Preparation of 4′-Substituted Thymidines by Substitution of the Thymidine 5′-Esters

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tert-Butyl thymidylate **3** was prepared from thymidine **1** in six steps and 67% overall yield. When the lithium trianion of **3** (prepared by treatment of **3** with excess LDA and then excess *tert*-butyllithum) is reacted with electrophiles, trapping occurs stereoselectively from either the α- or *β*-face depending on the electrophile (Scheme 1). Deuterioacetic acid in deuteriomethanol affords mainly the α-deuterated product (**4a**/**4b** = 2.4:1) while all other electrophiles, e.g., phenylselenenyl chloride, allyl bromide, and *N*-fluorobenzenesulfonimide (NFSI), give predominately (or completely) the products of attack from the *β*-face (**5bcd**/**4bcd** = 3.7:1 to 100:0). The structures of the products were determined by coupling constant analysis of both the initial compounds and the diols **6bcd** prepared by ester reduction and by formation of the acetonides **7bc**. The methyl ester of the 3′-epimer of thymidylic acid **9** was also prepared from thymidine **1** in nine steps and 74% overall yield. When the lithium trianion of **9** (prepared by treatment of **9** with excess LDA and then excess *tert*-butyllithum) is reacted with electrophiles, trapping also occurs stereoselectively with attack on either the α- or *β*-face depending on the electrophile (Scheme 2). Again, deuterioacetic acid in deuteriomethanol affords mainly the *β*-deuterated product (**11a**/**10a** = 1.6:1) while all other electrophiles, e.g., phenylselenenyl chloride, methyl iodide, allyl bromide, and NFSI, gave predominately (or completely) the product of attack from the α-face (8.7:1 to 100: 0). Again, the structures of the products were determined by coupling constant analysis of both the initial compounds, and the diols **12b**−**e** were prepared by reduction of the ester and by formation of the acetonides **13bcd**. A rationale has been developed using molecular mechanics calculations to explain the diastereoselectivity that involves staggered axial attack on the sp^2 carbon opposite to the pseudoaxial alkoxy group in the most stable half-chair conformation of the enolates, as shown in Schemes 3−5.

Introduction and Background

Modified nucleosides have become useful agents for the treatment of cancer and viral diseases due to their good antitumor and antiviral activity.[1] In particular, several nucleosides with substituents at the 4′-position are good candidates as antiviral agents.[2] For example, 4′-azidothymidine demonstrated very potent anti-HIV activity, but its high toxicity rendered it ineffectual as an antiviral drug.[3] Other 4′-substitutions, such as fluoro,[4] cyano,[5] and even an unusual oxetane,[5] have also afforded nucleosides with strong activity, including anti-HIV activity. Recently, in connection with biological studies of the mechanism of synthetic nucleases, we published a synthesis of 4′-deuteriothymidine,[6] which proceeded via deuteration of the anion of the corresponding 5′-ester. We now report the use of such anions of the 5′-esters of 2′-deoxy nucleosides and their analogues.

Most syntheses of 4′-carbon-branched nucleosides usually involve reactions of various 5′-oxo nucleoside derivatives, e.g., 4′-formyl and 4′-acyl nucleosides. Thus, 4′-carbon-substituted nucleosides were prepared years ago by the Syntex group via an aldol condensation−Cannizzaro reaction process to give the 4′,4′-bis-hydroxymethyl derivatives.[7] These diols could then be converted into other compounds since the α-hydroxymethyl group is generally more reactive than the *β*-hydroxymethyl group,[5a,8] an approach that has since been successfully applied often to the synthesis of more complex derivatives.[9] Another very interesting route employs dimethyl

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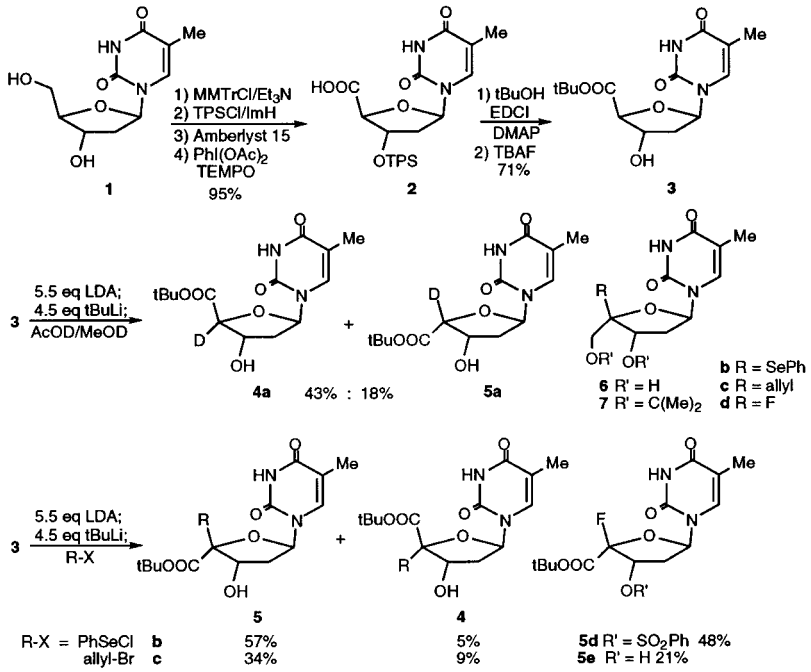
Scheme 1



L-tartrate and builds up the 4′-substituted nucleoside in a multistep sequence.[10] Although considerably longer, this sequence allows for the introduction of both purine and pyrimidine bases as well as modified bases. We decided to expand our earlier investigation on the use of the trianions of thymidine nucleosides[6] to determine if other electrophiles could also be added. Herein we report the results of our study of the stereochemistry of the addition of electrophiles to the anions of the 5′-esters of thymidine.

Results and Discussion

Although several methods exist for the preparation of thymidylic acid and its derivatives directly from thymidine,[11] we opted for a longer approach to guarantee the purity of the starting materials. Thus we prepared the *tert*-butyl ester of thymidylic acid **3** from thymidine **1** by a multistep route which gave very pure product. We protected first the 5′-hydroxyl group as the monomethoxytrityl (MMTr) ether and then the 3′-hydroxyl as the *tert*-butyldiphenylsilyl (TPS) ether. After hydrolysis of the MMTr ether, we carried out an oxidation with TEMPO and iodobenzene diacetate (BAIB)[12] to give the acid **2** in nearly quantitative yield over the four steps (Scheme 1). Formation of the *tert*-butyl ester with EDCI and *tert*-butyl alcohol and desilylation with TBAF afforded the desired substrate **3** in 71% yield.

In our earlier study of the triple deprotonation of the analogous methyl ester,[6] we found that it was necessary to remove the diisopropylamine from the complex with the trianion in order to produce the more reactive unchelated lithium salt. Thus, we routinely added a full equivalent of *n*- or *tert*-butyllithium to reform the LDA and thereby remove it from the trianion complex, a procedure first discovered by Seebach and co-workers and since often used.[13] Thus, deprotonation of the ester **3** using excess LDA (normally about 5−5.6 equiv) followed by reformation of the LDA with *tert*-butyllithium and deuteration gave mainly the α-deuterio thymidylate **4a** (43%), along with a smaller amount of the *β*-isomer **5a** (18%). This is in agreement with our earlier reported results, although we were unable at the time to isolate any of the minor *β*-isomer **5a**. Thus, as we reported, deuteration occurs primarily, but not exclusively, from the α-face.

However, when the lithium trianion of **3** was trapped with other electrophiles, the product of the reaction from the *β* face was the major isomer isolated. For example, phenylselenenyl chloride gave mainly **5b** (57%) along with a small amount of the α-isomer **4b** (5%) and allyl bromide gave mostly the *β*-isomer **5c** (34%) with 9% of the α-isomer **4c** being produced.[14] Using the strong, commercially available fluorinating agent *N*-fluorobenzenesulfonimide (NFSI) as the electrophile afforded mainly the *β*-fluoro 3′-sulfonate **5d** in 48% yield (under different conditions, one can isolate the free alcohol **5e**

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(14) It is known that phenylselenenylation of 3′-protected (acetate or silyl ether) 4′-formyl nucleoside derivatives using PhSeCl and triethylamine affords mostly the 4′*β*-selenophenyl aldehydes, although small amount of the α-isomer are obtained in some cases, e.g., 3−3.8:1 *β*/α from the dibenzoyladenine derivative, 15:1 from the *N*-benzoylcytidine derivative, and 100: 0 from the thymidine derivative. (a) Wackernagel, F.; Schwitter, U.; Giese, B. *Tetrahedron Lett.* **1997**, *38*, 2657. (b) Giese, B.; Erdmann, P.; Giraud, L.; Gobel, T.; Petretta, M.; Schafer, T.; Von Raumer, M. *Tetrahedron Lett.* **1994**, *35*, 2683. (c) Giese, B.; Dussy, A.; Elie, C.; Erdmann, P.; Schwitter, U. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1861. (d) Giese, B.; Erdmann, P.; Schäfer, T.; Schwitter, U. *Synthesis* **1994**, 1310.

Scheme 2

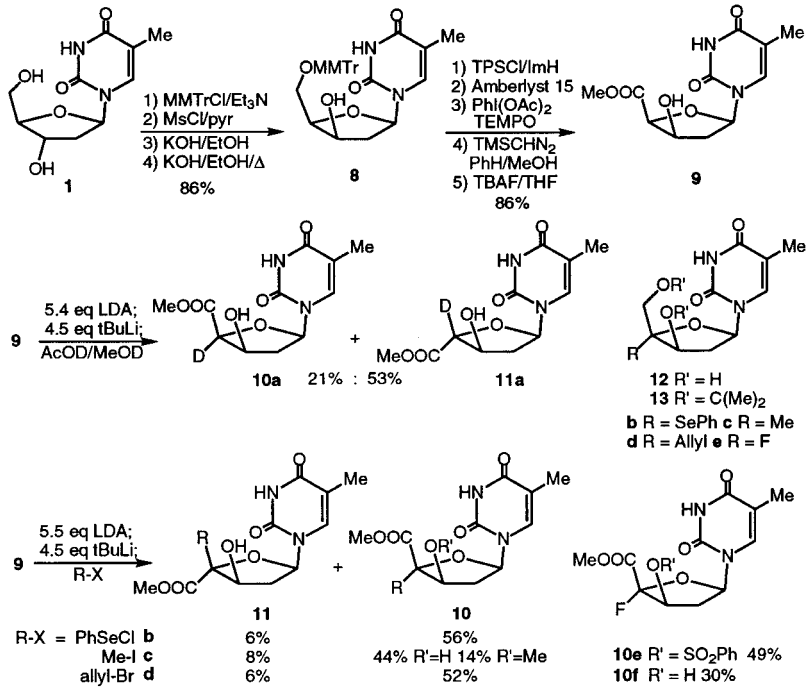


Table 1. Stereoselectivity of Addition of Electrophiles (E^+) to Ester Enolates

ester	E	α-product	β-product
3	D	2.4	1
3	SePh	1	11.4
3	allyl	1	3.8
3	F	0	1
9	D	1	1.6
9	SePh	9.3	1
9	allyl	7.3	1
9	Me	8.7	1
9	F	1	0

in 21% yield along with 19% of **5d**). The structures of the products **5bc** were proven by reduction of the esters to the corresponding primary alcohols **6bc** with lithium borohydride followed by formation of the acetonides **7bc** with acidic dimethoxypropane.[15] Control experiments showed that the trans-oriented diol did not form an acetonide under these conditions therefore proving that the ester group in **5** was cis to the hydroxyl group. The results of the addition of electrophiles to the trianion derived from **3** are shown in Table 1.

We also investigated deprotonations and functionalizations of the 3′-epimer of thymidylic esters, namely the methyl ester **9**.[16] This substrate was prepared as follows. First, inversion of the 3′-hydroxyl of **1** was carried out by a four-step sequence involving initial MMTr protection of the 5′-hydroxyl of **1** followed by mesylation, formation of the anhydro nucleoside, and hydrolysis to give **8** in 86% overall yield. Silylation of the 3′-hydroxyl, removal of the MMTr group, TEMPO-BAIB oxidation as before, formation of the methyl ester with trimethylsilyldiazomethane, and final desilylation with TBAF afforded the desired substrate **9** in 86% overall yield.

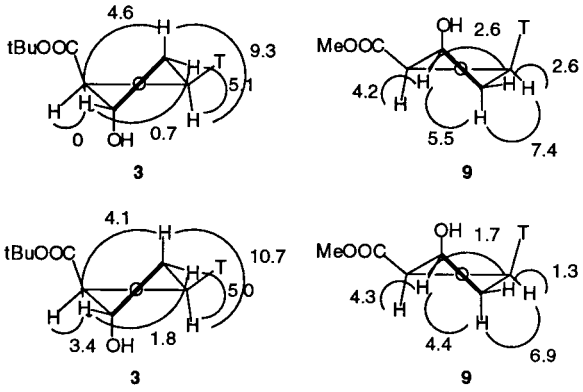
Deprotonation of the ester **9** under the same conditions as for **3**, namely excess LDA (5.4 equiv) followed by reformation of the LDA with *tert*-butyllithium (to give the more reactive unchelated lithium salt) and deuteration, gave mainly the β-deuterio thymidylate **11a** (53%) along with a smaller amount of the α-isomer **10a** (21%). This is again in general agreement with our earlier results in which the deuterium atom is introduced mostly cis to the existing hydroxyl group. However, when the lithium anion of **9** was trapped with other electrophiles, the α product was the major isomer isolated, e.g., phenylselenenyl chloride gave mainly **10b** (56%) along with a small amount of the α-isomer **11b** (6%), and methyl iodide gave mostly the α-isomer **10c** (44% and an additional 14% of the *O*-methyl derivative) with 8% of the β-isomer **11c** being produced. Allyl bromide afforded a similar mixture with the β-isomer **10d** greatly predominating (52%) over the α-isomer (6%). Again, use of the strong fluorinating agent (NFSI) as the electrophile afforded mainly the β-fluoro 3′-sulfonate **10e** in 49% yield (under different conditions, one can isolate the free alcohol **10f** in 30% yield along with 15% of **10e**). The structures of the products **10bcd** were again proven by reduction of the esters to the corresponding primary alcohols **12bcd** with $LiBH_4$ followed by formation of the acetonides **13bcd** with acidic dimethoxypropane.[15] Once more, control experiments showed that the trans-oriented diol did not form an acetonide under these conditions. The results of the addition of electrophiles to the trianion of **9** are shown in Table 1.

