X-ray analysis (Fig. 2); the ^{1}H NMR spectrum of **5a** is consistent with that of a standard sample.[13]

To demonstrate the efficiency and generality of this three component system, the reactions of various uracils **1** (0.5 mmol), Se powder (0.5 mmol), and boronic acids **2** (0.5 mmol) were investigated under the optimized conditions, the results of which are summarized in Table 2. Reactions of *N*,*N*-dimethyluracil **1a** with Se powder and arylboron reagents **2b–f** bearing various electron-donating and -withdrawing groups at the 4-position of the benzene ring afforded the corresponding products **5c–f** in good yields; however **5b**, which bears an electron-donating methoxy group, was obtained in poor yield (19%). Di(4-methoxyphenyl)selenide was unexpectedly isolated as the main product in 66% yield when 4-methoxyphenylboronic acid **2b** was used. The reaction of sterically hindered *ortho*-substituted boronic acids gave the corresponding 5-selanyluracils **5g** and **5h** without any difficulties. Unfortunately, the reaction of arylboronic acids containing heterocyclic rings, such as benzothiophene and pyridine, afforded **5i** in low yield (16%), and while **5j** was not produced. Moreover, reactions using vinyl and alkylboranoic acids did not yield the corresponding product **5k** and **5l**, and uracil **1a** were recovered.

Table 2 Study of substrate scope[a,b]



[a] Reagents and conditions: **1** (0.5 mmol), Se powder (0.5 mmol), **2** (0.5 mmol), and $AgNO_3$ (0.05 mmol) in DMSO at 120 °C under air. [b] Isolated yield.

Various uracils **1** were then treated with Se powder and phenylboronic acid **2a** under the same reaction conditions. Mono-substituted uracils **1m–o** bearing methyl, ethyl, and phenyl groups at their 1-position gave products **5m–o**, respectively, in satisfactory yields. Uracil **1p** bearing a triacetyl-D-ribosyl group also gave the desired product **5p**, albeit in low yield (32%). The reaction proceeded smoothly even with unsubstituted uracil **1q** to give the 5-selanyluracil **5q** in 84% yield. 6-Methyl and 6-chloro substituted uracils gave coupling

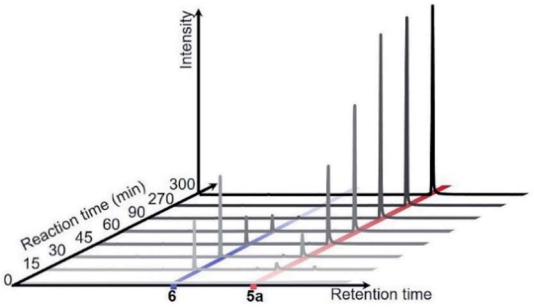
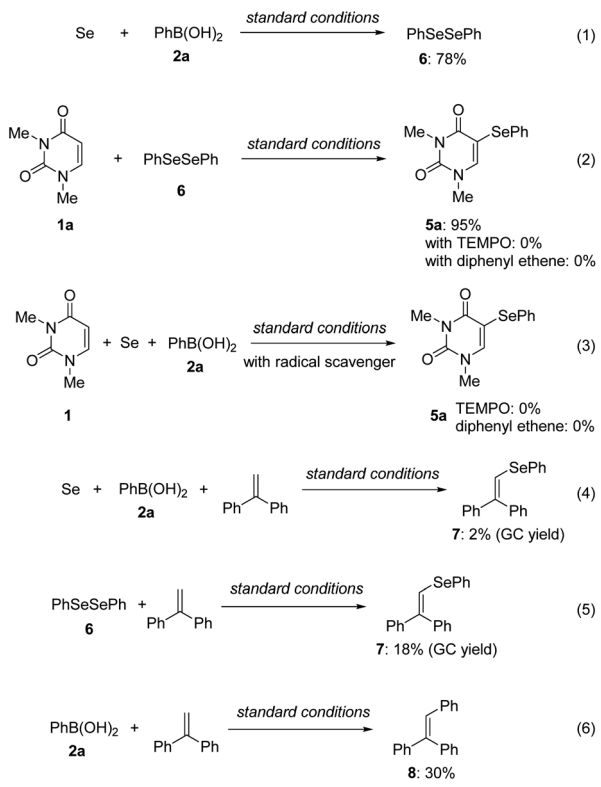


Fig. 3 Monitor of the reaction using 1a, 2a and Se powder by GC.

