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Synthesis of Chiral Acyclic Nucleosides by Sharpless Asymmetric Dihydroxylation: Access to Cidofovir and Buciclovir

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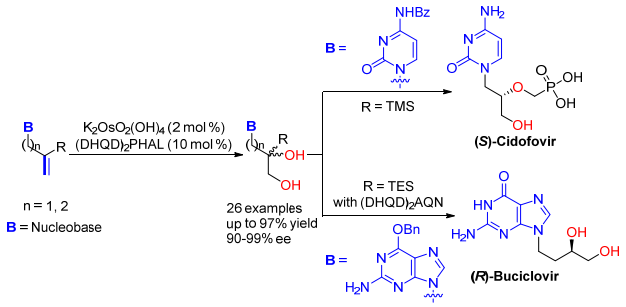


ABSTRACT

An efficient method to construct chiral acyclic nucleosides via Sharpless asymmetric dihydroxylation of N-allylpyrimidines or N-alkenylpurines is reported. A range of chiral acyclic nucleosides with two adjacent hydroxyl groups present on the side chains could be produced in good yields (up to 97% yield) and excellent enantioselectivities (90-99% ee). The synthetic utility of the reaction was demonstrated by the catalytic asymmetric synthesis of (*S*)-Cidofovir and (*R*)-Buciclovir.

Acyclic nucleosides and their phosphonates have emerged as a key class of antiviral nucleoside analogues.[1] Representative examples are shown in Figure 1. (*S*)-Cidofovir has been approved by the FDA in 1996 for the clinical use to treat cytomegalovirus retinitis in AIDS patients.[2] (*S*)-Cidofovir exhibits broad-spectrum activities against virtually all DNA viruses.[2b] (*R*)-Buciclovir is an anti-herpesvirus drug.[3] (*S*)-HPMPA is a potent and selective antiviral agent with activities against a broad-spectrum of DNA viruses.[4] D-Eritadenine is an inhibitor of *S*-adenosyl-L-homocysteine hydrolase.[5] For this list of chiral acyclic nucleosides and nucleotides exhibiting biological activities, one characteristic property is that two adjacent hydroxyl groups can always be found in the corresponding side chains. Therefore, developing an efficient method to construct chiral acyclic nucleosides and nucleotides with two adjacent hydroxyl groups connected to the side chains, is highly desirable.

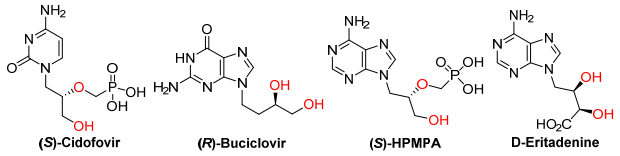
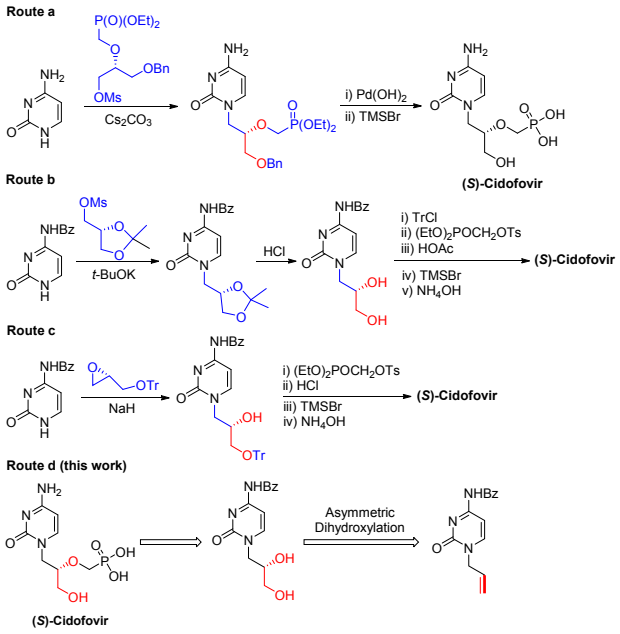


Figure 1. Selected biologically active chiral acyclic nucleosides and nucleotides

Conventional routes to synthesize chiral acyclic nucleosides and nucleotides, which contain two adjacent hydroxyl groups in the side chains, are based on a chiral pool strategy.[6] Take (*S*)-Cidofovir as the example, different synthetic routes are shown in Scheme 1. Webb II and co-workers first reported the synthesis of (*S*)-Cidofovir involving alkylation of cytosine with a chiral pre-assembled glycerol-phosphonate as the key step (Route a).[6a] Later, Bronson and co-workers developed an approach to produce (*S*)-Cidofovir based on coupling of (*S*)-2,3-O-isopropylideneglycerol with Bz-protected cytosine (Route b).[6b] Afterwards, Vemishetti and co-workers reported a practical route to synthesize (*S*)-Cidofovir starting from a ring-opening reaction of Bz-protected cytosine to (*S*)-tritylglycidol (Route c).[6c] Although remarkable progress has been achieved using the chiral pool strategy, the generation of chiral key starting materials often requires multiple steps from a chiral pool with necessary stereochemistry.[7] In 2014, our group reported an efficient route to synthesize chiral acyclic nucleoside Tenofovir through asymmetric transfer hydrogenation of α-purine-substituted acetone.[8-9] Considering that the

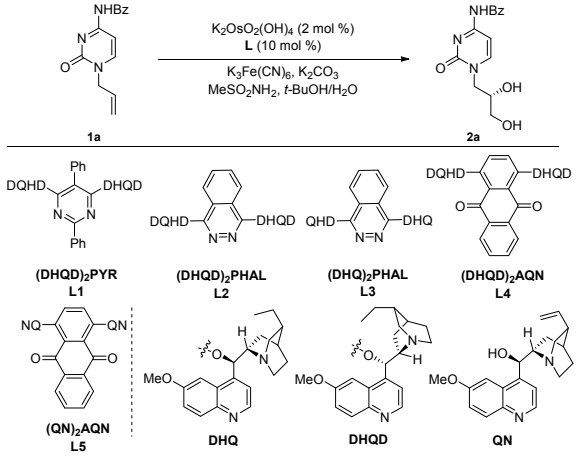
Sharpless asymmetric dihydroxylation (SAD) reaction represents a powerful strategy to construct optically active vicinal diols,[10-12] herein we report a catalytic asymmetric synthesis of chiral acyclic nucleosides, containing two adjacent hydroxyl groups in the side chains, via SAD of N1-allylcytosine (Route d).



Scheme 1. Different strategies to construct (*S*)-Cidofovir

Initially, Bz-protected N1-allylcytosine **1a** was selected as a model reactant in the asymmetric dihydroxylation reaction with $K_2OsO_2(OH)_4$ as the catalyst (Table 1). When $(DHQD)_2PYR$ **L1** was employed as the chiral ligand, the dihydroxylation proceeded well, affording the desired Bz-protected N^1-(2,3-dihydroxypropyl)cytosine **2a** in 95% yield and 29% ee (entry 1). Several known SAD ligands were screened (entries 2-5) and $(DHQD)_2PHAL$ **L2** proved to be the better choice, providing the diol **2a** in 97% yield and 55% ee (entries 2). The pseudoenantiomer $(DHQ)_2PHAL$ **L3** provided nearly identical results, along with an opposite enantiomer (entries 2). Upon lowering the reaction temperature from rt to 0 ^oC, the ee value of **2a** increased to 67% ee (entries 6). Optimization of reaction conditions demonstrated that the equivalents of $K_3Fe(CN)_6$ and K_2CO_3 could be decreased, and the ratio and concentration of *t*-BuOH/H_2O slightly influenced yield or ee value (entries 7-9). Several solvent mixtures were examined, and *t*-BuOH/H_2O proved to be better (entries 9). When the catalyst loading was reduced to 1 mol %, the ee value of **2a** decreased to 66% (entries 12).

Table 1. Optimization of reaction conditions[a]



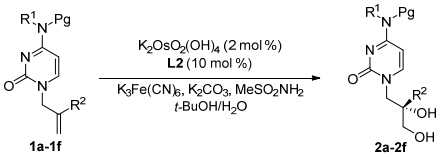
entry	L	*t* (°C)	solvent	yield (%)[b]	ee (%)[c]
1	**L1**	rt	*t*-BuOH/H_2O	95	29
2	**L2**	rt	*t*-BuOH/H_2O	97	55
3	**L3**	rt	*t*-BuOH/H_2O	96	-55
4	**L4**	rt	*t*-BuOH/H_2O	96	37
5	**L5**	rt	*t*-BuOH/H_2O	83	43
6	**L2**	0	*t*-BuOH/H_2O	95	67
7[d]	**L2**	0	*t*-BuOH/H_2O	94	70
8[d,]	**L2**	0	*t*-BuOH/H_2O (2:1), 1 mL	95	72
9[d]	**L2**	0	*t*-BuOH/H_2O (2:1), 2 mL	93	76
10[d]	**L2**	0	*i*-PrOH/H_2O (2:1), 2 mL	60	43
11[d]	**L2**	0	Acetone/H_2O (2:1), 2 mL	48	51
12[d,e]	**L2**	0	*t*-BuOH/H_2O (2:1), 2 mL	92	66

[a]Unless otherwise noted, reaction conditions were as follows: **1a** (0.05 mmol), $K_2OsO_2(OH)_4$ (2 mol %), **L** (10 mol %), $K_3Fe(CN)_6$ (6 equiv.), K_2CO_3 (6 equiv.), $MeSO_2NH_2$ (2 equiv.) in *t*-BuOH/H_2O (1.0 mL, 1:1) at rt for 12 h. [b]Isolated yield. [c]Determined by HPLC analysis. [d]$K_3Fe(CN)_6$ (3 equiv.) and K_2CO_3 (3 equiv.). [e]$K_2OsO_2(OH)_4$ (1 mol %), **L2** (5 mol %), 24 h.

Then, different protecting groups on N-allylcytosines were evaluated (Table 2). When Boc-protected N-allylcytosine **1b** was used, the enantioselectivity decreased (entry 2). In the case of isobutyryl or Bn-protected N-allylcytosines **1c**-**d**, the diols **2c** and **2d** were generated in 62% ee and 72% ee, respectively (entries 3-4). Therefore, a Bz protecting group proved to be the most suitable choice (entries 1-4). Next, a methyl group was introduced in the 2′-position of the side chain in N-allylcytosine. In doing so, the enantioselectivity of the diol product increased (**2e**, 90%

ee, entry 5). When an ethyl group was introduced in the 2′-position of the side chain, the diol **2f** was obtained in 93% ee (entry 6).

Table 2. Evaluation of protecting or substituent groups[a]

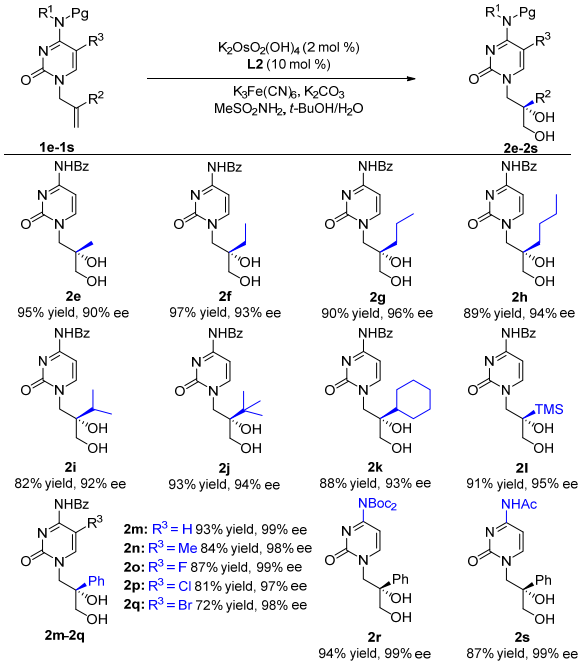


entry	**1**	R^1/Pg	R^2	**2**	yield (%)[b]	ee (%)[c]
1	**1a**	H/Bz	H	**2a**	93	76
2	**1b**	Boc/Boc	H	**2b**	91	38
3	**1c**	H/*i*-PrCO	H	**2c**	89	62
4	**1d**	H/Bn	H	**2d**	96	72
5	**1e**	H/Bz	Me	**2e**	95	90
6	**1f**	H/Bz	Et	**2f**	97	93

[a]Reaction conditions are same as Table 1, entry 9. [b]Isolated yield. [c]Determined by HPLC analysis.

