A New Route to the Improved Synthesis of 1-(Alkoxymethyl)-5-alkyl-6-(arylselenenyl)uracils

Namkyu Lee, Young-Woo Kim, Key H. Kim and Dae-Kee Kim*

Life Science Research Center, Sunkyong Industries, 600 Jungja-Dong, Changan-Ku, Suwon-Si, Kyungki-Do 440-745, Korea

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A new route to C-6-selenenyl analogs of compound **1a** from 5-alkyl-6-chlorouracils **6a-b** has been described. A mild and highly efficient synthesis of 1-(alkoxymethyl)-5-alkyl-6-(arylselenenyl)uracils **8a-e** has been accomplished from **6a-b** in good yields using a two step procedure. Silylation of 5-alkyl-6-chlorouracils **6a-b** using *N,O*-bis(trimethylsilyl)acetamide followed by regioselective alkylation of the silylated intermediate with ethyl or benzyl chloromethyl ether in dichloromethane afforded the desired 1-(alkoxymethyl)-5-alkyl-6-chlorouracils **7a-d** in 88-94% yields. Compounds **7a-d** readily underwent addition-elimination reaction with an appropriate arylselenol in the presence of ethanolic sodium hyroxide to produce the corresponding 1-(alkoxymethyl)-5-alkyl-6-(arylselenenyl)uracils **8a-e** in excellent yields (94-99%).

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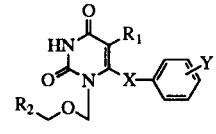
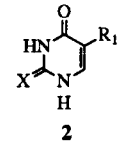
It has been reported by Tanaka *et al.* that 1-[(2-hydroxyethoxy)methyl]-6-(phenylthio)thymine **1a** and its analogs **1b-c** show potent and selective *in vitro* activity against human immunodeficiency virus type 1 [1-3]. Even though most analogs of compound **1a** were synthesized by regiospecific lithiation of 1-(alkoxymethyl)-5-alkyluracils or -2-thiouracils using lithium diisopropylamide followed by trapping the resulting C-6-lithiated species with appropriate electrophiles (diaryl disulfides and aryl aldehydes) [1-5], there are some problems associated with this approach, especially for large scale preparations. Direct application of the lithiation protocol to uracils with sterically demanding C-5-alkyl groups such as 1-(alkoxymethyl)-5-isopropyluracils generally suffered from very low yields. For example, lithium diisopropylamide lithiation of 1-(ethoxymethyl)-5-isopropyluracil **3c** followed by the reaction with benzaldehyde gave the alcohol product **4b** in only 18% yield, in contrast to the high yield (90%) of **4a** from 1-(ethoxymethyl)-5-ethyluracil **3a** [3]. This lithiation problem was overcome by using the corresponding 2-thiouracils since lithium diisopropylamide lithiation of 1-(alkoxymethyl)-5-alkyl-2-thiouracils followed by electrophile capture proceeded in much higher yields (>60%, in general), and the 2-thiouracils were shown to be readily converted to the desired uracil derivatives in reasonable to good yields (56-91%) by oxidative hydrolysis using hydrogen peroxide/sodium hydroxide condition [2,5]. However, the preparation of 1-(alkoxymethyl)-5-alkyl-2-thiouracils **3e-h** from the corresponding 5-alkyl-2-thiouracils **2c-d** by known procedure is rather complex with somewhat low yields (31-37%) [2] compared to those (62-83%) of 1-(alkoxymethyl)-5-alkyluracils **3a-d** from 5-alkyluracils **2a-b**, thus making 2-thiouracil route less practical. Furthermore, when R_1 is isopropyl and R_2 is phenyl as in compound **3h**, even though it is a 2-thiouracil, the lithiation protocol met with marginal success; *i.e.*, the C-6-lithiated derivative of **3h** reacted with phenyl disulfide in only 31% yield [2]. Another major limitation of this lithiation approach is that it cannot be used either when the introduction of an oxygen or nitrogen functionality at the C-6 position of uracils is required or when the appropriate electrophiles, for example, dialkyl or diaryl disulfides are not available for carbanion capture. In order to overcome this limitation, Tanaka *et al.* utilized a thymine with a phenylsulfinyl group at the C-6 position, **1e** which readily underwent addition-elimination reaction with various oxygen, nitrogen, or thiol nucleophiles [4,5]. This addition-elimination route, however, also confronted us with the same problems as described



