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A Linchpin Carbacyclization Approach for the Synthesis of Carbanucleosides

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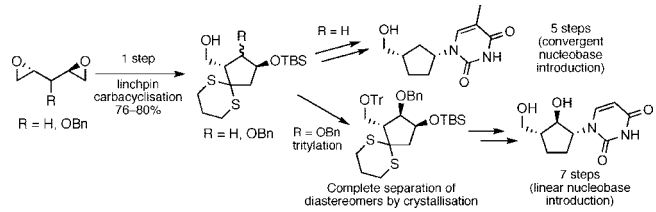

A convenient synthesis of carbanucleosides, with both enantiomers equally accessible, is reported. The key step is a tandem linchpin cyclization process to give access to substituted carbafuranose derivatives having the correct relative stereochemistry for subsequent nucleobase introduction with inversion of configuration at C1. This was illustrated by the synthesis of 2′,3′-dideoxycarbathymidine via a convergent nucleobase introduction and of 2′,3′-dideoxy-6′-hydroxycarbauridine via a linear nucleobase introduction. Both methods relied on Mitsunobu chemistry, and the first example of the Mukaiyama modification of the Mitsunobu reaction involving nucleobases as nucleophiles is reported.

Introduction

Many nucleoside-based drugs are currently in use against viral infections.[1] A particular class of nucleosides consist of carbanucleosides, in which the ring oxygen is replaced by a methylene unit. This modification alters the enzymatic stability and conformational properties, affecting biological activity.[2,3] Natural carbanucleosides include aristeromycin **1**[4] (Figure 1) and neplanocin A,[5] which show antibiotic and antitumor activity. The 6′β-fluoroaristeromycin **2** was found to be a potent inhibitor of AdoHcy hydrolase and to efficiently suppress vaccina virus replication.[6] Prominent synthetic carbanucleosides include carbovir,[7] a potent and selective inhibitor of HIV reverse transcriptase (as its triphosphate), and its pro-drug abacavir **3**.[8] The

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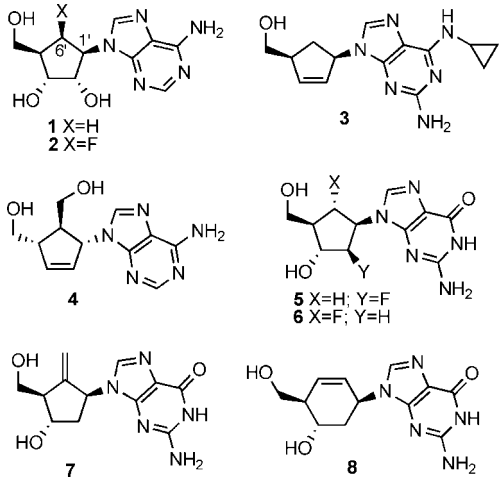

FIGURE 1. Carbanucleosides.

latter compound, with improved pharmacokinetics over carbovir, is currently employed in the treatment of HIV infections. In addition, the 6′-substitued carbanucleoside (−)-BCA **4** with the unnatural configuration also exhibits potent anti-HIV activity.[9] Thus, synthetic methodologies allowing access to both enantiomers of carbanucleosides are essential. Other biologically active carbanucleosides include the fluorine containing 2′β-fluoro and 6′α-fluorocarbocyclic guanosines **5** and **6**,[10] which are active against herpes virus. Interestingly, **5** displayed higher activity than its furanose parent. Entecavir **7**[11] has been approved in 2005 for the treatment of chronic hepatitis B (HBV) virus.[12] Cyclobutyl[13] and cyclohexyl[14] carbanucleosides have also been developed. For example, cyclohexenylguanine **8** displays potent and selective antiherpes activity.[14a,b]

The synthesis of carbanucleosides—and carbafuranose precursors—has been extensively reviewed[3] and generally follows a strategy in which the nucleobase unit is either introduced as a whole, for example, via a Mitsunobu process, epoxide opening, or Pd-mediated substitution process (convergent strategy), or in which the nucleobase is constructed in a stepwise manner starting from an aminocyclopentane derivative (linear strategy). Given the biological significance of this class of compounds, new synthetic methodology toward their synthesis continues to be of importance.[1]

We have reported a short synthesis of carbafuranose derivatives **11** and **12** via a dithiane-based linchpin cyclization process[15] starting from homochiral bis-epoxides such as **14**[16] and **15**[17] (Scheme 1),[18] of which both enantiomeric forms are equally available. It was envisioned that carbafuranose derivatives **11/12**, due to the relative *anti*-configuration of the 1′-OTBDMS and the 4′-hydroxymethyl group, would be suitable precursors for a convergent synthesis of carbanucleosides **9**, and that this would be a very convenient way to access 6′-substituted carbanucleosides which are interesting and topical targets.[19] In addition, 6′-substituted derivatives have been used as intermediates in the synthesis of unsaturated carbanucleosides.[20] Unlike many approaches strating from natural sugars, this approach would also allow access to both D- and L-carbanucleosides starting from the chiral pool. In this work, L-arabitol was chosen as starting material.

The linchpin cyclization process is propagated by a Brook rearrangement,[21] which regenerates the dithianyl anion making

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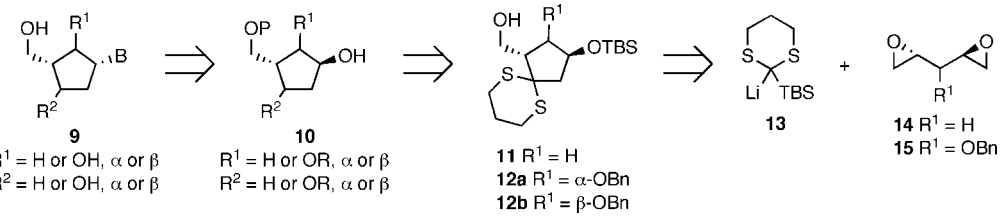
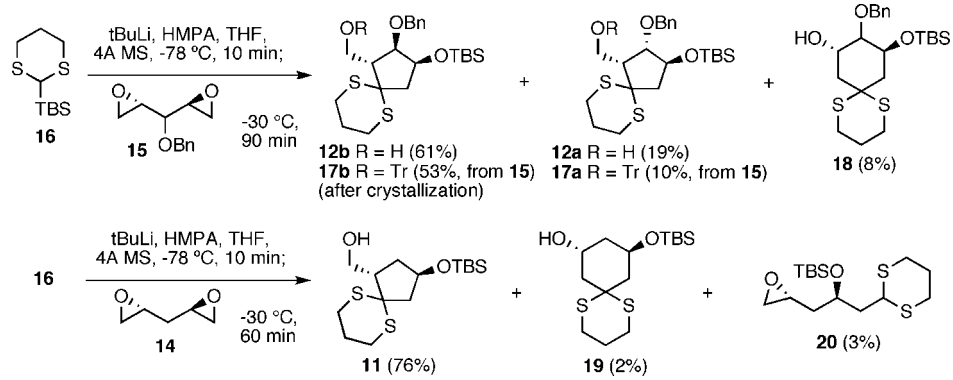
SCHEME 1. Synthetic Approach toward Carbanucleosides



SCHEME 2. Tandem Linchpin Carbacyclization Process Leading to Carbafuranose Derivatives



it available for further transformations (see below).[15,22] Though not required for our purposes, it is possible to control the timing of the Brook rearrangement[22a,23] which has enabled dithiane-based linchpin one-pot multicomponent coupling strategies for the construction of complex targets.[15,24] Recently, this concept has been extended to the development of anion-relay chemistry, which shows great promise for synthetic applications.[25] Prior to our work, the dithiane-based linchpin cyclization with 1,3-bis-epoxides to give cyclopentane derivatives,[26] and 1,5-bis-epoxides to give cyclohexane and cycloheptane derivatives,[26,27] had been described.