Subsequently, the scope of N1-allylcytosines in SAD reaction was explored (Scheme 2). Various straight-chain, branched, or cyclic alkyl substituents were introduced in the 2′-position of the side chains, and the chiral diols **2e**-**2k** were produced in excellent results. When TMS group was linked to the 2′-position of the side chain, the chiral acyclic nucleoside **2l** was obtained in 95% ee. In the case of the phenyl substituted N1-allylcytosine **1m**, the diol **2m** was generated in 99% ee. Several Bz-protected N1-allylcytosines with different substituents (Me, F, Cl, or Br) in the C5 position were evaluated, and the chiral acyclic nucleosides **2n**-**2q** were afforded in 97-99% ee. Upon changing the protecting group with a Boc or Ac group, the diols **2r**-**2s** could also be produced with excellent results. Therefore, various alkyl groups (linear chains, branched or cyclic) provided similar results with phenyl provided the highest ee.

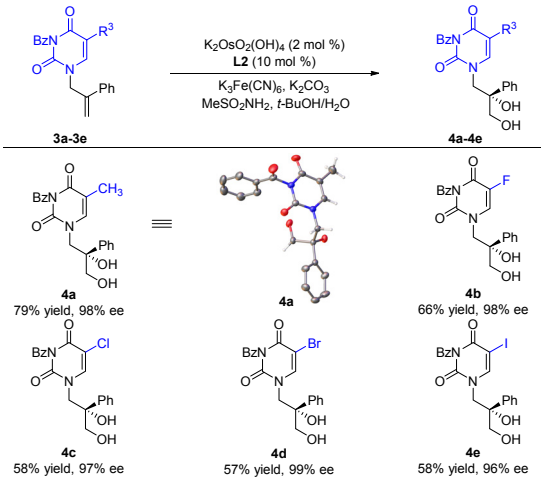
Scheme 2. Substrate scope of N-allylcytosines[a]



[a]Reaction conditions are same as Table 1, entry 9. Isolated yield are reported and the ee values were determined by HPLC analysis.

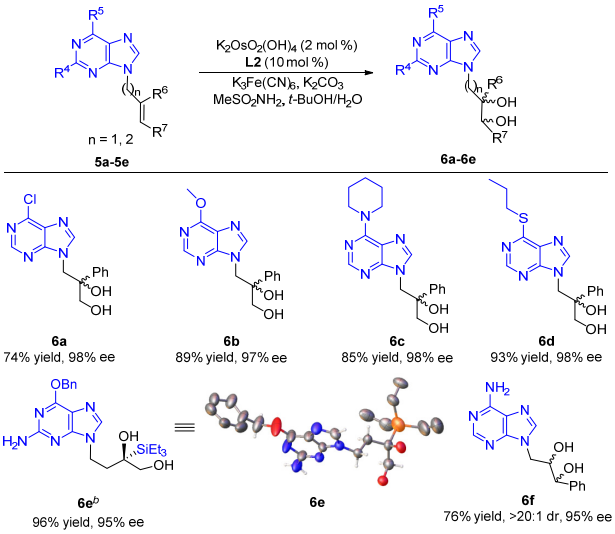
Other N1-allylpyrimidines were also screened (Scheme 3). When the Bz-protected N1-allylthymine **3a** was employed, the chiral diol **4a** was produced in 98% ee. The absolute configuration of the acyclic nucleoside **4a** was determined to be (*S*)-configuration by the single-crystal X-ray diffraction analysis.[13] N1-Allyluracils **3b-3e** with different halogen substituents (F, Cl, Br, or I) in the C5 position of uracil were examined, and the chiral diols **4b-4e** were produced in moderate yields and 96-99% ee. Therefore, this strategy also worked well with N-allylthymine and N-allyluracil.

Scheme 3. Substrate scope of other N-allylpyrimidines[a]



[a]Reaction conditions are same as Table 1, entry 9. Isolated yield are reported and the ee values were determined by HPLC analysis.

Scheme 4. Substrate scope of N-alkenylpurines[a]

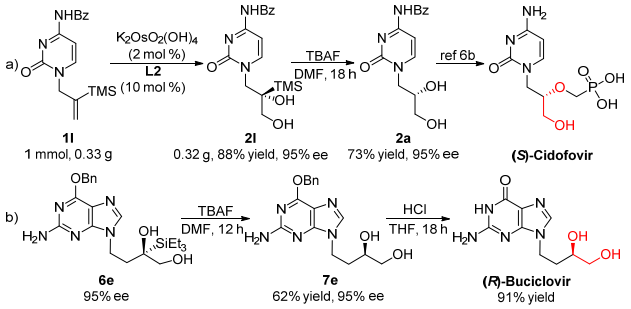


[a]Reaction conditions are same as Table 1, entry 9. Isolated yield are reported and the ee values were determined by chiral HPLC analysis. [b] **L4** was used instead of **L2**.

The substrate scope of N9-alkenylpurines in the reaction was further evaluated (Scheme 4). Several N9-allylpurines bearing a chloro (**5a**), alkoxy (**5b**), amino (**5c**), or alkyl sulfide (**5d**) group in the C6 position were screened, delivering **6a-6d** in good yields and 97-98% ee. Then, a triethylsilyl group was introduced in the 3′ position of the extended side chain, and the chiral diol **6e** was obtained in 95% ee. The absolute configuration of the acyclic nucleoside **6e** was determined to be (*S*)-configuration by the single-crystal X-ray diffraction analysis.[13] Then, the

N-allylpurine **5f** with a phenyl group at the terminal position was examined, the SAD reaction proceeded well, affording the acyclic nucleoside **6f** in 76% yield, >20:1 dr, and 95% ee. When N-allyladenine without additional substituent on the alkene was tested, only 35% ee was obtained (See SI for details).

Scheme 5. Synthesis of (*S*)-Cidofovir and (*R*)-Buciclovir



To further evaluate the applicability of this synthetic methodology, the SAD reaction of TMS-substituted N1-allylcytosine **1l** was performed on a 1 mmol scale (Scheme 5a). Under 2 mol % $K_2OsO_2(OH)_4$ and 10 mol % **L2**, the SAD reaction of **1l** proceeded smoothly, affording 0.32 g (88% yield) of the diol **2l** with 95% ee. Addition of TBAF resulted in the removal of the TMS group in diol **2l**,[14] affording the Bz-protected N^1-(2,3-dihydroxypropyl)cytosine **2a** in 73% yield and 95% ee, which could be transformed into the drug (*S*)-Cidofovir (Scheme 5a). Compared to Bronson group's work to construct Bz-protected-N^1-(2,3-dihydroxypropyl)cytosine **2a** in two steps with a 36% total yield, our developed route could afford a 64% total yield in two steps. The absolute configuration of product **2a** was determined to be (*S*)-configuration by comparison with the reported optical rotation. With the chiral acyclic purine nucleoside **6e** as the starting material in hand, the triethylsilyl group could also be removed by treatment with TBAF,[14] affording the chiral diol **7e** in 62% yield and 95% ee. After hydrolysis, (*R*)-Buciclovir could be obtained in 91% yield (Scheme 5b).

In summary, we have developed an efficient method to synthesize chiral acyclic nucleosides through SAD reaction of N-allylpyrimidines or N-alkenylpurines. Various of chiral acyclic nucleosides, bearing two adjacent hydroxyl groups in the corresponding side chains, could be afforded in 57-97% yields and 90-99% ee. Bz-protected-(*S*)-N^1-(2,3-dihydroxypropyl)-cytosine, the key intermediate for the synthesis of (*S*)-Cidofovir, could be obtained in two steps.

Furthermore, an efficient route to produce (*R*)-Buciclovir has been developed. Compared to conventional methods based on a chiral pool strategy, this method only employs catalytic amount of chiral catalyst, which avoids the use of equivalent chiral source and will provide a new route to synthesize chiral acyclic nucleosides.

■ EXPERIMENTAL SECTION

General information. ^{1}H, $^{13}C\{1H\}$ NMR spectra were recorded on Bruker (^{1}H 600 MHz, $^{13}C\{1H\}$ 150 MHz) and Bruker (^{1}H 400 MHz, $^{13}C\{1H\}$ 100 MHz) . Chemical shifts are recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, dt = doublet of triplets, t = triplet, q = quaternary, m = multiplet, br = broad). Coupling constants (*J*) are reported in Hertz (Hz). Enantiomer excesses were determined by chiral HPLC analysis on Chiralcel IA/ID/IE/AS-H/OD-H in comparison with the authentic racemates. Chiral HPLC analysis recorded on Thermo scientific Dionex Ultimate 3000 and Agilent Technologies 1260 Infinity. Optical rotations were reported as follows: $[\alpha]_D^T$ (c: = g/100mL, in solvent). Optical rotations recorded on Autopol Automatic Polarimeter. All products were further characterized by high-resolution mass spectra (HRMS). The HRMS was obtained using a Q-TOF instrument equipped with an ESI source. THF and Et_2O were freshly distilled from a sodium benzophenone ketyl. Other solvents used for work-up and purification purposes were purchased in technical grade quality and distilled by rotary evaporator before use.

Synthesis of *N*-allylated pyrimidines and *N*-alkenyl purines.

To a suspension of *N*-protected-cytosine (8.40 mmol) in THF/DMF (100 mL, 1/1), NaH (202 mg, 8.40 mmol, 60% dispersion in oil) was added. The reaction mixture was heated by oil bath at 60 °C for 45 min, (H, Alkyl, Aryl, TMS)-substituted allyl acetate[15] (4.20 mmol), DPPF (232 mg, 0.42 mmol) and $Pd(PPh_3)_4$ (485 mg, 0.42 mmol) were successively added. The reaction mixture was heated to 60 °C for 10 h. The mixture was cooled to room temperature, diluted with EtOAc (25 mL) and washed with an aqueous saturated solution of NH_4Cl. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. Purification by flash column chromatography on silica gel (petroleum ether/ethyl acetate 5:1 to 1:1) to give the products **1a-1s**.

In a dry 25 mL round bottom flask, *N*-protected-uracil or purine (8 mmol) and potassium carbonate (8 mmol) were dissolved in DMF, after add (3-bromoprop-1-en-2-yl)benzene[16] (4 mmol) at the room temperature, for over night, the reaction was complete monitored by TLC. Then, the reaction mixture was extracted with ethyl acetate and water for three times. The organic phases were combined and then dried by Na_2SO_4. Concentrated under the reduced pressure, the residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate 7:1) to give the products **3a-3e**, **5a-5d**.

In a dry 50 mL round bottom flask, 6-(benzyloxy)-9*H*-purin-2-amine (2.41 g, 10 mmol) and potassium carbonate (1.38 g, 10 mmol) were dissolved in DMF, (4-bromobut-1-en-2-yl)triethylsilane[17] (1.25 g, 5 mmol) was added at the room temperature. The reaction was complete monitored by TLC. Then, the reaction mixture was extracted with ethyl acetate and water for three times. The organic phases were combined and then dried by Na_2SO_4. Concentrated under the reduced pressure, the residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate 8:1) to give the product **5e** (1.33 g, 3.3 mmol, 65 % yield).

In a dry 25 mL round bottom flask, adenine (1.1 g, 8 mmol) and potassium carbonate (1.3 g, 9.6 mmol) were dissolved in DMF, (H, phenyl, ethoxycarbonyl, or TMS)-substituted allyl bromide (7.2 mmol) was added at the room temperature. The reaction was complete monitored by TLC. Then, the reaction mixture was extracted with ethyl acetate and water for three times. The organic phases were combined and then dried by Na_2SO_4. Concentrated under the reduced pressure, the residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate 3:1 to 1:2) to give the products **5f-5i**.

General procedure for the asymmetric dihydroxylation

To a mixture of *tert*-butyl alcohol and water (2:1, 2 mL) were added sequentially potassium ferricyanide (49.4 mg, 0.15 mmol), potassium carbonate (20.7 mg, 0.15 mmol), $(DHQD)_2PHAL$ **L2** (3.9 mg, 0.005 mmol), $MeSO_2NH_2$, (9.5 mg, 0.1 mmol) and $K_2OsO_2(OH)_4$ (0.36 mg, 0.001 mmol) at room temperature with stirring. The mixture stirred at room temperature for 30 minutes, then added to the alkene, and the heterogeneous slurry was stirred at 0 ^oC for 12 hours monitored by TLC. The reaction was quenched at 0 °C by addition of $Na_2S_2O_3$ and the mixture stirred at

room temperature for 2 hours. The reaction mixture was then dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to afford a crude product. Purification by flash column chromatography (V_{DCM}/V_{MeOH} = 20:1-60:1 as eluent) to afford afford the corresponding chiral dihydroxylation products **2a-2s**, **4a-4e**, **6a-6d** and **6f-6i**.