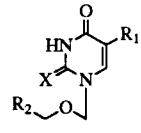
1

a, R_1 = Me, R_2 = CH_2OH, X = S, Y = H
b, R_1 = Et, R_2 = Me, X = S, Y = 3,5-Me_2
c, R_1 = *i*-Pr, R_2 = Me, X = CH_2, Y = 3,5-Me_2
d, R_1 = Me, R_2 = CH_2OH, X = Se, Y = H
e, R_1 = Me, R_2 = CH_2OTBS, X = S(O), Y = H



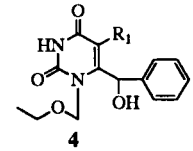
2

a, X = O, R_1 = Et
b, X = O, R_1 = *i*-Pr
c, X = S, R_1 = Et
d, X = S, R_1 = *i*-Pr



3

a, X = O, R_1 = Et, R_2 = Me
b, X = O, R_1 = Et, R_2 = Ph
c, X = O, R_1 = *i*-Pr, R_2 = Me
d, X = O, R_1 = *i* -Pr, R_2 = Ph
e, X = S, R_1 = Et, R_2 = Me
f, X = S, R_1 = Et, R_2 = Ph
g, X = S, R_1 = *i*-Pr, R_2 = Me
h, X = S, R_1 = *i*-Pr, R_2 = Ph



4

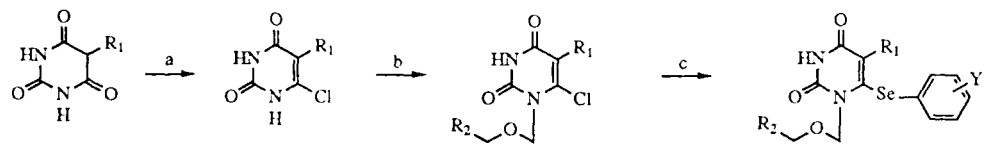
a, R_1 = Et
b, R_1 = *i*-Pr

earlier because the C-6-sulfinyl substituted uracil **1e** was prepared by the lithiation method and the subsequent oxidation of the resulting phenyl sulfide.

We have been also interested in developing 1-(alkoxymethyl)-5-alkyl-6-(arylselenenyl)uracils as potential chemotherapeutic agents for the treatment of human immunodeficiency virus type 1 since Goudgaon *et al.* [6] found that 1-[(2-hydroxyethoxy)methyl]-6-(phenylselenenyl)thymine **1d**, a C-6-selenenyl analog of compound **1a**, was more active than compound **1a** against human immunodeficiency virus type 1 in primary human lymphocytes. After our extensive structure-activity relationship study, four derivatives **8b-e** have been found to be the most potent against human immunodeficiency virus type 1 [7]. Unfortunately, it turned out to be very difficult to synthesize these compounds **8b-e** by adopting Tanaka's lithiation method; *i.e.*, the lithiation of uracils **3b-d** with lithium diisopropylamide followed by trapping with bis(3,5-dimethylphenyl) diselenide afforded the corresponding 6-arylselenenyluracils in extremely low yields (2-20%). It should be pointed out that our results are consistent with Tanaka's observations. In other words, Tanaka's lithiation approach is generally ineffective for those with either an isopropyl substituent at C-5 position or a phenyl group at the N-1 acyclic chain, irrespective of uracils or 2-thiouracils [2,3]. Thus, we have considered the conjugate addition-elimination process of 1-(alkoxymethyl)-5-alkyluracils with an appropriate leaving group at the C-6 position as an alternative route. It was conceived that 1-(alkoxymethyl)-5-alkyl-6-chlorouracils **7a-d** might serve as a good starting point for this purpose since 5-alkyl-6-chlorouracils **6a-b** are known to be readily available [8] and the chloro atom could act as an activator for conjugate addition and a good leaving group as well. It turned out to be the case.