Trapping of the anions of nucleosides having carbonyl groups at the 4′-position with the 3′α-hydroxyl protected with electrophiles are known and generally give mostly the β products.[14] We believe that the selectivity observed

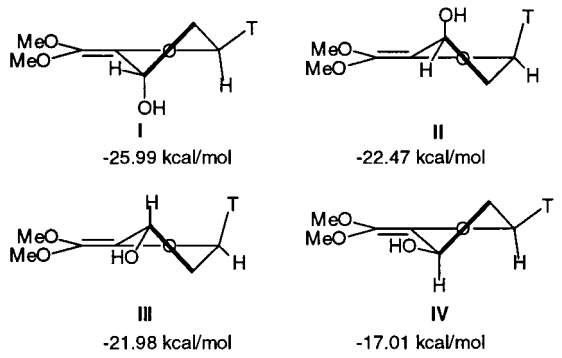
(15) The diols derived from the fluoro nucleosides, e.g., **6d** and **12e**, did not give clean acetonides under these conditions. Their structures were assigned by the pattern of coupling constants in the proton NMR, especially the $^3J_{H-F}$, and by analogy to the formation of the other derivatives.

(16) We were unable to prepare the corresponding *tert*-butyl ester due to steric hindrance caused by the large *tert*-butyldiphenylsilyl (TPS) ether at the 3′β position. Normally the methyl ester is not preferred since side products can arise via attack of some nucleophilic species (the ester enolate or LDA itself) on the methyl ester. However, presumably due to the steric hindrance around this methyl ester, we do not observe a significant amount of side products of the sort mentioned above during the formation and reaction of the trianion.

Scheme 3. Observed (Top) and Calculated (Bottom) *J* Values in ^{1}H NMR Spectra of 3 and 9



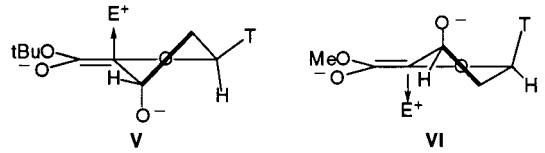
Scheme 4. Macromodel 5.0 Strain Energy Calculations



here is due to the conformation adopted by the nucleoside in its trianionic form. We have analyzed the conformations of the precursor esters **3** and **9** by coupling constant analysis and by molecular mechanics calculations (Macromodel 5.0). These two molecules exist in opposite half-chair conformations, with **3** preferring the 3′-exo conformation and **9** existing in the 3′-endo conformation, as shown in Scheme 3.[17] The key coupling constants are as follows: (a) the one between H3′ and H4′, which is very small (~0 Hz) in **3** and medium (4.2 Hz) in **9**; (b) the one between H1′ and H2′β, which is large (9.3 Hz) in **3** and small (2.6 Hz) in **9**. The corresponding calculated values for the minimized structures (both methyl esters) are also given in Scheme 3 for comparison purposes. The overall match is quite good. Thus, both molecules prefer conformations in which the hydroxyl group prefers a pseudoaxial position. We have also calculated the preferred conformations of the dimethylketene acetals **I**−**IV** as models for the lithium enolates of the esters **3** and **9** in the two possible half-chair conformations (Scheme 4). For the enolate derived from the ester **3**, the 3′-exo conformation **I** is greatly favored over the corresponding 3′-endo conformation **III** (by about 4 kcal/mol), while for the enolate derived from the ester **9**, the 3′-endo conformation **II** is greatly favored over the corresponding 3′-exo conformation **IV** (by about 5 kcal/mol). Presumably, this difference is due in part to the steric repulsion of the pseudoequatorial hydroxyl group with the alkoxy group on the alkene.

We rationalize the diastereoselectivity of the alkylation of the trianions of **3** and **9** as shown in Scheme 5, namely

Scheme 5. Presumed Transition States for Electrophilic Additions to the Enolates of 3 and 9



by assuming that the anions adopt conformations similar to those calculated for the dimethylketene acetals **I**−**IV**. Thus, we expect the trianion of **3** to adopt the conformation shown in **V** (analogous to **I**) while the trianion of **9** adopts the conformation shown in **VI** (analogous to **II**). The stereochemical course of the reaction can then be explained by assuming that the electrophilic agents approach the carbanionic center from the face opposite the 3′-alkoxide group which is in a pseudoaxial arrangement in both **V** and **VI**. Attack of the enolate on the electrophile would occur in the staggered axial orientation due to torsional strain, e.g., on the top face of **V** and on the bottom face of **VI** as shown. This "conformational transmission of chirality" via staggered axial attack on an sp^2 carbon center has been postulated to account for the high diastereoselectivity seen in additions to other half-chair conformations.[18]

The deuteration results can be rationalized by assuming that there is a small amount of net complexation of the deuterium source with the 3′-alkoxide group prior to protonation and this leads to a small preference for protonation cis to the alkoxy group, 2.4:1 and 1.6:1 for the trianions of **3** and **9** respectively.

We have just begun to examine the further chemistry of these novel 4′-substituted nucleoside derivatives, e.g., the transformation of the products into other useful nucleoside derivatives. The results of those experiments will be reported in due course. The preparation and testing of these and other novel nucleoside analogues is currently underway in our laboratories.

Conclusion

We have shown that electrophilic trapping of the lithium trianion of *tert*-butyl thymidylate **3** occurs stereoselectively from either the α- or β-face depending on the electrophile (Scheme 1). Deuterioacetic acid in deuteriomethanol affords mainly the α-deuterated product (**4a**/**4b** = 2.4:1) while all other electrophiles, e.g., phenylselenenyl chloride, allyl bromide, and *N*-fluorobenzenesulfonimide (NFSI), give predominately (or completely) the products of attack from the β-face (**5bcd**/**4bcd** = 3.7:1 to 100:0). The structures of the products were determined by coupling constant analysis of both the initial compounds and the diols **6bcd** prepared by ester reduction and by formation of the acetonides **7bc**. In similar fashion, electrophilic trapping of the lithium trianion of the methyl ester of the 3′-epimer of thymidylic acid **9** also occurs stereoselectively with attack on either the α- or β-face depending on the electrophile (Scheme 2). Again deuterioacetic acid in deuteriomethanol affords mainly the β-deuterated product (**11a**/**10a** = 1.6:1) while all other electrophiles, e.g., phenylselenenyl chloride, methyl iodide, allyl bromide, and NFSI, gave predominately (or completely) the product of attack from the

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α-face (8.7:1 to 100:0). Again, the structures of the products were determined by coupling constant analysis of both the initial compounds and the diols **12b**−**e** were prepared by reduction of the ester and by formation of the acetonides **13bcd**. A rationale has been developed using molecular mechanics calculations to explain the diastereoselectivity, which involves staggered axial attack on the sp^2 carbon opposite to the pseudoaxial alkoxy group in the most stable half-chair conformation of the enolates, as shown in Schemes 3−5.

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded on Bruker spectrometers at 200 or 400 MHz for proton and at 50 or 100 MHz for carbon and are so indicated. ^{1}H NMR and ^{13}C NMR data are reported in parts per million (δ) downfield from tetramethylsilane. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Infrared spectra were recorded on a Nicolet 510 infrared spectrophotometer as a liquid film or as a thin crystalline film. All IR data are reported in wavenumbers (cm^{-1}).

Thin-layer chromatography (TLC) was performed using Merck silica gel 60 F_{254} 0.25 mm plates. Visualization was accomplished using ultraviolet light or one of the following stains: Anisaldehyde (2 mL), acetic acid (1 mL), or sulfuric acid (2 mL) in 95% ethanol (85 mL). Flash chromatography was carried out using ICN Biomedicals silica gel 60 (230−400 mesh). Solvent systems are reported as volume percent mixtures. Concentration or evaporation of solvent refers to removal at reduced pressure using a Büchi rotary evaporator and a Büchi aspirator pump. All inorganic solutions are aqueous and concentrations are indicated in percent weight, except for saturated sodium chloride and saturated sodium bicarbonate.

The following solvents and reagents were distilled from the indicated agent under argon: tetrahydrofuran (THF) and diethyl ether from sodium benzophenone ketyl; dichloromethane and triethylamine from calcium hydride. All reactions were performed under argon unless otherwise noted.

1-[(2*R*,4*S*,5*R*)-5-[Bis(4-methoxyphenyl)phenylmethoxymethyl]-4-hydroxytetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione. To a solution of thymidine (157 mg, 0.648 mmol) in DMF (1.5 mL) were added triethylamine (0.23 mL, 1.65 mmol), DMAP (6 mg, 0.05 mmol), and 4-monomethoxytrityl chloride (400 mg, 1.30 mmol) at room temperature, and the mixture was stirred at the same temperature for 3.5 h. After being quenched with water, the mixture was extracted with CH_2Cl_2 (3 × 15 mL) and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography (hexane/ethyl acetate = 1:2, ethyl acetate) to give 1-[(2*R*,4*S*,5*R*)-5-[bis(4-methoxyphenyl)phenylmethoxymethyl]-4-hydroxytetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (330 mg, 99%) as a colorless foam: $[\alpha]^{22}_D = +10°$ (c = 0.33, $CHCl_3$); IR (neat) 3058, 1690, 1609, 1510, 1470, 1449, 1271, 1252, 1181, 1092, 1059, 1034, 831, 737, 702 cm^{-1}; 400 MHz ^{1}H NMR ($CDCl_3$) δ 1.45 (3H, d, J = 1.1 Hz), 2.31 (1H, ddd, J = 13.6, 8, 6 Hz), 2.44 (1H, ddd, J = 13.6, 5.8, 2.5 Hz), 3.10 (1H, d, J = 4.4 Hz), 3.37 (1H, dd, J = 10.5, 3 Hz), 3.45 (1H, dd, J = 10.5, 3 Hz), 3.78 (3H, s), 4.08 (1H, dt, J = 2.8, 2.8 Hz), 4.58 (1H, m), 6.44 (1H, dd, J = 8, 5.8 Hz), 6.84 (2H, m), 7.22−7.32 (8H, m), 7.38−7.43 (4H, m),7.60 (1H, d, J = 1.1 Hz), 9.41 (1H, br s); 100 MHz ^{13}C NMR ($CDCl_3$) δ 11.86 (C5-Me), 40.98 (C2′), 55.28 (OCH_3), 63.75 (C5′), 72.52 (C3′), 84.81 (C4′), 86.29 (C1′), 87.20 (CAr_3), 111.36 (C5), 113.31 (*o*-C × 2 of MeOAr), 127.30 (1C of Ph), 127.31 (1C of Ph), 128.04 (4C of Ph), 128.38 and 30.42 (2C of Ph), 134.87 (*p*-C of MeOAr), 135.73 (C4), 143.82 (*m*-C of MeOAr), 143.90 (*m*-C of MeOAr), 150.67 (C6), 158.80 (*C*-OMe), 164.02 (C2).

1-[(2*R*,4*S*,5*R*)-5-[Bis(4-methoxyphenyl)phenylmethoxymethyl]-4-(*tert*-butyldiphenylsilanyloxy)tetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione. To a solution of 1-[(2*R*,4*S*,5*R*)-5-[bis(4-methoxyphenyl)phenylmethoxymethyl]-4-hydroxytetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (498 mg, 0.968 mmol) in DMF (3.5 mL) were added imidazole (315 mg, 4.63 mmol) and TBDPSCl (0.40 mL, 1.54 mmol) at room temperature, and the mixture was stirred at the same temperature for 54 h. After being quenched with water, the mixture was extracted with Et_2O (3 × 25 mL) and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography (hexane/ethyl acetate = 3:1) to give 1-[(2*R*,4*S*,5*R*)-5-[bis(4-methoxyphenyl)phenylmethoxymethyl]-4-(*tert*-butyldiphenylsilanyloxy)tetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (726 mg, 100%) as a colorless foam: $[\alpha]^{21}_D = +41°$ (c = 0.58, $CHCl_3$); IR (neat) 3056, 2955, 2932, 1692, 1510, 1472, 1449, 1428, 1273, 1252, 1181, 1113, 1065, 1034, 999, 826, 756, 702, 613 cm^{-1}; 400 MHz ^{1}H NMR ($CDCl_3$) δ 1.06 (9H, s), 1.38 (3H, s), 2.09 (1H, ddd, J = 13.5, 7.5, 6.3 Hz), 2.40 (1H, dd, J = 13.5, 5.5 Hz), 2.92 (1H, dd, J = 10.5, 2.2 Hz), 3.24 (1H, dd, J = 10.5, 2.2 Hz), 3.79 (3H, s), 4.09 (1H, s), 4.57 (1H, m), 6.52 (1H, dd, J = 7.5, 5.5 Hz), 6.77 (2H, d, J = 8.5 Hz), 7.15 (2H, d, J = 8.5 Hz), 7.2−7.3 (12H, m), 7.35−7.47 (4H, m), 7.50 (1H, s), 7.56 (2H, d, J = 7.4 Hz), 7.63 (2H, d, J = 7.4 Hz), 9.09 (1H, br s); 100 MHz ^{13}C NMR ($CDCl_3$) δ 11.72 (C5-Me), 19.03 (CMe_3), 26.89 (CMe_3), 41.16 (C2′), 55.27 (OCH_3), 63.44 (C5′), 73.96 (C3′), 88.87 (C4′), 86.77 (C1′), 87.07 (CAr_3), 111.11 (C5), 113.23 (*o*-C × 2 of MeOAr), 127.16 (1C of Ph), 127.20 (1C of Ph), 127.87 (2C of Ph), 127.91 (2C of Ph), 127.96 (2C of Ph), 127.97 (2C of Ph), 128.31 (2C of Ph), 128.35 (2C of Ph), 130.00 (1C of Ph), 130.06 (1C of Ph), 130.35 (2C of Ph), 133.06 (1C of Ph), 133.09 (1C of Ph), 134.79 (*p*-C of MeOAr), 135.67 (2C of Ph), 135.72 (2C of Ph), 135.72 (C4), 143.75 (*m*-C of MeOAr), 143.84 (*m*-C of MeOAr), 150.46 (C6), 158.72 (*C*-OMe), 163.98 (C2).