To a mixture of *tert*-butyl alcohol and water (2:1, 2 mL) were added sequentially potassium ferricyanide (49.4 mg, 0.15 mmol), potassium carbonate (20.7 mg, 0.15 mmol), $(DHQD)_2AQN$ **L4** (4.3 mg, 0.005 mmol), $MeSO_2NH_2$, (9.5 mg, 0.1 mmol) and $K_2OsO_2(OH)_4$ (0.36 mg, 0.001 mmol) at room temperature with stirring. The mixture stirred at room temperature for 30 minutes, then added to the alkene, and the heterogeneous slurry was stirred at 0 ^oC for 12 hours monitored by TLC. The reaction was quenched at 0 °C by addition of $Na_2S_2O_3$ and the mixture stirred at room temperature for 2 hours. The reaction mixture was then dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to afford a crude product. Purification by flash column chromatography (V_{DCM}/V_{MeOH} = 60:1 as eluent) to afford **6e**.

Synthesis of (*S*)-Cidofovir and (*R*)-Buciclovir

To a mixture of *tert*-butyl alcohol and water (2:1, 25 mL) were added sequentially potassium ferricyanide (0.98 g, 3 mmol), potassium carbonate (0.41 g, 3 mmol), $(DHQD)_2PHAL$ **L2** (78 mg, 0.1 mmol), $MeSO_2NH_2$, (0.19 g, 2 mmol) and $K_2OsO_2(OH)_4$ (7.2 mg, 0.02 mmol) at room temperature with stirring. The mixture stirred at room temperature for 30 minutes, then added to the alkene **1l**, and the heterogeneous slurry was stirred at 0 ^oC for 18 hours monitored by TLC. The reaction was quenched at 0 °C by addition of $Na_2S_2O_3$ and the mixture stirred at room temperature for 2 hours. The reaction mixture was then dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to afford a crude product. Purification by flash column chromatography (V_{DCM}/V_{MeOH} = 50:1 as eluent) to afford **2l** (0.32 g, 88% yield, 95% ee). A solution of **2l** (36.1 mg, 0.1 mmol) in anhydrous DMF (2 mL) at 0 ^oC was added with TBAF (0.5 mL of an 1 M solution in THF, 0.5 mmol). The mixture was stirred at room temperature for 18 h. The mixture was quenched with saturated water and then extracted three times with AcOEt. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (V_{DCM}/V_{MeOH} =25:1 as eluent) to afford **2a** (26 mg, 73% yield, 95% ee).

A solution of **6e** (44.3 mg, 0.1 mmol) in anhydrous DMF (2 mL) at 0 ^{o}C, was added with TBAF (0.35 mL of an 1 M solution in THF, 0.35 mmol). The mixture was stirred at room temperature for 12 h. The mixture was quenched with saturated water and then extracted three times with AcOEt. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (V_{DCM}/V_{MeOH} = 30:1 as eluent) to afford **7e** (27 mg, 62% yield, 95% ee). A solution of 7e (33 mg, 0.1 mmol) in THF and methanol (1:1, 2 mL) at rt was added with 0.4 mL HCl (4 M). The mixture was stirred at room temperature for 18 h, and then NaOH (2 M) was added to adjust pH value with 7.1-7.3. The reaction mixture was extracted with ethyl acetate and water for three times. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography (V_{DCM}/V_{MeOH} = 4:1 as eluent) to afford **(*R*)-Buciclovir** (30 mg, 91% yield).

Characterization of Compounds

***N*-(1-Allyl-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (1a)**[18] White solid, 0.57 g, 53% yield m.p. 174.4-174.8 ^{o}C ^{1}H NMR (400 MHz, CD_3OD) δ 8.02 (d, *J* = 7.2 Hz, 1H), 8.00-7.93 (m, 2H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 6.8 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 2H), 6.06-5.97 (m, 1H), 5.31-5.23 (m, 2H), 4.55 (d, *J* = 6.0 Hz, 2H). HRMS (ESI-TOF) calcd for $C_{14}H_{13}N_3O_2Na$ $[M + Na]^+$ 278.0900, found 278.0902.

Di-*tert*-butyl-(1-allyl-2-oxo-1,2-dihydropyrimidin-4-yl)-4-azanedicarboxylate (1b) White solid, 0.83 g, 56% yield m.p. 102.1-103.2 ^{o}C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.2 Hz, 1H), 7.00 (d, *J* = 7.2 Hz, 1H), 5.97-5.87 (m, 1H), 5.30-5.22 (m, 2H), 4.47 (d, *J* = 6.0 Hz, 2H), 1.54 (s, 18H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.5, 155.0, 149.7, 147.3, 131.8, 119.7, 96.6, 85.0, 52.2, 27.8. **HRMS** (ESI-TOF) calcd for $C_{17}H_{25}N_3O_5Na$ $[M + Na]^+$ 374.1686, found 374.1687.

***N*-(1-Allyl-2-oxo-1,2-dihydropyrimidin-4-yl)isobutyramide (1c)** White solid, 0.55 g, 59% yield m.p. 160.2-160.9 ^{o}C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.41 (d, *J* = 7.2 Hz, 1H), 5.98-5.88 (m, 1H), 5.31-5.22 (m, 2H), 4.50 (d, *J* = 6.0 Hz, 2H), 2.69 (dt, *J* = 14.0, 6.8 Hz, 1H), 1.19 (d, *J* = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 177.5, 162.7, 155.9, 148.2, 131.7, 119.7, 96.9, 52.2, 36.6, 19.2. **HRMS** (ESI-TOF) calcd for $C_{11}H_{15}N_3O_2Na$ $[M + Na]^+$

244.1056, found 244.1052.

1-Allyl-4-(benzylamino)pyrimidin-2(1*H*)-one (1d) White solid, 0.62 g, 61% yield m.p. 172.1-173.2 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 15.2 Hz, 5H), 6.15-5.97 (m, 1H), 5.83 (s, 2H), 5.36 (t, *J* = 14.0 Hz, 2H), 4.82-4.65 (m, 2H), 4.52 (d, *J* = 5.2 Hz, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 163.8, 157.0, 143.8, 138.2, 133.0, 128.8, 128.2, 127.6, 118.5, 100.1, 95.2, 51.4, 44.9. **HRMS** (ESI-TOF) calcd for $C_{14}H_{16}N_3O$ $[M + H]^+$ 242.1288, found 242.1289.

***N*-(1-(2-Methylallyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (1e)** White solid, 0.56 g, 51% yield m.p. 138.4-139.6 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 7.89 (d, *J* = 6.6 Hz, 2H), 7.59 (t, *J* = 7.2 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 3H), 5.02 (s, 1H), 4.83 (s, 1H), 4.47 (s, 2H), 1.75 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.3, 155.7, 148.3, 139.7, 133.3, 133.2, 129.1, 127.7, 114.6, 97.0, 54.7, 20.1. **HRMS** (ESI-TOF) calcd for $C_{15}H_{15}N_3O_2Na$ $[M + Na]^+$ 292.1056, found 292.1054.

***N*-(1-(2-Methylenebutyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (1f)** White solid, 0.70 g, 59% yieldm.p. 145.5-146.7 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.90 (d, *J* = 5.4 Hz, 2H), 7.67-7.57 (m, 2H), 7.51 (t, *J* = 7.2 Hz, 3H), 5.05 (s, 1H), 4.87 (s, 1H), 4.52 (s, 2H), 2.06 (q, *J* = 7.2 Hz, 2H), 1.09 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.2, 148.3, 145.4, 133.3, 129.1, 127.7, 112.6, 97.0, 77.4, 53.8, 26.5, 11.9. **HRMS** (ESI-TOF) calcd for $C_{16}H_{17}N_3O_2Na$ $[M + Na]^+$ 306.1213, found 306.1211.

***N*-(1-(2-Methylenepentyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (1g)** White solid, 0.67 g, 54% yield m.p. 131.5-132.6 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.77 (s, 1H), 7.90 (d, *J* = 6.6 Hz, 1H), 7.66 (dd, *J* = 11.4, 7.8 Hz, 1H), 7.62-7.59 (m, 2H), 7.55-7.50 (m, 2H), 7.47-7.45 (m, 1H), 5.04 (s, 1H), 4.87 (s, 1H), 4.50 (s, 2H), 2.01 (t, *J* = 7.2 Hz, 2H), 1.53-1.50 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.2, 143.8, 133.3, 132.3, 132.2, 132.1, 129.2, 128.7, 128.6 127.7, 113.9, 97.0, 53.6, 35.7, 20.7, 13.8. **HRMS** (ESI-TOF) calcd for $C_{17}H_{20}N_3O_2$ $[M + H]^+$ 298.1550, found 298.1549.

***N*-(1-(2-Methylenehexyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (1h)** White solid, 0.47 g, 36% yield m.p. 119.6-120.1 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.90 (d, *J* = 5.4 Hz, 1H), 7.67 (dd, *J* = 11.4, 7.8 Hz, 1H), 7.62-7.59 (m, 2H), 7.54-7.50 (m, 2H), 7.46 (t, *J* = 6.0 Hz, 1H), 5.05 (s, 1H), 4.86 (s, 1H), 4.51 (s, 2H), 2.03 (t, *J* = 7.2 Hz, 2H), 1.48-1.45 (m, 2H), 1.35-1.30

(m, 2H), 0.90 (t, *J* = 7.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.2, 144.1, 133.3, 132.3, 132.2, 129.2, 128.7, 128.6, 127.7 113.7, 53.6, 33.4, 29.7, 22.5, 14.0. HRMS (ESI-TOF) calcd for $C_{18}H_{22}N_3O_2$ $[M + H]^+$ 312.1707, found 312.1711.

***N*-(1-(3-Methyl-2-methylenebutyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (1i)** White solid, 0.75 g, 63% yield m.p. 138.2-139.3 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.90 (d, *J* = 5.6 Hz, 2H), 7.59-7.51 (m, 5H), 5.07 (s, 1H), 4.78 (s, 1H), 4.56 (s, 2H), 2.28-2.45 (m, 1H), 1.11 (d, *J* = 6.4 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.2, 150.1, 148.4, 133.3, 132.2, 132.0, 129.1, 128.7, 128.5, 127.7, 111.4, 52.5, 31.8, 21.7. **HRMS** (ESI-TOF) calcd for $C_{17}H_{20}N_3O_2$ $[M + H]^+$ 298.1550, found 298.1555.

***N*-(1-(3,3-Dimethyl-2-methylenebutyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (1j)** White solid, 0.81 g, 62% yield m.p. 202.1-203.1 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.90 (d, *J* = 6.0 Hz, 2H), 7.62-7.60 (m, 2H), 7.51 (t, *J* = 7.2 Hz, 3H), 5.11 (s, 1H), 4.60 (s, 2H), 4.57 (s, 1H), 1.16 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.3, 152.1, 133.3, 132.3, 132.2, 129.2, 128.7, 128.6, 127.7, 110.2, 77.4, 50.6, 35.7, 29.3. **HRMS** (ESI-TOF) calcd for $C_{18}H_{22}N_3O_2$ $[M + H]^+$ 312.1707, found 312.1701.

***N*-(1-(2-Cyclohexylallyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (1k)** White solid, 0.87 g, 61% yield m.p. 207.2-208.2 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.77 (s, 1H), 7.90 (d, *J* = 6.0 Hz, 1H), 7.67 (dd, *J* = 12.0, 7.8 Hz, 1H), 7.62-7.50 (m, 4H), 7.47-7.45 (m, 1H), 5.06 (s, 1H), 4.79 (s, 1H), 4.54 (s, 2H), 1.88-1.77 (m, 6H), 1.68 (d, *J* = 12.0 Hz, 1H), 1.28 (d, *J* = 12.0 Hz, 1H), 1.24-1.14 (m, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 162.2, 149.3, 133.3, 132.3, 132.2, 132.1, 129.2, 128.7, 128.6, 127.7, 112.2, 52.7, 42.0, 32.3, 26.6, 26.3. **HRMS** (ESI-TOF) calcd for $C_{20}H_{24}N_3O_2$ $[M + H]^+$ 338.1863, found 338.1868.

***N*-(2-Oxo-1-(2-(trimethylsilyl)allyl)-1,2-dihydropyrimidin-4-yl)benzamide (1l)** White solid, 0.62 g, 45% yield m.p. 162.2-163.4 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.93 (s, 1H), 7.92 (d, *J* = 6.6 Hz, 2H), 7.70-7.55 (m, 2H), 7.50 (t, *J* = 7.2 Hz, 2H), 7.46 (d, *J* = 6.0 Hz, 1H), 5.57 (s, 1H), 5.52 (s, 1H), 4.65 (s, 2H), 0.13 (s, 9H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 162.2, 146.5, 133.3, 132.9, 132.3, 132.2, 132.1, 132.0, 129.1, 128.7, 128.6, 127.8, 127.2, 53.7, -1.7. **HRMS** (ESI-TOF) calcd for $C_{17}H_{22}N_3O_2Si$ $[M + H]^+$ 328.1476, found 328.1478.