We describe in full the synthesis of carbafuranoses **11**/**12** and their conversion to 2′,3′-dideoxycarbanucleosides. Both a convergent and a linear nucleobase introduction was investigated. The first use of the Mukaiyama modification of the Mitsunobu reaction with nucleobases is reported.

Results and Discussion

A summary of our results for the linchpin cyclization process is given in Scheme 2.[18] When the bis-epoxide **15** was used as a substrate, reaction with deprotonated **16** led to the desired 6′-benzyloxy epimers **12b** and **12a** in excellent combined yield (80%), together with a six-membered isomer **18**. Interestingly, **18** was obtained as a single diastereomer, but we were unable to determine its relative configuration. The relative configuration of **12b** was proven by X-ray crystallographic analysis of its trityl derivative **17b**.[18] The same linchpin cyclization process starting from the C_2-symmetric bis-epoxide **14** led to the desired carbafuranose derivative **11**. Whereas on small scale only **11** was isolated (in 83%), a larger scale experiment permitted isolation of a very small amount of six-membered ring isomer **19** and of a protonated acyclic intermediate **20**.

The separation of the diastereoisomers **12a/b** required tedious preparative HPLC, though **18** could be separated from **12** by column chromatography. Attempts to establish a convenient large-scale separation method by selective functionalization of the less hindered hydroxymethyl group proved unsuccessful. However, it was discovered that tritylation of the diastereomeric mixture induced selective crystallization of **17b**. Hence, after optimization of the tritylation of **12** (see Supporting Information), the separation protocol was then executed in sequence with the linchpin cyclization process: the crude reaction mixture of the carbacyclization, after aqueous workup, was directly subjected to tritylation which after column chromatography (EtOAc/hexanes) gave a mixture of **17a** and **17b**. Though we later discovered that **17a** and **17b** can be separated by chromatography using a DCM/hexanes mixture as eluent, a more convenient separation on large scale was achieved by slow recrystallization from EtOH, which afforded pure **17b** in 53% yield from **15**. The filtrate, which required another purification by column chromatography to remove traces of trityl alcohol, yielded **17a** in 10% yield.

The diastereoisomers **12b** and **12a** arise from attack of **13** onto the pro-*R* and pro-*S* epoxide groups of **15** respectively, which lead to intermediates **21** and **22** (Scheme 3). After Brook rearrangement to give **23**/**24**, a 5-*exo* cyclization leads to the furanose products **12b/a**, while a 6-*exo* (7-*endo*)[28] cyclization leads to the six-membered **18**. On the other hand, reaction with either **23** or **24** with **13** leads to **25**. However, the formation of

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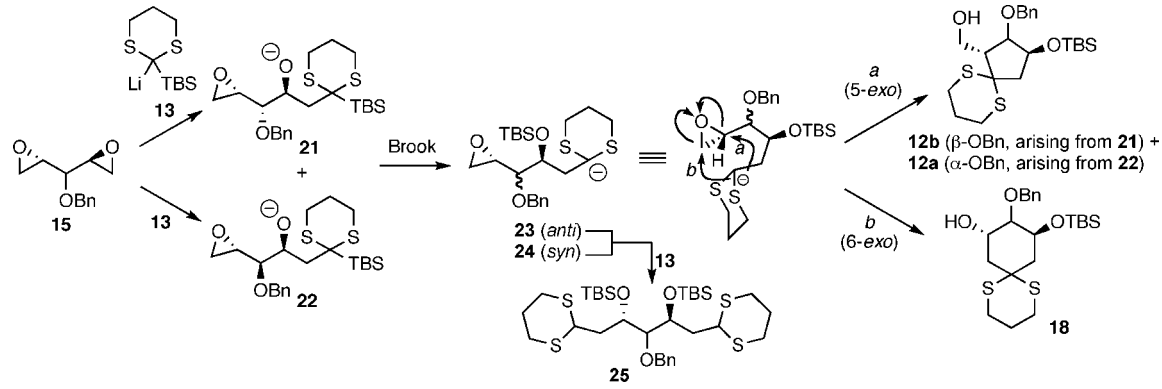
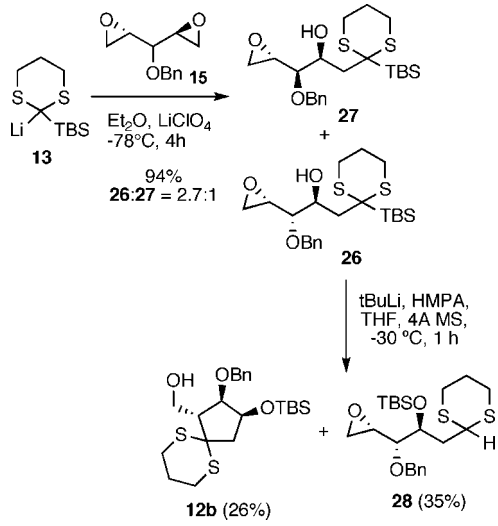
SCHEME 3. Formation of the Product Isomers and Byproducts



SCHEME 4. Brook Rearrangement of a Monoaddition Product To Give a Single Carbafuranose Diastereoisomer



25 was only observed on a few occasions during the optimization efforts. In addition, no products arising from protonation of **21**−**24** were isolated—all of which were independently synthesized, permitting their use as standards in TLC analysis. Nevertheless, when **14** was used as substrate, a very small amount of **20** was isolated. These observations suggest that both the Brook rearrangement[23,24] and the 5-*exo* cyclization are fast processes.

The fact that **18** is isolated as a single diastereomer suggests that only one of the intermediates **23** or **24** undergoes 6-*exo* cyclization. However, as **18** is only isolated in low yield (8%), this alone cannot be responsible for the unexpectedly large **12b**:**12a** ratio that was observed (3:1). As no protonated products arising from **21**−**24** were detected, it must be concluded that the two diastereotopic epoxide groups react with a considerable rate difference in the initial substitution reaction. As **12b** is the major isomer, the pro-*R* epoxide is the fastest reacting group.

A measure of this rate difference was obtained by model experiments (see the Supporting Information) in which **15** was reacted under conditions that did not allow Brook rearrangement, hence preventing the cyclization process. Interestingly, when the reaction was conducted in the presence of 1 equiv of $LiClO_4$ (Scheme 4), an excellent combined yield of **26**/**27** was achieved (94%) with no diaddition product isolated. Hence, the observed 2.7:1 ratio indicated that the diastereotopic epoxides of **15** indeed undergo opening with substantially different reaction rates. Franck and Figadère also reported on the diastereoselective (3:2 ratio) opening of **15** with an acetylide nucleophile, though the exact relative configuration of the diastereomers was not determined.[29]

Separation by preparative HPLC allowed isolation of **26** in diastereomerically pure form. As expected,[24] subjecting **26** to Brook rearrangement led to the formation of **12b**. This confirmed the structure of **26** (and **27**) as shown, as deprotonation of **26** to give **21** must have initiated Brook rearrangement to **23** (as in Scheme 3), leading to **12b** after cyclization. To our surprise, the noncyclized **28**, arising from protonation of **23**, was also isolated in appreciable quantity. Conveniently, this permitted stereochemical correlation with all possible monoaddition adducts of **15** (see Supporting Information).

Synthesis of 2′,3′-Dideoxycarbanucleosides. With a high-yielding cyclization process developed, including a practical large-scale separation of the 6′-diastereomers, further conversion into carbanucleosides was investigated. The first aim was to achieve a short convergent synthesis of the known 2′,3′-dideoxycarbathymidine **35**[30] from **11**, using a Mitsunobu process[31] (Scheme 5). Interestingly, in contrast to similar carbanucleosides, **35** has not yet been synthesized via a convergent process. The dithioketal group of the 6′-unsubstituted substrate **11** was removed by Raney nickel,[32a] followed by acylation of the hydroxymethyl group and desilylation of the secondary hydroxyl group, to give cyclopentanol **31**.