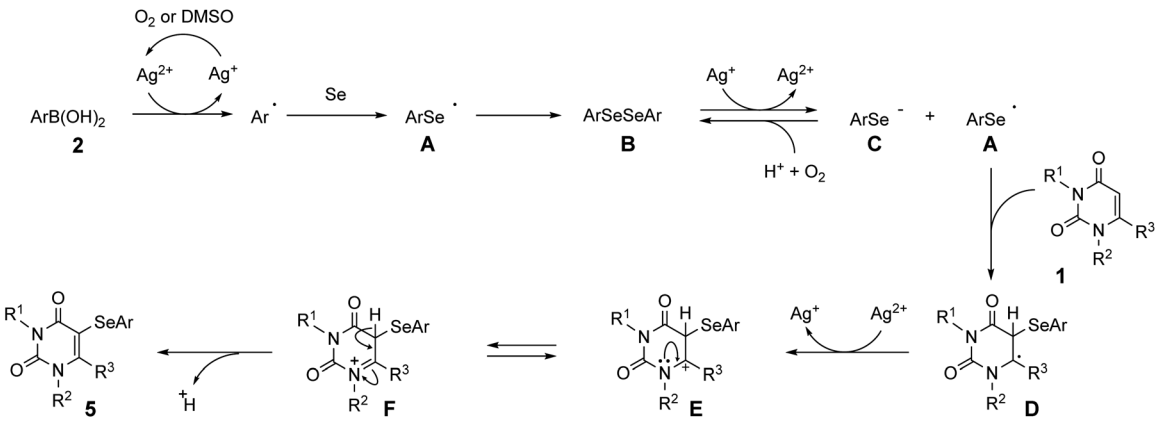


Scheme 2 Control experiments.

products **5r** and **5s** in good yields, whereas nitrile **1t** reacted to produce **5t** in extremely low yield (5%), while amine **5u** was not obtained. In the reaction of 5-methyluracil **1v**, selenation at 6-position did not proceed and 6-selanyluracil **5v** was not obtained. We also attempted to double C–H selenation of **1a** using 2 equiv. of Se powder and phenylboronic acid **2a**, but the corresponding diselanyluracil **5w** was not obtained; rather 5-selanyluracil **5a** was isolated in 95% yield. These results suggest that this reaction proceeds only at the 5-position of uracil. Finally, other chalcogen sources, such as sulfur and tellurium powder, were subjected to the reaction conditions with **1a** and **2a**; however, neither chalcogen reacted and the corresponding products **5aa** and **5ab** were not produced.

Diphenyl diselenide **6** and 5-selanyluracil **5a** were observed when the reaction of **1a**, **2a**, and Se powder was monitored by gas chromatography (Fig. 3). Therefore, we carried out a control experiment to investigate the reaction pathway and mechanism. The reaction of phenylboronic acid **2a** with Se powder under the standard conditions gave diphenyl diselenide **6** in 78% yield [Scheme 2, eqn (1)]. The two-component reaction of uracil **1a** with **6** gave the corresponding 5-selanyluracil **5a** in high yield [eqn (2)]; this reaction was completely inhibited when a radical scavenger, such as TEMPO [(2,2,6,6-tetramethyl-piperidin-1-yl) oxyl] or diphenylethylene, was included. In addition, the three-component reaction of **1a**, **2a**, and Se powder did not proceed in the presence of a radical scavenger [eqn (3)]. These results suggest that these reactions proceed by a radical mechanism that involves the formation of diphenyl diselenide. Selenide **7** was detected by GC-MS when phenylboronic acid **2a** was reacted with Se powder and diphenylethylene under the standard conditions [eqn (4)]; **7** was also formed when **6** was reacted with diphenylethylene [eqn (5)]. Moreover, the reaction of phenylboronic acid with diphenylethylene gave triphenylethylene **8** in 30% yield [eqn (6)]. These results suggest that phenylselanyl and phenyl radicals are generated in this reaction system.