In this report, we would like to describe a mild and highly efficient route to the synthesis of 1-(alkoxymethyl)-5-alkyl-6-(arylselenenyl)uracils, which involves the addition-elimination reaction of 1-(alkoxymethyl)-5-alkyl-6-chlorouracils with arylselenol as the key step. As shown in Scheme 1, the synthesis began with 6-chloro-5-ethyl- and -5-isopropyluracils, **6a** and **6b**, which were prepared in good yields (82-85%) from 5-ethyl- and 5-isopropylbarbituric acids, **5a** and **5b**, respectively, by modifying the known procedure [8]. Since there is no precedent for our approach, a model study with 6-chloro-5-ethyluracil **6a** was carried out in advance. First, the regioselective introduction of the benzyloxymethyl group was attempted according to the published method [2,9]. Treatment of **6a** with *N,O*-bis(trimethylsilyl)acetamide (2.2 equivalents, room temperature, 2 hours) in dichloromethane followed by alkylation of the *in situ* prepared silylated intermediate with benzyl chloromethyl ether (1.2 equivalents, reflux, 2 hours) in the presence of a catalytic amount of tetrabutylammonium iodide (0.01 equivalent) afforded a monoalkylated product in 68% yield (not optimized!) along with a small amount of N-1,3-dialkylated by-product. At this moment, it is not certain whether the alkylation occurred at N-1 or N-3 position because no one has studied the effect of C-6 substituents on the regioselectivity of this reaction. Thus, the resulting compound was further reacted with benzeneselenol (1.0 equivalent, room temperature) in ethanol in the presence of 1*N* ethanolic sodium hydroxide solution (1.0 equivalent) to obtain the addition-elimination product in 98% yield. Comparison of its spectral data (^{1}H and ^{13}C nmr) with those of authentic compound **8a**, prepared by Tanaka's lithiation method using 1-[(benzyloxy)methyl]-5-ethyluracil **3b** and phenyl disulfide in 46% yield, proved that the regioselective alkylation indeed occurred only at the N-1 position. It should be also stressed that the efficient conversion of C-6-chlorouracil **7b** to C-6-phenylselenenyl uracil derivative **8a** clearly demonstrated that 1-(alkoxymethyl)-5-alkyl-6-chlorouracils **7a-d** would be good substrates for addition-elimination process as we expected. With all the issues solved, the reaction conditions for each step were optimized as follows. Alkylation of 6-chloro-5-ethyl- and -5-isopropyluracils, **6a** and **6b** with benzyl chloromethyl ether (1.2

Scheme 1



5
a, R_1 = Et
b, R_1 = *i*-Pr

6
a, R_1 = Et (82%)
b, R_1 = *i*-Pr (85%)

7
a, R_1 = Et, R_2 = Me (93%)
b, R_1 = Et, R_2 = Ph (88%)
c, R_1 = *i*-Pr, R_2 = Me (89%)
d, R_1 = *i*-Pr, R_2 = Ph (94%)

8
a, R_1 = Et, R_2 = Ph, Y = H (98%)
b, R_1 = Et, R_2 = Me, Y = 3,5-Me_2 (94%)
c, R_1 = Et, R_2 = Ph, Y = 3,5-Me_2 (97%)
d, R_1 = *i*-Pr, R_2 = Me, Y = 3,5-Me_2 (99%)
e, R_1 = *i*-Pr, R_2 = Ph, Y = 3,5-Me_2 (99%)