The nucleobase was introduced by reaction of **31** with 3-*N*-benzoylthymine **32**, prepared by benzoylation of thymine following Reese's method (63% yield),[33] under Mitsunobu

(28) For nomenclature, see: (a) Narayan, R. S.; Sivakumar, M.; Bouhlel, E.; Borhan, B. *Org. Lett.* **2001**, *3*, 2489–2492, and references cited therein.

(29) Jalce, G.; Franck, X.; Seon-Meniel, B.; Hocquemiller, R.; Figadère, B. *Tetrahedron Lett.* **2006**, *47*, 5905–5908.

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(31) (a) Szarek, W. A.; Depew, C.; Jarrell, H. C.; Jones, J. K. N. *J. Chem. Soc., Chem. Commun.* **1975**, 648–649. (b) Iwakawa, M.; Pinto, B. M.; Szarek, W. A. *Can. J. Chem.* **1978**, *56*, 326–335. (c) Marquez, V. E.; Tseng, C. K. H.; Treanor, S. P.; Driscoll, J. S. *Nucleosides Nucleotides* **1987**, *6*, 239–244. (d) Bestmann, H. J.; Roth, D. *Angew. Chem., Int. Ed.* **1990**, *29*, 99–100. (e) Jenny, T. F.; Previsani, N.; Benner, S. A. *Tetrahedron Lett.* **1991**, *32*, 7029–7032. (f) Jenny, T. F.; Horlacher, J.; Previsani, N.; Benner, S. A. *Helv. Chim. Acta* **1992**, *75*, 1944–1954.

(32) (a) Hauptmann, H.; Walter, W. F. *Chem. Rev.* **1961**, *61*, 347–404. (b) Lipshutz, B. H.; Moretti, R.; Crow, R. *Tetrahedron Lett.* **1989**, *30*, 15–18.

(33) (a) Cruickshank, K. A.; Jiricny, J.; Reese, C. B. *Tetrahedron Lett.* **1984**, *25*, 681–684. (b) Frieden, M.; Giraud, M.; Reese, C. B.; Song, Q. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2827–2832.

SCHEME 5. Convergent Synthesis of 2′,3′-Dideoxycarbathymidine

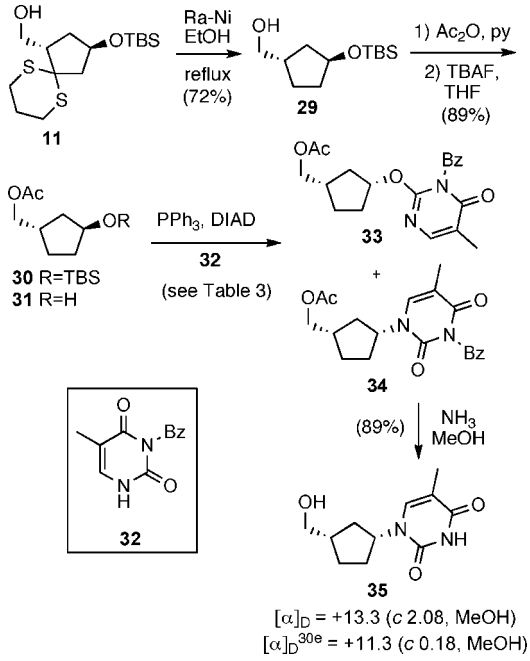


TABLE 1. Optimization of the Mitsunobu Reaction

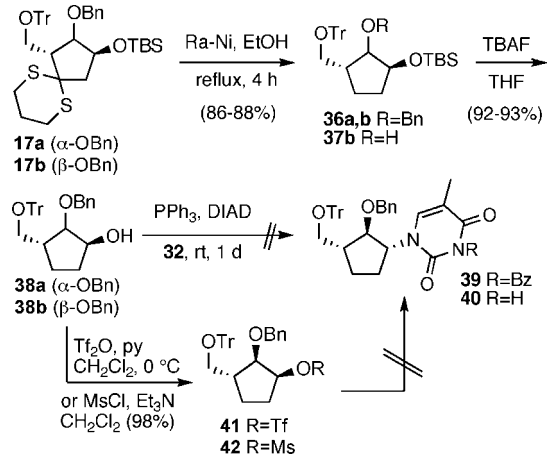
entry	PPh_3, DIAD (equiv)	**32** (equiv)	solvent (0.05 M)	*T* (°C)	yield of **34**[a] (%)	yield of **33**[a] (%)
1	2.5	1.5	CH_2Cl_2	rt	49	35
2	2.5	1.5	THF	rt	47	22
3	2.5	1.5	DMF	rt	53	8
4	2.5	1.5	DMF	0	33	12
5	1.5	3.0	DMF	0	48	20
6	1.5	3.0	DMF	rt	64	25

[a] Isolated yield.

conditions,[34] to give a mixture of 2-*O*- and 1-*N*-alkylated products **33** and **34** (Table 1). Extensive research efforts have been devoted to determining conditions favoring the 1-*N* alkylation of the pyrimidine nucleophiles.[35] In terms of *N*- vs *O*-selectivity, CH_2Cl_2 and THF are inferior solvents to DMF (entries 1 and 2 vs 3),[35c,d,i] although the best overall yield was obtained using CH_2Cl_2. Intriguingly,[35a] conducting the reaction at 0 °C (entry 4) did not improve the ratio at all. In addition, a side product was isolated arising from nucleophilic attack of the reduced azodicarboxylate byproduct. In order to facilitate purification, a reduced excess of DIAD and PPh_3 was used, and in order to minimize competing nucleophilic attack leading to the aforementioned side product, 3 equiv of **32** were used. This led to an increased yield of 48% for the desired product **34** (entry 5), and a further improvement in yield to 64% was achieved by conducting the experiment at ambient temperature (entry 6).

Finally, deprotection of **34** with methanolic ammonia smoothly led to acetate and benzoate removal in one operation, leading to (+)-2′,3′-dideoxycarbathymidine **35** in 89% yield. The optical rotation is in full agreement with the data reported.[30e] Hence, **35** was achieved in six linear steps in 28% overall yield from the 1,4-bis-epoxide **14**.

SCHEME 6. Attempted Synthesis of 6′-Hydroxycarbathymidine



Next, research was directed to a convergent synthesis of 6′-OH-substituted carbanucleosides. Both diastereomers **17a** and **17b** were treated with Raney nickel (Scheme 6) to give **36a/b**. Careful control (TLC) was required with regard to the amount of Ra−Ni used in order to avoid concomitant debenzylation to give **37**.[32b] Subsequent removal of the silyl group gave substrates **38a/b** in excellent yield. Unfortunately, introduction of the nucleobase via the Mitsunobu protocol failed, and virtually all of the starting material was recovered. Direct sulfonate displacement[36] was also unsuccessful. Reaction of the triflate **41**, synthesized in situ from **38b**, with deprotonated **32** in the presence of 18-C-6, led to decomposition and reaction of the mesylate **42**, synthesized in excellent yield from **38b**, with bis-silylated thymine led to the complete return of starting material.

The failure of the Mitsunobu reaction to give **39** was surprising given a control experiment (Scheme 7), in which **38b** was subjected to classic Mitsunobu conditions with *p*-nitrobenzoic acid, gave the corresponding benzoate **43** in almost quantitative yield. Alcohol deprotection of **43** led to **44**, which, being diastereomeric with **38b**, unambiguously proved the inversion of configuration at C1. Interestingly, Mitsunobu reaction with phthalimide led to the corresponding product **45** in excellent yield as well. A much longer reaction time was required with phthalimide (∼2 days) in comparison to *p*-nitrobenzoic acid (1 h), demonstrating the superiority of *p*-nitrobenzoic acid as a Mitsunobu substrate.[37]

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(35) Examples: (a) Bonnal, C.; Chavis, C.; Lucas, M. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1401–1410. (b) Borthwick, A. D.; Crame, A. J.; Exall, A. M.; Weingarten, G. G.; Mahmoudian, M. *Tetrahedron Lett.* **1995**, *36*, 6929–6932. (c) Chong, Y.; Gumina, G.; Chu, C. K. *Tetrahedron: Asymmetry* **2000**, *11*, 4853–4875. (d) Choo, H.; Chong, Y.; Chu, C. K. *Org. Lett.* **2001**, *3*, 1471–1473. (e) Ludek, O. R.; Meier, C. *Synthesis* **2003**, 2101–2109. (f) Ludek, O. R.; Meier, C. *Synlett* **2005**, 3145–3147. (g) Ludek, O. R.; Meier, C. *Eur. J. Org. Chem.* **2006**, 941–946. (h) Ludek, O. R.; Krämer, T.; Balzarini, J.; Meier, C. *Synthesis* **2006**, 1313–1324. (i) Ludek, O. R.; Meier, C. *Synlett* **2006**, 324–326, See also: (j) Comins, D. L.; Jianhua, G. *Tetrahedron Lett.* **1994**, *35*, 2819–2822.