Based on the above control experiments, a possible mechanism for the three-component reaction is proposed in Scheme 3. Initially, the aryl radical is generated from arylboronic acid **2**



Scheme 3 Proposed mechanism.

by the action of Ag^{2+}, which is formed by the aerobic or DMSO oxidation of $AgNO_3$. The aryl radical then reacts with selenium powder to form arylselanyl radical **A**, which immediately undergoes radical coupling to form diaryl diselenide **B**.[18,21] Diselenide **B** then receives one electron from Ag^+ to generate the aryl selenide anion **C** and **A**. Radical **A** then reacts with uracil **1** to produce intermediate **D**, which is then converted into 3-selenyluracil **5** *via* **E** and **F**. On the other hand, the generated selenide anion **C** is oxidized to the stable diaryl diselenide **B** and reused in our reaction system, which improves the reaction efficiency. As a more direct route, it is also possible that uracil **1** reacts with radical species **A** that was initially generated from boronic acid **2** and selenium, to produce the 3-selanyluracil **5**.

Conclusions

In conclusion, we developed a Ag-catalyzed three-component reaction for the synthesis of a 5-selanyluracils from a uracil, Se powder, and an arylboronic acid. This protocol enables various functionalized uracils and arylboronic acids to be converted into desired products. The reaction proceeds with high regioselectivity, the required reagents, including the arylboronic acid and Se powder, are inexpensive and easy to handle, and the protocol can easily be performed under aerobic conditions. Detailed mechanistic studies into this three-component reaction and its application to medicinal chemistry are currently in progress and will be reported in the future.

Experimental

General information

All chromatographic separations were accomplished with Silica Gel 60N (Kanto Chemical Co., Inc.). Thin-layer chromatography (TLC) was performed with Macherey-Nagel Sil G25 UV_{254} precoated TLC plates. Reagents were used without further purification unless otherwise specified. Melting points were recorded on a Yanagimoto micro melting point hot-stage apparatus (MP-S3) and are not corrected. IR spectra were recorded on a SHIMADZU FTIR-8400S spectrophotometer and are reported in frequency of absorption (cm^{-1}). Only selected IR peaks are reported. ^1H NMR (TMS: $\delta = 0.00$ ppm as an internal standard), ^{13}C NMR ($CDCl_3$: $\delta = 77.00$ ppm as an internal standard), ^{19}F NMR (trifluoromethylbenzene: $\delta = -64.0$ ppm as an external standard) and ^{77}Se NMR (Ph_2Se_2: $\delta = 436.15$ ppm as an internal standard) spectra were recorded on a JEOL ECZ-400S (400 MHz, 100 MHz, 376 MHz and 76 MHz) spectrometer in $CDCl_3$ unless otherwise stated. GC-MS (EI) spectra were recorded on Agilent 5977E Diff-SST MSD-230V spectrometer. HRMS (ESI) were recorded on Agilent 6230 Accurate-Mass TOF LC/MS system. The X-ray diffraction measurements carried out using a Rigaku XtaLAB Synergy, single source at home/near, HyPix3000 diffractometer. Spectroscopic data of 5-arylselanyluracils **5a**, **p**, **q**, and **5s** are in accordance with the literature.[8,11,13]

Synthesis of 5-arylselanyluracil

Arylboronic acid (**2**) (0.5 mmol, 1.0 eq.), Se powder (40 mg, 0.5 mmol, 1.0 eq.), $AgNO_3$ (8.5 mg, 0.05 mmol, 10 mol%), and *N*,*N*-dimethyluracil derivative (**1**) (0.5 mmol) were added to dimethylsulfoxide (3 mL) in around-bottom flask. After stirring at 120 °C for 5–24 h, the mixture was cooled to room temperature and evaporated to dryness under reduced pressure. The crude product was purified on a silica gel column chromatography to give the desired product **5a–i** and **5m–t**.