***N*-(2-Oxo-1-(2-phenylallyl)-1,2-dihydropyrimidin-4-yl)benzamide (1m)** White solid, 0.5 g,

36% yield m.p. 178.1-179.2 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.86 (d, *J* = 7.2 Hz, 2H), 7.60 (t, *J* = 7.2 Hz, 2H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.44 (d, *J* = 7.2 Hz, 3H), 7.34 (t, *J* = 7.2 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 1H), 5.68 (s, 1H), 5.28 (s, 1H), 5.01 (s, 2H). **^{13}C NMR** (100 MHz, CD_3OD) δ 164.7, 152.7, 143.3, 134.7, 134.1, 129.8, 129.3, 129.2, 128.6, 127.0, 98.0, 78.0, 68.4, 57.2. **HRMS** (ESI-TOF) calcd for $C_{20}H_{18}N_3O_2$ $[M + H]^+$ 332.1394, found 332.1398.

***N*-(5-Methyl-2-oxo-1-(2-phenylallyl)-1,2-dihydropyrimidin-4-yl)benzamide (1n)** White solid, 0.77 g, 53% yield m.p. 194.5-195.4 °C **^{1}H NMR** (400 MHz, CD_3OD) δ 7.76-7.70 (m, 3H), 7.54-7.50 (m, 3H), 7.47-7.44 (m, 2H), 7.38-7.35 (m, 3H), 5.57 (s, 1H), 5.31 (s, 1H), 4.87 (s, 2H), 1.87 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.7, 160.2, 148.7, 142.5, 140.2, 137.3, 137.0, 132.6, 130.0, 129.0, 128.9, 128.2, 126.2, 116.9, 112.1, 50.8, 13.6. **HRMS** (ESI-TOF) calcd for $C_{21}H_{20}N_3O_2$ $[M + H]^+$ 346.1550, found 346.1559.

***N*-(5-Fluoro-2-oxo-1-(2-phenylallyl)-1,2-dihydropyrimidin-4-yl)benzamide (1o)** Yellow solid, 0.82 g, 56% yield m.p. 207.2-208.2 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 12.93 (s, 1H), 8.26 (d, *J* = 7.2 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.45-7.42 (m, 4H), 7.40-7.31 (m, 4H), 5.70 (s, 1H), 5.36 (s, 1H), 4.86 (s, 2H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 153.0 (d, $J_{C\text{-}F}$ = 18.1 Hz), 147.7, 142.0, 139.9 (d, $J_{C\text{-}F}$ = 237.1 Hz), 136.5, 136.1, 133.1, 130.1, 129.1, 129.0, 128.4, 128.2 (d, $J_{C\text{-}F}$ = 30.2 Hz), 126.2, 118.2, 51.4. **HRMS** (ESI-TOF) calcd for $C_{20}H_{16}NaFN_3O_2$ $[M + Na]^+$ 372.1119, found 372.1127.

***N*-(5-Chloro-2-oxo-1-(2-phenylallyl)-1,2-dihydropyrimidin-4-yl)benzamide (1p)** Yellow solid, 0.80 g, 52% yield m.p. 163.3-164.5 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.12 (s, 1H), 8.31 (d, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.49-7.42 (m, 5H), 7.39-7.34 (m, 3H), 5.69 (s, 1H), 5.35 (s, 1H), 4.88 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.2, 147.9, 142.0, 140.7, 136.5, 133.8, 133.1, 130.3, 130.2, 129.1, 128.6, 128.4, 126.2, 118.1, 109.2, 51.3. **HRMS** (ESI-TOF) calcd for $C_{20}H_{16}NaClN_3O_2$ $[M + Na]^+$ 388.0823, found 388.0823.

***N*-(5-Bromo-2-oxo-1-(2-phenylallyl)-1,2-dihydropyrimidin-4-yl)benzamide (1q)** Yellow solid, 0.84 g, 49% yield m.p. 170.5-171.2 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.25 (s, 1H), 8.32 (d, *J* = 7.6 Hz, 2H), 7.59 (s, 1H), 7.56-7.52 (m, 1H), 7.49-7.30 (m, 7H), 5.69 (s, 1H), 5.34 (s, 1H), 4.87 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.4, 148.0, 143.4, 142.1, 136.6, 133.1, 130.3, 129.1, 128.6,

128.4, 126.3, 118.0, 97.3, 51.4. **HRMS** (ESI-TOF) calcd for $C_{20}H_{17}BrN_3O_2$ $[M + H]^+$ 410.0499, found 410.0492.

***N*-(2-Oxo-1-(2-phenylallyl)-1,2-dihydropyrimidin-4-yl)ditert-butoxycarbonylamide (1r)** White solid, 1.02 g, 57% yield m.p. 161.1-162.2 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.2 Hz, 1H), 7.42 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.36-7.27 (m, 3H), 6.93 (d, *J* = 7.6 Hz, 1H), 5.64 (s, 1H), 5.25 (s, 1H), 4.95 (s, 2H), 1.53 (s, 18H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 162.3, 155.2, 149.7, 146.6, 142.5, 137.1, 129.0, 128.7, 126.3, 117.4, 96.6, 85.0, 52.1, 27.8. **HRMS** (ESI-TOF) calcd for $C_{23}H_{30}N_3O_5$ $[M + H]^+$ 428.2180, found 428.2171.

3-Benzo-*N*-(2-oxo-1-(2-phenylallyl)-1,2-dihydropyrimidin-4-yl)acetamide (1s) Brown solid, 0.44 g, 39% yield m.p. 190.2-191.3 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.42-7.41 (m, *J* = 8.1, 2H), 7.34-7.29 (m, 4H), 5.64 (s, 1H), 5.24 (s, 1H), 4.98 (s, 2H), 2.23 (s, 3H). **^{13}C NMR** (150 MHz, CD_3OD) δ 173.0, 164.3, 158.7, 150.4, 144.7, 139.2, 129.7, 129.5, 127.4, 116.0, 98.2, 53.5, 24.5. **HRMS** (ESI-TOF) calcd for $C_{15}H_{16}N_3O_2$ $[M + H]^+$ 270.1237, found 270.1231.

3-Benzoyl-5-methyl-1-(2-phenylallyl)pyrimidine-2,4(1*H*,3*H*)-dione (3a) White solid, 0.50 g, 52% yield m.p. 134.0-135.2 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.47-7.42 (m, 4H), 7.37 (s, 3H), 7.06 (s, 1H), 5.63 (s, 1H), 5.34 (s, 1H), 4.83 (s, 2H), 1.89 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 168.9, 163.0, 150.1, 143.1, 138.5, 137.1, 135.1, 131.7, 130.6, 129.2, 129.0, 128.9, 126.5, 117.3, 111.4, 50.4, 12.6. **HRMS** (ESI-TOF) calcd for $C_{21}H_{18}N_2NaO_3$ $[M + Na]^+$ 369.1210, found 369.1207.

3-Benzoyl-5-fluoro-1-(2-phenylallyl)pyrimidine-2,4(1*H*,3*H*)-dione (3b) White solid, 0.82 g, 56% yield m.p. 129.9-130.3 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 2H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.42-7.38 (m, 5H), 7.31 (d, *J* = 5.6 Hz, 1H), 5.68 (s, 1H), 5.41 (s, 1H), 4.84 (s, 2H). **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 167.1, 156.1 (d, $J_{C\text{-}F}$ = 27.0 Hz), 148.6, 142.5, 140.3 (d, $J_{C\text{-}F}$ = 238.5 Hz), 136.5, 135.5, 131.0, 130.7, 129.4, 129.1, 129.0, 126.7 (d, $J_{C\text{-}F}$ = 35.0 Hz), 126.5, 118.5, 51.0. **HRMS** (ESI-TOF) calcd for $C_{20}H_{15}FN_2NaO_3$ $[M + Na]^+$ 373.0959, found 373.0959.

***N*-(5-Chloro-2-oxo-1-(2-phenylallyl)-1,2-dihydropyrimidin-4-yl)benzamide (3c)** Yellow solid, 0.97 g, 63% yield m.p. 151.5-151.9 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.76-7.74 (m, 2H), 7.66 (t, *J*

= 7.2 Hz, 1H), 7.48-7.45 (m, 3H), 7.42-7.40 (m, 2H), 7.39-7.36 (m, 3H), 5.68 (s, 1H), 5.41 (s, 1H), 4.87 (s, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 167.3, 158.1, 149.1, 142.5, 139.4, 136.5, 135.5, 131.0, 130.7, 129.4, 129.1, 129.0, 126.5, 118.4, 109.3, 51.0. **HRMS** (ESI-TOF) calcd for $C_{20}H_{15}ClN_2NaO_3$ $[M + Na]^+$ 389.0663, found 389.0659.

***N*-(5-Bromo-2-oxo-1-(2-phenylallyl)-1,2-dihydropyrimidin-4-yl)benzamide (3d)** White solid, 0.95 g, 55% yield m.p. 161.9-163.1 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 6.8 Hz, 2H), 7.66 (s, 1H), 7.57 (s, 1H), 7.46-7.34 (m, 7H), 5.68 (s, 1H), 5.40 (s, 1H), 4.87 (s, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 167.4, 158.1, 149.4, 142.5, 142.0, 136.6, 135.4, 131.0, 130.7, 129.4, 129.2, 129.1, 126.5, 118.3, 97.0, 51.1. **HRMS** (ESI-TOF) calcd for $C_{20}H_{15}BrN_2NaO_3$ $[M + Na]^+$ 433.0158, found 433.0150.

***N*-(5-Iodo-2-oxo-1-(2-phenylallyl)-1,2-dihydropyrimidin-4-yl)benzamide (3e)** White solid, 0.94 g, 49% yield m.p. 153.9-154.5 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.8 Hz, 2H), 7.70-7.62 (m, 2H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.39 (d, *J* = 13.8 Hz, 5H), 5.66 (s, 1H), 5.38 (s, 1H), 4.86 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.6, 159.0, 149.7, 147.2, 142.6, 136.7, 135.3, 131.0, 130.6, 129.3, 129.1, 129.0, 126.5, 118.1, 100.1, 68.2, 51.0. **HRMS** (ESI-TOF) calcd for $C_{20}H_{15}IN_2NaO_3$ $[M + Na]^+$ 481.0020, found 481.0014

6-Chloro-9-(2-phenylallyl)-9*H*-purine (5a) White solid, 0.61 g, 54% yield m.p. 87.1-88.2 °C **^{1}H NMR** (600 MHz, CD_3OD) δ 8.74 (s, 1H), 8.47 (s, 1H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.32-7.24 (m, 3H), 5.58 (s, 1H), 5.44 (s, 2H), 5.17 (s, 1H). **^{13}C NMR** (100 MHz, CD_3OD) δ 153.3, 153.1, 151.3, 148.3, 144.3, 138.9, 132.0, 129.7, 129.6, 127.3, 116.7, 48.6. **HRMS** (ESI-TOF) calcd for $C_{14}H_{12}ClN_4$ $[M + H]^+$ 271.0745, found 271.0755.

6-Methoxy-9-(2-phenylallyl)-9*H*-purine (5b) White solid, 0.70 g, 63% yield m.p. 110.8-111.5 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.86 (s, 1H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.31-7.27 (m, 3H), 5.59 (s, 1H), 5.27 (s, 2H), 5.13 (s, 1H), 4.17 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.2, 152.3, 152.2, 142.6, 142.2, 137.4, 128.9, 128.7, 126.1, 121.4, 116.3, 54.3, 47.3. **HRMS** (ESI-TOF) calcd for $C_{15}H_{15}N_4O$ $[M + H]^+$ 267.1240, found 267.1237.

9-(2-Phenylallyl)-6-(piperidin-1-yl)-9*H*-purine (5c) White solid, 0.60 g, 45% yield m.p. 105.5-106.4 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.67 (s, 1H), 7.45 (dd, *J* = 8.4, 2.0 Hz, 2H), 7.35-7.27 (m, 3H), 5.59 (s, 1H), 5.20 (s, 2H), 5.10 (s, 1H), 4.22 (s, 4H), 1.73-1.67 (m, 6H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 154.1, 152.8, 151.0, 142.8, 138.0, 137.7, 128.8, 128.6, 126.2, 119.7, 115.9, 46.8, 26.3, 25.0. **HRMS** (ESI-TOF) calcd for $C_{19}H_{22}N_5$ $[M + H]^+$ 320.1870, found 320.1863.