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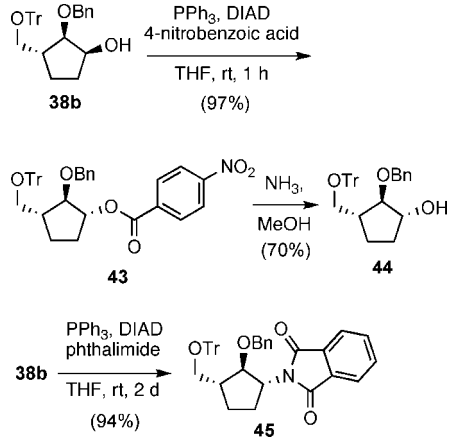
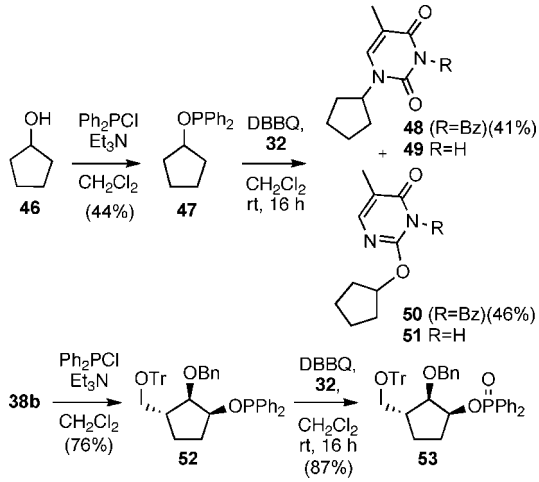
(37) (a) Martin, S. F.; Dodge, J. A. *Tetrahedron Lett.* **1991**, *32*, 3017–3020. (b) Hughes, D. L.; Reamer, R. A. *J. Org. Chem.* **1996**, *61*, 2967–2971.

SCHEME 7. Mitsunobu Reactions with 38b



SCHEME 8. Mukaiyama Process in Carbanucleoside Synthesis



We then investigated whether the nucleobase could be introduced by a Mukaiyama "oxidative−reductive condensation reaction",[38] in which an alcohol is converted into a phosphinite group prior to its activation with 2,6-di-*tert*-butyl-1,4-benzoquinone (DBBQ) in the presence of a nucleophile, leading to an S_N2 reaction. Whereas phthalimides, sulfonamides, and trifluoroacetamides have been used successfully in this process,[38e] the Mukaiyama procedure has not yet been demonstrated for nucleoside formation. Hence, a model compound **47** (Scheme 8) was synthesized. Though **47** was prone to decomposition, we were pleased to observe the formation of **48/50**[35g,i,39] in excellent yield upon addition of DBBQ and 3-*N*-benzoylthymine **32**, but essentially with no selectivity for *N*-alkylation over *O*-alkylation. Unfortunately, nucleoside formation from phosphinite **52**, obtained from **38b**, under similar conditions led to the isolation of the oxidized phosphinate **53**, which led us to abandon this method.

With a convergent nucleobase introduction being unsuccessful for **38b**, a linear approach was investigated. The successful assembly of **45** opened the way to a stepwise introduction of the nucleobase (see below). Unfortunately, all attempts to achieve phthalimide introduction via a Mitsunobu reaction with 6α-epimer **38a** (or derivatives) were unsuccessful (see the Supporting Information).

The completion of the linear synthesis for the carbauridine nucleoside **58** is shown in Scheme 9. Hydrazinolysis of the phthalimide derivative **45**, derived from **38b** as shown in Scheme 7, led to **54** in variable yields, together with a significant amount of a structurally related side product that was not identified. The purified amine **54** then underwent a sequence of reactions consisting of the condensation with acyl carbamate **55**,[40,41] cyclization with concomitant trityl removal,[30a,b,42] and benzyl hydrogenolysis to afford the desired 2′,3′-dideoxy-6′-hydroxycarbauridine **58**.

Conclusion

We have successfully achieved a facile construction of suitably protected carbafuranose sugars from 2-*tert*-butyldimethylsilyl-1,3-dithiane and symmetric 1,4-bis-epoxides. Convergent carbanucleoside formation from the synthesized carbasugars was demonstrated in the syntheses of 2′,3′-dideoxycarbathymidine **35** by a Mitsunobu coupling. For the synthesis of the 6′-substituted 6′-hydroxy-2′,3′-dideoxycarbauridine **58**, a stepwise approach had to be adopted, which also relied on a Mitsunobu process, using phthalimide.

Experimental Section

For general information, see the Supporting Information.

(2*R*,3*R*,4*S*)- and (2*R*,3*S*,4*S*)-[3-Benzyloxy-4-(*tert*-butyldimethylsilyloxy)-2-trityloxymethyl]cyclopent-1-one-1,3-propanedithioketal (17b and 17a). ^{t}BuLi (1.6 M solution in pentane, titrated concn 1.51 M; 4.2 mL, 6.30 mmol) was added to a solution of dithiane **16** (1.59 g, 6.79 mmol) and HMPA (10.8 mL) in THF (97.0 mL) containing 4 Å molecular sieves (∼20 g) at −78 °C, and the mixture was stirred for 10 min. Bis-epoxide **15** (1.0 g. 4.85 mmol) was added, and the mixture was stirred for 90 min at −30 °C. The reaction was quenched by the addition of satd NH_4Cl (50 mL) and H_2O (200 mL), and the aqueous phase was extracted with Et_2O (200 mL, then 2 × 100 mL). The organic layer was washed with brine (200 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude was dissolved in DMF (24.0 mL). Et_3N (1.35 mL, 9.70 mmol) was added followed by TrCl (2.70 g, 9.70 mmol). The mixture was stirred at 60 °C for 16 h. After cooling to room temperature, satd NH_4Cl (20 mL), H_2O (80 mL), and Et_2O (60 mL) were added. The aqueous phase was extracted with Et_2O (2 × 50 mL). The organic layer was washed with H_2O (100 mL) and brine (50 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification by column chromatography (EtOAc/petroleum ether 0→5%) and subsequent recrystallization from hot ethanol (1 week at 4 °C) afforded pure crystals of **17b** (1.72 g, 53%), with only traces of **17b** left in the filtrate. Concentration of the residual filtrate and successive chromatographic purifications first using DCM/petroleum ether 3: 7 and then toluene afforded **17a** (321 mg, 10%) as a foam.

(38) (a) Mukaiyama, T.; Shintou, T.; Fukumoto, K. *J. Am. Chem. Soc.* **2003**, *125*, 10538–10539. (b) Shintou, T.; Mukaiyama, T. *Chem. Lett.* **2003**, *32*, 984–985. (c) Shintou, T.; Fukumoto, K.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 1569–1579. (d) Shintou, T.; Mukaiyama, T. *J. Am. Chem. Soc.* **2004**, *126*, 7359–7367. (e) Mukaiyama, T.; Ikegai, K.; Aoki, H.; Pluempanupat, W.; Masutani, K. *Proc. Japan Acad., Ser. B* **2005**, *81*, 103–109. (f) Mukaiyama, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 5590–5614.

