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Stereoselective synthesis of both enantiomers of 1,4-anhydro-alditols, 1,4-anhydro-2-amino-alditols and D- and L-isonucleosides from 2,3-*O*-isopropylidene-D-glyceraldehyde using iodine-induced cyclization as the key step

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Abstract—We have stereoselectively prepared the enantiomeric 1,4-anhydro-alditols (−)-**15** and (+)-**15**, 1,4-anhydro-2-amino-alditols (−)-**19** and (+)-**19**, and isonucleosides (−)-**22**, (+)-**22** and **25**, from 2,3-*O*-isopropylidene-D-glyceraldehyde. The key step was the iodine-induced cyclization of 4-pentene-1,2,3-triols **2** and **3** to give, respectively, the tetrahydrofuran derivatives **4** and **5**. In these compounds we have optimized the substitution of iodine for oxygen-bearing groups. Results were best when we used potassium superoxide as a nucleophile. © 2001 Elsevier Science Ltd. All rights reserved.

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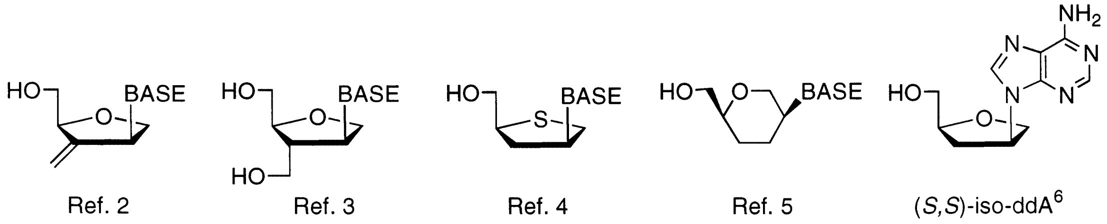
1. Introduction

Isonucleosides are a novel class of nucleosides that have attracted great interest.[1] Over the last few years many isonucleoside derivatives, such as exomethylene-,[2] branched-,[3] 4′-thio-,[4] pyranosyl-,[5] and others (Fig. 1) have been prepared. Isonucleosides are promising therapeutic reagents, as some of them combine strong and selective anti-HIV and anti-HSV activity, together with higher stability towards acids and enzymatic deamination. (*S*,*S*)-*iso*-ddA[6] is a good example (Fig. 1); its anti-HIV activity is similar to that of ddA, and it has no apparent toxicity. The enantiomeric (*R*,*R*)-*iso*-ddA is also active.

The 1,4-anhydro-alditol moieties in isonucleosides are usually prepared from carbohydrates. The most common method is to reduce methyl glycosides by treating them with triethylsilane in the presence of a Lewis acid (Scheme 1).[4a,6a,6c,7] The starting material for synthesizing deoxyderivatives is usually D-xylose, while for hydroxy derivatives, it is D-ribose. Alditol cyclization under Mitsunobu conditions has also been reported.[3f] 1,4-Anhydro-alditols are also synthesized through ring opening–ring closing protocols of sugar precursors.[3c,3d,8] Only a few reports describe the asymmetric synthesis of 1,4-anhydro-alditol units. 1,2,4-Butanetriol,[9] bis-epoxides,[4a] and glycidol,[6b] have been obtained by asymmetric synthesis and used to synthesize isonucleosides (Scheme 1).

The base can be directly introduced by nucleophilic substitution of a sulfonate with base salts.[10] This procedure is efficient for deoxyisonucleosides and purinic



Ref. 2 Ref. 3 Ref. 4 Ref. 5 (*S*,*S*)-iso-ddA[6]

Figure 1.

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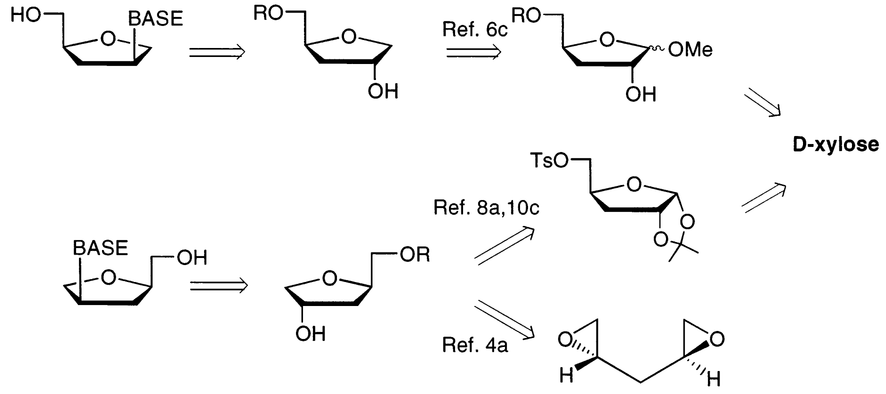


Scheme 1.

bases. For pyrimidinic bases, however, yields are lower. An alternative procedure involves preparing aminoalditols[11] by introducing an amino group, and further constructing the base. The ring opening of an epoxide with a base salt[3c,3d] or ammonia,[12] and the substitution of an alcohol with a base under Mitsunobu conditions[4b,5d,6b,10c] have also been reported.

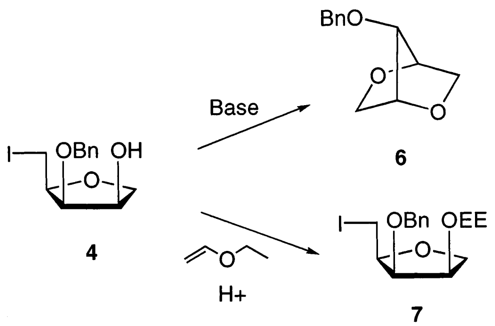
Herein, we report the synthesis of enantiomeric 1,4-anhydro-pentitols and 1,4-anhydro-2-amino-pentitols from 2,3-*O*-isopropylidene-D-glyceraldehyde as the common starting material, and their transformation into enantiomeric D- and L-isonucleosides.

2. Results and discussion

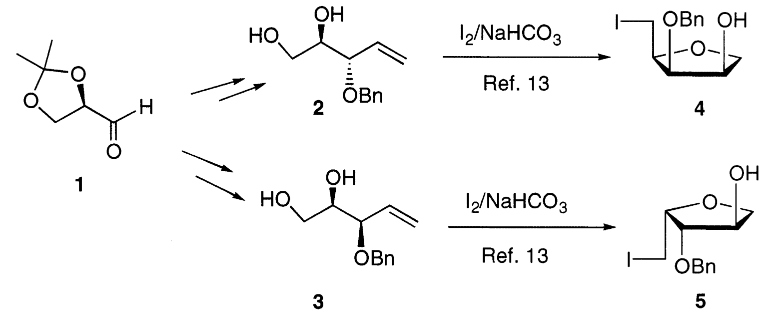
We recently reported the stereoselective synthesis of isomeric substituted tetrahydrofurans **4** and **5** by iodine-induced cyclization of the appropriately protected pentene-triols **2** and **3**, respectively (Scheme 2).[13] Triols **2** and **3** were obtained from 2,3-*O*-isopropylidene-D-glyceraldehyde **1** by reaction with vinylmagnesium bromide, protection of the generated hydroxyl group as its benzyl ether and subsequent acetal hydrolysis.

Tetrahydrofurans **4** and **5** can be transformed into 1,4-anhydro-pentitols by iodine substitution. The initial assays, which involved the treatment of compound **4** with potassium benzoate or potassium *p*-nitrobenzoate, produced the bicyclo derivative **6** via intramolecular substitution (Scheme 3). Similarly, any attempt to protect the hydroxyl group in basic medium led to the bicyclic compound **6**. The hydroxyl group was then protected in acid medium by reaction with ethyl vinyl ether to give **7** as a diastereomeric mixture.