9-(2-Phenylallyl)-6-(propylthio)-9*H*-purine (5d) Yellow oil, 0.76 g, 56% yield **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.68 (s, 1H), 7.84 (s, 1H), 7.37 (d, *J* = 7.2 Hz, 2H), 7.25-7.21 (m, 3H), 5.55 (s, 1H), 5.20 (s, 2H), 5.09 (s, 1H), 3.31 (t, *J* = 7.2 Hz, 2H), 1.76 (dd, *J* = 14.4, 7.2 Hz, 2H), 1.02 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.8, 152.2, 148.5, 142.5, 137.3, 131.2, 128.9, 128.8, 126.1, 116.4, 100.1, 47.1, 30.9, 23.0, 13.6. **HRMS** (ESI-TOF) calcd for $C_{17}H_{19}N_4S$ $[M + H]^+$ 311.1325, found 311.1318.

6-(Benzyloxy)-9-(3-(triethylsilyl)but-3-en-1-yl)-9*H*-purin-2-amine (5e) White solid, 0.61 g, 36% yield m.p. 123.3-123.9 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.50 (d, *J* = 6.8 Hz, 2H), 7.37-7.28 (m, 3H), 5.62 (s, 1H), 5.57 (s, 2H), 5.42 (s, 1H), 4.88 (s, 2H), 4.12 (t, *J* = 7.6 Hz, 2H), 2.61 (t, *J* = 7.2 Hz, 2H), 0.93 (t, *J* = 8.0 Hz, 9H), 0.63 (q, *J* = 8.0 Hz, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 161.2, 159.2, 154.1, 144.8, 139.6, 136.6, 128.5, 128.4, 128.3, 128.1, 115.8, 68.2, 43.1, 35.7, 7.4, 2.9. **HRMS** (ESI-TOF) calcd for $C_{22}H_{32}N_5OSi$ $[M + H]^+$ 410.2371, found 410.2372

9-Cinnamyl-9*H*-purin-6-amine (5f) White solid, 1.17 g, 65% yield m.p. 235.4-236.7 °C **^{1}H NMR** (400 MHz, d^6-DMSO) δ 8.18 (s, 1H), 8.15 (s, 1H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 3.6 Hz, 2H), 7.25 (d, *J* = 7.2 Hz, 1H), 7.22 (s, 2H), 6.53-6.51 (m, 2H), 4.94 (d, *J* = 4.0 Hz, 2H). **^{13}C NMR** (100 MHz, d^6-DMSO) δ 156.0, 152.5, 149.4, 140.6, 135.9, 132.4, 128.7, 127.9, 126.5, 124.7, 118.7, 44.6. **HRMS** (ESI-TOF) calcd for $C_{14}H_{14}N_5$ $[M + H]^+$ 252.1244, found 252.1241.

Ethyl (*E*)-4-(6-amino-9*H*-purin-9-yl)but-2-enoate (5g) White solid, 0.84 g, 47% yield m.p. 133.3-133.9 °C **^{1}H NMR** (400 MHz, d^6-DMSO) δ 8.43 (s, 1H), 8.20 (s, 1H), 7.35 (s, 2H), 7.22 (d, *J* = 14.4 Hz, 1H), 6.70-6.63 (m, 1H), 4.11 (q, *J* = 7.2 Hz, 2H), 3.32 (dd, *J* = 7.2, 1.2 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, d^6-DMSO) δ 170.9, 156.1, 153.1, 148.6, 138.8, 123.7, 119.1, 112.6, 60.4, 34.8, 14.1. **HRMS** (ESI-TOF) calcd for $C_{11}H_{14}N_5O_2$ $[M + H]^+$ 248.1142, found 248.1142.

9-Allyl-9*H*-purin-6-amine (5h) White solid, 1.29 g, 74% yield m.p. 73.9-75.3 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.80 (s, 1H), 6.07-6.00 (m, 3H), 5.31 (d, *J* = 10.2 Hz, 1H), 5.20 (d, *J*

= 16.8 Hz, 1H), 4.81 (d, *J* = 5.4 Hz, 2H). **HRMS** (ESI-TOF) calcd for $C_8H_{10}N_5$ $[M + H]^+$ 176.0931, found 176.0929.

(*E*)-9-(3-(Trimethylsilyl)allyl)-9*H*-purin-6-amine (5i) White solid, 1.24 g, 70% yield m.p. 198.2.3-199.9 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.79 (s, 1H), 6.15 (dt, *J* = 18.6, 4.8 Hz, 1H), 5.98 (s, 2H), 5.75 (d, *J* = 18.6 Hz, 1H), 4.84 (d, *J* = 3.6 Hz, 2H), 0.04 (s, 9H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 155.7, 153.3, 150.1, 140.6, 138.8, 134.6, 119.6, 47.8, -1.4. **HRMS** (ESI-TOF) calcd for $C_{11}H_{18}N_5Si$ $[M + H]^+$ 248.1326, found 248.1327.

(*S*)-4-(Benzoyl-l2-azanyl)-1-(2,3-dihydroxypropyl)pyrimidin-2(1*H*)-one (2a) White solid, 10.9 mg, 69% yield, 95% ee. $[\alpha]^{20}_D$ = -65.00 (c = 0.30, CH_3OH). (Reported: $[\alpha]^{20}_D$ = -81.95 (c = 1.09, CH_3OH), > 99% ee)[5] m.p. 189.1-191.9 °C. TLC: R_f = 0.36 (dichloromethane:methanol = 25:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 14.072 min (minor), 19.470 min (major). **^{1}H NMR** (400 MHz, CD_3OD) δ 8.03 (d, *J* = 7.2 Hz, 1H), 7.98 (d, *J* = 7.2 Hz, 2H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.57-7.53 (m, 3H), 4.28 (dd, *J* = 13.6, 3.6 Hz, 1H), 4.00 (dd, *J* = 8.4, 3.2 Hz, 1H), 3.74 (dd, *J* = 13.6, 8.4 Hz, 1H), 3.58 (d, *J* = 5.2 Hz, 2H). **^{13}C NMR** (150 MHz, *d*^{6}-DMSO) δ 167.7, 163.4, 156.0, 152.1, 133.7, 133.1, 128.9, 128.8, 95.7, 69.1, 64.2, 53.6. **HRMS** (ESI-TOF) calcd for $C_{14}H_{15}N_3NaO_4$ $[M + Na]^+$ 312.0955, found 312.0956.

(*S*)-*N*-(1-(2,3-Dihydroxy)-2-oxo-1,2-dihydropyrimidin-4-yl) di-tert-butoxycarbonylamide (2b) White solid, 17.5 mg, 91% yield, 38% ee. $[\alpha]^{25}_D$ = -7.94 (c = 1.0, CH_3OH), m.p. 128.1-128.9 °C. TLC: R_f = 0.42 (dichloromethane:methanol = 30:1) [UV]. The ee value was determined by chiral HPLC AS-H, *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, λ = 250 nm, retention time: 21.081 min (minor), 30.753 min (major). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.2 Hz, 1H), 7.04 (d, *J* = 7.2 Hz, 1H), 4.19 (s, 1H), 4.11-4.06 (m, 1H), 3.98 (s, 1H), 3.84-3.77 (m, 1H), 3.73 (s, 1H), 3.54 (s, 2H), 1.53 (s, 18H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.6, 156.6, 150.1, 149.6, 96.6, 85.2, 69.8, 63.6, 53.3, 27.8. **HRMS** (ESI-TOF) calcd for $C_{17}H_{27}N_3NaO_7$ $[M + Na]^+$ 408.1741, found 408.1741.

(*S*)-*N*-(1-(2,3-Dihydroxypropyl)-2-oxo-1,2-dihydropyrimidin-4-yl)isobutyramide (2c) White

solid, 11.3 mg, 89% yield, 62% ee. $[\alpha]^{25}_{D}$ = -15.3 (c = 0.5, CH_3OH), m.p. 181.2-182.3 °C. TLC: R_f = 0.32 (dichloromethane:methanol = 25:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, λ = 250 nm, retention time: 21.843 min (minor), 26.312 min (major). **^{1}H NMR** (400 MHz, CD_3OD) δ 7.95 (d, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.2 Hz, 1H), 4.24 (dd, *J* = 13.2, 3.2 Hz, 1H), 4.00-3.94 (m, 1H), 3.71 (dd, *J* = 13.6, 8.4 Hz, 1H), 3.56 (d, *J* = 5.2 Hz, 2H), 2.72-2.65 (m, 1H), 1.18 (d, *J* = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, CD_3OD) δ 179.7, 164.6, 159.1, 152.4, 97.6, 70.4, 64.9, 54.7, 37.2, 19.4. **HRMS** (ESI-TOF) calcd for $C_{11}H_{17}N_3NaO_4$ $[M + Na]^+$ 278.1111, found 278.1112.

(*S*)-4-(Benzylamino)-1-(2,3-dihydroxypropyl)pyrimidin-2(1*H*)-one (2d) White solid, 13.2 mg, 96% yield, 72% ee. $[\alpha]^{25}_{D}$ = -23.5 (c = 1.25, CH_3OH), m.p. 192.3-193.1 °C. TLC: R_f = 0.39 (dichloromethane:methanol = 25:1) [UV]. The ee value was determined by chiral HPLC IE, *n*-hexane/2-propanol = 60/40, flow rate 0.8 mL/min, λ = 250 nm, retention time: 17.112 min (major), 23.875 min (minor). **^{1}H NMR** (400 MHz, CD_3OD) δ 7.45 (d, *J* = 7.2 Hz, 1H), 7.34-7.28 (m, 4H), 7.26-7.25 (m, 1H), 5.84 (d, *J* = 7.2 Hz, 1H), 4.58 (dd, *J* = 18.0, 14.8 Hz, 2H), 4.05 (dd, *J* = 13.6, 3.6 Hz, 1H), 3.94-3.90 (m, 1H), 3.61 (dd, *J* = 13.6, 7.6 Hz, 1H), 3.52 (d, *J* = 5.2 Hz, 2H). **^{13}C NMR** (150 MHz, CD_3OD) δ 165.8, 160.0, 147.5, 139.8, 129.5, 128.8, 128.3, 96.2, 71.1, 64.7, 53.7, 45.2. **HRMS** (ESI-TOF) calcd for $C_{14}H_{17}N_3NaO_3$ $[M + Na]^+$ 298.1162, found 298.1163.

(*S*)-*N*-(1-(2,3-Dihydroxy-2-methylpropyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (2e) White solid, 14.5 mg, 95% yield, 90% ee. $[\alpha]^{25}_{D}$ = -31.6 (c = 1.7, CH_3OH), m.p. 177.2-178.3 °C. TLC: R_f = 0.41 (dichloromethane:methanol = 30:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, λ = 250 nm, retention time: 28.248 min (minor), 32.724 min (major). **^{1}H NMR** (600 MHz, CD_3OD) δ 8.05 (d, *J* = 7.2 Hz, 1H), 7.98 (d, *J* = 7.8 Hz, 2H), 7.67-7.63 (m, 1H), 7.59-7.53 (m, 3H), 4.06 (dd, *J* = 13.8, *J* = 9.6 Hz, 2H), 3.35 (dd, *J* = 11.4, 6.0 Hz, 2H), 1.20 (s, 3H). **^{13}C NMR** (100 MHz, CD_3OD) δ 169.1, 164.8, 159.9, 152.9, 134.7, 134.1, 129.8, 129.1, 98.2, 73.9, 68.2, 56.6, 22.8. **HRMS** (ESI-TOF) calcd for $C_{15}H_{17}N_3NaO_4$ $[M + Na]^+$ 326.1111, found 326.1116.

(*S*)-*N*-(1-(2-Hydroxy-2-(hydroxymethyl)butyl)-2-oxo-1,2-dihydropyrimidin-4-yl) benzamide (2f) White solid, 15.3 mg, 97% yield, 93% ee. $[\alpha]^{25}_{D}$ = -40.2 (c = 0.6, CH_3OH), m.p. 205.2-206.7 °C. TLC: R_f = 0.43 (dichloromethane:methanol = 30:1) [UV]. The ee value was determined by

chiral HPLC OD-H, *n*-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, λ = 250 nm, retention time: 27.259 min (minor), 33.641 min (major). **^{1}H NMR** (600 MHz, CD_3OD) δ 8.05 (d, *J* = 7.2 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 2H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 6.6 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 2H), 4.20 (d, *J* = 13.8 Hz, 1H), 3.91 (d, *J* = 13.8 Hz, 1H), 3.37 (d, *J* = 11.4 Hz, 1H), 3.27 (d, *J* = 11.4 Hz, 1H), 1.69-1.54 (m, 2H), 0.99 (t, *J* = 7.8 Hz, 3H). **^{13}C NMR** (100 MHz, CD_3OD) δ 164.9, 153.1, 134.7, 134.1, 130.9, 129.8, 129.2, 98.3, 75.7, 64.5, 55.9, 29.0, 7.3. **HRMS** (ESI-TOF) calcd for $C_{16}H_{19}N_3NaO_4$ $[M + Na]^+$ 340.1268, found 340.1270.