1-[(2*R*,4*S*,5*R*)-4-(*tert*-Butyldiphenylsilanyloxy)-5-hydroxymethyltetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione. To a solution of 1-[(2*R*,4*S*,5*R*)-5-[bis(4-methoxyphenyl)phenylmethoxymethyl]-4-(*tert*-butyldiphenylsilanyloxy)tetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (90 mg, 0.12 mmol) in MeOH (6 mL) was added Amberlyst 15-H (53 mg) at room temperature, and the mixture was stirred for 30 h. After filtration, the solvent was evaporated in vacuo. The residue was purified by flash chromatography (hexane/ethyl acetate = 1:1−1:2) to give 1-[(2*R*,4*S*,5*R*)-4-(*tert*-butyldiphenylsilanyloxy)-5-hydroxymethyltetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (58 mg, 100%) as a colorless foam: $[\alpha]^{22}_D = +39°$ (c = 0.60, $CHCl_3$); IR (neat) 3440, 3071, 2932, 2859, 1690, 1472, 1428, 1364, 1275, 1198, 1105, 1061, 1032, 960, 824, 756, 741, 702, 612 cm^{-1}; 400 MHz ^{1}H NMR ($CDCl_3$) δ 1.09 (9H, s), 1.82 (3H, s), 2.14 (1H, ddd, J = 13.5, 8, 6 Hz), 2.26 (1H, ddd, J = 13.5, 6, 3 Hz), 2.45 (1H, br), 3.25 (1H, dd, J = 12, 2.5 Hz), 3.63 (1H, dd, J = 12, 2.5 Hz), 3.98 (1H, dt, J = 3, 2.5 Hz), 4.45 (1H, ddd, J = 6, 3 Hz), 6.26 (1H, dd, J = 8, 6 Hz), 7.30 (1H, s), 7.35−7.5 (6H, m), 7.62−7.66 (4H, m), 9.20 (1H, br); 100 MHz ^{13}C NMR ($CDCl_3$) δ 12.47 (C5-Me), 19.04 (CMe_3), 26.91 (CMe_3), 40.27 (C2′), 62.02 (C5′), 73.01 (C3′), 86.67 (C4′), 87.72 (C1′), 110.95 (C5), 127.92 (4C of Ph), 130.11 (1C of Ph), 130.15 (1C of Ph), 133.10 (1C of Ph), 133.24 (1C of Ph), 135.72 (2C of Ph), 135.77 (2C of Ph), 136.91 (C4), 150.45 (C6), 163.94 (C2).

(2*S*,3*S*,5*R*)-3-(*tert*-Butyldiphenylsilanyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-tetrahydrofuran-2-carboxylic Acid (2). To a solution of 1-[(2*R*,4*S*,5*R*)-4-(*tert*-butyldiphenylsilanyloxy)-5-hydroxymethyltetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (124 mg, 0.258 mmol) in CH_2Cl_2 (1.3 mL) were added 2,2,6,6-tetramethyl-1-piperidinyloxy, free radical (TEMPO) (9 mg, 0.06 mmol), and iodobenzene diacetate (BAIB) (184 mg, 0.570 mmol) at room temperature. After the mixture was stirred for 2 h, a mixture of MeCN−water (1:1) (0.014 mL) was added to the reaction mixture, and the mixture was stirred for 24 h. After removal of the solvent, the residue was purified by flash chromatography ($CHCl_3$−MeOH = 10:1) to give (2*S*,3*S*,5*R*)-3-(*tert*-butyldiphenylsilanyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid **2** (128 mg, 100%) as a colorless foam: $[\alpha]^{22}_D = +72°$ (c = 0.60, $CHCl_3$−MeOH = 10:1); IR (neat) 3071, 2957, 2932, 2859, 1713, 1674,

1472, 1428, 1279, 1227, 1107, 1084, 741, 702, 610 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3-CD_3OD$ = 10:1) δ 1.00 (9H, s), 1.67 (1H, ddd, J = 13.5, 9.5, 4.4 Hz), 1.78 (3H, s), 2.13 (1H, dd, J = 13.5, 5 Hz), 4.48 (1H, s), 4.52 (1H, d, J = 4.4 Hz), 6.53 (1H, dd, J = 9.5, 5 Hz), 7.29 (6H, m), 7.56 (4H, m), 8.04 (1H, s); 50 MHz ^{13}C NMR ($CDCl_3-CD_3OD$ = 10:1) δ 16.25 (C5-Me), 22.92 (CMe_3), 30.65 (CMe_3), 43.28 (C2′), 80.65 (C3′), 89.30 (C4′), 90.62 (C1′), 114.86 (C5), 131.74 (2C of Ph), 131.80 (2C of Ph), 133.92 (1C of Ph), 134.00 (1C of Ph), 136.47 (1C of Ph), 136.67 (1C of Ph), 139.60 (2C of Ph), 139.66 (2C of Ph), 141.07 (C4), 154.65 (C6), 168.54 (C2), 177.8 (C5′).

(2*S*,3*S*,5*R*)-3-(*tert*-Butyldiphenylsilanyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic Acid *tert*-Butyl Ester. To a solution of **2** (430 mg, 0.870 mmol) in CH_2Cl_2 (3.2 mL) were added *t*-BuOH (0.80 mL, 8.37 mmol), DMAP (304 mg, 2.49 mmol), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (1.05 g, 5.48 mmol) at 0 °C, and the mixture was stirred at 0 °C for 30 min and room temperature for 23 h. After being quenched with water, the mixture was extracted with CH_2Cl_2 and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography (hexane/ethyl acetate = 3:1) to give (2*S*,3*S*,5*R*)-3-(*tert*-butyldiphenylsilanyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-tetrahydrofuran-2-carboxylic acid *tert*-butyl ester (333 mg, 100%) as a colorless foam: $[\alpha]^{22}_D$ = +65° (c = 0.70, $CHCl_3$); IR (neat) 3071, 2961, 2932, 1738, 1696, 1472, 1427, 1279, 1221, 1130, 1105, 1084, 739, 702, 608 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.10 (9H, s), 1.36 (9H, s), 1.77 (1H, ddd, J = 13.5, 9.6, 5 Hz), 1.94 (3H, d, J = 1 Hz), 2.25 (1H, dd, J = 13.5, 5 Hz), 4.47 (1H, s), 4.49 (1H, d, J = 5 Hz), 6.68 (1H, dd, J = 9.6, 5 Hz), 7.38−7.5 (6H, m), 7.66 (4H, m), 8.11 (1H, d, J = 1 Hz), 9.3 (1H, br); ^{13}C NMR ($CDCl_3-CD_3OD$ = 10:1) δ 12.69 (C5-Me), 19.14 (CMe_3), 26.85 (CMe_3), 27.91 (CMe_3), 39.38 (C2′), 76.60 (C3′), 82.61 (CMe_3), 85.49 (C4′), 86.44 (C1′), 111.17 (C5), 127.94 (2C of Ph), 128.00 (2C of Ph), 130.12 (1C of Ph), 130.19 (1C of Ph), 132.61 (1C of Ph), 132.72 (1C of Ph), 135.71 (2C of Ph), 135.73 (2C of Ph), 136.48 (C4), 150.64 (C6), 164.14 (C2), 170.34 (C5′).

(2*S*,3*S*,5*R*)-3-Hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic Acid *tert*-Butyl Ester (3). To (2*S*,3*S*,5*R*)-3-(*tert*-butyldiphenylsilanyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester (333 mg, 0.605 mmol) in THF (6.8 mL) was added TBAF (1 M in THF, 0.60 mL) at 0 °C, and the mixture was stirred at the same temperature for 1.5 h. After being quenched with water, the mixture was extracted with CH_2Cl_2 and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography (hexane/ethyl acetate = 1:2−1:4) to give **3** (184 mg, 97%) as a colorless foam: $[\alpha]^{22}_D$ = +23° (c = 0.32, $CHCl_3$−MeOH = 20:1); IR (neat) 3389, 3241, 1734, 1717, 1657, 1476, 1372, 1333, 1292, 1275, 1213, 1161, 1121, 1096, 1071, 621 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3-CD_3OD$ = 20:1) δ 1.44 (9H, s), 1.89 (1H, ddd, J = 13.5, 9.3, 4.6 Hz), 1.89 (3H, d, J = 1.2 Hz), 2.33 (1H, ddd, J = 13.5, 5.1, 0.7 Hz), 4.35 (1H, s), 4.42 (1H, d, J = 4.6 Hz), 6.43 (1H, dd, J = 9.3, 5.1 Hz), 8.11 (1H, d, J = 1.2 Hz); ^{13}C NMR ($CDCl_3-CD_3OD$ = 20:1) δ 16.41 (C5-Me), 31.82 (CMe_3), 42.93 (C2′), 78.44 (C3′), 86.79 (CMe_3), 89.25 (C4′), 90.38 (C1′), 115.09 (C5), 140.50 (C4), 154.81 (C6), 168.43 (C2), 174.53 (C5′).

(2*S*,3*S*,5*R*)-4-Deuterio-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic Acid *tert*-Butyl Ester (4a). The ester **3** (30 mg) was coevaporated with benzene, dried in vacuo, dissolved in THF (3.9 mL)−HMPA (0.48 mL), and dried under molecular sieves 4 Å with stirring for 1 h. To the solution of **3** (28 mg, 0.090 mmol) was added lithium diisopropylamide mono(tetrahydrofuran) (LDA) (Aldrich, 1.5 M in cyclohexane, 0.35 mL, 0.53 mmol) at −78 °C, and the mixture was stirred at −78 °C for 5 min, −78 °C → room temperature for 10 min, and at room temperature for 30 min. *tert*-Butyllithium (1.7 M in pentane, 0.25 mL, 0.43 mmol) was added to the solution at −78 °C, and the mixture was stirred at −78 °C for 1 h. To the solution were added CD_3OD (0.34 mL) and CD_3CO_2D (0.11 mL) at −78 °C, and the mixture was stirred at −78 °C → room temperature for 30 min. After removal of the solvent, the residue was purified by flash chromatography (hexane/ethyl acetate = 2:3−1:2) to give a 7:1 mixture of **4a** and **3** (14 mg, 50%) and a 7:1 mixture of **5a** and the C4′-stereoisomer of **3** (5.2 mg, 18%).

(2*S*,3*S*,5*R*)-4-Deuterio-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **4a** (colorless foam): $[\alpha]^{21}_D$ = +27° (c = 0.29, $CHCl_3$−MeOH = 20:1); IR (neat) 3386, 3241, 1732, 1717, 1655, 1476, 1372, 1294, 1273, 1204, 1088 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3-CD_3OD$ = 20:1) δ 1.45 (9H, s), 1.90 (1H, ddd, J = 13.5, 9.2, 4.3 Hz), 1.90 (3H, d, J = 1.2 Hz), 2.33 (1H, ddd, J = 13.5, 5.1, 1 Hz), 4.43 (1H, d, J = 4.3 Hz), 6.43 (1H, dd, J = 9.2, 5.1 Hz), 8.11 (1H, d, J = 1.2 Hz); ^{13}C NMR ($CDCl_3-CD_3OD$ = 20:1) δ 16.41 (C5-Me), 31.83 (CMe_3), 42.94 (C2′), 78.38 (C3′), 86.79 (CMe_3), 89.25 (small peak, C4′), 90.37 (C1′), 115.10 (C5), 140.46 (C4), 154.77 (C6), 168.34 (C2), 174.51 (C5′).

(2*R*,3*S*,5*R*)-4-Deuterio-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **5a** (colorless foam): $[\alpha]^{22}_D$ = +32° (c = 0.20, $CHCl_3$−MeOH = 20:1); IR (neat) 3455, 3208, 1742, 1723, 1673, 1267, 1105, 1086 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3-CD_3OD$ = 20:1) δ 1.46 (9H, s), 1.85 (3H, d, s), 2.29 (1H, ddd, J = 13.5, 7.3, 5.7 Hz), 2.46 (1H, ddd, J = 13.5, 6.5, 2 Hz), 4.68 (1H, dd, J = 5.7, 2 Hz), 4.73 (1/7 H, d, J = 4.4 Hz), 6.20 (1H, dd, J = 7.3, 6.5 Hz), 7.09 (1H, s); ^{13}C NMR ($CDCl_3-CD_3OD$ = 20:1) δ 16.21 (C5-Me), 31.88 (CMe_3), 44.06 (C2′), 76.05 (C3′), 85,19 (small peak, C4′), 86.77 (CMe_3), 92.49 (C1′), 114.81 (C5), 140.53 (C4), 154.25 (C6), 168.25 (C2), 172.19 (C5′).

(2*S*,4*S*,5*R*)-3-Hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-2-(phenylselenenyl)tetrahydrofuran-2-carboxylic Acid *tert*-Butyl Ester (5b). The ester **3** (8 mg) was coevaporated with benzene, dried in vacuo, dissolved in THF (1.0 mL)−HMPA (0.13 mL), and dried under molecular sieves 4A (three pieces) with stirring for 1 h. To the solution of **3** (7.5 mg, 0.024 mmol) was added lithium diisopropylamide mono(tetrahydrofuran) (LDA) (Aldrich, 1.5 M in cyclohexane, 0.090 mL, 0.14 mmol) at −78 °C, and the mixture was stirred at −78 °C for 5 min, −78 °C → room temperature for 10 min, and room temperature for 30 min. *tert*-Butyllithium (1.7 M in pentane, 0.065 mL, 0.11 mmol) was added to the solution at −78 °C, and the mixture was stirred at −78 °C for 1 h. To the solution was added phenylselenenyl chloride (52 mg, 0.27 mmol) in THF (0.1 mL) at −78 °C, and the mixture was stirred at the same temperature for 1 h. After the reaction was quenched with MeOH (0.09 mL)−AcOH (0.03 mL), the solvent was evaporated in vacuo. The residue was purified by flash chromatography (hexane/ethyl acetate = 2:3) to give (2*S*,4*S*,5*R*)-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-2-(phenylselenenyl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **5b** (6.4 mg, 57%) as a colorless foam and (2*R*,3*S*,5*R*)-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-2-(phenylselenenyl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **4b** (0.6 mg, 5%) as a colorless foam.