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(40) Acyl carbamate **55** was synthesized from (*E*)-methyl-3-methoxyacrylate in four steps: (a) Shaw, G.; Warrener, R. *J. Chem. Soc.* **1958**, 153–156. (b) Shaw, G.; Warrener, R. *J. Chem. Soc.* **1958**, 157–161. See also: (c) Tietze, L. F.; Schneider, C.; Pretor, M. *Synthesis* **1993**, 1079–1080.

(41) Wyatt, P. G.; Anslow, A. S.; Coomber, B. A.; Cousins, R. P. C.; Evans, D. N.; Gilbert, V. S.; Humber, D. C.; Paternoster, I. L.; Sollis, S. L.; Tapolczay, D. J.; Weingarten, G. G. *Nucleosides Nucleotides* **1995**, *14*, 2039–2049.

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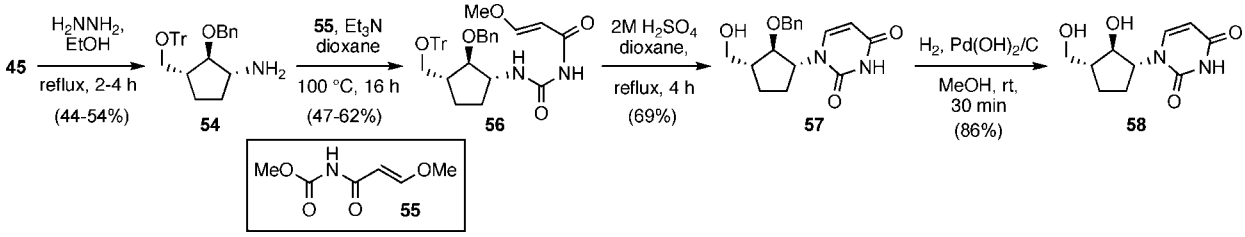
SCHEME 9. Synthesis of 2′,3′-Dideoxy-6′-hydroxycarbauridine



Data for 17a: mp 50−54 °C; $[\alpha]_D$ +20.8 (*c* 1.3, $CHCl_3$, 24 °C); IR 2950 (m), 2929 (m), 2898 (m), 2856 (m), 1453 (m), 1363 (m), 1090 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.56−7.48 and 7.40−7.20 (20H, m, ArH), 4.63 (1H, d, J = 12.5 Hz, CH_aH$_b$Ph), 4.58 (1H, d, J = 12.5 Hz, CH$_a$$H_b$Ph), 4.45 (1H, ddd, J = 7.0, 5.5, 3.0 Hz, CHOSi), 4.21 (1H, dd, J = 6.0, 3.0 Hz, CHOBn), 3.69 (1H, dd, J = 9.5, 4.5 Hz, CH_aH$_b$OTr), 3.60 (1H, dd, J = 9.5, 8.0 Hz, CH$_a$$H_b$OTr), 3.04 (1H, ddd, J = 14.0, 10.5, 3.0 Hz, SCH_aH$_b$), 2.97 (1H, dd, J = 14.0, 7.0 Hz, CCH_aH$_b$), 2.88−2.75 (3H, m, SCH$_a$$H_b$ + SCH_cH$_d$ + CHCH$_2$OTr), 2.68 (1H, ddd, J = 14.0, 6.0, 3.5 Hz, SCH$_c$$H_d$), 2.16 (1H, dd, J = 14.0, 5.5 Hz, CCH$_a$$H_b$), 2.03 (1H, m, SCH$_2CH_aH_b$), 1.87 (1H, m, SCH$_2CH_a$$H_b$), 0.98 (9H, s, SiC(CH$_3$)$_3$), 0.13 (6H, s, SiCH$_3$ × 2); ^{13}C NMR (100 MHz, $CDCl_3$) 144.4 (C$_{Ar}$ × 3), 138.9 (C$_{Ar}$), 129.1 (CH$_{Ar}$ × 6), 128.3 (CH$_{Ar}$ × 2), 127.8 (CH$_{Ar}$ × 6), 127.6 (CH$_{Ar}$ × 2), 127.3 (CH$_{Ar}$), 127.0 (CH$_{Ar}$ × 3), 87.5 (CPh$_3$), 87.0 (CHOBn), 77.4 (CHOSi), 72.6 (CH$_2$Ph), 59.9 (CH$_2$OTr), 55.1 (SCS), 53.9 (*C*HCH$_2$OTr), 50.3 (C*C*H$_2$), 28.9 (SCH$_2$), 27.7 (SCH$_2$), 26.0 (SiC(*C*H$_3$)$_3$), 25.1 (SCH$_2$*C*H$_2$), 18.1 (SiC), −4.4 (SiCH$_3$), −4.6 (SiCH$_3$); ES$^+$ *m*/*z* 705 ((M + Na)$^+$, 100); HRMS (ES$^+$) for $C_{41}H_{50}O_3S_2SiNa$ (M + Na)$^+$ calcd 705.2863; Measured 705.2859.

Data for 17b. mp 102−105 °C (EtOH). $[\alpha]_D$ +37.5 (*c* 0.65, $CHCl_3$, 24 °C). IR 2949 (w), 2929 (w), 2898 (w), 2855 (w), 1491 (w), 1462 (w), 1138 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 7.59−7.56 and 7.48−7.23 (20H, m, ArH), 4.76 (1H, d, J = 12.0 Hz, CH_aH$_b$Ph), 4.51 (1H, d, J = 12.0 Hz, CH$_a$$H_b$Ph), 4.37 (1H, dt, J = 7.5, 6.0 Hz, CHOSi), 3.73 (1H, t, J = 6.0 Hz, CHOBn), 3.61 (1H, dd, J = 9.5, 6.0 Hz, CH_aH$_b$OTr), 3.38 (1H, dd, J = 9.5, 6.0 Hz, CH$_a$$H_b$OTr), 3.08 (1H, ddd, J = 14.0, 10.5, 3.0 Hz, SCH_aH$_b$), 2.92−2.84 (2H, m, SCH$_a$$H_b$ + SCH_cH$_d$), 2.84 (1H, dd, J = 13.0, 6.0 Hz, CCH_aH$_b$), 2.73 (1H, q, 6.0 Hz, CHCH$_2$OTr), 2.68 (1H, ddd, J = 14.0, 6.0, 3.0 Hz, SCH$_c$$H_d$), 2.43 (1H, dd, J = 13.0, 8.0 Hz, CCH$_a$$H_b$), 2.04 (1H, m, SCH$_2CH_aH_b$), 1.90 (1H, m, SCH$_2CH_a$$H_b$), 0.99 (9H, s, SiC(CH$_3$)$_3$), 0.15 (3H, s, SiCH$_3$), 0.14 (3H, s, SiCH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) 144.3 (C$_{Ar}$ × 3), 139.0 (C$_{Ar}$), 129.1 (CH$_{Ar}$ × 6), 128.2 (CH$_{Ar}$ × 2), 127.8 (CH$_{Ar}$ × 6), 127.6 (CH$_{Ar}$ × 2), 127.2 (CH$_{Ar}$), 127.0 (CH$_{Ar}$ × 3), 87.6 (CPh$_3$), 81.7 (CHOBn), 72.1 (CH$_2$Ph), 71.3 (CHOSi), 62.1 (CH$_2$OTr), 57.3 (*C*HCH$_2$OTr), 52.4 (SCS), 50.0 (C*C*H$_2$), 28.8 (SCH$_2$), 27.8 (SCH$_2$), 26.1 (SiC(*C*H$_3$)$_3$), 25.4 (SCH$_2$*C*H$_2$), 18.4 (SiC), −4.5 × 2 (Si(CH$_3$)$_2$); ES$^+$ *m*/*z* (%) 705 ((M + Na)$^+$, 100); HRMS (ES$^+$) for $C_{41}H_{50}O_3S_2SiNa$ (M + Na)$^+$ calcd 705.2863, measured 705.2864.