1,3-Dimethyl-5-[(4-methoxyphenyl)selanyl]pyrimidine-2,4-(1*H*,3*H*)-dione (5b). Colorless needles (32 mg, 19%). $R_f = 0.4$ (EtOAc/hexane 1 : 1). Mp 119–121 °C (CH_2Cl_2–hexane). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.56$ (dt, $J = 9.1$, 2.5 Hz, 2H, Ar-H), 7.14 (s, 1H, H-6), 6.86 (dt, $J = 9.1$, 2.5 Hz, 2H, Ar-H), 3.81 (s, 3H, OCH_3), 3.37 (s, 3H, N–CH_3), 3.34 (s, 3H, N–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 161.9$ (s, C), 160.0 (s, C), 151.5 (s, C), 143.7 (s, CH), 136.3 (s, CH), 118.1 (s, C), 115.2 (s, CH), 105.2 (s, C), 55.3 (s, CH_3), 37.1 (s, CH_3), 28.6 (s, CH_3). ^{77}Se NMR (76 MHz, $CDCl_3$): $\delta = 321.5$ (s). IR (KBr): ν_{max}/cm^{-1} 1711 *vs.* (C=O), 1670 *vs.* (C=O). HRMS (ESI): *m*/*z* calcd for $C_{13}H_{14}N_2O_3Se + H^+$; 327.0248 $[M + H]^+$: found: 327.0251.

1,3-Dimethyl-5-[(4-methylphenyl)selanyl]pyrimidine-2,4-(1*H*,3*H*)-dione (5c). Colorless plates (111 mg, 72%). $R_f = 0.5$ (EtOAc/hexane 1 : 1). Mp 113–114 °C (CH_2Cl_2–hexane). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.46$ (d, $J = 8.2$ Hz, 2H, Ar-H), 7.30 (s, 1H, H-6), 7.11 (d, $J = 7.8$ Hz, 2H, Ar-H), 3.38 (s, 3H, N–CH_3), 3.36 (s, 3H, N–CH_3), 2.33 (s, 3H, 4′-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 161.9$ (s, C), 151.6 (s, C), 145.0 (s, CH), 138.3 (s, C), 133.6 (s, CH), 130.3 (s, CH), 125.0 (s, C), 104.2 (s, C), 37.1 (s, CH_3), 28.6 (s, CH_3), 21.2 (s, CH_3). ^{77}Se NMR (76 MHz, $CDCl_3$): $\delta = 324.9$ (s). IR (KBr): ν_{max}/cm^{-1} 1705 *vs.* (C=O), 1651 *vs.* (C=O). HRMS (ESI): *m*/*z* calcd for $C_{13}H_{14}N_2O_2Se + H^+$; 311.0299 $[M + H]^+$: found: 311.0301.

1,3-Dimethyl-5-[(4-fluorophenyl)selanyl]pyrimidine-2,4-(1*H*,3*H*)-dione (5d). Colorless plates (132 mg, 85%). $R_f = 0.5$ (EtOAc/hexane 1 : 1). Mp 85–87 °C (ether). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.56$ (dd, $J = 8.7$, 5.5 Hz, 2H, Ar-H), 7.41 (s, 1H, H-6), 7.00 (t, $J = 8.9$ Hz, 2H, Ar-H), 3.40 (s, 3H, N–CH_3), 3.38 (s, 3H, N–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 162.8$ (d, $^1J_{C,F} = 249$ Hz, CF), 161.9 (s, C), 151.5 (s, C), 145.9 (s, CH), 135.5 (d, $^3J_{C,F} = 8.7$ Hz, CH), 123.6 (d, $^4J_{C,F} = 3.9$ Hz, C), 116.6 (d, $^2J_{C,F} = 21.2$ Hz, CH), 103.6 (s, C), 37.2 (s, CH_3), 28.7 (s, CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -114.3$ (s). ^{77}Se NMR (76 MHz, $CDCl_3$): $\delta = 326.0$ (s). IR (KBr): ν_{max}/cm^{-1} 1715 *vs.* (C=O), 1655 *vs.* (C=O). HRMS (ESI): *m*/*z* calcd for $C_{12}H_{11}FN_2O_2Se + H^+$; 315.0048 $[M + H]^+$: found: 315.0048.