(*S*)-*N*-(1-(2-Hydroxy-2-(hydroxymethyl)pentyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (2g) White solid, 14.0 mg, 90% yield, 96% ee. $[\alpha]^{25}_D$ = -43.1 (c = 0.8, CH_3OH), m.p. 151.9-152.6 ^oC. TLC: R_f = 0.39 (dichloromethane:methanol = 35:1) [UV].The ee value was determined by chiral HPLC IA, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 36.190 min (minor), 43.572 min (major). **^{1}H NMR** (400 MHz, CD_3OD) δ 8.04 (d, *J* = 7.2 Hz, 1H), 7.98 (d, *J* = 7.6 Hz, 2H), 7.67-7.53 (m, 4H), 4.19 (d, *J* = 13.9 Hz, 1H), 3.91 (d, *J* = 13.6 Hz, 1H), 3.36 (d, *J* = 11.6 Hz, 1H), 3.26 (d, *J* = 11.6 Hz, 1H), 1.61-1.39 (m, 4H), 0.96 (t, *J* = 6.4 Hz, 3H). **^{13}C NMR** (100 MHz, CD_3OD) δ 164.9, 153.1, 134.7, 134.1, 129.8, 129.2, 101.4, 98.3, 75.6, 65.1, 56.1, 39.0, 17.0, 15.0. **HRMS** (ESI-TOF) calcd for $C_{17}H_{21}N_3NaO_4$ $[M + Na]^+$ 354.1424, found 354.1428.

(*S*)-*N*-(1-(2-Hydroxy-2-(hydroxymethyl)hexyl)-2-oxo-1,2-dihydropyrimidin-4-yl) benzamide (2h) White solid, 15.4 mg, 89% yield, 94% ee. $[\alpha]^{25}_D$ = 31.6 (c =2.2, CH_3OH), m.p. 157.9-158.3 ^oC. TLC: R_f = 0.41 (dichloromethane:methanol = 35:1) [UV]. The ee value was determined by chiral HPLC IE, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 23.802 min (minor), 35.495 min (major). **^{1}H NMR** (400 MHz, CD_3OD) δ 8.04 (d, *J* = 7.2 Hz, 1H), 8.01-7.97 (m, 2H), 7.67-7.53 (m, 4H), 4.19 (d, *J* = 13.6 Hz, 1H), 3.91 (d, *J* = 14.0 Hz, 1H), 3.36 (d, *J* = 11.6 Hz, 1H), 3.26 (d, *J* = 11.6 Hz, 1H), 1.67-1.48 (m, 2H), 1.47-1.31 (m, 4H), 0.95 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, CD_3OD) δ 164.9, 153.1, 134.7, 134.1, 129.8, 129.2, 98.3, 75.6, 65.1, 56.1, 36.4, 25.9, 24.4, 14.4. **HRMS** (ESI-TOF) calcd for $C_{18}H_{23}N_3NaO_4$ $[M + Na]^+$ 368.1581, found 368.1591.

(*S*)-*N*-(1-(2-Hydroxy-2-(hydroxymethyl)-3-methylbutyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (2i) White solid, 13.7 mg, 82% yield, 92% ee. $[\alpha]^{25}_D$ = -40.9 (c = 0.2, CH_3OH), m.p.

162.3-163.2 °C. TLC: R_f = 0.39 (dichloromethane:methanol = 35:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 16.276 min (minor), 19.138 min (major). **^{1}H NMR** (400 MHz, CD_3OD) δ 8.05 (d, *J* = 7.6 Hz, 1H), 7.98-7.97 (m, 2H), 7.66-7.52 (m, 4H), 4.33 (d, *J* = 14.0 Hz, 1H), 3.89 (d, *J* = 14.0 Hz, 1H), 3.44 (d, *J* = 11.6 Hz, 1H), 3.24 (d, *J* = 11.6 Hz, 1H), 2.03-1.96 (m, 1H), 1.04 (t, *J* = 7.2 Hz, 6H). **^{13}C NMR** (100 MHz, CD_3OD) δ 169.1, 164.8, 160.5, 153.3, 134.7, 134.1, 129.8, 129.2, 98.3, 97.0, 77.1, 63.5, 54.7, 33.6, 17.2, 17.0. **HRMS** (ESI-TOF) calcd for $C_{17}H_{21}N_3NaO_4$ $[M + Na]^+$ 354.1424, found 354.1430.

(*S*)-*N*-(1-(2-Hydroxy-2-(hydroxymethyl)-3,3-dimethylbutyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (2j) White solid, 16.1 mg, 93% yield, 94% ee. $[\alpha]^{25}_D$ = 47.33 (c = 1.7, CH_3OH), m.p. 74.9-75.6 °C. TLC: R_f = 0.38 (dichloromethane:methanol = 40:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 23.010 min (minor), 28.112 min (major). **^{1}H NMR** (600 MHz, CD_3OD) δ 8.08 (d, *J* = 7.2 Hz, 1H), 7.99 (d, *J* = 7.8 Hz, 2H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 6.6 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 2H), 4.58 (d, *J* = 14.4 Hz, 1H), 3.96 (d, *J* = 13.8 Hz, 1H), 3.66 (d, *J* = 12.0 Hz, 1H), 3.28 (d, *J* = 12.6 Hz, 1H), 1.10 (s, 9H). **^{13}C NMR** (100 MHz, CD_3OD) δ 164.8, 153.7, 134.7, 134.1, 129.9, 129.2, 98.3, 77.9, 63.7, 53.5, 38.2, 26.1. **HRMS** (ESI-TOF) calcd for $C_{18}H_{23}N_3NaO_4$ $[M + Na]^+$ 368.1581, found 368.1582.

(*S*)-*N*-(1-(2-Cyclohexyl-2,3-dihydroxypropyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (2k) White solid, 16.3 mg, 88% yield, 93% ee. $[\alpha]^{25}_D$ = -30.76 (c = 1.5, CH_3OH), m.p. 214.9-215.7 °C. TLC: R_f = 0.36 (dichloromethane:methanol = 35:1) [UV]. The ee value was determined by chiral HPLC IA, *n*-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, λ = 250 nm, retention time: 13.956 min (minor), 16.616 min (major). **^{1}H NMR** (600 MHz, d^6-DMSO) δ 11.20 (s, 1H), 8.03 (d, *J* = 6.6 Hz, 1H), 8.01 (d, *J* = 7.8 Hz, 2H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 2H), 7.34 (d, *J* = 5.4 Hz, 1H), 4.68-4.62 (m, 2H), 4.12 (d, *J* = 13.8 Hz, 1H), 3.81 (d, *J* = 13.8 Hz, 1H), 3.23 (dd, *J* = 11.4, 7.8 Hz, 1H), 3.09 (dd, *J* = 11.4, 4.2 Hz, 1H), 1.81 (dd, *J* = 23.4, 10.8 Hz, 2H), 1.73 (s, 2H), 1.61 (d, *J* = 10.8 Hz, 1H), 1.50 (t, *J* = 10.2 Hz, 1H), 1.22-1.05 (m, 5H). **^{13}C NMR** (100 MHz, d^6-DMSO) δ 167.2, 163.0, 157.2, 152.1, 133.1, 132.7, 128.5, 95.8, 75.3, 62.1, 52.7, 42.4, 26.5, 26.4, 26.2, 26.1. **HRMS** (ESI-TOF) calcd for $C_{20}H_{25}N_3NaO_4$ $[M + Na]^+$ 394.1737,

found 394.1739.

(*R*)-*N*-(1-(2,3-Dihydroxy-2-(trimethylsilyl)propyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (2l) White solid, 16.4 mg, 91% yield, 95% ee. $[\alpha]^{25}_{D}$ = 53.15 (c =1.0, CH_3OH), m.p. 151.2-152.8 °C. TLC: R_f = 0.34 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, λ = 250 nm, retention time: 24.481 min (minor), 39.200 min (major). **^{1}H NMR** (600 MHz, CD_3OD) δ 8.06 (d, *J* = 7.2 Hz, 1H), 7.98 (d, *J* = 7.8 Hz, 2H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.59 (d, *J* = 7.2 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 2H), 4.47 (d, *J* = 14.4 Hz, 1H), 4.01 (d, *J* = 14.4 Hz, 1H), 3.54 (d, *J* = 11.4 Hz, 1H), 3.40 (d, *J* = 11.4 Hz, 1H), 0.16 (s, 9H). **^{13}C NMR** (150 MHz, CD_3OD) δ 164.8, 153.2, 134.7, 134.1, 129.8, 129.2, 98.1, 70.6, 65.2, 55.0, -3.4. **HRMS** (ESI-TOF) calcd for $C_{17}H_{23}N_3NaSiO_4$ $[M + Na]^+$ 384.1350, found 384.1359.

(*S*)-*N*-(1-(2,3-Dihydroxy-2-phenylpropyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (2m) White solid, 16.9 mg, 93% yield, 99% ee. $[\alpha]^{25}_{D}$ = -38.3 (c = 1.4, CH_3OH), m.p. 147.5-148.2 °C. TLC: R_f = 0.38 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 18.287 min (major), 24.454 min (minor). **^{1}H NMR** (400 MHz, CD_3OD) δ 7.96 (d, *J* = 7.2 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.2 Hz, 1H) 7.54 (dd, *J* = 15.2, 7.6 Hz, 4H), 7.46 (d, *J* = 7.2 Hz, 1H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.27 (t, *J* = 7.2 Hz, 1H), 4.62 (d, *J* = 14.0 Hz, 1H), 4.17 (d, *J* = 14.0 Hz, 1H), 3.78 (d, *J* = 11.6 Hz, 1H), 3.69 (d, *J* = 11.6 Hz, 1H). **^{13}C NMR** (100 MHz, CD_3OD) δ 164.7, 152.7, 143.3, 134.7, 134.1, 129.8, 129.3, 129.2, 128.6, 127.0, 98.0, 78.0, 68.4, 57.2. **HRMS** (ESI-TOF) calcd for $C_{20}H_{19}N_3NaO_4$ $[M + Na]^+$ 388.1268, found 388.1267.

(*S*)-*N*-(1-(2,3-Dihydroxy-2-phenylpropyl)-5-methyl-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (2n) White solid, 15.9 mg, 84% yield, 98% ee. $[\alpha]^{25}_{D}$ = -93.0 (c = 0.4, CH_3OH), m.p. 171.0-171.8 °C. TLC: R_f = 0.36 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC IA, *n*-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, λ = 250 nm, retention time: 23.040 min (minor), 27.874 min (major). **^{1}H NMR** (400 MHz, CD_3OD) δ 8.22 (s, 2H), 7.54 (d, *J* = 7.2 Hz, 3H), 7.45 (t, *J* = 7.2 Hz, 3H), 7.38-7.33 (m, 2H), 7.30-7.26 (m, 1H), 4.37 (d, *J* = 7.2 Hz, 1H), 4.08 (d, *J* = 14.0 Hz, 1H), 3.83 (d, *J* = 11.6 Hz, 1H), 3.73 (d, *J* = 11.6 Hz, 1H), 2.00 (s, 3H).**^{13}C NMR** (100 MHz, CD_3OD) δ 170.2, 165.0, 144.6, 136.2, 132.8, 131.4, 130.9,

130.3, 129.2, 129.0, 128.6, 127.1, 126.5, 109.9, 78.1, 68.7, 12.2. **HRMS** (ESI-TOF) calcd for $C_{21}H_{21}N_3NaO_4$ $[M + Na]^+$ 402.1424, found 402.1429.

(*S*)-*N*-(1-(2,3-Dihydroxy-2-phenylpropyl)-5-fluoro-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (2o) White solid, 16.7 mg, 87% yield, 99% ee. $[\alpha]^{25}_D$ = -79.3 (c = 0.6, CH_3OH), m.p. 162.7-163.5 ^oC. TLC: R_f = 0.37 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 15.469 min (minor), 19.806 min (major). **^{1}H NMR** (600 MHz, CD_3OD) δ 7.99 (d, *J* = 24.0 Hz, 3H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.27 (t, *J* = 7.2 Hz, 1H), 4.48 (d, *J* = 6.0 Hz, 1H), 4.15 (d, *J* = 14.4 Hz, 1H), 3.80 (d, *J* = 11.4 Hz, 1H), 3.71 (d, *J* = 11.4 Hz, 1H). **^{13}C{^{1}H} NMR** (150 MHz, CD_3OD) δ 143.0, 140.5, 138.9, 134.2, 130.5, 130.0, 129.6, 129.5, 129.3，129.2, 128.6, 126.9, 126.3, 77.9, 68.4, 56.9. **HRMS** (ESI-TOF) calcd for $C_{20}H_{18}FN_3NaO_4$ $[M + Na]^+$ 406.1174, found 406.1183.