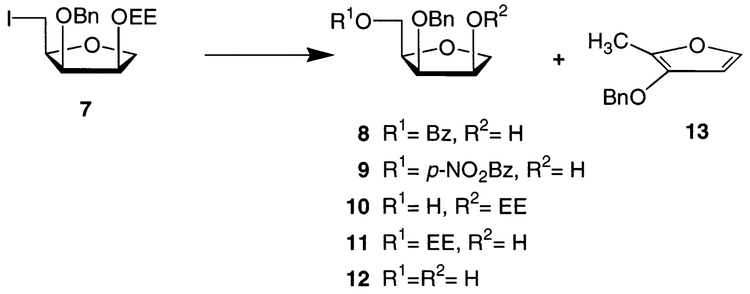
Attempts at the substitution of iodine in compound **7** by reaction with potassium benzoate resulted in formation of the furan derivative **13**, together with small amounts of the substitution product **8** (Table 1, entry 1; Scheme 4). Using potassium *p*-nitrobenzoate as a nucleophile also produced the furan as the major product (entry 2), with small amounts of compound **9**. The presence of the endocyclic oxygen and the β-tertiary carbon hinder the substitution reaction.[3a]



Scheme 3.



Scheme 2.



Scheme 4.

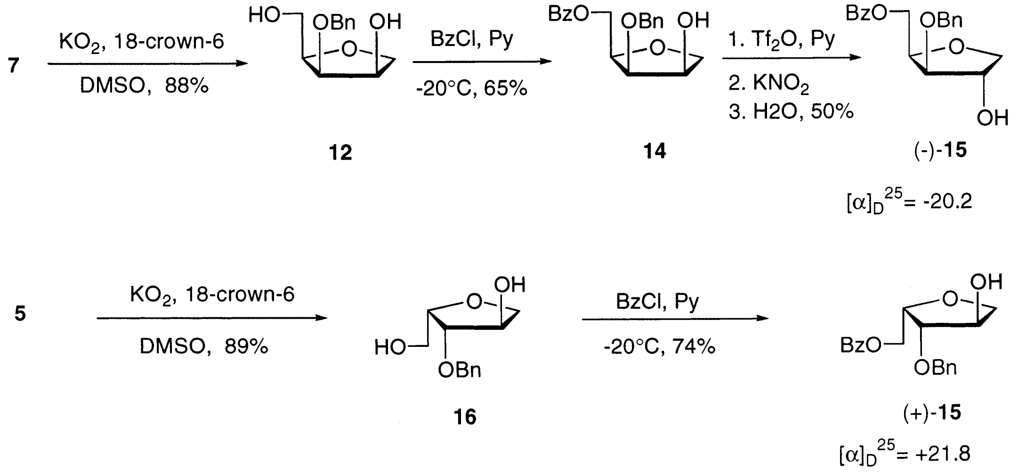
Table 1. Results of iodine substitution reactions of compound **7**

Entry	Conditions	Products	Yields (%)
1	KBzO	**8**, **13**	25, 69
2	K*p*-NO_2BzO	**9**, **13**	30, 50
3	$(Bu_3Sn)_2O/AgNO_3$	–	–
4	KNO_2, 18-crown-6	–	–
5	Co(II)(salen), $NaBH_4$, NaOH, O_2	**2**	37
6	KO_2, 18-crown-6, PPh_3, H_2O	**10**, **11**	53, 24
7	KO_2, 18-crown-6, PPh_3, HCl	**12**	88

We then used bis(tributyltin)oxide in the presence of silver nitrate,[14] but we obtained a complex mixture after several days of reaction (entry 3). The reaction of **7** with potassium nitrite, following a similar procedure to that used for inverting the configuration of secondary alcohols,[15] also gave a complex mixture. We also investigated the substitution of iodine using radical conditions by treating **7** with $NaBH_4$, a catalytic amount of Co(II)(salen), and flushing with dry air. After treatment with acid to deprotect the acetal group, compound **2** was isolated (entry 5). This result can be explained by the formation of a carbanion, instead of a radical and subsequent β-elimination, which opens the ring, and is the opposite of the process that forms **4** from **2** (Scheme 2). When we used potassium superoxide, the nucleophilic substitution was fast and efficient, although the ethyl ethoxide group migrated after the reaction mixture was treated with water, to provide a mixture of compounds **10** and **11**. We solved this problem by treating the reaction mixture with dilute aqueous HCl to deprotect the acetal group, to give 1,4-anhydro-pentitol **12** in 88% yield.

The primary hydroxyl group in compound **12** was protected by reaction with benzoyl chloride to give compound **14** (Scheme 5). The configuration of the secondary alcohol in **14** was inverted by formation of the triflate derivative, reaction with KNO_2 and hydrolysis of the nitrite intermediate to give compound (–)-**15** in a total yield of 50%.

We also used this method starting from the iodo derivative **5**. In this case, intramolecular nucleophilic substitution cannot take place, and compound **5** was treated without protection with potassium superoxide in DMSO to give compound **16** (Scheme 5) in 89% yield. Protecting the primary alcohol by reaction with benzoyl chloride afforded 1,4-anhydro-alditol (+)-**15** in 74% yield. The NMR spectrum and the melting point of compounds (–)-**15** and (+)-**15** were identical, and specific rotation values were very close in absolute value but with opposite sign ($[\alpha]_D^{25}=-20.2$ for (–)-**15** and $[\alpha]_D^{25}=+21.8$ for (+)-**15**), which confirms their enantiomeric nature.