1,3-Dimethyl-5-[(4-bromophenyl)selanyl]pyrimidine-2,4-(1*H*,3*H*)-dione (5e). Colorless plates (134 mg, 72%). $R_f = 0.5$ (EtOAc/hexane 1 : 1). Mp 115–117 °C (CH_2Cl_2–hexane). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.53$ (s, 1H, H-6), 7.42–7.37 (m, 4H, Ar-H), 3.42 (s, 3H, N–CH_3), 3.39 (s, 3H, N–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 161.8$ (s, C), 151.6 (s, C), 147.1 (s, CH), 133.9 (s, CH), 132.4 (s, CH), 128.5 (s, C), 122.1 (s, C), 102.4 (s, C), 37.2 (s, CH_3), 28.8 (s, CH_3). ^{77}Se NMR (76 MHz, $CDCl_3$): $\delta = 328.2$ (s). IR (KBr): ν_{max}/cm^{-1} 1707 *vs.* (C=O), 1647 *vs.* (C=O). HRMS (ESI): *m*/*z*

calcd for $C_{12}H_{11}BrN_2O_2Se$ + H^+; 374.9247 $[M + H]^+$: found: 374.7246.

1,3-Dimethyl-5-{[(4-trifluoromethyl)phenyl]selanyl}-pyrimidine-2,4-(1*H*,3*H*)-dione (5f). Colorless needles (145 mg, 80%). R_f = 0.5 (EtOAc/hexane 1 : 1). Mp 139–141 °C (CH_2Cl_2–hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (s, 1H, H-6), 7.54–7.48 (m, 4H, Ar-H), 3.46 (s, 3H, N–CH_3), 3.41 (s, 3H, N–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8 (s, C), 151.6 (s, C), 148.8 (s, CH), 135.6 (s, C), 130.7 (s, CH), 129.3 (q, $^2J_{C,F}$ = 32.8 Hz, C), 126.0 (q, $^3J_{C,F}$ = 3.9 Hz, CH), 123.9 (q, $^1J_{C,F}$ = 272 Hz, CF_3), 100.9 (s, C), 37.3 (s, CH_3), 28.9 (s, CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): δ = −63.9 (s). ^{77}Se NMR (76 MHz, $CDCl_3$): δ = 335.0 (s). IR (KBr): ν_{max}/cm^{-1} 1711 *vs.* (C=O), 1655 *vs.* (C=O). HRMS (ESI): *m*/*z* calcd for $C_{13}H_{11}F_3N_2O_2Se$ + H^+; 365.0016 $[M + H]^+$: found: 365.0017.

1,3-Dimethy-5-[(2-methylphenyl)selanyl]pyrimidine-2,4-(1*H*,3*H*)-dione (5g). Colorless plates (113 mg, 73%). R_f = 0.6 (EtOAc/hexane 1 : 1). Mp 147–149 °C (CH_2Cl_2–hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (dd, *J* = 8.0, 1.4 Hz, 1H, Ar-H), 7.25 (s, 1H, H-6), 7.23–7.18 (m, 2H, Ar-H), 7.10 (td, *J* = 7.2, 2.1 Hz, 1H, Ar-H), 3.40 (s, 3H, N–CH_3), 3.38 (s, 3H, N–CH_3), 2.46 (s, 3H, 2′-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (s, C), 151.6 (s, C), 145.6 (s, CH), 139.2 (s, C), 132.4 (s, CH), 130.4 (s, CH), 129.9 (s, C), 127.9 (s, CH), 126.9 (s, CH), 102.5 (s, C), 37.2 (s, CH_3), 28.7 (s, CH_3), 22.0 (s, CH_3). ^{77}Se NMR (76 MHz, $CDCl_3$): δ = 290.5 (s). IR (KBr): ν_{max}/cm^{-1} 1701 s (C=O), 1651 *vs.* (C=O). HRMS (ESI): *m*/*z* calcd for $C_{13}H_{14}N_2O_2Se$ + H^+; 311.0299 $[M + H]^+$: found: 311.0298.