(*S*)-*N*-(5-Chloro-1-(2,3-dihydroxy-2-phenylpropyl)-2-oxo-1,2-dihydropyrimidin-4-yl) benzamide (2p) White solid, 16.2 mg, 81% yield, 97% ee. $[\alpha]^{25}_D$ = -73.1 (c = 1.2, CH_3OH), m.p. 71.4-72.5 ^oC. TLC: R_f = 0.38 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC AS-H, *n*-hexane/2-propanol = 50/50, flow rate 0.8 mL/min, λ = 250 nm, retention time: 18.957 min (minor), 28.531 min (major). **^{1}H NMR** (400 MHz, CD_3OD) δ 8.36-7.78 (m, 3H), 7.62-7.51 (m, 3H), 7.47 (d, *J* = 6.4 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.27 (t, *J* = 7.2 Hz, 1H), 4.39 (s, 1H), 4.13 (d, *J* = 13.6 Hz, 1H), 3.84 (d, *J* = 11.2 Hz, 1H), 3.72 (d, *J* = 11.6 Hz, 1H). **^{13}C NMR** (100 MHz, CD_3OD) δ 167.4, 150.3, 142.4, 140.1, 135.5, 131.0, 130.7, 129.4, 129.1, 128.6, 125.5, 108.4, 67.4, 55.0, 29.5. **HRMS** (ESI-TOF) calcd for $C_{20}H_{18}ClN_3NaO_4$ $[M + Na]^+$ 422.0878, found 422.0888.

(*S*)-*N*-(5-Bromo-1-(2,3-dihydroxy-2-phenylpropyl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (2q) White solid, 15.9 mg, 72% yield, 98% ee. $[\alpha]^{25}_D$ = -87.7 (c = 0.8, CH_3OH), m.p. 73.9-74.6 ^oC. TLC: R_f = 0.36 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC AS-H, *n*-hexane/2-propanol = 60/40, flow rate 0.8 mL/min, λ = 250 nm, retention time: 23.567 min (minor), 35.255 min (major). **^{1}H NMR** (600 MHz, CD_3OD) δ 8.28 (s, 1H), 7.97 (s, 1H), 7.54 (d, *J* = 7.8 Hz, 4H), 7.46 (s, 2H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.28 (t, *J* = 7.2 Hz, 1H), 4.36 (d, *J* = 12.0 Hz, 1H), 4.13 (d, *J* = 12.6 Hz, 1H), 3.85 (d, *J* = 7.2 Hz, 1H), 3.73 (d, *J* = 11.4 Hz,

1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 156.6, 146.8, 140.4, 133.2, 130.1, 129.0, 128.8, 128.5, 128.4 127.5, 125.5, 100.0, 76.7, 67.1, 55.9. **HRMS** (ESI-TOF) calcd for $C_{20}H_{18}N_3BrNaO_4$ $[M + Na]^+$ 466.0373, found 466.0378.

(*S*)-*N*6-(1-(2,3-Dihydroxy-2-phenylpropyl)-2-oxo-1,2-dihydropyrimidin-4-yl) ditert-butoxycarbonylamide (2r) White solid, 21.7 mg, 94 % yield, 99% ee. $[\alpha]^{25}_D$ =81.1 (c = 1.1, CH_2Cl_2), m.p. 73.1-74.2 °C. TLC: R_f = 0.41 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC IA, *n*-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, λ = 250 nm, retention time: 12.075 min (major), 14.332 min (minor). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.8 Hz, 2H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.91 (d, *J* = 7.2 Hz, 1H), 4.58 (s, 1H), 4.36 (d, *J* = 15.6 Hz, 1H), 4.04 (d, *J* = 14.4 Hz, 1H), 3.87 (d, *J* = 7.8 Hz, 1H), 3.72 (s, 1H), 3.64 (d, *J* = 12.0 Hz, 1H), 1.54 (s, 18H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 162.7, 157.5, 149.5, 149.5, 141.0, 128.8, 128.1, 125.5, 96.6, 85.4, 76.6, 66.8, 57.9, 27.8. **HRMS** (ESI-TOF) calcd for $C_{23}H_{31}N_3NaO_7$ $[M + Na]^+$ 484.2054, found 484.2053.

(*S*)-*N*-(1-(2,3-Dihydroxy-2-phenylpropyl)-2-oxo-1,2-dihydropyrimidin-4-yl)acetamide (2s) White solid, 13.1 mg, 87% yield, 99% ee. $[\alpha]^{25}_D$ =70.8 (c = 1.2, CH_3OH), m.p. 113.1-114.5 °C. TLC: R_f = 0.33 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 21.519 min (major), 31.785 min (minor). **^{1}H NMR** (600 MHz, CD_3OD) δ 7.78 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 2H), 4.59 (d, *J* = 13.8 Hz, 1H), 4.13 (d, *J* = 13.8 Hz, 1H), 3.75 (d, *J* = 11.4 Hz, 1H), 3.67 (d, *J* = 11.4 Hz, 1H), 2.15 (s, 3H). **^{13}C NMR** (100 MHz, CD_3OD) δ 173.0, 164.2, 160.1, 152.5, 143.3, 129.3, 128.6, 127.0, 97.6, 78.0, 68.4, 57.3, 24.5. **HRMS** (ESI-TOF) calcd for $C_{15}H_{17}N_3NaO_4$ $[M + Na]^+$ 326.1111, found 326.1119.

(*S*)-3-Benzoyl-1-(2,3-dihydroxy-2-phenylpropyl)pyrimidine-2,4(1*H*,3*H*)-dione (4a) White solid, 14.9 mg, 79% yield, 98% ee. $[\alpha]^{25}_D$ = 59.5 (c = 0.6, CH_3OH), m.p. 138.4-139.2 °C. TLC: R_f = 0.44 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 15.430 min (major), 20.891 min (minor). **^{1}H NMR** (600 MHz, CD_3OD) δ 7.70 (t, *J* = 7.2Hz, 3H), 7.52 (dd, *J* = 13.2, 7.2 Hz, 5H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 1H), 4.20 (s, 2H), 3.86 (d, *J* = 11.4 Hz, 1H), 3.71 (d, *J* = 11.4 Hz, 1H), 1.84 (s, 3H). **^{13}C NMR** (100 MHz, CD_3OD) δ 170.2,

165.0, 151.9, 144.6, 142.8, 136.2, 132.8, 131.4, 130.3, 129.2, 128.6, 127.1, 109.8, 78.1, 68.7, 54.8, 12.2. **HRMS** (ESI-TOF) calcd for $C_{21}H_{20}N_2NaO_5$ $[M + Na]^+$ 403.1264, found 403.1258.

(*S*)-3-Benzoyl-1-(2,3-dihydroxy-2-phenylpropyl)-5-fluoropyrimidine-2,4(1*H*,3*H*)-dione (4b) White solid, 12.8 mg, 66% yield, 98% ee. $[\alpha]^{25}_D$ = 48.7 (c = 0.5, CH_3OH), m.p. 60.9-61.5 °C. TLC: R_f = 0.42 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 15.812 min (minor), 20.708 min (major). ^{1}H NMR (400 MHz, CD_3OD) δ 7.96 (d, *J* = 6.4 Hz, 1H), 7.77-7.60 (m, 3H), 7.55-7.50 (m, 4H), 7.38-7.28 (m, 3H), 4.24 (d, *J* = 10.4 Hz, 1H), 4.16 (d, *J* = 12.8 Hz, 1H), 3.88 (d, *J* = 11.6 Hz, 1H), 3.70 (d, *J* = 11.2 Hz, 1H). **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 167.1, 156.3 (d, $J_{C\text{-}F}$ = 27 Hz), 149.7, 140.1, 139.6 (d, $J_{C\text{-}F}$ = 237 Hz), 135.6, 132.3, 130.9, 130.7, 130.1 (d, $J_{C\text{-}F}$ = 33 Hz), 129.4, 129.0, 128.8, 128.5, 127.5, 125.5, 77.0, 67.5, 43.5. **HRMS** (ESI-TOF) calcd for $C_{20}H_{17}FN_2NaO_5$ $[M + Na]^+$ 407.1014, found 407.1016.

(*S*)-3-Benzoyl-5-chloro-1-(2,3-dihydroxy-2-phenylpropyl)pyrimidine-2,4(1*H*,3*H*)-dione (4c) White solid, 11.5 mg, 58% yield, 97% ee. $[\alpha]^{25}_D$ = 32.2 (c =0.8, CH_3OH), m.p. 121.3-122.8 °C. TLC: R_f = 0.46 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 15.127 min (major), 19.893 min (minor). **^{1}H NMR** (600 MHz, CD_3OD) δ 8.00 (s, 3H), 7.62 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 2H), 7.51 (d, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.28 (t, *J* = 7.2 Hz, 1H), 4.47 (s, 1H), 4.16 (d, *J* = 13.2 Hz, 1H), 3.81 (d, *J* = 11.4 Hz, 1H), 3.71 (d, *J* = 11.4 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.4, 158.3, 150.3, 142.4, 140.1, 135.5, 131.0, 130.7, 129.4, 129.1, 128.6, 125.5, 108.4, 77.4, 67.4, 55.1. **HRMS** (ESI-TOF) calcd for $C_{20}H_{17}ClN_2NaO_5$ $[M + Na]^+$ 423.0718, found 423.0712.

(*S*)-3-Benzoyl-5-bromo-1-(2,3-dihydroxy-2-phenylpropyl)pyrimidine-2,4(1*H*,3*H*)-dione (4d) White solid, 16.2 mg, 57% yield, 99% ee. $[\alpha]^{25}_D$ = 54.6 (c = 2.1, CH_3OH), m.p. 102.1-103.3 °C. TLC: R_f = 0.44 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 14.675 min (major), 20.778 min (minor). **^{1}H NMR** (600 MHz, CD_3OD) δ 8.03 (s, 1H), 7.74-7.70 (m, 3H), 7.54-7.50 (m, 4H), 7.38-7.28 (m, 3H), 4.23 (s, 2H), 3.89 (d, *J* = 11.2 Hz, 1H), 3.71 (d, *J* = 11.6 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.4, 158.3, 150.3, 142.4, 140.1, 135.5, 131.0,

130.7, 129.4, 129.1, 128.6, 125.5, 108.4, 77.4, 67.4. **HRMS** (ESI-TOF) calcd for $C_{20}H_{17}BrN_2NaO_5$ $[M + Na]^+$467.0213, found 467.0220.

(*S*)-3-Benzoyl-1-(2,3-dihydroxy-2-phenylpropyl)-5-iodopyrimidine-2,4(1*H*,3*H*)-dione (4e) White solid, 11.5 mg, 58% yield, 96% ee. $[\alpha]^{25}_D$ = 58.1 (c = 0.6, CH_3OH), m.p. 150.6-152.1 °C. TLC: R_f= 0.45 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC IA, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 17.465 min (minor), 22.058 min (major). **^{1}H NMR** (600 MHz, CD_3OD) δ 7.96 (d, *J* = 6.0 Hz, 1H), 7.72 (t, *J* = 7.2 Hz, 3H), 7.53 (d, *J* = 7.2 Hz, 4H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.31 (t, *J* = 7.2 Hz, 1H), 4.26 (s, 1H), 4.17 (s, 1H), 3.88 (d, *J* = 11.4 Hz, 1H), 3.70 (d, *J* = 11.4 Hz, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 167.6, 159.2, 150.9, 150.1, 140.1, 135.5, 130.9, 130.6, 129.4, 129.0, 128.5, 125.5, 76.8, 67.3, 67.0. **HRMS** (ESI-TOF) calcd for $C_{20}H_{17}IN_2NaO_5$ $[M + Na]^+$ 515.0074, found 515.0079.

3-(6-Chloro-9*H*-purin-9-yl)-2-phenylpropane-1,2-diol (6a) White solid, 11.2 mg, 74% yield, 98% ee. $[\alpha]^{25}_D$ = -66.8 (c = 1.2, CH_2Cl_2), m.p. 90.1-91.7 °C. TLC: R_f = 0.38 (dichloromethane:methanol = 60:1) [UV]. The ee value was determined by chiral HPLC OD-H, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 10.770 min (major), 18.116 min (minor). **^{1}H NMR** (600 MHz, CD_3OD) δ 8.58 (s, 1H), 8.31 (s, 1H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.21 (t, *J* = 7.2 Hz, 2H), 7.16 (t, *J* = 7.2 Hz, 1H), 4.82-4.70 (m, 2H), 3.90 (d, *J* = 11.4 Hz, 1H), 3.75 (d, *J* = 11.4 Hz, 1H). **^{13}C NMR** (100 MHz, CD_3OD) δ 153.9, 152.6, 150.8, 149.1, 142.5, 131.4, 129.1, 128.6, 126.8, 77.5, 68.6, 52.1. **HRMS** (ESI-TOF) calcd for $C_{14}H_{13}ClN_4O_2$ $[M + H]^+$ 305.0800, found 305.0792.