(2*S*,4*S*,5*R*)-3-Hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)- 2-(phenylselenenyl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **5b**: $[\alpha]^{22}_D$ = +84° (c = 0.5, $CHCl_3$); IR (neat) 3400, 1698, 1474, 1370, 1273, 1159, 1084, 1063, 747, 667 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.35 (9H, s), 1.89 (3H, d, J = 1.2 Hz), 2.50 (1H, ddd, J = 13.5, 9.2, 4.3 Hz), 2.57 (1H, ddd, J = 13.5, 6, 1.2 Hz), 3.31 (1H, br s), 4.71 (1H, m), 6.86 (1H, dd, J = 9.2, 6 Hz), 7.33 (2H, m), 7.39 (1H, m), 7.62 (3H, m), 8.74 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 12.61 (C5-Me), 27.81 (CMe_3), 37.55 (C2′), 71.11 (C3′), 84.28 (CMe_3), 87.64 (C4′), 92.97 (C1′), 111.97 (C5), 126.88 (*p*-C of Ph), 129.28 (C-Se), 129.31 (2C of Ph), 135.71 (2C of Ph), 135.91 (C4), 150.28 (C6), 163.39 (C2), 167.23 (C5′).

(2*R*,3*S*,5*R*)-3-Hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-2-(phenylselenenyl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **4b**: 400 MHz ^1H NMR ($CDCl_3$) δ 1.35 (9H, s), 1.92 (3H, d, J = 1.2 Hz), 2.29 (1H, ddd, J = 13.7, 7.6, 5.2 Hz), 2.65 (1H, ddd, J = 13.6, 7.4, 6.8 Hz), 3.25 (1H, br s), 4.76 (1H, m), 6.38 (1H, dd, J = 7.4, 5.2 Hz), 7.33 (2H, m), 7.39 (1H, m), 7.62 (3H, m), 8.74 (1H, br s).

1-(2*R*,4*S*,5*R*)-4-Hydroxy-5-hydroxymethyl-5-phenylselenenyltetrahydrofuran-2-yl)-5-methyl-1*H*-pyrimidine-2,4-dione (6b). To a solution of **5b** (12 mg, 0.026 mmol) in

THF (0.8 mL) was added $LiBH_4$ (2 mg, 0.092 mmol) at room temperature, and the mixture was stirred for 1 h. After the reaction was quenched with EtOH (0.25 mL) for 0.5 h and neutralized with AcOH (0.01 mL) for 0.5 h, the solvent was evaporated in vacuo. The residue was purified by flash chromatography (hexane/ethyl acetate = 1:2 to ethyl acetate) to give 1-(2*R*,4*S*,5*R*)-4-hydroxy-5-hydroxy-methyl-5-phenylselenenyltetrahydrofuran-2-yl)-5-methyl-1*H*-pyrimidine-2,4-dione **6b** (7 mg, 68%) as a colorless foam: $[\alpha]^{22}_D = +181°$ (c = 0.15, $CHCl_3$); IR (neat) 3397, 2924, 2853, 1692, 1468, 1275, 1042, 741 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.94 (3H, s), 2.56 (2H, m), 3.29 (1H, br), 3.87 (1H, d, J = 13 Hz), 3.92 (1H, d, J = 13 Hz), 4.26 (1H, br s), 4.68 (1H, br s), 6.82 (1H, dd, J = 7.9, 7.4 Hz), 7.31 (2H, dd, J = 7.7, 7.1 Hz), 7.38 (1H, m), 7.56 (2H, m), 7.84 (1H, d, J = 1.2 Hz), 9.17 (1H, br s); ^{13}C NMR ($CDCl_3$) δ: 12.60 (C5-Me), 39.37 (C2′), 64.27 (C5′), 78.07 (C3′), 87.21 (C1′), 97.85 (C4′), 112.14 (C5), 126.08 (*p*-C of Ph), 129.22 (C-Se), 129.54 (2C of Ph), 135.88 (2C of Ph), 136.19 (C4), 150.77 (C6), 163.61 (C2).

1-[(4a*R*,6*R*,7a*S*)-2,2-Dimethyl-4a-phenylselenenyltetrahydrofuro[3,2-*d*][1,3]dioxin-6-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (7b). To a solution of **6b** (9 mg, 0.023 mmol) in 2,2-dimethoxypropane (0.33 mL)−DMF (0.08 mL) was added pyridinium *p*-toluenesulfonate (<1 mg) at room temperature, and the mixture was stirred for 48 h. After removal of the solvent, the residue was purified by preparative thin-layer chromatography (ethyl acetate) to give 1-(4a*R*,6*R*,7a*S*)-2,2-dimethyl-4a-phenylselenenyltetrahydrofuro[3,2-*d*][1,3]dioxin-6-yl)-5-methyl-1*H*-pyrimidine-2,4-dione **7b** (6.5 mg, 65%) as a colorless foam: $[\alpha]^{21}_D = +57°$ (c = 0.15, $CHCl_3$); IR (neat) 3183, 2926, 1694, 1470, 1375, 1267, 1078, 999, 866 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.23 (3H, s), 1.35 (3H, s), 1.96 (3H, s), 2.51 (2H, m), 3.94 (1H, d, J = 12.9 Hz), 4.23 (1H, d, J = 12.9 Hz), 4.61 (1H, br s), 6.77 (1H, dd, J = 8, 7 Hz), 7.35 (2H, dd, J = 7.5, 7.3 Hz), 7.42 (1H, dd, J = 7.5, 7.5 Hz), 7.65 (1H, d, J = 7.3 Hz), 7.86 (1H, s), 8.34 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 12.64 (C5-Me), 19.45 and 27.91 (Me_2C), 37.92 (C2′), 66.31 (C5′), 75.00 (C3′), 87.61 (C1′), 88.88 (Me_2C), 98.35 (C4′), 111.74 (C5), 125.80 (*p*-C of Ph), 129.47 (C-Se), 129.59 (2C of Ph), 136.11 (C4), 136.47 (2C of Ph), 150.23 (C6), 163.29 (C2).

(2*R*,3*S*,5*R*)-3-Hydroxy-2-methyl-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic Acid *tert*-Butyl Ester (5c). The ester **3** (8 mg) was coevaporated with benzene, dried in vacuo, dissolved in THF (1.0 mL)−HMPA (0.13 mL), and dried under molecular sieves 4A (three pieces) with stirring for 1 h. To the solution of **3** (7.5 mg, 0.024 mmol) was added lithium diisopropylamide mono(tetrahydrofuran) (LDA) (Aldrich, 1.5 M in cyclohexane, 0.090 mL, 0.14 mmol) at −78 °C, and the mixture was stirred at −78 °C for 5 min, −78 °C → room temperature for 10 min, and at room temperature for 30 min. *tert*-Butyllithium (1.7 M in pentane, 0.065 mL, 0.11 mmol) was added to the solution at −78 °C, and the mixture was stirred at −78 °C for 1 h. To the solution was added allyl bromide (0.035 mL, 0.40 mmol) at −78 °C, and the mixture was stirred at −78 °C → −30 °C for 1 h and at 0 °C for 40 min. After the reaction was quenched with MeOH (0.09 mL)−AcOH (0.03 mL), the solvent was evaporated in vacuo. The residue was purified by flash chromatography (hexane/ethyl acetate = 1:1−1:2) to give (2*R*,3*S*,5*R*)-2-methyl-3-(2-propenyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **5c′** (1.5 mg, 16%), (2*R*,3*S*,5*R*)-3-hydroxy-2-methyl-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **5c** (2.9 mg, 34%), and (2*S*,3*S*,5*R*)-3-hydroxy-2-methyl-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **4c** (0.8 mg, 9%).

(2*R*,3*S*,5*R*)-3-Hydroxy-2-methyl-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **5c** (colorless foam): $[\alpha]^{22}_D = +33°$ (c = 0.22, $CHCl_3$); IR (neat) 3492, 2930, 1740, 1709, 1674, 1476, 1370, 1275, 1235, 1140, 1086 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.52 (9H, s), 1.92 (3H, s), 2.25 (1H, ddd, J = 13.7, 6.8, 6.5 Hz), 2.47 (1H, ddd, J = 13.5, 6.5, 4.4 Hz), 2.54 (1H, dd, J = 14, 7 Hz), 2.82 (1H, dd, J = 14, 7.2 Hz), 4.46 (1H, m), 5.22 (2H, m), 5.83 (1H, m), 6.35 (1H, dd, J = 6.6, 6.6 Hz), 7.19 (1H, d, J = 1 Hz), 8.70 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 12.60 (C5-Me), 28.11 (CMe_3), 39.00 (C2′), 40.64 (allyl), 75.46 (C3′), 83.45 (CMe_3), 86.20 (C4′), 89.81 (C1′), 111.08 (C5), 119.91 and 131.64 (vinyl of allyl), 135.84 (C4), 149.99 (C6), 163.58 (C2), 170.33 (C5′).

(2*R*,3*S*,5*R*)-2-Methyl-3-(2-propenyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **5c′** (colorless foam): 400 MHz ^1H NMR ($CDCl_3$) δ 1.49 (9H, s), 1.91 (3H, d, J = 1.2 Hz), 2.18 (1H, ddd, J = 13.5, 6.8, 6.5 Hz), 2.54 (2H, m), 2.47 (1H, dd, J = 13.5, 6.6 Hz), 4.05 (2H, m), 4.15 (1H, m), 5.15−5.35 (4H, m), 5.75−5.95 (2H, m), 6.32 (1H, dd, J = 6.6, 6.5 Hz), 7.19 (1H, d, J = 1.2 Hz), 8.16 (1H, br).

(2*S*,3*S*,5*R*)-3-Hydroxy-2-methyl-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **4c** (colorless foam): 400 MHz ^1H NMR ($CDCl_3$) δ 1.50 (9H, s), 1.96 (3H, d, J = 1.2 Hz), 2.03 (1H, ddd, J = 13.5, 8.8, 5 Hz), 2.46 (1H, ddd, J = 13.5, 5, 2 Hz), 2.66 (2H, m), 4.59 (1H, dd, J = 5, 1.8 Hz), 4.46 (1H, m), 5.19 (2H, m), 5.84 (1H, m), 6.43 (1H, dd, J = 8.8, 5 Hz), 8.02 (1H, d, J = 1.2 Hz), 8.22 (1H, br).

1-[(2*R*,4*S*,5*S*)-4-Hydroxy-5-hydroxymethyl-5-(2-propenyl)tetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (6c). To a solution of **5c** (4.2 mg, 0.012 mmol) in THF (0.4 mL) was added $LiBH_4$ (1 mg, 0.046 mmol) at room temperature, and the mixture was stirred for 3 h. After the reaction was quenched with EtOH (0.25 mL) for 0.5 h and neutralized with AcOH (0.01 mL) for 0.5 h, the solvent was evaporated in vacuo. The residue was purified by flash chromatography (ethyl acetate) to give 1-(2*R*,4*S*,5*S*)-4-hydroxy-5-hydroxymethyl-5-(2-propenyl)tetrahydrofuran-2-yl)-5-methyl-1*H*-pyrimidine-2,4-dione **6c** (3 mg, 89%) as a colorless foam: $[\alpha]^{22}_D = +18°$ (c = 0.10, $CHCl_3$); IR (neat) 3413, 2926, 1684, 1472, 1271, 1053 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.91 (3H, d, J = 1.1 Hz), 2.21 (1H, ddd, J = 14, 7.2, 7.1 Hz), 2.39 (1H, dd, J = 14, 6.9 Hz), 2.44 (1H, dd, J = 14, 7.3 Hz), 2.51 (1H, ddd, J = 14, 6.2, 3.3 Hz), 3.44 (1H, br s, OH), 3.82 (1H, d, J = 13 Hz), 3.85 (1H, d, J = 13 Hz), 3.98 (1H, d, J = 5.4 Hz, OH), 4.44 (1H, m), 5.21 (2H, m), 5.84 (1H, m), 6.40 (1H, dd, J = 7.2, 6.2 Hz), 7.25 (1H, d, J = 1.1 Hz), 9.43 (1H, br s); ^{13}C NMR ($CDCl_3$) δ: 12.61 (C5-Me), 40.49 and 40.70 (C2′ and allyl), 65.26 (C5′), 75.61 (C3′), 84.97 (C4′), 87.71 (C1′), 111.41 (C5), 119.80 and 132.36 (vinyl of allyl), 135.41 (C4), 150.72 (C6), 163.89 (C2).

5-Methyl-1-[(4a*S*,6*R*,7a*S*)-2,2-dimethyl-4a-(2-propenyl)-tetrahydrofuro[3,2-*d*][1,3]dioxin-6-yl]-1*H*-pyrimidine-2,4-dione (7c). To a solution of **6c** (8 mg, 0.028 mmol) in 2,2-dimethoxypropane (0.28 mL)−DMF (0.08 mL) was added pyridinium *p*-toluenesulfonate (<1 mg) at room temperature, and the mixture was stirred for 35 h. After removal of the solvent, the residue was purified by preparative thin-layer chromatography (ethyl acetate) to give 5-methyl-1-(4a*S*,6*R*,7a*S*)-2,2-dimethyl-4a-(2-propenyl)tetrahydrofuro[3,2-*d*][1,3]dioxin-6-yl)-1*H*-pyrimidine-2,4-dione **7c** (5.6 mg, 62%) as a colorless foam: $[\alpha]^{21}_D = +32°$ (c = 0.17, $CHCl_3$); IR (neat) 3187, 2928, 1692, 1468, 1373, 1264, 851, 756 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.37 (6H, s), 1.92 (3H, s), 2.00 (1H, ddd, J = 13, 8.5, 5.5 Hz), 2.41 (1H, dd, J = 13, 4.5 Hz), 2.50 (2H, m), 3.64 (1H, d, J = 11.7 Hz), 3.69 (1H, d, J = 11.7 Hz), 4.21 (1H, d, J = 5 Hz), 5.26 (2H, m), 5.86 (1H, m), 6.38 (1H, dd, J = 9, 4.5 Hz), 7.31 (1H, s), 8.37 (1H, br s); ^{13}C NMR ($CDCl_3$) δ: 12.65 (C5-Me), 22.48 and 25.62 (Me_2C), 37.77 and 40.94 (C2′ and allyl), 63.90 (C5′), 73.90 (C3′), 84.03 (C4′), 85.79 (C1′), 99.47 (Me_2C), 111.11 (C5), 120.11 and 131.89 (vinyl of allyl), 134.97 (C4), 150.05 (C6), 163.35 (C2).