1,3-Dimethy-5-[(2,4,6-trimethylphenyl)selanyl]pyrimidine-2,4-(1*H*,3*H*)-dione (5h). Colorless plates (141 mg, 84%). R_f = 0.6 (EtOAc/hexane 1 : 1). Mp 142–144 °C (CH_2Cl_2–hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.01 (s, 2H, 3′,5′-H), 6.27 (s, 1H, H-6), 3.38 (s, 3H, N–CH_3), 3.25 (s, 3H, N–CH_3), 2.49 (s, 6H, 2′,6′-CH_3), 2.31 (s, 3H, 4′-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (s, C), 151.4 (s, C), 143.8 (s, C), 139.7 (s, C), 137.3 (s, CH), 129.2 (s, CH), 123.7 (s, C), 105.7 (s, C), 37.2 (s, CH_3), 28.4 (s, CH_3), 24.0 (s, CH_3), 21.1 (s, CH_3). ^{77}Se NMR (76 MHz, $CDCl_3$): δ = 221.7 (s). IR (KBr): ν_{max}/cm^{-1} 1701 *vs.* (C=O), 1684 *vs.* (C=O). HRMS (ESI): *m*/*z* calcd for $C_{15}H_{18}N_2O_2Se$ + H^+; 339.0612 $[M + H]^+$: found: 339.0612.

1,3-Dimethy-5-(benzothien-2-ylselanyl)pyrimidine-2,4-(1*H*,3*H*)-dione (5i). Colorless needles (28 mg, 16%). R_f = 0.5 (EtOAc/hexane 1 : 1). Mp 148–150 °C (CH_2Cl_2–hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.67 (m, 2H, Ar-H), 7.51 (d, *J* = 0.9 Hz, 1H, benzothiophene-3′H), 7.30–7.23 (m, 3H, H-6, Ar-H), 3.31 (s, 3H, N–CH_3), 3.28 (s, 3H, N–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.6 (s, C), 151.4 (s, C), 144.6 (s, CH), 143.6 (s, C), 140.0 (s, C), 132.8 (s, CH), 125.0 (s, CH), 124.7 (s, C), 124.6 (s, CH), 123.5 (s, CH), 121.8 (s, CH), 104.2 (s, C), 37.3 (s, CH_3), 28.7 (s, CH_3). ^{77}Se NMR (76 MHz, $CDCl_3$): δ = 263.6 (s). IR (KBr): ν_{max}/cm^{-1} 1709 s (C=O), 1655 *vs.* (C=O). HRMS (ESI): *m*/*z* calcd for $C_{14}H_{12}N_2O_2SSe$ + H^+; 352.9863 $[M + H]^+$: found: 352.9869.

1-Methyl-5-(phenylselanyl)pyrimidine-2,4-(1*H*,3*H*)-dione (5m). Colorless plates (99 mg, 70%). R_f = 0.5 (EtOAc/hexane 2 : 1). Mp 190–193 °C (CH_2Cl_2–hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.79 (s, 1H, N–H), 7.53–7.50 (m, 2H, Ar-H), 7.47 (s, 1H, H-6), 7.30–7.27 (m, 3H, Ar-H), 3.37 (s, 3H, N–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (s, C), 150.8 (s, C), 149.0 (s, CH), 132.5 (s, CH), 129.5 (s, CH), 129.3 (s, C), 127.9 (s, CH), 103.9 (s, C), 36.1 (s, CH_3). ^{77}Se NMR (76 MHz, $CDCl_3$): δ = 319.6 (s). IR (KBr): ν_{max}/cm^{-1} 1717 *vs.* (C=O), 1697 *vs.* (C=O). HRMS (ESI): *m*/*z* calcd for $C_{11}H_{10}N_2O_2Se$ + H^+; 282.9986 $[M + H]^+$: found: 282.9981.

1-Ethyl-5-(phenylselanyl)pyrimidine-2,4-(1*H*,3*H*)-dione (5n). Colorless plates (136 mg, 92%). R_f = 0.5 (EtOAc/hexane 1 : 1). Mp 173–175 °C (CH_2Cl_2–hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.22 (brs, 1H, N–H), 7.54–7.50 (m, 2H, Ar-H), 7.49 (s, 1H, H-6), 7.30–7.27 (m, 3H, Ar-H), 3.78 (q, *J* = 7.3 Hz, 2H, CH_2), 1.29 (t, *J* = 7.3 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.0 (s, C), 150.5 (s, C), 148.0 (s, CH), 132.4 (s, CH), 129.4 (s, CH), 127.8 (s, CH), 104.0 (s, C), 44.2 (s, CH_2), 14.4 (s, CH_3). ^{77}Se NMR (76 MHz, $CDCl_3$): δ = 319.4 (s). IR (KBr): ν_{max}/cm^{-1} 1697 *vs.* (C=O), 1668 *vs.* (C=O). HRMS (ESI): *m*/*z* calcd for $C_{12}H_{12}N_2O_2Se$ + H^+; 297.0142 $[M + H]^+$: found: 297.0143.