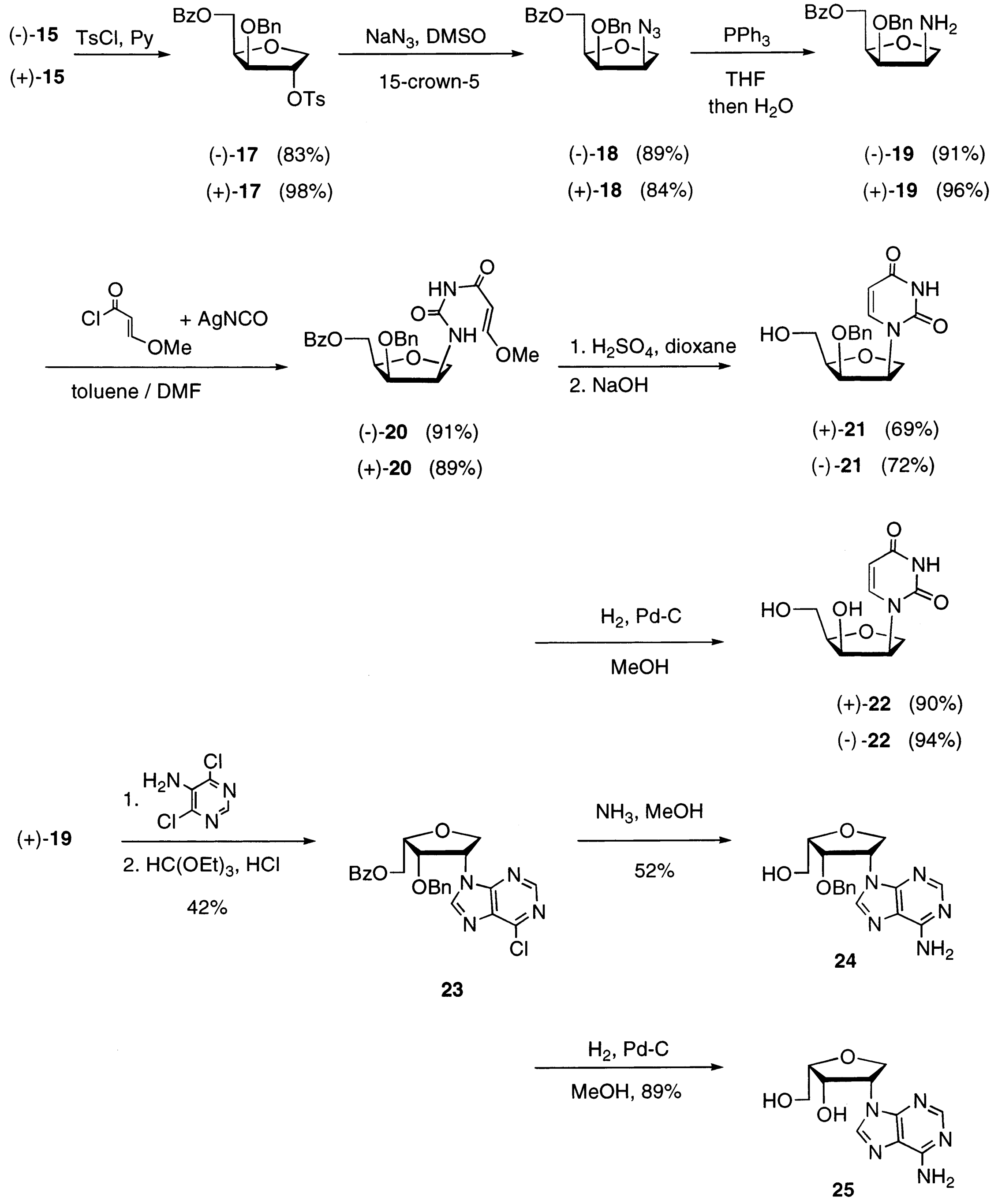


Scheme 5.

Bimolecular nucleophilic substitution starting from a sulfonate is the most common way of introducing the base in isonucleoside synthesis.[6c,7b,8] For this, alcohols (−)-**15** and (+)-**15** were treated with tosyl chloride to obtain tosylates (−)-**17** and (+)-**17** in 83 and 98% yield, respectively (Scheme 6).

To obtain the isonucleoside, we initially treated tosylate (−)-**17** with the potassium salt of adenine, the base that usually produces better yields in this reaction, but only deprotection of the benzoate group was observed. We tried several reaction conditions, but detected no nucleoside. We had obtained good yields in the synthesis of (*S*,*S*)-*iso*-ddA by introducing the bases under Mitsunobu conditions.[6b] However, when we treated (−)-**15** with 3-benzoylthymine using these conditions, isonucleosides were not obtained.

We then decided to introduce an amino group from which the different pyrimidinic and purinic bases could be built up.[11] Compounds (−)-**17** and (+)-**17** were treated with sodium azide in DMF in the presence of 15-crown-5 to provide azido derivatives (−)-**18** and (+)-**18** in goods yields. These compounds were reduced by treatment with triphenylphosphine–water[16] to afford the 1,4-anhydro-2-amino-alditols (−)-**19** and (+)-**19**, respectively, in >90% yield.



Scheme 6.

Treating compounds (−)-**19** and (+)-**19** with *trans*-methoxyacryloyl chloride and silver isocyanate afforded enantiomers (−)-**20** and (+)-**20**, respectively. These were treated first in acid and then in basic medium to give the isonucleosides (+)-**21** and (−)-**21**. Hydrogenolysis of these compounds led to the unprotected enantiomeric isonucleosides (+)-**22** and (−)-**22** in excellent yields.

Purinic nucleosides were also obtained by reaction of (−)-**19** with 5-amino-4,6-dichloropyrimidine and then with trimethylorthoformate in acid medium, to give the 6-chloropurine derivative **23** in 42% yield. The 6-chloropurine moiety in **23** was converted by reaction with ammonia in methanol with concomitant deprotection of the primary hydroxyl group to give **24**. Finally treating **24** under hydrogenolytic conditions provided the fully deprotected isonucleoside **25**.

3. Conclusion

In summary, starting from a common precursor (2,3-*O*-isopropylidene-D-glyceraldehyde), we have synthesized enantiomeric 1,4-anhydro-alditols (−)-**15** and (+)-**15**, 1,4-anhydro-2-aminoalditols (−)-**19** and (+)-**19**, and isonucleosides (+)-**22**, (−)-**22**, and **25**. The synthesis of (+)-**22** from the pentenetriol **2** required 12 steps and the overall yield was 8%. Its enantiomer (−)-**22** required ten steps from the pentenetriol **3** and the overall yield was 27%. Compound **25** was prepared in nine steps from **3** in an overall yield of 10%.

4. Experimental

General comments: melting points are uncorrected. Optical rotations were measured at 25°C in 10 cm cells. ^{1}H and ^{13}C NMR spectra were recorded in a 300 and 400 MHz (75.4 and 100.5 MHz, respectively) apparatus. Coupling constants are given in hertz (Hz). Elemental analyses were determined at the Servei de Recursos Científics (Universitat Rovira i Virgili). TLC was carried out on aluminium sheets precoated with silica gel 60 F_{254}. Flash column chromatography was performed using Kieselgel 60 (particle size: 40–63 μm). Radial chromatography was performed on 1, 2 or 4 mm plates of silica gel, depending on the amount of product. Band separation was monitored by UV. Medium-pressure chromatography (MPLC) was performed using silica gel 60 A CC (6–35 μm). All chromatographic solvents were distilled at atmospheric pressure prior to use. Dry solvents were obtained by conventional methods.[17]

4.1. (2*S*,3*S*,4*R*)-3-Benzyloxy-4-((1*R*/*S*)-(1-ethoxy)-ethoxy)-2-(iodomethyl)tetrahydrofuran 7

Ethyl vinyl ether (1.6 mL, 16.71 mmol) was added to a solution of **4** (1.82 g, 5.44 mmol) in anhydrous CH_2Cl_2. Pyridinium *p*-toluenesulfonate (140 mg, 0.56 mmol) was then added, and the reaction was maintained at rt for 3 h. The reaction was quenched by adding ethyl ether (20 mL), and washed with saturated aqueous $NaHCO_3$ (8 mL), brine (8 mL) and water (16 mL). The organic phase was separated, dried with $MgSO_4$, filtered and evaporated to dryness. The residue was purified by MPLC using a linear gradient [hexane to hexane/ethyl acetate (4:1)] to obtain diastereoisomeric mixture **7** as a syrup (2.13 g, 96%). Data from the spectrum of the diastereomeric mixture. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.5–7.2 (m, 10H, 2×Ph), 5.0–4.5 (m, 6H, 2×CH_2Ph, 2×H_{acetal}), 4.5–3.8 (m, 10H, 2×H-5, 2×H-5′, 2×H-4, 2×H-3, 2×H-2), 3.7–3.2 (m, 8H, 2×OCH_2Me, 2×H-6, 2×H-6′), 1.4–1.1 (m, 12H, 4×CH_3); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 138.3, 138.0, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7 (2×Ph), 99.7, 99.2 (2C_{acetal}), 80.5, 80.2 (2×C-2), 78.2 (C-3, 2 C), 75.3, 74.1 (2×CH_2Ph), 73.8, 73.6 (2×C-5), 70.6, 69.8 (2×C-4), 61.4, 59.7 (2×OCH_2Me), 20.1 (CH_3), 19.9 (CH_3), 15.1 (CH_3, 2C), 4.1, 3.8 (2×C-6).