(2*S*,3*S*,5*R*)-3-Benzenesulfonyloxy-2-fluoro-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic Acid *tert*-Butyl Ester (5d). The ester **3** (16 mg) was coevaporated with benzene, dried in vacuo, dissolved in THF (2.0 mL)−HMPA (0.25 mL), and dried under molecular sieves 4A (eight pieces) with stirring for 1 h. To the solution of **3** (14.5 mg, 0.046 mmol) was added lithium diisopropylamide mono(tetrahydrofuran) (LDA) (Aldrich, 1.5 M in cyclohexane, 0.18 mL, 0.27 mmol) at −78 °C, and the mixture was stirred at −78 °C for 5 min, −78 °C → room temperature for 10 min,

and room temperature for 30 min. *tert*-Butyllithium (1.7 M in pentane, 0.13 mL, 0.22 mmol) was added to the solution at −78 °C, and the mixture was stirred at −78 °C for 1 h. To the solution was added *N*-fluorobenzenesulfonimide (NFSI) (155 mg, 0.490 mmol) in THF (0.42 mL) at −78 °C, and the mixture was stirred at −78 °C → −25 °C for 1 h and at −25 °C → 0 °C for 5 min. After the reaction was quenched with MeOH (0.18 mL)−AcOH (0.06 mL), the solvent was evaporated in vacuo. The residue was purified by flash chromatography (hexane/ethyl acetate = 1:1−1:2) to give (2*S*,3*S*,5*R*)-3-benzenesulfonyloxy-2-fluoro-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **5d** (10.3 mg, 48%) and the 3′-*O*-benzenesulfonyl derivative of **3** (3.4 mg, 16%).

(2*S*,3*S*,5*R*)-3-Benzenesulfonyloxy-2-fluoro-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **5d** (colorless foam): $[\alpha]^{24}_D = +19°$ ($c = 0.43$, $CHCl_3$); IR (neat) 1759, 1713, 1474, 1451, 1373, 1335, 1260, 1194, 1117, 1051, 1001, 918, 899, 835, 781, 752, 689, 588 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3$) δ 1.49 (9H, s), 1.92 (3H, d, $J = 0.9$ Hz), 2.29 (1H, m), 2.64 (1H, dd, $J = 15$, 6 Hz), 5.38 (1H, dd, $J = 3.7$, 3.7 Hz), 6.80 (1H, ddd, $J = 8.5$, 8.5, 6 Hz), 7.14 (1H, s), 7.61 (2H, m), 7.70 (1H, m), 7.92 (2H, m), 8.42 (1H, br); ^{13}C NMR ($CDCl_3$) δ: 12.67 (C5-Me), 27.61 (C*Me*$_3$), 35.10 (C2′), 81.29 (C3′, d, $J = 169$ Hz), 85.51 (*C*Me$_3$), 87.22 (C1′), 112.80 (C5), 112.95 (C4′, d, $J = 936$ Hz), 127.91 (2C of Ph), 129.67 (2C of Ph), 133.74 (1C of Ph), 134.76 (1C of Ph), 135.82 (C4), 149.92 (C6), 160.17 (C5′, d, $J = 130$ Hz), 162.92 (C2).

(2*S*,3*S*,5*R*)-2-Fluoro-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic Acid *tert*-Butyl Ester (5e). The ester **3** (52 mg) was coevaporated with benzene, dried under vacuo, dissolved in THF (6.5 mL)−HMPA (0.81 mL), and dried under molecular sieves 4A (25 pieces) with stirring for 1 h. To the solution of **3** (51 mg, 0.16 mmol) was added lithium diisopropylamide mono(tetrahydrofuran) (LDA) (Aldrich, 1.5 M in cyclohexane, 0.61 mL, 0.92 mmol) at −78 °C, and the mixture was stirred at −78 °C for 5 min, −78 °C → room temperature for 15 min, and room temperature for 27 min. *tert*-Butyllithium (1.7 M in pentane, 0.44 mL, 0.75 mmol) was added to the solution at −78 °C, and the mixture was stirred at −78 °C for 1 h. To the solution was added *N*-fluorobenzenesulfonimide (NFSI) (545 mg, 1.73 mmol) in THF (1.5 mL) at −78 °C, and the mixture was stirred at −78 °C for 10 min. After the reaction was quenched with MeOH (0.63 mL)−AcOH (0.19 mL), the solvent was evaporated in vacuo. The residue was purified by flash chromatography (hexane/ethyl acetate = 1:1) to give (2*S*,3*S*,5*R*)-2-fluoro-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **5e** (10.9 mg, 21%) and **5d** (14 mg, 19%).

(2*S*,3*S*,5*R*)-2-Fluoro-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid *tert*-butyl ester **5e** (colorless foam): $[\alpha]^{22}_D = +34°$ ($c = 0.08$, $CHCl_3$); IR (neat) 3463, 3204, 2928, 1755, 1725, 1682, 1478, 1335, 1279, 1115 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.56 (9H, s), 1.95 (3H, d, $J = 1.2$ Hz), 2.21 (1H, m), 2.56 (1H, dd, $J = 14$, 6 Hz), 3.48 (1H, br s, OH), 4.66 (1H, m), 6.94 (1H, ddd, $J = 8.9$, 8.9, 6 Hz), 7.22 (1H, dd, $J = 1.2$, 1.2 Hz), 8.57 (1H, br); ^{13}C NMR ($CDCl_3$) δ 12.72 (C5-Me), 27.84 (C*Me*$_3$), 36.47 (C2′, d, $J = 10$ Hz), 75.66 (C3′, d, $J = 143$ Hz), 85.52 (*C*Me$_3$), 87.79 (C1′, d, $J = 12$ Hz), 112.59 (C5), 113.89 (C4′, d, $J = 941$ Hz), 134.43 (C4, d, $J = 22$ Hz), 150.38 (C6), 163.43 (C2), 163.28 (C5′, d, $J = 139$ Hz).

1-[(2*R*,4*S*,5*R*)-5-Fluoro-4-hydroxy-5-hydroxymethyltetrahydrofuran-2-yl)-5-methyl-1*H*-pyrimidine-2,4-dione (6d). To a solution of **5d** (9.5 mg, 0.029 mmol) in THF (1.0 mL) was added $LiBH_4$ (3 mg, 0.14 mmol) at room temperature, and the mixture was stirred for 2 h. After the reaction was quenched with EtOH (0.5 mL) for 10 min and neutralized with AcOH (0.02 mL) for 10 min, the solvent was evaporated in vacuo. The residue was purified by flash chromatography (ethyl acetate) to give 1-[(2*R*,4*S*,5*R*)-5-fluoro-4-hydroxy-5-hydroxymethyltetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione **6d** (6.2 mg, 82%) as a colorless foam: $[\alpha]^{22}_D = +0°$ ($c = 0.1$, $CHCl_3$−MeOH = 20:1); IR (neat) 3397, 1701, 1474, 1283, 1071 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$−CD_3OD = 20:1) δ 1.88 (3H, s), 2.16 (1H, m), 2.43 (1H, dd, $J = 14$, 6 Hz), 3.86 (1H, dd, $J = 18$, 12.6 Hz), 3.91 (1H, dd, $J = 23$, 12.6 Hz), 4.48 (1H, dd, $J = 3$, 3 Hz), 6.69 (1H, ddd, $J = 8.3$, 8.3, 6 Hz), 7.28 (1H, s); ^{13}C NMR ($CDCl_3$−CD_3OD = 20:1) δ 16.42 (C5-Me), 41.18 (C2′), 64.57 (C5′, d, $J = 129$ Hz), 77.73 (C3′, d, $J = 157$ Hz), 90.85 (C1′, d, $J = 13$ Hz), 116.05 (C5), 124.94 (C4′, d, $J = 906$ Hz), 138.79 (C4, d, $J = 24$ Hz), 154.60 (C6), 167.86 (C2).

Methanesulfonic Acid (2*R*,3*S*,5*R*)-2-[Bis(4-methoxyphenyl)phenylmethoxymethyl]-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-3-yl Ester. To a solution of 1-[(2*R*,4*S*,5*R*)-5-[bis(4-methoxyphenyl)phenylmethoxymethyl]-4-hydroxytetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (56 mg, 0.11 mmol) in pyridine (0.3 mL) was added methanesulfonyl chloride (0.011 mL, 0.14 mmol) at 0 °C, and the mixture was stirred for 6 h at the same temperature and refrigerated for 12 h. After the reaction was quenched with ice−water (5 mL), the mixture was extracted with CH_2Cl_2 and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography (hexane/ethyl acetate = 1:2) to give methanesulfonic acid (2*R*,3*S*,5*R*)-2-[bis(4-methoxyphenyl)phenylmethoxymethyl]-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-3-yl ester (61 mg, 94%) as a colorless foam: $[\alpha]^{22}_D = +21°$ ($c = 0.45$, $CHCl_3$); IR (neat) 3031, 1694, 1510, 1360, 1252, 1177, 756 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.46 (3H, d, $J = 1.1$ Hz), 2.48 (1H, ddd, $J = 14.5$, 8.7, 6.5 Hz), 2.68 (1H, ddd, $J = 14.5$, 5.5, 1.4 Hz), 3.02 (3H, s), 3.45 (1H, dd, $J = 10.8$, 2.5 Hz), 3.54 (1H, dd, $J = 10.8$, 2.8 Hz), 3.79 (3H, s), 4.32 (1H, m), 4.09 (1H, s), 5.40 (1H, m), 6.44 (1H, dd, $J = 8.7$, 5.5 Hz), 6.86 (2H, m), 7.24−7.35 (8H, m), 7.37−7.4 (4H, m), 7.54 (1H, d, $J = 1.1$ Hz), 9.36 (1H, s); ^{13}C NMR ($CDCl_3$) δ 11.84 (C5-Me), 38.47 (C2′), 38.66 (MeS), 55.31 (O*C*H$_3$), 63.03 (C5′), 79.91 (C3′), 83.77 (C4′), 84.29 (C1′), 87.64 (*C*Ar$_3$), 111.89 (C5), 113.44 (*o*-C × 2 of MeOAr), 127.49 (2C of Ph), 128.16 (4C of Ph), 128.29 (2C of Ph), 128.34 (2C of Ph), 130.38 (2C of Ph), 134.45 (p-C of MeOAr), 135.04 (C4), 143.52 (*m*-C × 2 of MeOAr), 150.53 (C6), 158.96 (*C*-OMe), 163.78 (C2).

(1*R*,9*R*,10*R*)-10-[[(4-Methoxyphenyl)diphenyl]-methoxymethyl]-4-methyl-8,11-dioxa-2,6-diazatricyclo-[7.2.1.0^{2,7}]dodeca-3,6-dien-5-one. To a solution of methanesulfonic acid (2*R*,3*S*,5*R*)-2-[bis(4-methoxyphenyl)phenylmethoxymethyl]-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-3-yl ester (1.58 g, 2.67 mmol) in EtOH (267 mL) were added 1 N aqueous NaOH (2.67 mL) and water (19.2 mL) at room temperature, and the mixture was refluxed for 2 h. After removal of the solvent, the residue was purified by flash chromatography ($CHCl_3$−MeOH = 10:1) to give (1*R*,9*R*,10*R*)-10-[[(4-methoxyphenyl)diphenyl]methoxymethyl]-4-methyl-8,11-dioxa-2,6-diazatricyclo[7.2.1.0^{2,7}]dodeca-3,6-dien-5-one (1.19 g, 91%) as a colorless foam: $[\alpha]^{22}_D = +4°$ ($c = 0.45$, $CHCl_3$); IR (neat) 1661, 1634, 1532, 1472, 1136, 1078, 880, 704 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.89 (3H, s), 2.34 (1H, ddd, $J = 12.8$, 3.3, 3 Hz), 2.65 (1H, d, $J = 12.8$ Hz), 3.30 (1H, dd, $J = 10$, 6 Hz), 3.34 (1H, dd, $J = 10$, 7 Hz), 3.77 (3H, s), 4.24 (1H, ddd, $J = 7$, 6, 2 Hz), 5.10 (1H, s), 5.47 (1H, d, $J = 3.3$ Hz), 6.80 (2H, m), 6.93 (1H, s), 7.15−7.3 (10H, m), 7.41 (4H, m); ^{13}C NMR ($CDCl_3$) δ 13.44 (C5-Me), 33.64 (C2′), 55.27 (O*C*H$_3$), 62.28 (C5′), 76.80 (C3′), 84.54 (C4′), 87.00 (*C*Ar$_3$), 87.53 (C1′), 113.22 (*o*-C × 2 of MeOAr), 118.31 (C5), 127.04 (2C of Ph), 127.91 (2C of Ph), 127.93 (2C of Ph), 128.25 (2C of Ph), 128.29 (2C of Ph), 130.38 (2C of Ph), 134.84 (*p*-C of MeOAr), 135.19 (C4), 143.84 (*m*-C of MeOAr), 143.97 (*m*-C of MeOAr), 153.31 (C6), 158.68 (*C*-OMe), 171.70 (C2).

(2*R*,4*R*,5*R*)-1-[5-[Bis(4-methoxyphenyl)phenylmethoxymethyl]-4-hydroxytetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (8). To a solution of (1*R*,9*R*,10*R*)-10-[[(4-methoxyphenyl)diphenyl]methoxymethyl]-4-methyl-8,11-dioxa-2,6-diazatricyclo[7.2.1.0^{2,7}]dodeca-3,6-dien-5-one (1.19 g, 2.40 mmol) in EtOH (240 mL) were added 1 N aqueous NaOH (5.4 mL) and water (40 mL) at room temperature, and the mixture was refluxed for 3 h. After removal of the solvent, the residue was purified by flash chromatography (ethyl acetate) to give (2*R*,4*R*,5*R*)-5-[[bis(4-methoxyphenyl)phenylmethoxy-

methyl]-4-hydroxytetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione **8** (1.25 g, 100%) as a colorless foam: $[\alpha]^{22}_D = +18°$ ($c = 0.35$, $CHCl_3$); IR (neat) 3391, 3026, 1698, 1509, 1271, 1252, 1069, 756 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.77 (3H, s), 2.20 (1H, dd, $J = 14.5$, 2 Hz), 2.56 (1H, ddd, $J = 14.5$, 8, 5 Hz), 3.50 (1H, dd, $J = 10$, 5.4 Hz), 3.64 (1H, dd, $J = 10$, 5.3 Hz), 3.80 (3H, s), 4.05 (1H, ddd, $J = 5.4$, 5.3, 3 Hz), 4.46 (1H, ddd, $J = 5$, 3, 3 Hz), 6.19 (1H, dd, $J = 8$, 2 Hz), 6.86 (2H, m), 7.22−7.36 (8H, m), 7.45−7.5 (4H, m), 7.65 (1H, d, $J = 1.2$ Hz), 9.21 (1H, br s); 400 MHz ^{13}C NMR ($CDCl_3$) δ: 12.53 (C5-Me), 40.81 (C2′), 55.27 (O*C*H$_3$), 61.99 (C5′), 70.96 (C3′), 82.84 (C4′), 85.22 (C1′), 87.24 (*C*Ar$_3$), 110.11 (C5), 113.37 (*o*-C × 2 of MeOAr), 127.24 (1C of Ph), 127.26 (1C of Ph), 128.09 (2C of Ph), 128.10 (2C of Ph), 128.21 (2C of Ph), 128.25 (2C of Ph), 130.29 (2C of Ph), 134.85 (*p*-C of MeOAr), 137.22 (C4), 143.78 (*m*-C of MeOAr), 143.86 (*m*-C of MeOAr), 150.75 (C6), 158.81 (*C*-OMe), 164.06 (C2).