[a] $BnEt_3Cl$ (2.0 equivalents), $POCl_3$, 50°, 7 hours; [b] *N,O*-bis(trimethylsilyl)acetamide (2.2 equivalents), dichloromethane, room temperature, 2 hours, then benzyl or ethyl chloromethyl ether (1.2 equivalents), $(n\text{-}Bu)_4NI$ (0.01 equivalent), reflux or 0°, 2 hours, N_2 atmosphere; [c] benzeneselenol or (3,5-dimethylphenyl)selenol (1.05 equivalents), 1*N* ethanolic NaOH solution (1.05 equivalents), ethanol, room temperature, 2 hours, N_2 atmosphere.

equivalents, freshly distilled!) using the afore-mentioned conditions proceeded in excellent yields to afford 1-[(benzyloxy)methyl]-6-chloro-5-ethyluracil **7b** (88%) and 1-[(benzyloxy)methyl]-6-chloro-5-isopropyluracil **7d** (94%), respectively. In contrast, the same reaction with freshly distilled chloromethyl ethyl ether under identical conditions produced the desired N-1 alkylated compounds in rather low yields (45-56%) together with about 2% of dialkylated by-products. In order to find optimum conditions, a series of reactions were examined with 6-chloro-5-ethyluracil **6a**. Whereas the use of another solvent (acetonitrile), triethylamine as an acid scavenger, or Lewis acid such as stannic chloride did not improve the yield, increasing the amount of chloromethyl ethyl ether to 3.0 equivalents enhanced not only the yield of desired product up to 75% but also that of by-product to 7%. It was later found that the best results were realized when the silylated 6-chlorouracils (*N,O*-bis(trimethylsilyl)acetamide, 2.2 equivalents, room temperature, 2 hours) were reacted with 1.2 equivalents of chloromethyl ethyl ether at lower temperature (0°) for 2 hours in dichloromethane; *i.e.*, 6-chloro-1-(ethoxymethyl)-5-ethyluracil **7a** and 6-chloro-1-(ethoxymethyl)-5-isopropyluracil **7c** were obtained in 93% and 89% yields from 6-chloro-5-ethyluracil **6a** and 6-chloro-5-isopropyluracil **6b**, respectively. Finally, the transformations of 1-(alkoxymethyl)-5-alkyl-6-chlorouracils **7a-d** into the most active 1-(alkoxymethyl)-5-alkyl-6-[(3,5-dimethylphenyl)selenenyl]uracil derivatives **8b-e** were carefully investigated. It was exciting to find that the addition-elimination reaction of uracils **7a-d** with a slight excess of (3,5-dimethylphenyl)selenol (1.05 equivalents, freshly distilled prior to use) in ethanol containing 1*N* ethanolic sodium hydroxide solution (1.05 equivalents) at room temperature under a nitrogen atmosphere proceeded in almost quantitative yields (94-99%) to produce the corresponding 1-(alkoxymethyl)-5-alkyl-6-[(3,5-dimethylphenyl)selenenyl]uracils **8b-e**. This reaction seemed to be very fast and might be completed in less than 30 minutes at room temperature since a sudden formation of massive white precipitates (sodium chloride salt) was observed in about 10 minutes after the addition of (3,5-dimethylphenyl)selenol. Even though it is not shown here, our approach could be extended to the synthesis of various other uracil derivatives with C-6 nitrogen or oxygen functional group since **7a** also reacted with 3,5-dimethylthiophenol to afford C-6-phenylthio uracil **1b** in almost quantitative yield (99%). These four compounds **8b-e** have been evaluated for their inhibitory effects on the replication of human immunodeficiency virus type 1 in the National Cancer Institute (Bethesda, USA) and found to be active in the nanomolar concentration range [7]. Of these compounds, 6-[(3,5-dimethylphenyl)selenenyl]-1-(ethoxymethyl)-5-isopropyluracil **8d** was the most inhibitory to human immunodeficiency virus type 1 replication with an EC_{50} of 0.0047 μM and a selective index of >42600.

In conclusion, a quite efficient route to the analogs of compound **1a** from readily available 5-alkyl-6-chlorouracils **6a-b** in two steps has been developed. Employing this approach, a mild and highly efficient synthesis of 1-(alkoxymethyl)-5-alkyl-6-(arylselenenyl)uracils **8a-e**, which have been up to now troublesome to synthesize, has been accomplished.