(1*S*,3*S*)-[3-(*tert*-Butyldimethylsilyloxy)cyclopent-1-yl]methanol (29). Raney Ni (50% slurry in water, rinsed with EtOH; ∼1 mL) was added to a solution of **11** (0.0964 g, 0.288 mmol) in EtOH (3.5 mL) at reflux for 2 h. Similar quantities of Raney Ni were added after 30, 60, and 90 min. The reaction mixture was cooled and then filtered through Celite, washed with EtOH, concentrated in vacuo, and purified by column chromatography (EtOAc/petroleum ether 25:75) to give **29** as a colorless oil (47.0 mg, 72%): $[\alpha]_D$ +0.9 (*c* 0.8, $CHCl_3$, 23 °C); IR 3338 (m, br), 2954 (m), 2928 (m), 2895 (w), 2857 (m), 1471 (w), 1361 (w), 1252 (m), 1052 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 4.27 (1H, m, CHOSi), 3.51 (2H, AB system, CH_2OH), 2.37 (1H, septet, J = 7.5 Hz, CHCH$_2$OH), 1.91 (1H, dtd, J = 12.5, 8.5, 6.0 Hz, CH_aH$_b$CH$_2$CHOSi), 1.79 (1H, m, CH$_2$CH_aH$_b$CHOSi), 1.71 (1H, m, CHCH_aH$_b$CH), 1.57 (1H, m, CH$_2$CH$_a$$H_b$CHOSi), 1.42 (1H, ddd, J = 13.5, 8.5, 6.0 Hz, CHCH$_a$$H_b$CH), 1.34 (1H, bs, OH), 1.24 (1H, ddt, J = 12.5, 8.6, 7.1 Hz, CH$_a$$H_bCH_2$CHOSi), 0.87 (9H, s, SiC(CH$_3$)$_3$), 0.04 (6H, s, SiCH$_3$ × 2); ^{13}C NMR (100 MHz, $CDCl_3$) 74.1 (CHOSi), 67.5 (CH$_2$OH), 39.8 (*C*HCH$_2$OH), 39.1 (CH*C*H$_2$CH), 35.6 (CH$_2$*C*H$_2$CHOSi), 26.6 (*C*H$_2$CH$_2$CHOSi), 26.0 (SiC(*C*H$_3$)$_3$), 18.3 (SiC), −4.6 (Si(CH$_3$)$_2$); EIMS *m*/*z* 173 ((M − ^{t}Bu)$^+$, 80), 75 (100); HRMS (EI) for $C_8H_{17}O_2Si$ (M − ^{t}Bu)$^+$calcd 173.0998, measured 173.0998.

(1*S*,3*S*)-[(3-*tert*-Butyldimethylsilanyloxycyclopent-1-yl)methyl] Acetate (30). Acetic anhydride (39 μL, 0.413 mmol) was added to a solution of alcohol **29** (48 mg, 0.208 mmol) in pyridine (1.0 mL). The mixture was stirred at rt for 16 h, and the solvent was evaporated in vacuo. The crude was purified by column chromatography (EtOAc/petroleum ether 5:95) to afford **30** as a colorless oil (57 mg, quant): $[\alpha]_D$ +7.7 (*c* 1.08, $CHCl_3$, 26 °C); IR 2954 (m), 2929 (m), 2893 (w), 2856 (m), 1743 (s), 1472 (w), 1463 (w), 1435 (w), 1364 (m), 1235 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 4.29 (1H, tt, J = 5.5, 3.5 Hz, CHOSi), 3.95 (2H, d, J = 7.0 Hz, CH_2OAc), 2.48 (1H, m, CHCH$_2$OAc), 2.05 (3H, s, COCH$_3$), 1.93 (1H, m, CH_aH$_b$CH$_2$CHOSi), 1.81 (1H, ddt, J = 13.0, 8.8, 5.6 Hz, CH$_2$CH_aH$_b$CHOSi), 1.73 (1H, dddd, J = 13.0, 8.0, 3.0, 1.5 Hz, CHCH_aH$_b$CH), 1.57 (1H, m, CH$_2$CH$_a$$H_b$CHOSi), 1.41 (1H, ddd, J = 13.0, 8.5, 5.5 Hz, CHCH$_a$$H_b$CH), 1.25 (1H, ddt, J = 13.0, 9.0, 7.0 Hz, CH$_a$$H_bCH_2$CHOSi), 0.88 (9H, s, SiC(CH$_3$)$_3$), 0.04 (6H, s, SiCH$_3$ × 2); ^{13}C NMR (100 MHz, $CDCl_3$) 171.4 (C═O), 73.9 (CHOSi), 68.6 (CH$_2$OAc), 39.5 (CH*C*H$_2$CH), 36.3 (*C*HCH$_2$OAc), 35.5 (CH$_2$*C*H$_2$CHOSi), 26.9 (*C*H$_2$CH$_2$CHOSi), 26.0 (SiC(*C*H$_3$)$_3$), 21.1 (CO*C*H$_3$), 18.2 (SiC), −4.6 (SiCH$_3$ × 2); ES$^+$ *m*/*z* 295 ((M + Na)$^+$, 70), 567 ((2M + Na)$^+$, 100); HRMS (ES$^+$) for $C_{14}H_{28}O_3SiNa$ (M + Na)$^+$ calcd 295.1670, measured 295.1699.

(1*S*,3*S*)-[(3-Hydroxycyclopent-1-yl)methyl] Acetate (31). TBAF (1.0 M solution in THF; 0.15 mL, 0.150 mmol) was added to a solution of acetate **30** (27.0 mg, 0.0991 mmol) in THF (1.0 mL). The mixture was stirred at room temperature for 4 h, and the solvent was evaporated in vacuo. The crude was filtered through silica gel and purified by HPLC (acetone/hexane 34:66) to afford **31** as a colorless oil (14.0 mg, 89%): $[\alpha]_D$ +9.4 (*c* 0.41, $CHCl_3$, 26 °C). IR 3411 (m, br), 2954 (m, br), 1740 (s), 1367 (m), 1241 (s), 1033 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 4.39 (1H, m, CHOH), 3.99 (1H, dd, J = 11.3, 6.8 Hz, CHHOAc), 3.97 (1H, dd, J = 11.3, 6.8 Hz, CHHOAc), 2.53 (1H, m, CHCH$_2$OAc), 2.06 (3H, s, COCH$_3$), 2.02−1.88 (2H, m, CH_aH$_b$CH$_2$CHOH + CH$_2$CH_aH$_b$CHOH), 1.80 (1H, ddt, J = 14.0, 8.0, 2.0 Hz, CHCH_aH$_b$CH), 1.61 (1H, m, CH$_2$CH$_a$$H_b$CHOH), 1.50 (1H, ddd, J = 14.0, 9.0, 5.0 Hz, CHCH$_a$$H_b$CH), 1.38 (1H, d, J = 1.5 Hz, OH), 1.33 (1H, m, CH$_a$$H_bCH_2$CHOH); ^{13}C NMR (100 MHz, $CDCl_3$) 171.4 (C═O), 73.7 (CHOH), 68.3 (CH$_2$OAc), 39.3 (CH*C*H$_2$CH), 36.4 (*C*HCH$_2$OAc), 35.1 (CH$_2$*C*H$_2$CHOH), 27.0 (*C*H$_2$CH$_2$CHOH), 21.1 (CO*C*H$_3$); ES$^+$ *m*/*z* 181 ((M + Na)$^+$, 100); HRMS (ES$^+$) for $C_8H_{14}O_3Na$ (M + Na)$^+$ calcd 181.0835, measured 181.0837.