(2*R*,4*R*,5*R*)-1-[5-[Bis(4-methoxyphenyl)phenylmethoxymethyl]-4-(*tert*-butyldiphenylsilanyloxy)tetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione. To a solution of **8** (1.06 g, 2.06 mmol) in DMF (15.4 mL) were added imidazole (1.83 g, 26.9 mmol) and TBDPSCl (2.31 mL, 8.88 mmol) at room temperature, and the mixture was gently refluxed for 1.5 h. After the reaction was quenched with water, the mixture was extracted with Et_2O and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography (hexane/ethyl acetate = 2:1) to give (2*R*,4*R*,5*R*)-1-[5-[bis(4-methoxyphenyl)phenylmethoxymethyl]-4-(*tert*-butyldiphenylsilanyloxy)tetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (1.46 g, 94%) as a colorless foam: $[\alpha]^{22}_D = +36°$ ($c = 0.52$, $CHCl_3$); IR (neat) 2932, 1686, 1510, 1472, 1269, 1252, 1115, 1071, 741, 704 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 0.89 (9H, s), 1.84 (3H, d, $J = 1$ Hz), 2.06 (1H, dd, $J = 15$, 1.8 Hz), 2.38 (1H, ddd, $J = 15$, 7.7, 5.5 Hz), 3.04 (1H, dd, $J = 10.7$, 2 Hz), 3.73 (1H, dd, $J = 10.7$, 9 Hz), 3.79 (3H, s), 4.06 (1H, ddd, $J = 9$, 3, 2 Hz), 4.18 (1H, dd, $J = 5$, 3 Hz), 6.17 (1H, dd, $J = 7.6$, 1.8 Hz), 6.76 (2H, m), 7.15−7.5 (22H, m), 7.17 (1H, d, $J = 1$ Hz), 9.05 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 12.56 (C5-Me), 19.06 (*C*Me$_3$), 26.85 (C*Me*$_3$), 41.94 (C2′), 55.23 (O*C*H$_3$), 64.08 (C5′), 72.49 (C3′), 84.91 (C4′), 85.77 (C1′), 86.69 (*C*Ar$_3$), 109.67 (C5), 113.14 (*o*-C × 2 of MeOAr), 126.88 (1C of Ph), 126.94 (1C of Ph), 127.67 (2C of Ph), 127.89 (2C of Ph), 127.91 (2C of Ph), 127.94 (2C of Ph), 128.31 (2C of Ph), 128.54 (2C of Ph), 129.96 (1C of Ph), 130.30 (1C of Ph), 130.47 (2C of Ph), 131.99 (1C of Ph), 132.40 (1C of Ph), 135.29 (*p*-C of MeOAr), 135.63 (2C of Ph), 135.89 (2C of Ph), 136.51 (C4), 143.96 (*m*-C of MeOAr), 144.49 (*m*-C of MeOAr), 150.35 (C6), 158.57 (*C*-OMe), 164.13 (C2).

(2*R*,4*R*,5*R*)-1-[4-(*tert*-Butyldiphenylsilanyloxy)-5-hydroxymethyltetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione. To a solution of (2*R*,4*R*,5*R*)-1-[5-[bis(4-methoxyphenyl)phenylmethoxymethyl]-4-(*tert*-butyldiphenylsilanyloxy)tetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (1.50 g, 1.92 mmol) in MeOH (100 mL) was added Amberlyst 15-H (1.03 g) at room temperature, and the mixture was stirred for 37 h. After filtration, the solvent was evaporated in vacuo. The residue was purified by flash chromatography (hexane/ethyl acetate = 1:2−1:4) to give (2*R*,4*R*,5*R*)-1-[4-(*tert*-butyldiphenylsilanyloxy)-5-hydroxymethyltetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (923 mg, 100%) as a colorless foam: $[\alpha]^{20}_D = -21°$ ($c = 0.48$, $CHCl_3$); IR (neat) 2932, 1686, 1472, 1428, 1271, 1113, 1074, 702, 611 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.08 (9H, s), 1.93 (3H, s), 2.01 (1H, ddd, $J = 14.6$, 3.8, 2 Hz), 2.41 (1H, ddd, $J = 14.6$, 7.4, 6.6 Hz), 3.77 (1H, dd, $J = 12$, 3 Hz), 3.88 (1H, m), 4.01 (1H, dd, $J = 12$, 5.4 Hz), 4.54 (1H, m), 6.09 (1H, dd, $J = 7.4$, 3.8 Hz), 7.35−7.5 (6H, m), 7.56 (2H, m), 7.64 (2H, m), 7.81 (1H, s), 9.08 (1H, br); ^{13}C NMR ($CDCl_3$) δ: 12.63 (C5-Me), 19.16 (*C*Me$_3$), 26.99 (C*Me*$_3$), 41.67 (C2′), 62.02 (C5′), 72.45 (C3′), 83.82 (C4′), 83.85 (C1′), 110.65 (C5), 128.07 (2C of Ph), 128.17 (2C of Ph), 130.48 (1C of Ph), 130.49 (1C of Ph), 132.07 (1C of Ph), 132.35 (1C of Ph), 135.75 (4C of Ph), 136.21 (C4), 150.43 (C6), 164.02 (C2).

(2*S*,3*R*,5*R*)-3-(*tert*-Butyldiphenylsilanyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic Acid. To a solution of (2*R*,4*R*,5*R*)-1-[4-(*tert*-Butyldiphenylsilanyloxy)-5-hydroxymethyltetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione (864 mg, 1.80 mmol) in CH_2Cl_2 (8.5 mL) were added 2,2,6,6-tetramethyl-1-piperidinyl-oxy, free radical (TEMPO) (62 mg, 0.39 mmol), and iodobenzene diacetate (BAIB) (1.28 g, 3.97 mmol) at room temperature. After the mixture was stirred for 2 h, a mixture of MeCN−water (1:1) (0.1 mL) was added to the reaction mixture, and the mixture was stirred for 24 h. After removal of the solvent, the residue was purified by flash chromatography ($CHCl_3$−MeOH = 10:1) to give (2*S*,3*R*,5*R*)-3-(*tert*-butyldiphenylsilanyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid (890 mg, 100%) as a colorless foam: $[\alpha]^{21}_D = -3°$ ($c = 0.25$, $CHCl_3$−MeOH = 40:1); IR (neat) 2932, 1686, 1474, 1428, 1277, 1113, 1076, 704, 612 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$−CD_3OD = 40:1) δ 0.96 (9H, s), 1.90 (3H, s), 2.07 (1H, ddd, $J = 14.5$, 2, 2 Hz), 2.17 (1H, ddd, $J = 14.5$, 6.5, 5.2 Hz), 4.59 (1H, d, $J = 4.4$ Hz), 4.75 (1H, m), 6.00 (1H, dd, $J = 6.5$, 2 Hz), 7.3−7.45 (6H, m), 7.49 (2H, m), 7.62 (2H, m), 8.38 (1H, s); ^{13}C NMR ($CDCl_3$−CD_3OD = 40:1) δ 16.45 (C5-Me), 22.88 (*C*Me$_3$), 30.62 (C*Me*$_3$), 44.18 (C2′), 76.74 (C3′), 87.87 (C4′), 90.79 (C1′), 113.41 (C5), 131.68 (2C of Ph), 131.75 (2C of Ph), 133.98(1C of Ph), 134.11 (1C of Ph), 135.50 (1C of Ph), 136.55 (1C of Ph), 139.47 (2C of Ph), 139.89 (2C of Ph), 141.67 (C4), 154.13 (C6), 168.70 (C2), 174.78 (C5′).

(2*S*,3*R*,5*R*)-3-(*tert*-Butyldiphenylsilanyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic Acid Methyl Ester. To a solution of (2*S*,3*R*,5*R*)-3-(*tert*-butyldiphenylsilanyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid (74 mg, 0.15 mmol) in benzene (2 mL)−MeOH (1.6 mL) was added (trimethylsilyl)diazomethane (2 M in hexane, 0.17 mL, 3.4 mmol) at room temperature, and the mixture was stirred for 10 h. After removal of the solvent, the residue was purified by flash chromatography (hexane/ethyl acetate = 1:1) to give (2*S*,3*R*,5*R*)-3-(*tert*-butyldiphenylsilanyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid methyl ester (70 mg, 92%) as a colorless foam: $[\alpha]^{22}_D = +4°$ ($c = 0.35$, $CHCl_3$); IR (neat) 2953, 1759, 1694, 1472, 1429, 1277, 1219, 1113, 1051, 941, 702 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 0.99 (9H, s), 1.96 (3H, d, $J = 1.2$ Hz), 2.12 (1H, ddd, $J = 14.2$, 3.9, 3.6 Hz), 2.20 (1H, ddd, $J = 14.2$, 6.5, 5.3 Hz), 4.59 (1H, d, $J = 5$ Hz), 4.75 (1H, ddd, $J = 5.3$, 5, 3.6 Hz), 6.04 (1H, dd, $J = 6.5$, 3.9 Hz), 7.35−7.5 (6H, m), 7.53 (2H, m), 7.59 (2H, m), 8.30 (1H, d, $J = 1.2$ Hz), 8.87 (1H, br); ^{13}C NMR ($CDCl_3$) δ 12.77 (C5-Me), 19.00 (*C*Me$_3$), 26.78 (C*Me*$_3$), 39.87 (C2′), 52.28 (ester Me), 72.81 (C3′), 83.10 (C4′), 86.13 (C1′), 110.08 (C5), 127.92 (2C of Ph), 128.02 (2C of Ph), 130.25 (1C of Ph), 130.43 (1C of Ph), 131.82 (1C of Ph), 132.34 (1C of Ph), 135.68 (2C of Ph), 135.80 (2C of Ph), 137.01 (C4), 150.26 (C6), 164.02 (C2), 169.28 (C5′).

(2*S*,3*R*5*R*)-3-Hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic Acid Methyl Ester (9). To (2*S*,3*R*,5*R*)-3-(*tert*-butyldiphenylsilanyloxy)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid methyl ester (800 mg, 1.57 mmol) in THF (17 mL) was added TBAF (1 M in THF, 1.6 mL) at 0 °C, and the mixture was stirred at the same temperature for 1.5 h. After the reaction was quenched with water, the mixture was extracted with CH_2Cl_2 and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography (ethyl acetate/MeOH = 50:1) to give (2*S*,3*R*,5*R*)-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid methyl ester **9** (424 mg, 100%) as a colorless foam: $[\alpha]^{23}_D = +18°$ ($c = 0.45$, $CHCl_3$−MeOH = 10:1); IR (neat) 3381, 1746, 1686, 1476, 1279, 1221, 1100 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3$−CD_3OD = 10:1) δ 1.84 (3H, s), 2.14 (1H, dm, $J = 14.5$ Hz), 2.49 (1H, ddd, $J = 14.5$, 7, 5.5 Hz), 3.77 (3H, s), 4.53 (1H, d, $J = 4.2$ Hz), 4.60 (1H, m), 6.08 (1H, dd, $J = 7.4$, 2.6 Hz), 8.03 (1H, s); ^{13}C NMR ($CDCl_3$−CD_3OD = 10:1) δ 16.16 (C5-Me), 44.50 (C2′), 56.04 (ester Me), 74.44 (C3′), 87.70 (C4′), 90.34 (C1′), 113.66 (C5), 141.87 (C4), 154.89 (C6), 169.09 (C2), 173.28 (C5′).

(2*R*,3*R*,5*R*)-2-Deuterio-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yltetrahydrofuran-2-carbox-

ylic Acid Methyl Ester (11a) and (2*S*,3*R*,5*R*)-2-Deuterio-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic Acid Methyl Ester (10a). The ester **9** (29 mg) was coevaporated with benzene, dried in vacuo, dissolved in THF (4.3 mL)−HMPA (0.52 mL), and dried under molecular sieves 4A (18 pieces) with stirring for 1 h. To the solution of **9** (28.0 mg, 0.104 mmol) was added lithium diisopropylamide mono(tetrahydrofuran) (LDA) (Aldrich, 1.5 M in cyclohexane, 0.40 mL, 0.60 mmol) at −78 °C, and the mixture was stirred at −78 °C for 5 min, −78 °C → room temperature for 10 min, and room temperature for 10 min. *tert*-Butyllithium (1.7 M in pentane, 0.30 mL, 0.51 mmol) was added to the solution at −78 °C, and the mixture was stirred at −78 °C for 1 h. To the solution were added CD_3OD (0.38 mL) and CD_3CO_2D (0.12 mL) at −78 °C, and the mixture was stirred at −78 °C → room temperature for 30 min. After removal of the solvent, the residue was purified by flash chromatography (hexane/ethyl acetate = 1:2 to ethyl acetate) to give (2*R*,3*R*,5*R*)-2-deuterio-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid methyl ester **11a** (15 mg, 53%) and (2*S*,3*R*,5*R*)-2-deuterio-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-tetrahydrofuran-2-carboxylic acid methyl ester **10a** (6 mg, 21%), both as colorless foams.

(2*R*,3*R*,5*R*)-2-Deuterio-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid methyl ester **11a**: $[\alpha]^{21}_D = -21°$ ($c = 0.25$, $CHCl_3$); IR (neat) 3401, 2928, 1744, 1694, 1472, 1277, 1103, 756 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$−CD_3OD = 8:1) δ 1.86 (3H, d, J = 1.1 Hz), 2.17 (1H, ddd, J = 14.7, 3, 2 Hz), 2.68 (1H, ddd, J = 14.7, 7.4, 5.5 Hz), 3.80 (3H, s), 4.28 (1H, dd, J = 5.5, 2 Hz), 6.15 (1H, dd, J = 7.4, 3 Hz), 8.00 (1H, s); ^{13}C NMR ($CDCl_3$−CD_3OD = 8:1) δ 16.23 (C5-Me), 42.99 (C2′), 56.43 (ester Me), 76.92 (C3′), 91.24 (C1′), 114.49 (C5), 141.56 (C4), 154.80 (C6), 168.50 (C2), 174.90 (C5′).