EXPERIMENTAL

Melting points were determined on either an Electrothermal F500MA digital or a Mettler FP62 melting point apparatus and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 1600 FTIR spectrophotometer. The ^1H nmr and ^{13}C nmr spectra were run in deuteriochloroform on a Varian Unity 300 spectrometer. The chemical shifts are reported in parts per million (ppm) relative to internal tetramethylsilane for ^1H nmr, and deuteriochloroform served as the internal standard at δ 77.0 for ^{13}C nmr. The electron impact mass spectra were obtained on a VG Quattro mass spectrometer. The tlc analysis was performed on Merck silica gel 60F-254 glass plates. Flash chromatography was performed using Merck silica gel 60 (230-400 mesh). Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer.

General Procedure for the Conversion of 5-Alkyl barbituric Acids **5a-b** to 5-Alkyl-6-chlorouracils **6a-b**.

A stirred suspension of barbituric acid (0.07 mole) **5a-b** [8] and benzyltriethylammonium chloride (0.14 mole) in phosphorus oxychloride (1.75 moles, 163 ml) was heated at 50° for 7 hours under a nitrogen atmosphere. The reaction mixture was cooled to room temperature and evaporated to dryness *in vacuo*. The residue was carefully quenched with 200 g of ice chips at 0°, and the slurry was kept in a refrigerator (about -5°) for 7 hours. The resulting white precipitate was collected and washed thoroughly with hot hexanes to afford the corresponding 6-chlorouracils **6a-b**.

6-Chloro-5-ethyluracil (**6a**).

This compound was obtained from **5a** in 82% yield as a white powder, and its melting point and ^1H nmr were identical with those reported in the literature [8].

6-Chloro-5-isopropyluracil (**6b**).

This compound was obtained from **5b** in 85% yield as a white powder, and its melting point and ^1H nmr were identical with those reported in the literature [8].

General Procedure for the Preparation of 5-Alkyl-6-chloro-1-(ethoxymethyl)uracils **7a** and **7c** from 5-Alkyl-6-chlorouracils **6a-b**.

To a stirred suspension of 5-alkyl-6-chlorouracil **6a-b** (3.0 mmoles) in anhydrous dichloromethane (9 ml) at room temperature under a nitrogen atmosphere was slowly added *N,O*-bis-(trimethylsilyl)acetamide (1.41 g, 6.6 mmoles, 1.72 ml) *via* a syringe, and the mixture was stirred for 2 hours at room temper-

ature. To the resulting clear reaction mixture was added tetrabutylammonium iodide (11 mg, 0.03 mmole) in one portion at room temperature, and the mixture was immediately cooled to 0°. Chloromethyl ethyl ether (591 mg, 6.0 mmoles, 0.58 ml) was slowly added to the reaction mixture at 0°, and the mixture was stirred for an additional 2 hours in an ice bath. The reaction mixture was poured into saturated sodium bicarbonate solution (25 ml) and ice (25 g), and was stirred for 30 minutes. The organic phase was separated, and the aqueous phase was extracted with dichloromethane (20 ml). The combined dichloromethane solution was washed with brine (20 ml), dried over anhydrous magnesium sulfate, and evaporated to dryness *in vacuo* to afford a yellow solid. The crude product was purified by flash column chromatography on silica gel with a mixture of ethyl acetate and hexane (1:2, v/v) as eluent.

6-Chloro-1-(ethoxymethyl)-5-ethyluracil (**7a**).

This compound was obtained from **6a** in 93% yield as white crystals, mp 125.6-126.1° (ethyl acetate-hexane); ir (potassium bromide): 1722, 1667, 1455 cm^{-1}; ^1H nmr: δ 1.10 (t, J = 7.4 Hz, 3H, CH_2CH_3), 1.23 (t, J = 7.1 Hz, 3H, OCH_2CH_3), 2.56 (q, J = 7.4 Hz, 2H, CH_2CH_3), 3.67 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 5.50 (s, 2H, NCH_2O), 9.68 (br s, 1H, NH); ^{13}C nmr: δ 12.2, 15.0, 20.1, 65.4, 74.8, 116.1, 143.1, 150.3, 161.5; ms: m/z 232 (M^+- H).