4.2. (3*R*,4*R*,5*R*)-4-(Benzyloxy)-5-(hydroxymethyl)-tetrahydrofuranol 12

Melted 18-crown-6 (1.48 g, 5.60 mmol) and potassium superoxide (400 mg, 5.63 mmol) were added to a solution of the diastereomeric mixture **7** (569 mg, 1.40 mmol) in anhydrous dimethylsulfoxide (14 mL). After 1 min the reaction mixture was diluted with ethyl ether and poured into brine. The organic phase was separated and the aqueous phase was extracted with ethyl acetate. Triphenylphosphine (a few mg) was added to the organic phase, which was then washed with aqueous HCl (1N), water, dried with $MgSO_4$ and evaporated. The resulting reaction crude was purified by CC (CH_2Cl_2/MeOH 50:1) to obtain **12** as a syrup (275 mg, 88%); $[\alpha]_D^{25}=-25.4$ (*c* 1.70, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.5–7.3 (m, 5H, Ph), 4.76 (d, 1H, $J_{AB}=11.8$ Hz, CH_2Ph), 4.53 (d, 1H, $J_{AB}=11.8$ Hz, CH_2Ph), 4.23 (bs, 1H, H-3), 4.21 (dd, 1H, $J_{4,5}=7.7$ Hz, $J_{3,4}=5.0$ Hz, H-4), 4.07 (dt, 1H, $J_{5,6}\approx J_{5,6'}=3.3$ Hz, H-5), 3.95 (dd, 1H, $J_{2,2'}=10.3$ Hz, $J_{2,3}=1.2$ Hz, H-2), 3.80 (m, 2H, H-2′, H-6), 3.71 (dd, 1H, $J_{6,6'}=12.2$ Hz, $J_{5,6'}=3.4$ Hz, H-6′), 3.14 (bs, 1H, OH), 2.14 (bs, 1H, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 137.2, 128.5, 128.0, 127.7 (Ph), 78.9 (C-4), 78.2 (C-5), 73.3 (C-2), 72.5 (CH_2Ph), 69.2 (C-3), 60.9 (C-6). Anal. calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 63.92, H, 7.21%.

4.3. (3*R*,4*R*,5*R*)-5-[(Benzoyloxy)methyl]-4-(benzyloxy)-tetrahydrofuran-3-ol 14

A solution of diol **12** (192 mg, 0.86 mmol) in anhydrous pyridine (1 mL) was cooled at −20°C and benzoyl chloride (100 μL, 0.86 mmol) was then added. After 1.5 h the reaction was quenched by pouring into aqueous HCl (1N) and extracted five times with CH_2Cl_2. The organic phase was dried with $MgSO_4$ and evaporated. The remaining residue was purified by CC (hexane/ethyl acetate 2:1) to obtain **14** as a syrup (183 mg, 65%); $[\alpha]_D^{25}=+13.4$ (*c* 1.80, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.06 (d, 2H, $J=8.4$ Hz, Ph), 7.5 (t, 1H, $J=7.2$ Hz, Ph), 7.4 (t, 2H, $J=7.6$ Hz, Ph), 7.4–7.2 (m, 5H, Ph), 4.69 (s, 2H, 2×CH_2Ph), 4.64 (dd, 1H, $J_{6,6'}=11.7$ Hz, $J_{5,6}=3.9$ Hz, H-6), 4.49 (dd, 1H, $J_{6,6'}=11.7$ Hz, $J_{5,6'}=7.2$ Hz, H-6′), 4.38–4.26 (m, 2H, H-5, H-3), 4.21 (dd, 1H, $J=6.3$ Hz, $J'=5.4$ Hz, H-4), 3.93 (dd, 1H, $J_{2,2'}=10.0$ Hz, $J_{2,3}=3.2$ Hz, H-2), 3.85 (dd, 1H, $J_{2,2'}=10.0$ Hz, $J_{2',3}=4.5$ Hz, H-2′), 2.74 (d, 1H, $J_{3,\mathrm{OH}}=6.0$ Hz, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 166.2 (C=O), 136.7, 132.8, 129.8, 129.4, 128.4, 128.1, 128.1, 127.7 (Ph), 78.9 (C-4), 77.0 (C-5), 73.6 (C-2), 72.5 (CH_2Ph), 70.3 (C-3), 63.9 (C-6). Anal. calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.55, H, 6.47%.

4.4. (3*S*,4*R*,5*R*)-5-[(Benzoyloxy)methyl]-4-(benzyloxy)tetrahydrofuran-3-ol (−)-15

Anhydrous pyridine (140 μL, 1.73 mmol) was added to a solution of **14** (122 mg, 0.37 mmol) in anhydrous CH_2Cl_2 (1.5 mL) under an argon atmosphere. The resulting solution was cooled in ice/salt for 10 min. Triflic anhydride (70 μL, 0.42 mmol) was then added dropwise, and the reaction was allowed to warm to rt. After 30 min the reaction mixture was filtered over a neutral silica gel pad and the solution was evaporated to dryness. The resulting syrup was dissolved in DMF (12 mL) and potassium nitrite (190 mg, 2.23 mmol), and 18-crown-6 (100 mg, 0.38 mmol) was added. The reaction mixture was stirred at rt until it became homogeneous and greenish (1 h approx.). The reaction was quenched by adding water (40 μL, 2.20 mmol) via syringe and maintaining the stirring overnight. The reaction mixture was then poured into an aqueous solution of ammonium chloride and was extracted five times with CH_2Cl_2. The organic phase was dried with $MgSO_4$ and evaporated. The resulting reaction crude was purified by CC (hexane/ethyl acetate 2:1) to obtain **15** as a white powder (61 mg, 50%); mp 74–76°C; $[\alpha]_D^{25}=-20.2$ (*c* 1.10, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.04 (d, 2H, $J=7.2$ Hz, Ph), 7.56 (t, 1H, $J=7.4$ Hz, Ph), 7.42 (t, 2H, $J=7.5$ Hz, Ph), 7.34–7.26 (m, 5H, Ph), 4.69 (d, 1H, $J=12.0$ Hz, CH_2Ph), 4.64–4.46 (m, 3H, H-6, H-6′, H-5), 4.56 (d, 1H, $J=12.0$ Hz, CH_2Ph), 4.42 (bs, 1H, H-3), 4.21 (dd, 1H, $J_{2,2'}=9.8$ Hz, $J_{2,3}=4.2$ Hz, H-2), 3.99 (dd, 1H, $J_{4,5}=4.2$ Hz, $J_{3,4}=1.8$ Hz, H-4), 3.78 (dd, 1H, $J_{2,2'}=9.8$ Hz, $J_{2',3}=1.9$ Hz, H-2′), 2.00 (bs, 1H, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 166.5 (C=O), 137.4, 133.0, 129.9, 129.6, 128.5, 128.3, 127.9, 127.6 (Ph), 84.4 (C-4), 77.9 (C-5), 74.3 (C-3), 73.7 (C-2), 72.0 (CH_2Ph), 63.5 (C-6). Anal. calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.25, H, 6.36%.