(2*S*,3*R*,5*R*)-2-Deuterio-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid methyl ester **10a**: IR (neat) 1281, 1103, 758 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$−CD_3OD = 5:1) δ 1.81 (3H, s), 2.11 (1H, dm, J = 14.5 Hz), 2.47 (1H, ddd, J = 14.5, 6, 6 Hz), 3.74 (3H, s), 4.55 (1H, d, J = 6 Hz), 6.06 (1H, dm, J = 6 Hz), 8.03 (1H, s); ^{13}C NMR ($CDCl_3$−CD_3OD = 5:1) δ 16.20 (C5-Me), 44.47 (C2′), 56.14 (ester Me), 74.39 (C3′), 90.39 (C1′), 113.73 (C5), 141.75 (C4), 154.75 (C6), 169.00 (C2), 173.21 (C5′).

(2*R*,3*R*,5*R*)-3-Hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-2-(phenylselenenyl)tetrahydrofuran-2-carboxylic Acid Methyl Ester (10b). The ester **9** (7.3 mg) was coevaporated with benzene, dried in vacuo, dissolved in THF (1.1 mL)−HMPA (0.14 mL), and dried under molecular sieves 4A (three pieces) with stirring for 1 h. To the solution of **9** (6.7 mg, 0.025 mmol) was added lithium diisopropylamide mono(tetrahydrofuran) (LDA) (Aldrich, 1.5 M in cyclohexane, 0.093 mL, 0.14 mmol) at −78 °C, and the mixture was stirred at −78 °C for 5 min, −78 °C → room temperature for 5 min, and room temperature for 11 min. *tert*-Butyllithium (1.7 M in pentane, 0.075 mL, 0.12 mmol) was added to the solution at −78 °C, and the mixture was stirred at −78 °C for 1 h. To the solution was added phenylselenenyl chloride (55 mg, 0.29 mmol) in THF (0.15 mL) at −78 °C, and the mixture was stirred at the same temperature for 1 h. After the reaction was quenched with MeOH (0.09 mL)−AcOH (0.03 mL), the solvent was evaporated in vacuo. The residue was purified by flash chromatography (hexane/ethyl acetate = 1:1) to give (2*R*,3*R*,5*R*)-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-2-(phenylselenenyl)tetrahydrofuran-2-carboxylic acid methyl ester **10b** (6 mg, 56%) together with recovery of **9** (1 mg, 15%) and (2*S*,3*R*,5*R*)-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)- 2-(phenylselenenyl)tetrahydrofuran-2-carboxylic acid methyl ester **11b** (0.6 mg, 6%), all as colorless foams.

(2*R*,3*R*,5*R*)-3-Hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-2-(phenylselenenyl)tetrahydrofuran-2-carboxylic acid methyl ester **10b**: $[\alpha]^{22}_D = -153°$ ($c = 0.27$, $CHCl_3$); IR (neat) 3063, 1686, 1476, 1279, 1090, 742, 692 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.87 (3H, d, J = 1.2 Hz), 2.19 (1H, dd, J = 15, 3.2 Hz), 3.08 (1H, ddd, J = 15, 8.5, 6 Hz), 3.71 (1H, s), 3.75 (1H, br s), 4.70 (1H, dd, J = 6, 3.4 Hz), 6.50 (1H, dd, J = 8.5, 3.2 Hz), 7.35 (2H, m), 7.42 (1H, m), 7.56 (1H, d, J = 1.2 Hz), 7.62 (2H, m), 8.90 (1H, br s); ^{13}C NMR ($CDCl_3$) δ: 12.61 (C5-Me), 38.02 (C2′), 52.94 (ester Me), 75.92 (C3′), 85.60 (C4′), 93.20 (C1′), 111.87 (C5), 125.59 (*p*-C of Ph), 129.35 (2C of Ph), 129.86 (C-Se), 137.04 (C4), 137.25 (2C of Ph), 150.44 (C6), 163.64 (C2), 168.02 (C5′).

1-(2*R*,4*R*,5*S*)-4-Hydroxy-5-hydroxymethyl-5-phenylselenenyltetrahydrofuran-2-yl)-5-methyl-1*H*-pyrimidine-2,4-dione (12b). To a solution of (2*R*,3*R*,5*R*)-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)-2-(phenylselenenyl)tetrahydrofuran-2-carboxylic acid methyl ester **10b** (24 mg, 0.056 mmol) in THF (0.75 mL)−EtOH (1.0 mL) was added $LiBH_4$ (3 mg, 0.14 mmol) at room temperature, and the mixture was stirred for 1 h. After the mixture was neutralized with AcOH (0.015 mL) for 30 min, the solvent was evaporated in vacuo. The residue was purified by flash chromatography (hexane/ethyl acetate = 1:2) to give 1-(2*R*,4*R*,5*S*)-4-hydroxy-5-hydroxymethyl-5-phenylselenenyltetrahydrofuran-2-yl)-5-methyl-1*H*-pyrimidine-2,4-dione **12b** (14 mg, 63%) as a colorless foam: $[\alpha]^{22}_D = -158°$ ($c = 0.08$, $CHCl_3$); IR (neat) 3386, 2926, 1686, 1474, 1279, 1057, 741, 693 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.89 (3H, s), 2.16 (1H, dd, J = 15, 3 Hz), 2.93 (1H, br s, OH), 3.10 (1H, ddd, J = 15, 8.5, 7 Hz), 3.88 (2H, m), 4.08 (1H, br s, OH), 4.54 (1H, s), 6.55 (1H, dd, J = 8.5, 3 Hz), 7.35 (2H, dd, J = 7, 7 Hz), 7.40 (1H, dd, J = 7, 7 Hz), 7.59 (1H, s), 7.62 (2H, d, J = 7 Hz), 8.31 (1H, br s); ^{13}C NMR ($CDCl_3$) δ: 12.55 (C5-Me), 39.37 (C2′), 63.45 (C5′), 77.02 (C3′), 85.97 (C1′), 98.23 (C4′), 111.88 (C5), 125.30 (*p*-C of Ph), 129.36 (C−Se), 129.40 (2C of Ph), 137.13 (2C of Ph), 137.44 (C4), 150.27 (C6), 163.34 (C2).

1-(4a*S*,6*R*,7a*R*)-2,2-Dimethyl-4a-phenylselenenyltetrahydrofuro[3,2-*d*][1,3]dioxin-6-yl)-5-methyl-1*H*-pyrimidine-2,4-dione (13b). To a solution of **12b** (3 mg, 0.0076 mmol) in 2,2-dimethoxypropane (0.24 mL)−DMF (0.06 mL) was added pyridinium *p*-toluenesulfo-nate (<1 mg) at room temperature, and the mixture was stirred for 30 h. After removal of the solvent, the residue was purified by preparative thin-layer chromatography (ethyl acetate) to give 1-(4a*S*,6*R*,7a*R*)-2,2-dimethyl-4a-phenylselenenyltetrahydrofuro[3,2-*d*]-[1,3]dioxin-6-yl)-5-methyl-1*H*-pyrimidine-2,4-dione **13b** (3.3 mg, 100%) as a colorless foam: $[\alpha]^{22}_D = -78°$ ($c = 0.14$, $CHCl_3$); IR (neat) 2924, 1692, 1468, 1283, 1202, 1117 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.32 (3H, s), 1.36 (3H, s), 1.92 (3H, d, J = 1.2 Hz), 2.04 (1H, dd, J = 15, 2.2 Hz), 3.08 (1H, ddd, J = 15, 8.5, 5 Hz), 4.08 (1H, d, J = 13.4 Hz), 4.38 (1H, d, J = 13.4 Hz), 4.52 (1H, d, J = 5 Hz), 6.40 (1H, dd, J = 8.5, 2.2 Hz), 7.35 (2H, m), 7.42 (1H, m), 7.67 (2H, m), 7.94 (1H, d, J = 1.2 Hz), 8.13 (1H, br); ^{13}C NMR ($CDCl_3$) δ: 12.59 (C5-Me), 18.68 and 28.64 (Me_2C), 39.39 (C2′), 65.94 (C5′), 73.96 (C3′), 84.80 (C1′), 88.05 (Me_2C), 98.55 (C4′), 110.48 (C5), 125.05 (*p*-C of Ph), 129.40 (2C of Ph), 129.56 (C-Se), 137.17 (C4), 137.42 (2C of Ph), 150.20 (C6), 163.45 (C2).

(2*S*,3*R*,5*R*)-3-Hydroxy-2-methyl-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimi-din-1-yl)tetrahydrofuran-2-carboxylic Acid Methyl Ester (10c). The ester **9** (34 mg) was coevaporated with benzene, dried in vacuo, dissolved in THF (5.0 mL)−HMPA (0.61 mL), and dried under molecular sieves 4A (15 pieces) with stirring for 1 h. To the solution of **9** (33 mg, 0.12 mmol) was added lithium diisopropylamide mono-(tetrahydrofuran) (LDA) (Aldrich, 1.5 M in cyclohexane, 0.45 mL, 0.68 mmol) at −78 °C, and the mixture was stirred at −78 °C for 5 min, −78 °C → room temperature for 10 min, and room temperature for 10 min. *tert*-Butyllithium (1.7 M in pentane, 0.34 mL, 0.58 mmol) was added to the solution at −78 °C, and the mixture was stirred at −78 °C for 1 h. To the solution were added iodomethane (0.12 mL, 1.93 mmol) at −78 °C and the mixture was stirred at −78 °C for 20 min and at −78 °C → −20 °C for 1 h. After the reaction was quenched with MeOH (0.42 mL)−AcOH (0.14 mL), the solvent was evaporated in vacuo. The residue was purified by flash chromatography (ethyl acetate) to give (2*S*,3*R*,5*R*)-3-hydroxy-2-methyl-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid methyl ester **10c** (15 mg,

44%) as a colorless foam: $[\alpha]^{22}_D = -98°$ ($c = 0.33$, $CHCl_3$); IR (neat) 3399, 1740, 1690, 1476, 1281, 1107 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.48 (3H, s), 1.81 (3H, s), 2.51 (1H, dm, J = 15 Hz), 2.72 (1H, ddd, J = 15, 7, 6 Hz), 3.86 (3H, s), 4.00 (1H, br s), 4.39 (1H, d, J = 4.4 Hz), 6.19 (1H, d, J = 7 Hz), 8.03 (1H, s), 9.86 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 12.49 (C5-Me), 22.67 (C4′-Me), 39.30 (C2′), 52.52 (ester Me), 75.65 (C3′), 85.74 (C4′), 90.56 (C1′), 109.94 (C5), 137.66 (C4), 150.66 (C6), 164.60 (C2), 171.90 (C5′).

1-(2*R*,4*R*,5*R*)-4-Hydroxy-5-hydroxymethyl-5-methyltetrahydrofuran-2-yl)-5-methyl-1*H*-pyrimidine-2,4-dione (12c). To a solution of **10c** (11.5 mg, 0.040 mmol) in THF (1.1 mL) was added $LiBH_4$ (2 mg, 0.092 mmol) at room temperature, and the mixture was stirred for 1 h. After the mixture was stirred with EtOH (0.33 mL) for 15 min and neutralized with AcOH (0.013 mL) for 30 min, the solvent was evaporated in vacuo. The residue was purified by flash chromatography (ethyl acetate) to give 1-(2*R*,4*R*,5*R*)-4-hydroxy-5-hydroxymethyl-5-methyltetrahydrofuran-2-yl)-5-methyl-1*H*-pyrimidine-2,4-dione **12c** (7.5 mg, 73%) as a colorless foam: $[\alpha]^{22}_D = -14°$ ($c = 0.10$, $CHCl_3$−MeOH = 20:1); IR (neat) 3407, 1690, 1476, 1279, 1055 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$−CD_3OD = 20:1) δ 1.09 (3H, s), 1.82 (3H, d, J = 1.1 Hz), 1.97 (1H, ddd, J = 14.7, 3.9, 2.6 Hz), 2.70 (1H, ddd, J = 14.7, 7.8, 6 Hz), 3.69 (1H, d, J = 11.6 Hz), 3.76 (1H, d, J = 11.6 Hz), 4.12 (1H, dd, J = 6, 2.6 Hz), 6.09 (1H, dd, J = 7.8, 3.9 Hz), 7.84 (1H, d, J = 1.1 Hz); ^{13}C NMR ($CDCl_3$) δ: 16.24 (C5-Me), 25.57 (C4′-Me), 44.50 (C2′), 69.45 (C5′), 79.36 (C3′), 87.67 (C4′), 90.82 (C1′), 114.49 (C5), 141.46 (C4), 154.87 (C6), 168.67 (C2).

5-Methyl-1-[(4a*S*,6*R*,7a*R*)-2,2,4a-trimethyltetrahydrofuro[3,2-*d*][1,3]dioxin-6-yl]-1*H*-pyrimidine-2,4-dione (13c). To a solution of **12c** (7 mg, 0.027 mmol) in 2,2-dimethoxypropane (0.28 mL)−DMF (0.08 mL) was added pyridinium *p*-toluenesulfonate (<1 mg) at room temperature, and the mixture was stirred for 50 h. After removal of the solvent, the residue was purified by preparative thin-layer chromatography (ethyl acetate) to give 5-methyl-1-[(4a*S*,6*R*,7a*R*)-2,2,4a-trimethyltetrahydrofuro[3,2-*d*][1,3]dioxin-6-yl]-1*H*-pyrimidine-2,4-dione **13c** (8 mg, 100%) as a colorless foam: $[\alpha]^{22}_D = -3°$ (c = 0.15, $CHCl_3$); IR (neat) 3189, 1694, 1472, 1379, 1283, 1094, 1028 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.12 (3H, s), 1.40 (3H, s), 1.46 (3H, s), 1.95 (3H, s), 2.07 (1H, d, J = 15.4 Hz), 2.79 (1H, ddd, J = 15.4, 7.8, 4.6 Hz), 3.88 (1H, d, J = 13.3 Hz), 4.01 (1H, d, J = 13.3 Hz), 4.19 (1H, d, J = 4.6 Hz), 6.19 (1H, d, J = 7.8 Hz), 8.06 (1H, s), 8.53 (1H, br); ^{13}C NMR ($CDCl_3$) δ: 12.61 (C5-Me), 18.82 and 21.24 (Me_2C), 28.53 (C4′-Me), 39.66 (C2′), 65.08 (C5′), 73.17 (C3′), 79.60 (C4′), 83.92 (C1′), 98.01 (Me_2C), 109.55 (C5), 137.44 (C4), 150.46 (C6), 163.91 (C2).