Anal. Calcd. for $C_9H_{13}ClN_2O_3$: C, 46.46; H, 5.63; N, 12.04. Found: C, 46.62; H, 5.71; N, 11.86.

6-Chloro-1-(ethoxymethyl)-5-isopropyluracil (**7c**).

This compound was obtained from **6b** in 89% yield as white crystals, mp 93.5-93.9° (ethyl acetate-hexane); ir (potassium bromide): 1714, 1643, 1453 cm^{-1}; ^1H nmr: δ 1.24 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 1.30 (d, J = 6.9 Hz, 6H, $CH(CH_3)_2$), 3.21 (septet, J = 6.9 Hz, 1H, $CH(CH_3)_2$), 3.67 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 5.50 (s, 2H, NCH_2O), 9.00 (br s, 1H, NH); ^{13}C nmr: δ 15.0, 29.2, 65.4, 74.9, 118.6, 142.5, 150.2, 160.8; ms: m/z 246 (M^+- H).

Anal. Calcd. for $C_{10}H_{15}ClN_2O_3$: C, 48.69; H, 6.13; N, 11.36. Found: C, 48.55; H, 6.18; N, 11.29.

General Procedure for the Preparation of 5-Alkyl-1-[(benzyloxy)methyl]-6-chlorouracils **7b** and **7d** from 5-Alkyl-6-chlorouracils **6a-b**.

To a stirred suspension of 5-alkyl-6-chlorouracil **6a-b** (3.0 mmoles) in anhydrous dichloromethane (9 ml) at room temperature under a nitrogen atmosphere was slowly added *N,O*-bis-(trimethylsilyl)acetamide (1.41 g, 6.6 mmoles, 1.72 ml) *via* a syringe, and the mixture was stirred for 2 hours at room temperature. To the resulting clear reaction mixture at room temperature was added tetrabutylammonium iodide (11 mg, 0.03 mmole) in one portion followed by benzyl chloromethyl ether (593 mg, 3.6 mmoles, 0.53 ml), and the mixture was refluxed in an oil bath for 2 hours. The reaction mixture was cooled to room temperature and poured into saturated sodium bicarbonate solution (25 ml) and ice (25 g), and the mixture was stirred for an additional 30 minutes. The organic phase was separated, and the aqueous phase was extracted with dichloromethane (20 ml). The combined dichloromethane solution was washed with brine (20 ml), dried over anhydrous magnesium sulfate, and evaporated to dryness *in vacuo* to afford a yellow solid. The crude product was purified by flash column chromatography on silica gel with a mixture of ethyl acetate and hexane (1:2, v/v) as eluent.

1-[(Benzyloxy)methyl]-6-chloro-5-ethyluracil (**7b**).

This compound was obtained from **6a** in 88% yield as white crystals, mp 117.4-118.2° (ethyl acetate-hexane); ir (potassium bromide): 1700, 1671, 1446 cm^{-1}; ^1H nmr: δ 1.08 (t, J = 7.5 Hz, 3H, CH_2CH_3), 2.52 (q, J = 7.5 Hz, 2H, CH_2CH_3), 4.70 (s, 2H, OCH_2Ph), 5.58 (s, 2H, NCH_2O), 7.26-7.34 (m, 5H, Ar H), 9.50 (br s, 1H, NH); ^{13}C nmr: δ 12.2, 20.2, 72.0, 74.7, 76.6, 116.2, 127.6, 127.9, 128.4, 137.1, 142.9, 150.3, 161.3; ms: m/z 294 (M^+- H).

Anal. Calcd. for $C_{14}H_{15}ClN_2O_3$: C, 57.05; H, 5.13; N, 9.50. Found: C, 57.23; H, 5.26; N, 9.25.