(1′*R*,4′*S*)-3-Benzoyl-1-(4′-acetoxymethylcyclopentan-1′-yl)thymine (34). DIAD (64 μL, 0.304 mmol) was added to a solution of PPh_3 (80.0 mg, 0.304 mmol) in DMF (2.0 mL) at 0 °C, and the mixture was stirred for 1 h. A solution of 3-benzoylthymine **32** (140 mg, 0.609 mmol) and alcohol **31** (32.1 mg, 0.203 mmol) in DMF (2.0 mL) was then added, and the mixture was stirred at rt for 1 h. H_2O (10 mL) was added, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude was purified by column chromatography (acetone/petroleum ether 35:

65) and then by HPLC (EtOAc/hexane 6:4) to afford **34** (48.0 mg, 64%) and **33** (18.6 mg, 25%) as colorless oils.

Data for 34: $[\alpha]_D$ +23.5 (*c* 0.66, $CHCl_3$, 26 °C); IR 2954 (w), 1741 (s), 1695 (s), 1648 (vs), 1599 (w), 1441 (m), 1367 (m), 1240 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.94−7.91 (2H, m, CH_{Ar}), 7.64 (1H, m, CH_{Ar}), 7.52−7.47 (2H, m, CH_{Ar}), 7.14 (1H, q, J = 1.0 Hz, *C*=CH), 4.91 (1H, dtd, J = 11.0, 9.0, 7.5 Hz, C*H*N), 4.09 (2H, d, J = 6.5 Hz, CH_2OAc), 2.42−2.24 (2H, m, C*H*CH_2OAc + CHC$H_a$$H_b$CH), 2.15 (1H, m, $CH_2CH_aH_b$CH), 2.08 (3H, s, $COCH_3$), 2.00 (3H, s, CH_3), 1.91 (1H, m, C$H_a$$H_b$$CH_2$CH), 1.77 (1H, m, $CH_2CH_aH_b$CH), 1.61 (1H, dddd, J = 13.0, 9.5, 7.5, 6.0 Hz, $CH_aH_bCH_2$CH), 1.45 (1H, dt, J = 12.0, 10.0 Hz, $CHCH_aH_b$CH); ^{13}C NMR (100 MHz, $CDCl_3$) 171.2 (C=O), 169.3 (C=O), 162.8 (C=O), 150.1 (C=O), 136.4 (*C*=*C*H), 135.0 (CH_{Ar}), 131.9 (C_{Ar}), 130.6 (CH_{Ar} × 2), 129.2 (CH_{Ar} × 2), 111.3 (*C*=CH), 67.9 (CH_2OAc), 56.6 (CHN), 36.8 (*C*HCH_2OAc), 35.1 (CH*C*H_2CH), 29.8 (CH_2CH_2CH), 27.0 (*C*H_2CH_2CH), 21.0 (CO*C*H_3), 12.8 (CH_3); ES$^+$ *m*/*z* 393 ((M + Na)$^+$, 82), 371 ((M + H)$^+$, 100); HRMS (ES$^+$) for $C_{20}H_{22}N_2O_5Na$ (M + Na)$^+$ calcd 393.1421, measured 393.1417.

Data for *O*^{2}-(1′*R*,4′*S*)-3-benzoyl-1-(4′-acetoxymethylcyclopentan-1′-yl)thymine (33): IR 2960 (m,br), 1737 (s), 1611 (m), 1552 (m), 1429 (s), 1335 (m), 1236 (s), 1052 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 8.39 (1H, d, J = 1.0 Hz, CH=C), 8.21−8.18 (2H, m, CH_{Ph}), 7.67 (1H, m, CH_{Ph}), 7.55−7.51 (2H, m, CH_{Ph}), 5.37 (1H, tt, J = 6.0, 4.0 Hz, C*H*O), 4.08 (1H, dd, J = 11.0 6.5 Hz, C$H_a$$H_b$OAc), 4.05 (1H, dd, J = 11.0, 6.5 Hz, CH_aH_bOAc), 2.37−2.25 (2H, m, C*H*CH_2OAc + CHC$H_a$$H_b$CH), 2.15 (3H, d, J = 1.0 Hz, CH_3), 2.04 (3H, s, $COCH_3$) 2.00−1.92 (2H, m, C$H_a$$H_b$CHO), 1.84 (1H, m, C$H_a$$H_b$$CH_2$CH), 1.70−1.57 (2H, m, $CHCH_aH_b$CH + $CH_aH_bCH_2$CH); ^{13}C NMR (100 MHz, $CDCl_3$) 171.2 (C), 165.4 (C), 164.0 (C), 163.3 (C), 161.9 (*C*=*C*H), 134.3 (CH_{Ar}), 130.6 (CH_{Ph} × 2), 129.2 (CH_{Ph} × 2), 128.6 (C_{Ph}), 115.5 (*C*=CH), 79.5 (CHO), 68.6 (CH_2OAc), 37.4 (*C*HCH_2OAc), 35.9 (CH*C*H_2CH), 32.4 (CH_2CH_2CHO), 27.4 (*C*H_2CH_2CHO), 21.1 (CO*C*H_3), 12.3 (CH_3); ES$^+$ *m*/*z* 231 (100), 371 ((M + H)$^+$, 88), 393 ((M + Na)$^+$, 70); HRMS (ES$^+$) for $C_{20}H_{23}N_2O_5Na$ (M + H)$^+$ calcd 371.1601, measured 371.1603.

(1′*R*,4′*S*)-1-(4′-Hydroxymethylcyclopentan-1′-yl)thymine (6′-Carba-2′,3′-dideoxythymidine) (35). A mixture of **34** (38.2 mg, 0.103 mmol) and NH_3 (7 N solution in MeOH; 1.5 mL, 10.5 mmol) was stirred at rt for 24 h. The solvent was evaporated in vacuo, and the crude was purified by column chromatography (acetone/petroleum ether 6:4) to afford **35** as white crystals (20.6 mg, 89%): $[\alpha]_D$ +13.3 (*c* 2.08, MeOH, 29 °C) [lit.[30e] +11.30 (*c* 0.18, MeOH, 28 °C)]; ^1H NMR (400 MHz, DMSO-d_6) 11.14 (1H, s), 7.55 (1H, s), 4.72 (1H, m), 4.53 (1H, t, J = 5.5 Hz), 3.39 (2H, t, J = 5.5 Hz), 2.06 (1H, m), 1.95 (1H, dt, J = 12.0, 7.5 Hz), 1.86 (1H, m), 1.78 (3H, s), 1.75−1.62 (2H, m), 1.53 (1H, m), 1.37 (1H, m); ^{13}C NMR (100 MHz, DMSO-d_6) 163.7 (C=O), 150.9 (C=O), 137.6 (CH), 109.0 (CH), 64.8 (CH_2), 55.3 (CH), 39.5 (CH), 33.9 (CH_2), 29.1 (CH_2), 26.1 (CH_2), 12.0 (CH_3); ^1H NMR corresponds to the previously reported values.[30b,e] ^{13}C NMR corresponds to the previously reported values.[30c]