(2*S*,3*R*,5*R*)-3-Hydroxy-2-(2-propenyl)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic Acid Methyl Ester (10d). The ester **9** (9 mg) was coevaporated with benzene, dried in vacuo, dissolved in THF (1.3 mL)−HMPA (0.17 mL), and dried under molecular sieves 4A (5 pieces) with stirring for 1 h. To the solution of **9** (8.5 mg, 0.031 mmol) was added lithium diisopropylamide mono(tetrahydrofuran) (LDA) (Aldrich, 1.5 M in cyclohexane, 0.12 mL, 0.17 mmol) at −78 °C, and the mixture was stirred at −78 °C for 5 min, −78 °C → room temperature for 5 min, and room temperature for 10 min. *tert*-Butyllithium (1.7 M in pentane, 0.09 mL, 0.15 mmol) was added to the solution at −78 °C, and the mixture was stirred at −78 °C for 1 h. To the solution was added allyl bromide (0.042 mL, 0.49 mmol) at −78 °C, and the mixture was stirred at −78 °C for 30 min and at −78 °C → −15 °C for 1.5 h. After the reaction was quenched with MeOH (0.11 mL)−AcOH (0.036 mL), the solvent was evaporated in vacuo. The residue was purified by flash chromatography (ethyl acetate) to give (2*S*,3*R*,5*R*)-3-hydroxy-2-(2-propenyl)-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid methyl ester **10d** (5 mg, 52%) as a colorless foam: $[\alpha]^{24}_D = -21°$ ($c = 0.20$, $CHCl_3$); IR (neat) 3370, 2930, 1752, 1696, 1474, 1281, 1101 cm^{-1}; 200 MHz ^1H NMR ($CDCl_3$) δ 1.88 (3H, d, J = 0.9 Hz), 2.32 (1H, m), 2.32 (1H, m), 2.34 (1H, m), 2.67 (2H, m), 3.20 (1H, br s), 3.85 (3H, s), 4.44 (1H, m), 5.16 (2H, m), 5.75 (1H, m), 6.23 (1H, dd, J = 7.6, 2.8 Hz), 7.92 (1H, s), 8.68 (1H, br s); ^{13}C NMR ($CDCl_3$) δ: 12.48 (C5-Me), 39.89 (C2′), 40.60 (allyl), 52.53 (ester Me), 75.00 (C3′), 87.23 (C4′), 94.76 (C1′), 109.14 (C5), 119.90 and 130.97 (vinyl of allyl), 138.19 (C4), 150.92 (C6), 164.70 (C2), 170.57 (C5′).

1-(2*R*,4*R*,5*R*)-4-Hydroxy-5-hydroxymethyl-5-(2-propenyl)tetrahydrofuran-2-yl)-5-methyl-1*H*-pyrimidine-2,4-dione (12d). To a solution of **10d** (15 mg, 0.048 mmol) in THF (1 mL) was added $LiBH_4$ (10 mg, 0.46 mmol) at room temperature, and the mixture was stirred for 18 h. After the mixture was stirred with EtOH (1 mL) for 30 min and neutralized with AcOH (0.06 mL) for 30 min, the solvent was evaporated in vacuo. The residue was purified by flash chromatography (ethyl acetate) to give 1-[(2*R*,4*R*,5*R*)-4-hydroxy-5-hydroxymethyl-5-(2-propenyl)tetrahydrofuran-2-yl]-5-methyl-1*H*-pyrimidine-2,4-dione **12d** (6.9 mg, 51%) as a colorless foam: $[\alpha]^{22}_D = -24°$ ($c = 0.10$, $CHCl_3$); IR (neat) 3403, 1686, 1474, 1277, 1076 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.91 (3H, s), 2.27 (3H, m), 2.78 (1H, ddd, J = 14.7, 7.7, 7 Hz), 3.03 (1H, br, s, OH), 3.89 (2H, s), 4.37 (1H, m), 5.17 (2H, m), 5.81 (1H, m), 6.04 (1H, dd, J = 7, 6 Hz), 7.71 (1H, s), 8.77 (1H, br s); ^{13}C NMR ($CDCl_3$) δ 12.54 (C5-Me), 39.88 (C2′), 40.29 (allyl), 65.07 (C5′), 75.28 (C3′), 85.44 (C4′), 88.07 (C1′), 111.08 (C5), 119.70 and 131.96 (vinyl of allyl), 137.82 (C4), 150.53 (C6), 163.77 (C2).

5-Methyl-1-[(4a*R*,6*R*,7a*R*)-2,2-dimethyl-4a-(2-propenyl)-tetrahydrofuro[3,2-*d*] [1,3]dioxin-6-yl]-1*H*-pyrimidine-2,4-dione (13d). To a solution of **12d** (5 mg, 0.018 mmol) in 2,2-dimethoxypropane (0.28 mL)−DMF (0.06 mL) was added pyridinium *p*-toluenesulfonate (<1 mg) at room temperature, and the mixture was stirred for 30 h. After removal of the solvent, the residue was purified by preparative thin-layer chromatography (ethyl acetate) to give 5-methyl-1-[(4a*R*,6*R*,7a*R*)-2,2-dimethyl-4a-(2-propenyl)tetrahydrofuro[3,2-*d*][1,3]-dioxin-6-yl]-1*H*-pyrimidine-2,4-dione **13d** (5 mg, 86%) as a colorless foam: $[\alpha]^{22}_D = -29°$ ($c = 0.15$, $CHCl_3$); IR (neat) 1686, 1470, 1279, 1202, 1096 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.39 (3H, s), 1.44 (3H, s), 1.95 (3H, s), 2.08 (1H, d, J = 15.4 Hz), 2.15 (1H, dd, J = 14, 7.8 Hz), 2.23 (1H, dd, J = 14, 6.5 Hz), 2.79 (1H, ddd, J = 15.4, 8, 5 Hz), 3.93 (1H, d, J = 14.5 Hz), 3.95 (1H, d, J = 14.5 Hz), 4.25 (1H, d, J = 5 Hz), 5.18 (2H, m), 5.79 (1H, m), 6.22 (1H, d, J = 8 Hz), 8.04 (1H, s), 8.25 (1H, br); ^{13}C NMR ($CDCl_3$) δ 12.60 (C5-Me), 19.41 and 28.12 (Me_2C), 39.74 (C2′), 39.96 (allyl), 63.96 (C5′), 72.22 (C3′), 81.91 (C4′), 84.21 (C1′), 98.05 (Me_2C), 109.66 (C5), 120.08 and 130.97 (vinyl of allyl), 137.31 (C4), 150.38 (C6), 163.75 (C2).

(2*R*,3*R*,5*R*)-3-Benzenesulfonyloxy-2-fluoro-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic Acid Methyl Ester (10e). The ester **9** (9.5 mg) was coevaporated with benzene, dried in vacuo, dissolved in THF (1.4 mL)−HMPA (0.17 mL), and dried under molecular sieves 4A (five pieces) with stirring for 1 h. To the solution of **9** (9 mg, 0.033 mmol) was added lithium diisopropylamide mono(tetrahydrofuran) (LDA) (Aldrich, 1.5 M in cyclohexane, 0.13 mL, 0.19 mmol) at −78 °C, and the mixture was stirred at −78 °C for 5 min, −78 °C → room temperature for 5 min, and room temperature for 10 min. *tert*-Butyllithium (1.7 M in pentane, 0.095 mL, 0.16 mmol) was added to the solution at −78 °C, and the mixture was stirred at −78 °C for 1 h. To the solution was added *N*-fluorobenzenesulfonimide (NFSI) (110 mg, 0.35 mmol) in THF (0.3 mL) at −78 °C, and the mixture was stirred at −78 °C → 30 °C for 1 h and at −30 °C → 0 °C for 15 min. After the reaction was quenched with MeOH (0.12 mL)−AcOH (0.04 mL), the solvent was evaporated in vacuo. The residue was purified by flash chromatography (hexane/ethyl acetate = 1:2) to give (2*R*,3*R*,5*R*)-3-benzenesulfonyloxy-2-fluoro-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid methyl ester **10e** (7 mg, 49%) as a colorless foam: $[\alpha]^{24}_D = -16°$ ($c = 0.4$, $CHCl_3$); IR (neat) 2924, 1771, 1696, 1451, 1377, 1285, 1194, 1115, 743, 586 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.84 (3H, d, J = 1.2 Hz), 2.37 (1H, ddd, J = 16, 2.5, 1 Hz), 2.99 (1H, dddd, J = 16, 7.5, 5.5, 1.4 Hz), 3.78 (3H, s), 5.26 (1H, ddd, J = 5.5, 5.5, 1 Hz), 6.60 (1H, ddd, J = 7.5, 2.5, 2.5 Hz), 7.46 (1H, d, J = 1.2 Hz), 7.60 (2H, m), 7.74 (1H, m), 7.85 (2H, m), 8.90 (1H, br); ^{13}C NMR ($CDCl_3$) δ 12.64 (C5-Me), 35.98 (C2′), 53.75 (ester Me), 79.70 (C3′, d, J = 165 Hz), 86.49 (C1′, d, J = 8 Hz), 111.95

(C5), 113.28 (C4′, d, J = 939 Hz), 127.73 (2C of Ph), 129.69 (2C of Ph), 134.72 (1C of Ph), 134.96 (1C of Ph), 135.45 (C4), 150.04 (C6), 162.25 (C5′, d, J = 129 Hz), 163.30 (C2).

(2*R*,3*R*,5*R*)-2-Fluoro-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimi-din-1-yl)tetrahydrofuran-2-carboxylic Acid Methyl Ester (10f). The ester **9** (13 mg) was coevaporated with benzene, dried in vacuo, dissolved in THF (1.9 mL)−HMPA (0.24 mL), and dried under molecular sieves 4A (eight pieces) with stirring for 1 h. To the solution of **9** (12.5 mg, 0.046 mmol) was added lithium diisopropylamide mono(tetrahydrofuran) (LDA) (Aldrich, 1.5 M in cyclohexane, 0.18 mL, 0.27 mmol) at −78 °C, and the mixture was stirred at −78 °C for 5 min, −78 °C → room temperature for 7 min, and room temperature for 10 min. *tert*-Butyllithium (1.7 M in pentane, 0.13 mL, 0.22 mmol) was added to the solution at −78 °C, and the mixture was stirred at −78 °C for 1 h. To the solution were added *N*-fluorobenzenesulfonimide (NFSI) (156 mg, 0.495 mmol) in THF (0.48 mL) at −78 °C, and the mixture was stirred at −78 °C for 20 min. After the reaction was quenched with MeOH (0.2 mL)−AcOH (0.045 mL), the solvent was evaporated in vacuo. The residue was purified by flash chromatography (hexane/ethyl acetate = 1:2) to give **10e** (3 mg, 15%) and (2*R*,3*R*,5*R*)-2-fluoro-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid methyl ester **10f** (4.6 mg, 30%), both as colorless foams.

(2*R*,3*R*,5*R*)-2-Fluoro-3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2*H*-pyrimidin-1-yl)tetrahydrofuran-2-carboxylic acid methyl ester **10f**: $[\alpha]^{24}_D = -32°$ (c = 0.2, $CHCl_3$); IR (neat) 2926, 1761, 1694, 1472, 1318, 1285, 1115, 756 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$) δ 1.88 (3H, s), 2.39 (1H, dm, J = 15 Hz), 2.87 (1H, ddd, J = 15, 8.5, 6 Hz), 3.94 (3H, s), 4.28 (br s), 4.62 (1H, m), 6.42 (1H, ddd, J = 8.5, 2.5, 2.5 Hz), 7.67 (1H, s), 9.29 (1H, br); ^{13}C NMR ($CDCl_3$) δ: 12.53 (C5-Me), 36.16 (C2′), 53.57 (ester Me), 74.11 (C3′, d, J = 145 Hz), 88.30 (C1′, d, J = 10 Hz), 111.35 (C5), 114.99 (C4′, d, J = 930 Hz), 137.53 (C4), 150.48 (C6), 163.68 (C2), 164.33 (C5′, d, J = 130 Hz).

1-(2*R*,4*R*,5*S*)-5-Fluoro-4-hydroxy-5-hydroxymethyltetrahydrofuran-2-yl)-5-methyl-1*H*-pyrimidine-2,4-dione (12e). To a solution of **10f** (3.5 mg, 0.012 mmol) in THF (0.2 mL) was added $LiBH_4$ (1 mg, 0.046 mmol) at room temperature, and the mixture was stirred for 2.5 h. After the mixture was stirred with EtOH (0.2 mL) for 10 min and neutralized with AcOH (0.01 mL) for 10 min, the solvent was evaporated in vacuo. The residue was purified by flash chromatography (ethyl acetate) to give 1-(2*R*,4*R*,5*S*)-5-fluoro-4-hydroxy-5-hydroxymethyltetrahydrofuran-2-yl)-5-methyl-1*H*-pyrimidine-2,4-dione **12e** (2.5 mg, 80%) as a colorless foam: $[\alpha]^{23}_D = -40°$ (c = 0.05, $CHCl_3$−MeOH = 20:1); IR (neat) 3382, 2926, 1689, 1472, 1285, 1140, 1067 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$−CD_3OD = 20:1) δ 1.90 (3H, d, J = 1.2 Hz), 2.04 (1H, ddd, J = 15, 2.7 Hz), 2.86 (1H, dddd, J = 15, 9.0, 6.4, 1.4 Hz), 3.93 (1H, dd, J = 12.6, 10.2 Hz), 4.00 (1H, dd, J = 22.5, 12.6 Hz), 4.46 (1H, dd, J = 5.4, 5.3 Hz), 6.43 (1H, ddd, J = 8.8, 2.4, 2.4 Hz), 7.65 (1H, d, J = 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ: 12.39 (C5-Me), 36.64 (C2′), 60.80 (C5′, d, J = 124 Hz), 72.20 (C3′, d, J = 159 Hz), 86.04 (C1′, d, J = 13 Hz), 111.58 (C5), 120.75 (C4′, d, J = 920 Hz), 137.14 (C4), 150.65 (C6), 163.94 (C2).

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Supporting Information Available: Proton and carbon NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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