4.5. (3*R*,4*S*,5*S*)-4-(Benzyloxy)-5-(hydroxymethyl)tetrahydrofuran-3-ol (−)-16

Melted 18-crown-6 (310 mg, 1.17 mmol) and potassium superoxide (83 mg, 1.17 mmol) was added to a solution of **5** (97 mg, 0.29 mmol) in anhydrous DMSO (3 mL). After 5 min at rt, the reaction was quenched by pouring it into brine and extracted three times with ethyl acetate. The aqueous solution was acidified with aqueous HCl (1N) and extracted with ethyl acetate. Triphenylphosphine (a few mg) was added to the organic phase, which was dried with $MgSO_4$ and evaporated. The resulting crude product was purified by CC (CH_2Cl_2 to CH_2Cl_2/MeOH 50:1) to obtain (−)-**16** as a syrup (58 mg, 89%); mp 45–47°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.4–7.2 (m, 5H, Ph), 4.68 (d, 1H, $J_{AB}=11.8$ Hz, CH_2Ph), 4.52 (d, 1H, $J_{AB}=11.8$ Hz, CH_2Ph), 4.36 (dt, 1H, $J_{2,3}=4.1$ Hz, $J_{3,4}\approx J_{2',3}=2.0$ Hz, H-3), 4.18 (q, 1H, $J_{4,5}\approx J_{5,6}\approx J_{5,6'}=5.0$ Hz, H-5), 4.12 (dd, 1H, $J_{2,2'}=9.8$ Hz, $J_{2,3}=4.4$ Hz, H-2), 4.00 (dd, 1H, $J_{4,5}=4.8$ Hz, $J_{3,4}=1.5$ Hz, H-4), 3.86 (dd, 1H, $J_{6,6'}=12.1$ Hz, $J_{5,6}=5.4$ Hz, H-6), 3.79 (dd, 1H, $J_{6,6'}=12.1$ Hz, $J_{5,6'}=4.8$ Hz, H-6′), 3.72 (dd, 1H, $J_{2,2'}=9.8$ Hz, $J_{2',3}=2.4$ Hz, H-2′), 3.0 (bs, 1H, OH), 2.8 (bs, 1H, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 137.4, 128.6, 128.0, 127.6 (Ph), 85.2 (C-4), 80.0 (C-5), 74.9 (C-3), 73.3 (C-2), 72.3 (CH_2Ph), 61.6 (C-6). Anal. calcd for $C_{12}H_{16}O_4$: C, 69.27; H, 7.50. Found: C, 69.42, H, 7.50%.

4.6. (3*R*,4*S*,5*S*)-5-[(Benzoyloxy)methyl]-4-(benzyloxy)tetrahydrofuran-3-ol (+)-15

The procedure used for preparing (−)-**15** was followed starting from (+)-**16** (65 mg, 0.29 mmol), anhydrous pyridine (1 mL) and benzoyl chloride (35 μL, 0.30 mmol) to obtain (+)-**15** as a white solid (70 mg, 74%); mp 75–76°C; $[\alpha]_D^{25}=+21.8$ (*c* 1.215, $CHCl_3$). Anal. calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.63, H, 6.51%.

4.7. (2*R*,3*S*,4*S*)-2-[(Benzoyloxy)methyl]-3-(benzyloxy)-4-(*p*-toluensulfonyloxy)tetrahydrofuran (−)-17

A solution of alcohol (−)-**15** (108 mg, 0.33 mmol) in anhydrous pyridine (1 mL) was cooled at −10°C for 1 h and tosyl chloride (190 mg, 0.50 mmol) was then added. The reaction mixture was maintained at 4°C for 3 days and then quenched by pouring it into HCl 1N. The aqueous solution was extracted with CH_2Cl_2, and the organic phase was dried with $MgSO_4$, filtered and evaporated. The residue was purified by CC (hexane/ethyl acetate 5:1) to obtain (−)-**17** as a syrup (132 mg, 83%); $[\alpha]_D^{25}=-32.50$ (*c* 1.178, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.98 (d, 2H, $J=7.8$ Hz, Bz), 7.78 (d, 2H, $J=8.0$ Hz, Ts), 7.56 (t, 1H, $J=7.4$ Hz, Bz), 7.42 (t, 2H, $J=7.5$ Hz, Bz), 7.35 (d, 2H, $J=8.0$ Hz, Ts), 7.32–7.22 (m, 5H, Ph), 5.01 (dt, 1H, $J_{5,4}=4.4$ Hz, $J_{4,3}\approx J_{5',4}=1.6$ Hz, H-4), 4.61 (d, 1H, $J_{AB}=12.0$ Hz, CH_2Ph), 4.52 (dd, 1H, $J_{6,6'}=11.4$ Hz, $J_{2,6}=5.1$ Hz, H-6), 4.46 (dd, 1H, $J_{6,6'}=11.4$ Hz, $J_{2,6'}=6.4$ Hz, H-6′), 4.45 (d, 1H, $J_{AB}=12.0$ Hz, CH_2Ph), 4.33 (ddd, 1H, $J_{2,6'}=6.4$ Hz, $J_{2,6}=5.1$ Hz, $J_{3,2}=4.2$ Hz, H-2), 4.22 (dd, 1H, $J_{3,2}=4.2$ Hz, $J_{4,3}=1.2$ Hz, H-3), 4.18 (dd, 1H, $J_{5,5'}=10.8$ Hz, $J_{5,4}=4.4$ Hz, H-5), 3.81 (dd, 1H, $J_{5,5'}=10.8$ Hz, $J_{5',4}=1.8$ Hz, H-5′), 2.44 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 166.2 (C=O), 145.4, 136.8, 133.2, 133.0, 130.0, 129.7, 129.6, 128.5, 128.3, 128.1, 127.8, 127.7 (Ar), 82.1 (C-3), 81.4 (C-4), 78.1 (C-2), 72.1 (CH_2Ph), 70.9 (C-5), 62.6 (C-6), 21.6 (CH_3). Anal. calcd for $C_{26}H_{26}O_7S$: C, 64.72; H, 5.43; S, 6.64. Found: C, 64.63; H, 6.51; S, 6.73%.

4.8. (2*S*,3*R*,4*R*)-2-[(Benzoyloxy)methyl)]-3-(benzyloxy)-4-(*p*-toluensulfonyloxy)tetrahydrofuran (+)-17

The procedure used for preparing (−)-**17** was followed starting from (+)-**15** (195 mg, 0.59 mmol), anhydrous pyridine (1 mL) and tosyl chloride (340 mg, 0.90 mmol) to give (+)-**17** as a syrup (280 mg, 98%); $[\alpha]_D^{25}=+31.5$ (*c* 1.230, $CHCl_3$). Anal. calcd for $C_{26}H_{26}O_7S$: C, 64.72; H, 5.43; S, 6.64. Found: C, 64.58; H, 6.41; S, 6.59%.

4.9. (2*R*,3*R*,4*R*)-4-Azido-2-[(benzoyloxy)methyl]-3-(benzyloxy)tetrahydrofuran (−)-18

To a solution of **17** (111 mg, 0.23 mmol) in anhydrous DMSO (1 mL), NaN_3 (45 mg, 0.69 mmol) and 15-crown-5 (140 μL, 0.70 mmol) was added. The reaction mixture was heated to 100°C overnight, quenched by pouring it into brine, and the resulting solution was extracted five times with ethyl ether. The organic phase was dried with $MgSO_4$, filtered and evaporated. The residue was purified by CC (hexane/ethyl acetate 5:1) to afford (−)-**18** as a syrup (72 mg, 89%); ^1H NMR ($CDCl_3$, 300 MHz): δ 8.04 (d, 2H, $J=8.1$ Hz, Bz), 7.55 (t, 1H, $J=7.5$ Hz, Bz), 7.42 (t, 2H, $J=7.4$ Hz, Bz), 7.4–7.2 (m, 5H, Ph), 4.82 (d, 1H, $J_{AB}=11.8$ Hz, CH_2Ph), 4.63 (d, 1H, $J_{AB}=11.8$ Hz, CH_2Ph), 4.62 (dd, 1H, $J_{6,6'}=11.7$ Hz, $J_{2,6}=3.9$ Hz, H-6), 4.50 (dd, 1H, $J_{6,6'}=11.7$ Hz, $J_{2,6'}=7.5$ Hz, H-6′), 4.4–4.3 (m, 2H, H-5, H-2), 4.0–3.9 (m, 3H, H-5′, H-4, H-3); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 166.3 (C=O), 136.9, 133.0, 129.9, 129.6, 128.5, 128.3, 128.1, 127.8 (Ph), 79.3 (C-2), 77.6 (C-3), 73.8 (CH_2Ph), 69.2 (C-5), 63.9 (C-6), 61.0 (C-4); IR (CH_2Cl_2, cm^{-1}): 2924 (m), 2107 (s), 1717 (s), 1455 (m), 1328 (w), 1266 (s), 1104 (m), 967 (w), 703 (m), 545 (w).