3-(6-Methoxy-9*H*-purin-9-yl)-2-phenylpropane-1,2-diol (6b) White solid, 11.4 mg, 89% yield, 97% ee. $[\alpha]^{25}_D$ = -63.7 (c = 0.3, CH_2Cl_2), m.p. 102.1-103.4 °C. TLC: R_f = 0.42 (dichloromethane:methanol = 60:1) [UV]. The ee value was determined by chiral HPLC ID, *n*-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, λ = 250 nm, retention time: 24.380 min (minor), 26.692 min (major). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.49 (s, 1H), 7.34-7.26 (m, 5H), 4.59 (d, *J* = 14.4 Hz, 1H), 4.52 (d, *J* = 14.4 Hz, 1H), 4.41 (s, 1H), 4.36 (s, 1H), 4.18 (s, 3H), 3.79 (d, *J* = 12.0 Hz, 1H), 3.65 (d, *J* = 12.0 Hz, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 161.4, 152.2, 152.0, 143.8, 140.6, 128.8, 128.2, 125.3, 121.2, 76.4, 66.8, 54.6, 51.5. **HRMS** (ESI-TOF) calcd for $C_{15}H_{16}N_4NaO_3$ $[M + Na]^+$ 323.1115, found 323.1117.

2-Phenyl-3-(6-(piperidin-1-yl)-9*H*-purin-9-yl)propane-1,2-diol (6c) White solid, 15.8 mg, 85% yield, 98% ee. $[\alpha]^{25}_{D}$ = -82.7 (c = 1.2, CH_2Cl_2), m.p. 113.1-114.2 °C. TLC: R_f = 0.41 (dichloromethane:methanol = 60:1) [UV]. The ee value was determined by chiral HPLC IA, *n*-hexane/2-propanol = 95/5, flow rate 0.8 mL/min, λ = 250 nm, retention time: 60.961 min (minor), 66.002 min (major). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.31-7.27 (m, 5H), 7.21 (s, 1H), 4.52 (d, *J* = 14.4 Hz, 1H), 4.37 (d, *J* = 15.0 Hz, 1H), 4.23 (s, 4H), 3.79 (d, *J* = 12.0 Hz, 1H), 3.56 (d, *J* = 12.0 Hz, 1H), 1.73-1.69 (m, 6H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.9, 152.0, 150.8, 141.1, 139.4, 128.6, 128.0, 125.3, 119.3, 76.2, 66.5, 51.3, 46.5, 26.2, 24.8. **HRMS** (ESI-TOF) calcd for $C_{19}H_{23}N_5NaO_2$ $[M + Na]^+$ 376.1744, found 376.1737.

2-Phenyl-3-(6-(propylthio)-9*H*-purin-9-yl)propane-1,2-diol (6d) Colorless oil, 15.9 mg, 93% yield, 98% ee. $[\alpha]^{25}_{D}$ = -75.9 (c = 1.5, CH_2Cl_2); TLC: R_f = 0.44 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC IA, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 7.883 min (minor), 8.643 min (major). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.52 (s, 1H), 7.38-7.26 (m, 5H), 4.54 (dd, *J* = 22.8, 14.4 Hz, 2H), 4.28 (s, 1H), 4.22 (s, 1H), 3.78 (d, *J* = 12.0 Hz, 1H), 3.65 (d, *J* = 12.0 Hz, 1H), 3.36 (t, *J* = 7.2 Hz, 2H), 1.81 (dd, *J* = 14.4, 7.2 Hz, 2H), 1.08 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 162.7, 151.5, 148.5, 144.1, 140.6, 131.1, 128.9, 128.3, 125.3, 76.3, 66.7, 51.3, 30.9, 23.0, 13.6. **HRMS** (ESI-TOF) calcd for $C_{17}H_{20}N_4NaO_2S$ $[M + Na]^+$ 367.1199, found 367.1205.

(*S*)-4-(2-Amino-6-(benzyloxy)-9*H*-purin-9-yl)-2-(triethylsilyl)butane-1,2-diol (6e) Colorless oil, 21.3 mg, 96% yield, 95% ee $[\alpha]^{25}_{D}$ = 43.17 (c = 0.99, CH_3OH); TLC: R_f = 0.38 (dichloromethane:methanol = 50:1) [UV]. The ee value was determined by chiral HPLC IE, *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 17.813 min (major), 29.852 min (minor). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.41 (d, *J* = 6.8 Hz, 2H), 7.26-7.20 (m, 3H), 5.47 (s, 2H), 5.38 (s, 2H), 4.18 (s, 2H), 3.78 (d, *J* = 11.2 Hz, 1H), 3.65 (d, *J* = 11.2 Hz, 1H), 2.05 (s, 2H), 0.91 (t, *J* = 7.2 Hz, 9H), 0.58 (d, *J* = 7.6 Hz, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 161.2, 159.3, 153.4, 139.6, 136.4, 128.5, 128.3, 128.1, 115.6, 69.7, 68.3, 67.0, 39.8, 36.6, 7.9, 2.0. **HRMS** (ESI-TOF) calcd for $C_{22}H_{34}N_5O_3Si^+$ $[M + H]^+$ 444.2425, found 444.2427.

3-(6-Amino-9*H*-purin-9-yl)-1-phenylpropane-1,2-diol (6f) White solid, 10.8 mg, 76% yield, >20:1 dr, 95% ee $[\alpha]^{25}_{D}$ = 29.56 (c = 0.60, CH_3OH), m.p. 114.3-115.2 °C. TLC: R_f = 0.25

(dichloromethane:methanol = 30:1) [UV]. The ee value was determined by chiral HPLC ID, *n*-hexane/2-propanol = 60/40, flow rate 0.8 mL/min, λ = 250 nm, retention time: 21.720 min (major), 33.050 min (minor). **^{1}H NMR** (600 MHz, d^6-DMSO) δ 8.11 (s, 1H), 8.00 (s, 1H), 7.40 (d, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.25 (t, *J* = 7.2 Hz, 1H), 7.15 (s, 2H), 5.55 (d, *J* = 4.8 Hz, 1H), 5.14 (d, *J* = 6.0 Hz, 1H), 4.58 (d, *J* = 4.8 Hz, 1H), 4.20 (dd, *J* = 13.8, 3.0 Hz, 1H), 4.00-3.98 (m, 1H), 3.90 (dd, *J* = 13.8, 9.6 Hz, 1H). **^{13}C NMR** (150 MHz, d^6-DMSO) δ 155.9, 152.2, 149.6, 142.4, 141.6, 127.8, 127.0, 126.9, 118.6, 73.9, 72.5, 46.1. **HRMS** (ESI-TOF) calcd for $C_{14}H_{16}N_5O_2^+$ $[M + H]^+$ 286.1299, found 286.1293.

3-(6-amino-9H-purin-9-yl)propane-1,2-diol (6h) White solid, 8.6 mg, 82% yield, 35% ee $[\alpha]^{25}_D$ = -7.82 (c = 0.29, CH_3OH). m.p. 212.6-213.3 °C. TLC: R_f = 0.25 (dichloromethane:methanol = 20:1) [UV]. The ee value was determined by chiral HPLC AD-H, *n*-hexane/2-propanol = 80/20, flow rate 0.8 mL/min, λ = 250 nm, retention time: 16.798 min (minor), 20.835 min (major). **^{1}H NMR** (400 MHz, d^6-DMSO) δ 8.13 (s, 1H), 8.02 (s, 1H), 7.17 (s, 2H), 5.09 (d, *J* = 5.6 Hz, 1H), 4.83 (t, *J* = 5.6 Hz, 1H), 4.29 (dd, *J* = 14.0, 3.6 Hz, 1H), 3.99 (dd, *J* = 14.0, 8.0 Hz, 1H), 3.86-3.79 (m, 1H), 3.41-3.36 (m, 1H), 3.31-3.27 (m, 1H). **^{13}C NMR** (150 MHz, d^6-DMSO) δ 155.9, 152.2, 149.7, 141.7, 118.6, 69.7, 63.5, 46.4. **HRMS** (ESI-TOF) calcd for $C_8H_{12}N_5O_2^+$ $[M + H]^+$ 210.0986, found 210.0988.

3-(6-Amino-9*H*-purin-9-yl)-1-(trimethylsilyl)propane-1,2-diol (6i) White solid, 8.9 mg, 63% yield, 98:2 dr, 65% ee $[\alpha]^{25}_D$ = 12.00 (c = 0.30, CH_3OH), m.p. 102.5-103.6 °C. TLC: R_f = 0.45 (dichloromethane:methanol = 40:1) [UV]. The ee value was determined by chiral HPLC AD-H, *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, λ = 250 nm, retention time: 26.622 min (major), 39.662 min (minor), 62.843 min (minor), 73.258 min (minor). **^{1}H NMR** (400 MHz, CD_3OD) δ 8.21 (s, 1H), 8.09 (s, 1H), 4.41-4.29 (m, 2H), 4.04 (ddd, *J* = 8.0, 5.6, 2.4 Hz, 1H), 3.27 (d, *J* = 2.4 Hz, 1H), 0.09 (s, 9H). **^{13}C NMR** (150 MHz, CD_3OD) δ 157.3, 153.6, 150.8, 143.6, 120.0, 72.5, 67.7, 48.6, -2.8. **HRMS** (ESI-TOF) calcd for $C_{11}H_{20}N_5O_2Si^+$ $[M + H]^+$ 282.1381, found 282.1379.

(*R*)-4-(2-Amino-6-(benzyloxy)-9*H*-purin-9-yl)butane-1,2-diol (7e) White solid, 20.3 mg, 62% yield, 95% ee $[\alpha]^{25}_D$ = 59.25 (c = 1.13, CH_3OH), m.p. 143.1-144.2 °C. **TLC**: R_f = 0.35 (dichloromethane:methanol = 30:1) [UV]. The ee value was determined by chiral HPLC IE,

n-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, λ = 250 nm, retention time: 28.148 min (major), 36.647 min (minor). ^{1}H NMR (400 MHz, DMSO) δ 7.83 (s, 1H), 7.54-7.48 (m, 2H), 7.43-7.30 (m, 3H), 6.46 (s, 2H), 5.49 (s, 2H), 4.76 (s, 1H), 4.54 (s, 1H), 4.19-4.01 (m, 2H), 3.32-3.30 (m, 2H), 3.24-3.20 (m, 1H), 2.04-1.89 (m, 1H), 1.71-1.56 (m, 1H). **^{13}C NMR** (150 MHz, d^6-DMSO) δ 160.0, 159.6, 154.4, 140.0, 136.7, 128.5, 128.4, 128.0, 113.7, 68.5, 66.8, 65.8, 39.9, 33.5. **HRMS** (ESI-TOF) calcd for $C_{16}H_{20}N_5O_3^+$ $[M + H]^+$ 330.1561, found 330.1560.

(*R*)-9-(3,4-Dihydroxybutyl)guanine (Buciclovir) White solid, 21.7 mg, 91% yield $[\alpha]^{25}_D$ = 30.12 (c = 0.65, CH_3OH), m.p. 252.1-254.6 ^{o}C. **TLC**: R_f= 0.32 (dichloromethane:methanol = 3:1) [UV]. Due to the analysis conditions of racemic Buciclovir unable to be built, the ee value can not be determined by chiral HPLC. **^{1}H NMR** (400 MHz, d^6-DMSO) δ 10.85 (s, 1H), 7.65 (s, 1H), 6.78 (s, 2H), 4.85 (d, *J* = 4.8 Hz, 1H), 4.65 (t, *J* = 5.6 Hz, 1H), 4.09-3.94 (m, 2H), 3.34-.29 (m, 2H), 3.24-3.19 (m, 1H), 1.95-1.87 (m, 1H), 1.64-1.57 (m, 1H). **^{13}C NMR** (100 MHz, d^6-DMSO) δ 156.8, 153.8, 151.1, 137.5, 116.5, 68.5, 65.8, 39.9, 33.8. **HRMS** (ESI-TOF) calcd for $C_9H_{13}N_5NaO_3^+$ $[M + Na]^+$ 262.0911, found 262.0910.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Details for the optimization of conditions, substrate scope of other N-alkenyladenine, copies of ^{1}H and ^{13}C NMR spectra for all compounds, and HPLC spectra for chiral compounds (PDF)

X-ray data for compounds **4a** and **6e** (CIF)

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Notes

The authors declare no competing financial interest.

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