1-[(Benzyloxy)methyl]-6-chloro-5-isopropyluracil (**7d**).

This compound was obtained from **6b** in 94% yield as white crystals, mp 142.5-142.8° (ethyl acetate-hexane); ir (potassium bromide): 1705, 1678, 1439 cm^{-1}; ^1H nmr: δ 1.27 (d, J = 6.9 Hz, 6H, $CH(CH_3)_2$), 3.20 (septet, J = 6.9 Hz, 1H, $CH(CH_3)_2$), 4.70 (s, 2H, OCH_2Ph), 5.59 (s, 2H, NCH_2O), 7.26-7.40 (m, 5H, Ar H), 8.68 (br s, 1H, NH); ^{13}C nmr: δ 19.5, 29.2, 72.1, 74.9, 118.7, 137.2, 142.3, 150.1, 160.5; ms: m/z 308 (M^+- H).

Anal. Calcd. for $C_{15}H_{17}ClN_2O_3$: C, 58.35; H, 5.55; N, 9.07. Found: C, 58.61; H, 5.72; N, 8.76.

General Procedure for the Displacement of Chloro Atom in 1-(Alkoxymethyl)-5-alkyl-6-chlorouracils **7a-d** with Arylselenols.

To a stirred solution of 1-(alkoxymethyl)-5-alkyl-6-chlorouracils **7a-d** (4.06 mmoles) in absolute ethanol (15 ml) at room temperature under a nitrogen atmosphere were added 1*N* ethanolic sodium hydroxide solution (4.26 mmoles, 4.3 ml) and arylselenol (4.26 mmoles), and the resulting slurry was stirred at room temperature for 2 hours. The reaction mixture was cooled to 0°, and the resulting white precipitate was collected and washed with cold ethanol. The crude white solid was dissolved in dichloromethane, and insoluble sodium chloride was removed by passing through a Celite pad. Evaporation to dryness *in vacuo* gave a white crystalline product. The ethanolic portion was acidified with concentrated hydrogen chloride solution to *p*H 5-6 and evaporated to dryness *in vacuo* to afford a yellow residue. Brine (30 ml) was added to the residue, and the aqueous phase was extracted with dichloromethane (2 x 20 ml). The combined dichloromethane solution was dried over anhydrous magnesium sulfate and evaporated to dryness *in vacuo* to afford a yellow oil. The crude oil was purified by flash column chromatography on silica gel with a mixture of ethyl acetate and hexane (1:2, v/v) as eluent to give an additional white solid.

1-[(Benzyloxy)methyl]-5-ethyl-6-(phenylselenenyl)uracil (**8a**).

This compound was obtained from **7b** and benzeneselenol in 98% yield as white crystals, and its physical and spectral data were identical with those reported in the literature [7].

6-[(3,5-Dimethylphenyl)selenenyl]-1-(ethoxymethyl)-5-ethyluracil (**8b**).

This compound was obtained from **7a** and (3,5-dimethylphenyl)selenol in 94% yield as white crystals, and its physical and spectral data were identical with those reported in the literature [7].

1-[(Benzyloxy)methyl]-6-[(3,5-dimethylphenyl)selenenyl]-5-ethyluracil (**8c**).

This compound was obtained from **7b** and (3,5-dimethylphenyl)selenol in 97% yield as white crystals, and its physical and spectral data were identical with those reported in the literature [7].

6-[(3,5-Dimethylphenyl)selenenyl]-1-(ethoxymethyl)-5-isopropyluracil (**8d**).

This compound was obtained from **7c** and (3,5-dimethylphenyl)selenol in 99% yield as white crystals, and its physical and spectral data were identical with those reported in the literature [7].

1-[(Benzyloxy)methyl]-6-[(3,5-dimethylphenyl)selenenyl]-5-isopropyluracil (**8e**).

This compound was obtained from **7d** and (3,5-dimethylphenyl)selenol in 99% yield as white crystals, and its physical and spectral data were identical with those reported in the literature [7].

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* To whom correspondence should be addressed.

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