4.10. (2*S*,3*S*,4*S*)-4-Azido-2-[(benzoyloxy)methyl]-3-(benzyloxy)tetrahydrofuran (+)-18

A similar procedure to that used for the preparation of (−)-**17** was followed starting from (+)-**17** (186 mg, 0.39 mmol), anhydrous DMSO (1 mL), NaN_3 (75 mg, 1.15 mmol) and 15-crown-5 (230 μL, 1.15 mmol) to afford (+)-**18** as a syrup (114 mg, 84%).

4.11. (2*R*,3*R*,4*R*)-4-Amino-2-[(benzoyloxy)methyl]-3-(benzyloxy)tetrahydrofuran (−)-19

Triphenylphosphine (70 mg, 0.27 mmol) was added to a solution of (−)-**18** (69 mg, 0.20 mmol) in anhydrous THF (1 mL). The reaction mixture was maintained at rt for 2.5 h. Water (60 μL, 3.33 mmol) was then added and the reaction mixture was heated under reflux for 1 h. The solvent was evaporated and the residue was purified by CC (CH_2Cl_2 and then CH_2Cl_2/MeOH 50:1) to obtain **19** as a white solid (58 mg, 91%); mp 53–54°C; $[\alpha]_D^{25}=-7.1$ (*c* 0.824, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 8.05 (d, 2H, $J=8.4$ Hz, Bz), 7.56 (t, 1H, $J=7.5$ Hz, Bz), 7.43 (t, 2H, $J=7.6$ Hz, Bz), 7.4–7.2 (m, 5H, Ph), 4.70 (s, 2H, CH_2Ph), 4.60 (dd, 1H, $J_{6,6'}=11.5$ Hz, $J_{2,6}=5.0$ Hz, H-6), 4.50 (dd, 1H, $J_{6,6'}=11.5$ Hz, $J_{2,6'}=7.2$ Hz, H-6′), 4.36 (dt, 1H, $J_{2,6'}=7.2$ Hz, $J_{3,2}\approx J_{2,6}=4.8$ Hz, H-2), 4.05 (t, 1H, $J_{4,3}\approx J_{3,2}=4.6$ Hz, H-3), 3.94 (bs, 1H, H-4), 3.65–3.55 (m, 2H, H-5, H-5′), 1.58 (bs, 2H, NH_2); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 166.4 (C=O), 137.5, 133.0, 129.9, 129.6, 128.5, 128.3, 128.1, 127.9 (Ph), 80.3 (C-3), 78.8 (C-2), 74.3 (C-5), 72.5 (CH_2Ph), 64.1 (C-6), 54.7 (C-4); IR (CH_2Cl_2, cm^{-1}): 3500 (s), 2924 (m), 2856 (m), 1714 (s), 1449 (s), 1270 (s), 1114 (m), 707 (m). Anal. calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.61; H, 6.61; N, 4.20%.

4.12. (2*S*,3*S*,4*S*)-4-Amino-2-[(benzoyloxy)methyl]-3-(benzyloxy)tetrahydrofuran (+)-19

A similar procedure to that used in the preparation of (−)-**19** was followed starting from (+)-**18** (72 mg, 0.20 mmol), anhydrous THF (1 mL), triphenylphosphine (75 mg, 0.29 mmol) and water (60 μL, 3.33 mmol) to give (+)-**19** as a white solid (64 mg, 96%); mp 50–53°C; $[\alpha]_D^{25}=+6.5$ (*c* 1.1045, $CHCl_3$). Anal. calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.41; H, 6.71; N, 4.09%.

4.13. (2*R*,3*R*,4*R*)-2-[(Benzoyloxy)methyl]-3-(benzyloxy)-4-[[[(3-methoxy-1-oxo-2-(*E*)-propenyl)amino]carbonyl]-amino]tetrahydrofuran (−)-20

trans-Methoxyacryloyl chloride (34 mg, 0.28 mmol) was added under an argon atmosphere to a suspension of silver isocyanate (65 mg, 0.43 mmol) in anhydrous toluene (1 mL). The reaction mixture was heated under reflux for 0.5 h and cooled to rt. Compound **19** (31 mg, 0.09 mmol) dissolved in DMF (1 mL) was then added. The reaction was maintained for 1 day at rt and then evaporated under vacuum. The residue was purified by CC (CH_2Cl_2 to CH_2Cl_2/MeOH 50:1) to give (−)-**20** as a white solid (39 mg, 91%); mp 119–121°C; $[\alpha]_D^{25}=-32.5$ (*c* 1.520, $CHCl_3$); UV ($CHCl_3$) λ_{max} 244 nm; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.61 (s, 1H, NH), 9.25 (d, 1H, $J_{NH,3}=7.6$ Hz, NH), 8.04 (d, 2H, $J=8.0$ Hz, Bz), 7.70 (d, 1H, $J_{2',3'}=12.2$ Hz, H-3′), 7.56 (t, 1H, $J=7.4$ Hz, Bz), 7.43 (t, 2H, $J=7.8$ Hz, Bz), 7.4–7.2 (m, 5H, Ph), 5.33 (d, 1H, $J_{2',3'}=12.2$ Hz, H-2′), 4.78 (d, 1H, $J_{AB}=11.6$ Hz, CH_2Ph), 4.62–4.52 (m, 2H, H-4, H-6a, CH_2Ph), 4.48 (dd, 1H, $J_{6a,6b}=11.8$ Hz, $J_{2,6b}=7.3$ Hz, H-6b), 4.34 (dt, 1H, $J_{2,6b}=7.3$ Hz, $J_{3,2}\approx J_{2,6a}=4.8$ Hz, H-2), 4.25 (t, 1H, $J_{4,3}\approx J_{3,2}=5.2$ Hz, H-3), 4.05 (dd, 1H, $J_{5a,5b}=8.4$ Hz, $J_{5a,4}=7.2$ Hz, H-5a), 3.86 (t, 1H, $J_{5a,5b}\approx J_{5b,4}=8.0$ Hz, H-5b), 3.74 (s, 1H, OCH_3); ^{13}C NMR ($CDCl_3$, 100.5 MHz): δ 167.6 (C=O), 166.3 (C=O), 163.8 (C-3′), 155.2 (C=O), 136.9, 133.0, 129.8, 129.6, 128.5, 128.4, 128.3, 128.1 (Ph), 97.3 (C-2′), 78.9 (C-3), 77.9 (C-2), 74.4 (C-5), 70.3 (CH_2Ph), 63.6 (C-6), 57.9 (OCH_3), 52.2 (C-4). Anal. calcd for $C_{24}H_{26}N_2O_7$: C, 63.43; H, 5.77; N, 6.26. Found: C, 63.11; H, 5.92; N, 5.92%.