1-Phenyl-5-(phenylselanyl)pyrimidine-2,4-(1*H*,3*H*)-dione (5o). Colorless needles (135 mg, 79%). R_f = 0.6 (EtOAc/CH_2Cl_2 1 : 3). Mp 198–201 °C (CH_2Cl_2–hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.87 (s, 1H, N–H), 7.64 (s, 1H, H-6), 7.57 (dd, *J* = 6.2, 3.0 Hz, 2H, Ar-H), 7.49–7.41 (m, 3H, Ar-H), 7.32–7.26 (m, 5H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.7 (s, C), 150.0 (s, C), 147.9 (s, CH), 137.9 (s, CH), 132.8 (s, C), 129.6 (s, CH), 129.5 (s, CH), 129.1 (s, CH), 129.0 (s, C), 128.0 (s, CH), 126.1 (s, CH), 105.0 (s, CH). ^{77}Se NMR (76 MHz, $CDCl_3$): δ = 322.7 (s). IR (KBr): ν_{max}/cm^{-1} 1726 s (C=O), 1663 *vs.* (C=O). HRMS (ESI): *m*/*z* calcd for $C_{16}H_{12}N_2O_2Se$ + H^+; 345.0142 $[M + H]^+$: found: 345.0142.

1,3,6-Trimethyl-5-(phenylselanyl)pyrimidine-2,4-(1*H*,3*H*)-dione (5r). Yellow oil (108 mg, 70%). R_f = 0.5 (EtOAc/hexane 1 : 1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.35 (m, 2H, Ar-H), 7.25–7.20 (m, 3H, Ar-H), 3.52 (s, 3H, N–CH_3), 3.40 (m, 3H, N–CH_3), 2.71 (s, 3H, 6-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.5 (s, C), 157.1 (s, C), 151.9 (s, C), 131.5 (s, C), 130.2 (s, CH), 129.2 (s, CH), 126.7 (s, CH), 103.3 (s, C), 33.6 (s, CH_3), 29.2 (s, CH_3), 21.9 (s, CH_3). ^{77}Se NMR (76 MHz, $CDCl_3$): δ = 302.8 (s). IR (KBr): ν_{max}/cm^{-1} 1701 s (C=O), 1647 *vs.* (C=O). HRMS (ESI): *m*/*z* calcd for $C_{13}H_{14}N_2O_2Se$ + H^+; 333.0113 $[M + H]^+$: found: 333.0115.

1,2,3,6-Tetrahydro-1,3-dimethyl-2,6-dioxo-5-(phenylselanyl)-pyrimidinecarbonitrile (5t). Yellow plates (8.7 mg, 5%). R_f = 0.5 (EtOAc/hexane 2 : 3). Mp 127–129 °C (CH_2Cl_2–hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (dd, *J* = 7.8, 1.8 Hz, 2H, Ar-H), 7.35–7.30 (m, 3H, Ar-H), 3.65 (s, 3H, N–CH_3), 3.38 (m, 3H, N–CH_3), 2.71 (s, 3H, 6-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.1 (s, C), 150.5 (s, C), 134.2 (s, CH), 131.6 (s, C), 129.5 (s, CH), 128.9 (s, CH), 128.3 (s, C), 113.9 (s, C), 111.1 (s, C), 35.8 (s, CH_3), 29.4 (s, CH_3). ^{77}Se NMR (76 MHz, $CDCl_3$): δ = 365.0 (s). IR (KBr): ν_{max}/cm^{-1} 2234 w (C≡N), 1711 s (C=O), 1663 *vs.* (C=O). HRMS (ESI): *m*/*z* calcd for $C_{13}H_{11}N_3O_2Se$ + H^+; 322.0095 $[M + H]^+$: found: 322.0099.

Conflicts of interest

There are no conflicts to declare.

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