4.14. (2*S*,3*S*,4*S*)-2-[(Benzoyloxy)methyl]-3-(benzyloxy)-4-[[[(3-methoxy-1-oxo-2-(*E*)-propenyl)amino]carbonyl]-amino]tetrahydrofuran (+)-20

A similar procedure to that used for the preparation of (−)-**19** was followed starting from (+)-**19** (156 mg, 0.48 mmol) *trans*-methoxyacryloyl chloride (172 mg, 1.42 mmol), silver isocyanate (330 mg, 2.20 mmol) and DMF (2 mL) to give (+)-**20** as a white solid (193 mg, 89%); mp 118–120°C; $[\alpha]_D^{25}=+30.7$ (*c* 0.832, $CHCl_3$). Anal. calcd for $C_{24}H_{26}N_2O_7$: C, 63.43; H, 5.77; N, 6.26. Found: C, 63.13; H, 5.93; N, 6.24%.

4.15. 1-[(3*R*,4*R*,5*R*)-4-(Benzyloxy)-5-(hydroxymethyl)-tetrahydrofuran-3-yl]uracil (+)-21

Aqueous H_2SO_4 (2 M, 2 mL) was added to a solution of (−)-**20** (89 mg, 0.20 mmol) in dioxane (2 mL). The reaction mixture was heated under reflux for 18 h, cooled, neutralized with aqueous NaOH solution (2 M) and the solvent was evaporated under vacuum. The residue was dissolved in ethanol and the solids were filtered off. The solution was evaporated and the residue purified by radial chromatography (CH_2Cl_2/MeOH 50:1) to give (+)-**21** as a white foam (43 mg, 69%); mp 45°C (dec.); $[\alpha]^{25}_{\mathrm{D}} = +81.6$ (*c* 1.513, $CHCl_3$); UV ($CHCl_3$) $\lambda_{\max}$ 266 nm; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.04 (bs, 1H, NH), 7.61 (d, 1H, $J_{5,6} = 8.1$ Hz, H-6), 7.4–7.2 (m, 5H, Ph), 5.72 (d, 1H, $J_{5,6} = 8.1$ Hz, H-5), 5.46 (td, 1H, $J_{2'',3'} \approx J_{3',4'} = 6.9$ Hz, $J_{2',3'} = 3.5$ Hz, H-3′), 4.43 (d, 1H, $J_{\mathrm{AB}} = 11.4$ Hz, CH_2Ph), 4.40 (m, 1H, H-4′), 4.35 (d, 1H, $J_{\mathrm{AB}} = 11.4$ Hz, CH_2Ph), 4.10 (dd, 1H, $J_{2',2''} = 10.6$ Hz, $J_{2',3'} = 3.5$ Hz, H-2′), 4.0–3.8 (m, 4H, H-2′, H-5′, H-6′, H-6″), 2.4 (bs, 1H, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 163.7 (C=O), 151.5 (C=O), 143.5 (C-6), 136.1, 128.7, 128.5, 128.0 (Ph), 101.8 (C-5), 82.2 (C-5′), 78.7 (C-4′), 74.2 (CH_2Ph), 70.0 (C-2′), 61.0 (C-6′), 55.8 (C-3′). Anal. calcd for $C_{16}H_{18}N_2O_5$: C, 60.37; H, 5.70; N, 8.80. Found: C, 60.17; H, 5.83; N, 8.65%.

4.16. 1-[(3*S*,4*S*,5*S*)-4-(Benzyloxy)-5-(hydroxymethyl)-tetrahydrofuran-3-yl]uracil (−)-21

A similar procedure to that used for the preparation of (+)-**21** was followed, starting from (+)-**20** (159 mg, 0.65 mmol), H_2SO_4 (2 M, 3.5 mL), and dioxane (3.5 mL) to give (−)-**21** as a white foam (80 mg, 72%); mp 45°C (dec.); $[\alpha]^{25}_{\mathrm{D}} = -83.5$ (*c* 1.214, $CHCl_3$). Anal. calcd for $C_{16}H_{18}N_2O_5$: C, 60.37; H, 5.70; N, 8.80. Found: C, 60.43; H, 5.85; N, 8.61%.

4.17. 1-[(3*R*,4*R*,5*R*)-4-Hydroxy-5-(hydroxymethyl)-tetrahydrofuran-3-yl]uracil (+)-22

To a solution of (+)-**21** (37 mg, 0.12 mmol) in MeOH (3 mL) was added Pd/C (10%, 40 mg). The reaction mixture was maintained overnight under hydrogen (1 atm) with vigorous stirring. The catalyst was removed by filtration and the solvent was evaporated. The residue was purified by radial chromatography (CH_2Cl_2/MeOH 8:1) to give (+)-**22** as a syrup (24 mg, 90%); $[\alpha]^{25}_{\mathrm{D}} = +83.1$ (*c* 0.835, MeOH); UV (MeOH) $\lambda_{\max}$ 272 nm; ^{1}H NMR (CD_3OD, 300 MHz): δ 7.66 (d, 1H, $J_{5,6} = 7.8$ Hz, H-6), 5.65 (d, 1H, $J_{5,6} = 7.8$ Hz, H-5), 5.24 (dt, 1H, $J_{2'',3'} = 8.0$ Hz, $J_{2',3'} \approx J_{3',4'} = 5.8$ Hz, H-3′), 4.44 (dd, 1H, $J_{3',4'} = 6.0$ Hz, $J_{4',5'} = 4.2$ Hz, H-4′), 4.08 (dd, 1H, $J_{2',2''} = 9.8$ Hz, $J_{2',3'} = 5.8$ Hz, H-2′), 3.98 (dd, 1H, $J_{2',2''} = 9.8$ Hz, $J_{2'',3'} = 8.0$ Hz, H-2″), 3.90 (dt, 1H, $J_{5',6''} = 6.7$ Hz, $J_{4',5'} \approx J_{5',6'} = 4.4$ Hz, H-5′), 3.84 (dd, 1H, $J_{6',6''} = 11.6$ Hz, $J_{5',6'} = 4.4$ Hz, H-6′), 3.77 (dd, 1H, $J_{6',6''} = 11.6$ Hz, $J_{5',6''} = 6.7$ Hz, H-6″); ^{13}C NMR (CD_3OD, 75.4 MHz): δ 162.3 (C-4), 149.8 (C-2), 146.1 (C-6), 101.3 (C-5), 84.6 (C-5′), 71.8 (C-4′), 69.6 (C-2′), 61.7 (C-6′), 58.9 (C-3′). Anal. calcd for $C_9H_{12}N_2O_5$: C, 47.37; H, 5.30; N, 12.28. Found: C, 47.12; H, 5.60; N, 12.11%.

4.18. 1-[(3*S*,4*S*,5*S*)-4-Hydroxy-5-(hydroxymethyl)-tetrahydrofuran-3-yl]uracil (−)-22

A similar procedure was followed starting from (+)-**21** (61 mg, 0.19 mmol), Pd/C (10%, 60 mg) and MeOH (6 mL) to give (−)-**22** as a syrup (41 mg, 94%); $[\alpha]^{25}_{\mathrm{D}} = -85.2$ (*c* 0.720, MeOH). Anal. calcd for $C_9H_{12}N_2O_5$: C, 47.37; H, 5.30; N, 12.28. Found: C, 47.10; H, 5.16; N, 12.06%.

4.19. 9-[(3*S*,4*S*,5*S*)-5-[(Benzoyloxy)methyl]-4-(benzyloxy)tetrahydrofuran-3-yl]-6-chloropurine 23

The amine (+)-**13** (170 mg, 0.52 mmol) was dissolved in anhydrous butanol (2 mL) and then triethylamine (2 mL) was added. After a few minutes at rt 5-amino-4,6-dichloropyrimidine (105 mg, 0.64 mmol) was added, and the mixture obtained was heated under reflux for 72 h. The reaction was cooled to rt and then hot ethyl acetate was added. A precipitate appeared on standing which was filtered off. The filtrate was concentrated and the resulting residue purified by CC (hexane/ethyl acetate 1:1) to obtain 148 mg of an inseparable mixture. This mixture was directly treated with trimethylorthoformate (3 mL) and concentrated HCl (80 μL) for 3 days. The reaction mixture was then directly purified by CC (CH_2Cl_2/MeOH 15:1) to give **23** as a syrup (101 mg, 42% yield for the two steps); $[\alpha]^{25}_{\mathrm{D}} = -56.2$ (*c* 1.296, $CHCl_3$); UV ($CHCl_3$) $\lambda_{\max}$ 266 nm; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.67 (s, 1H, H-8), 8.36 (s, 1H, H-2), 8.08 (d, 2H, $J = 7.2$ Hz, Bz), 7.59 (t, 1H, $J = 7.4$ Hz, Bz), 7.46 (t, 2H, $J = 7.86$ Hz, Bz), 7.2–6.8 (m, 5H, Ph), 5.52 (q, 1H, $J_{2',3'} \approx J_{2'',3'} \approx J_{3',4'} = 6.4$ Hz, H-3′), 4.70 (dd, 1H, $J_{6',6''} = 11.7$ Hz, $J_{5',6'} = 5.1$ Hz, H-6′), 4.64 (dd, 1H, $J_{6',6''} = 11.7$ Hz, $J_{5',6''} = 6.6$ Hz, H-6″), 4.52–4.43 (m, 2H, H-4′, H-5′), 4.34 (d, 1H, $J_{\mathrm{AB}} = 11.6$ Hz, CH_2Ph), 4.33 (dd, 1H, $J_{2',2''} = 9.6$ Hz, $J_{2',3'} = 6.3$ Hz, H-2′), 4.22 (dd, 1H, $J_{2',2''} = 9.6$ Hz, $J_{2',3''} = 7.5$ Hz, H-2″), 4.05 (d, 1H, $J_{\mathrm{AB}} = 11.6$ Hz, CH_2Ph); ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 166.1 (C=O), 151.6 (C-2), 150.8 (C-4), 144.8 (C-8), 135.3, 133.2, 129.6, 128.4, 128.2, 128.1, 127.9 (Ar), 79.8 (C-4′), 77.4 (C-5′), 74.4 (C-2′), 69.9 (CH_2Ph), 62.6 (C-6′), 55.6 (C-3′). Anal. calcd for $C_{24}H_{20}ClN_4O_4$: C, 62.00; H, 4.55; Cl, 7.63; N, 12.31. Found: C, 62.23; H, 4.61; Cl, 7.86; N, 12.21%.

4.20. 6-Amino-9-[(3*S*,4*S*,5*S*)-4-benzyloxy-5-(hydroxymethyl)tetrahydrofuran-3-yl]purine 24

A solution of **23** (82 mg, 0.18 mmol) in MeOH saturated with ammonia (3 mL) was allowed to stand at rt overnight. The solvent was then evaporated and the residue was purified by CC (CH_2Cl_2/MeOH 20:1 to 10:1) to give compound **24** (31 mg, 52%); $[\alpha]^{25}_{\mathrm{D}} = -46.3$ (*c* 1.353, MeOH); UV ($CHCl_3$) $\lambda_{\max}$ 270 nm; ^{1}H NMR (CD_3OD, 400 MHz): δ 8.17 (s, 1H, H-8), 8.16 (s, 1H, H-2), 7.2–6.8 (m, 5H, Ph), 5.38 (dt, 1H, $J_{2',3'} = 7.2$ Hz, $J_{2'',3'} \approx J_{3',4'} = 6.0$ Hz, H-3′), 4.43 (dd, 1H, $J_{3',4'} = 5.6$ Hz, $J_{4',5'} = 4.8$ Hz, H-4′), 4.34 (d, 1H, $J_{\mathrm{AB}} = 11.2$ Hz, CH_2Ph), 4.29 (dd, 1H, $J_{2',2''} = 9.6$ Hz, $J_{2',3'} = 6.0$ Hz, H-2′), 4.17–4.12 (m, 2H, H-2″, H-5′), 3.99 (d, 1H, $J_{\mathrm{AB}} = 11.2$ Hz, CH_2Ph), 3.87–3.84 (m, 2H, H-6′, H-6″); ^{13}C NMR (CD_3OD, 100.5 MHz): δ 157.0 (C-6), 153.6

(C-2), 150.8 (C-4), 141.9 (C-8), 137.9, 129.1, 128.9, 128.8 (Ph), 119.5 (C-5), 83.8 (C-4′), 79.1 (C-5′), 75.0 (C-2′), 70.4 (CH_2Ph), 61.4 (C-6′), 57.1 (C-3′). Anal. calcd for $C_{17}H_{19}N_5O_3$: C, 59.81; H, 5.61; N, 20.52. Found: C, 60.01; H, 5.50; N, 20.21%.

4.21. 6-Amino-9-[(3*S*,4*S*,5*S*)-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-3-yl]purine 25

To a solution of **24** (27 mg, 0.079 mmol) in MeOH (2 mL), Pd/C (10%, 27 mg) was added. The reaction mixture was maintained overnight under hydrogen (1 atm) with vigorous stirring. The catalyst was filtered off and the solvent was evaporated. The residue was dissolved in ethanol and the resultant solution was filtered and evaporated The residue was purified by radial chromatography (CH_2Cl_2/MeOH 8:2) to give **25** as a foam (18 mg, 89%); $[\alpha]_D^{25} = -26.6$ (*c* 0.275, MeOH); UV (CH_3OH) λ_{max} 262 nm; ^1H NMR (CD_3OD, 400 MHz): δ 8.26 (s, 1H, H-8), 8.21 (s, 1H, H-2), 5.33 (td, 1H, $J_{3',4} = 5.2$ Hz, $J_{3',2'} \approx J_{3',2''} = 8.0$ Hz, H-3′), 5.49 (dd, 1H, $J_{4',3'} = 5.2$ Hz, $J_{4',5'} = 4.0$ Hz, H-4′), 4.32 (pseudo t, 1H, $J_{2',3'} \approx J_{2',2''} = 8.0$ Hz, H-2′), 4.25 (pseudo t, 1H, $J_{2'',3'} \approx J_{2'',2'} = 8.0$ Hz, H-2″), 4.14 (ddd, 1H, $J_{5',6''} = 6.8$ Hz, $J_{5',6'} = 4.8$ Hz, $J_{5',4'} = 4.0$ Hz, H-5′), 3.87 (dd, 1H, $J_{6',6''} = 12.0$ Hz, $J_{6',5'} = 4.8$ Hz, H-6′), 3.81 (dd, 1H, $J_{6'',6'} = 12.0$ Hz, $J_{6'',5'} = 6.8$ Hz, H-6″); ^{13}C NMR (CD_3OD, 100.5 MHz): δ 157.4 (C-6), 153.8 (C-2), 151.3 (C-4), 142.5 (C-8), 119.6 (C-5), 83.4 (C-5′), 71.82 (C-4′), 69.6 (C-2′), 62.0 (C-6′), 58.5 (C-3′). Anal. calcd for $C_{10}H_{13}N_5O_3$: C, 47.81; H, 5.22; N, 27.87. Found: C, 47.99; H, 5.26; N, 28.20%.

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