(1*S*,2*S*,3*R*)-(2-Benzyloxy-3-trityloxymethylcyclopentyloxy)-*tert*-butyldimethylsilane (36a). Raney nickel (slurry in water, rinsed with EtOH; ∼2 mL) was added to a solution of **17a** (126.0 mg, 0.184 mmol) in ethanol (1.85 mL). The mixture was stirred at reflux with the addition of Raney nickel (∼2 mL) every 30 min until complete conversion was evident by TLC (∼4 h). The suspension was cooled and filtered through Celite. The resulting solution was concentrated in vacuo and purified by column chromatography (EtOAc/petroleum ether 3:97) to afford **36a** as a colorless oil (92.0 mg, 86%): $[\alpha]_D$ +11.6 (*c* 2.1, $CHCl_3$, 24 °C); IR 3057 (w), 3029 w, 2949 (m), 2854 (m), 1490 (m), 1447 (m), 1359 (w), 1064 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.43−7.39 and 7.24−7.07 (20H, m, ArH), 4.46 (1H, d, J = 12.0 Hz, C$H_a$$H_b$Ph), 4.36 (1H, d, J = 12.0 Hz, CH_aH_bPh), 4.14 (1H, dt, J = 6.0, 2.5 Hz, CHOSi), 3.72 (1H, dd, J = 5.0, 2.5 Hz, CHOBn), 3.18 (1H, dd, J = 9.0, 7.5 Hz, C$H_a$$H_b$OTr), 3.16 (1H, dd, J = 9.0, 6.5 Hz, CH_aH_bOTr), 2.45 (1H, m, C*H*CH_2OTr), 1.95 (1H, m, C$H_a$$H_b$CHOSi), 1.80 (1H, m, C$H_a$$H_b$$CH_2$CHOSi), 1.44 (1H, m, CH_aH_bCHOSi), 1.34 (1H, m, $CH_aH_b$$CH_2$CHOSi), 0.85 (9H, s, SiC$(CH_3)_3$), 0.01 (3H, s, $SiCH_3$), 0.00 (3H, s, $SiCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) 144.7 (C_{Ar} × 3), 139.2 (C_{Ar}), 129.0 (CH_{Ar} × 6), 128.3 (CH_{Ar} × 2), 128.0 (CH_{Ar} × 6), 127.5 (CH_{Ar} × 2), 127.4 (CH_{Ar}), 126.9 (CH_{Ar} × 3), 86.7 (CHOBn), 86.6 (*C*Ph_3), 76.9 (CHOSi), 71.9 (CH_2Ph), 63.2 (CH_2OTr), 41.7 (*C*HCH_2OTr), 32.4 (*C*H_2CHOSi), 26.0 (SiC(*C*H_3)$_3$), 25.2 (*C*H_2CH_2CHOSi), 18.4 (SiC), −4.5 ($SiCH_3$ × 2); ES$^+$ *m*/*z* 601 ((M + Na)$^+$, 100); HRMS (ES$^+$) for $C_{38}H_{46}O_3SiNa$ (M + Na)$^+$ calcd 601.3108, measured 601.3119.

(1*S*,2*R*,3*R*)-(2-Benzyloxy-3-trityloxymethylcyclopentyloxy)-*tert*-butyldimethylsilane (36b). Raney nickel (slurry in water, rinsed with EtOH; ∼1 cm^3) was added to a solution of **17b** (94.0 mg, 0.138 mmol) in ethanol (1.46 mL), and the mixture was stirred at reflux for 4 h. The suspension was cooled, filtered through Celite, and concentrated in vacuo. The crude was purified by column chromatography (EtOAc/petroleum ether 1:9) to afford **36b** as a colorless oil (70 mg, 88%): $[\alpha]_D$ +36.0 (*c* 0.50, $CHCl_3$, 24 °C); IR 3058 (w), 3027 (w), 2950 (m), 2853 (m), 1489 (m), 1447 (m), 1358 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 7.36−7.32 and 7.23−7.13 (20H, m, ArH), 4.60 (1H, d, J = 12.0 Hz, C$H_a$$H_b$Ph), 4.40 (1H, d, J = 12.0 Hz, CH_aH_bPh), 4.07 (1H, m, CHOSi), 3.52 (1H, dd, J = 6.0, 4.0 Hz, CHOBn) see spectrum, 3.02 (1H, dd, J = 9.0, 6.0 Hz, C$H_a$$H_b$OTr), 3.00 (1H, dd, J = 9.0, 5.5 Hz, CH_aH_bOTr), 2.32 (1H, m, C*H*CH_2OTr), 1.87 (1H, m, C$H_a$$H_b$$CH_2$CHOSi), 1.69−1.64 (2H, m, CH_2CHOSi), 1.29 (1H, m, $CH_aH_b$$CH_2$CHOSi), 0.84 (9H, s, SiC$(CH_3)_3$), 0.00 (3H, s, $SiCH_3$), −0.01 (3H, s, $SiCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) 144.5 (C_{Ar} × 3), 139.3 (C_{Ar}), 128.9 (CH_{Ar} × 6), 128.3 (CH_{Ar} × 2), 127.8 (CH_{Ar} × 6), 127.7 (CH_{Ar} × 2), 127.3 (CH_{Ar}), 127.0 (CH_{Ar} × 3), 86.4 (CPh_3), 83.1 (CHOBn), 73.5 (CHOSi), 71.8 (CH_2Ph), 64.9 (CH_2OTr), 42.6 (*C*HCH_2OTr), 31.5 (*C*H_2CHOSi), 26.1 (SiC(*C*H_3)$_3$), 23.2 (*C*H_2CH_2CHOSi), 18.4 (SiC), −4.4 ($SiCH_3$), −4.5 ($SiCH_3$); ES$^+$ *m*/*z* 601 ((M + Na)$^+$, 100); HRMS (ES$^+$) for $C_{38}H_{46}O_3SiNa$ (M + Na)$^+$ calcd 601.3108, measured 601.3119.

The reaction requires careful monitoring in order to avoid benzyl hydrogenolysis leading to (1*R*,2*S*,5*R*)-2-*tert*-butyldimethylsilanyloxy-5-trityloxymethylcyclopentanol (**37b**): $[\alpha]_D$ +34.9 (*c* 0.78, $CHCl_3$, 27 °C); IR 3546 (m,br), 3058 (w), 2953 (m), 2928 (m), 2857 (m), 1597 (w), 1490 (m), 1448 (m), 1101 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.49−7.46 and 7.34−7.23 (15H, m, ArH), 4.11 (1H, q, J = 5.5 Hz, CHOSi), 3.73 (1H, q, J = 5.5 Hz, C*H*OH), 3.15 (1H, dd, J = 9.0, 5.0 Hz, C$H_a$$H_b$OTr), 3.10 (1H, dd, J = 9.0, 6.0 Hz, CH_aH_bOTr), 2.54 (1H, d, J = 5.5 Hz, OH), 2.17 (1H, m, C*H*CH_2OTr), 1.96 (1H, dtd, J = 13.0, 8.5, 4.0 Hz, C$H_a$$H_b$$CHCH_2$), 1.85 (1H, m, C$H_a$$H_b$CHOSi), 1.66 (1H, m, CH_aH_bCHOSi), 1.34 (1H, dq, J = 13.0 8.5 Hz, $CH_aH_b$$CHCH_2$), 0.92 (9H, s, SiC$(CH_3)_3$), 0.10 (6H, s, Si$(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) 144.5 (C_{Ar} × 3), 128.9 (CH_{Ar} × 6), 127.9 (CH_{Ar} × 6), 127.0 (CH_{Ar} × 3), 86.5 (CPh_3), 76.2 (CHOH), 74.6 (CHOSi), 65.3 (CH_2OTr), 45.0 (*C*HCH_2OTr), 31.6 (*C*H_2CHOH), 26.0 (SiC$(CH_3)_3$), 24.1 (*C*H_2CH_2CH), 18.3 (SiC), −4.4 ($SiCH_3$), −4.8 ($SiCH_3$); ES$^+$ *m*/*z* 511 ((M + Na)$^+$, 20); HRMS (ES$^+$) for $C_{31}H_{40}O_3SiNa$ (M + Na)$^+$ calcd 511.2639, measured 511.2653.

(1*S*,2*S*,3*R*)-2-Benzyloxy-3-trityloxymethylcyclopentan-1-ol (38a). TBAF (1.0 M solution in THF; 0.285 mL, 0.285 mmol) was added to a solution of **36a** (110 mg, 0.190 mmol) in THF (1.9 mL). The mixture was stirred at rt for 16 h. The solvent was removed in vacuo, and the residue was purified by column chromatography (EtOAc/petroleum ether 3:7) to afford **38a** as a white solid (81.0 mg, 92%): mp 38−40 °C; $[\alpha]_D$ +9.2 (*c* 0.80, $CHCl_3$, 24 °C); IR 3388 (w, br), 3059 (w), 3031 (w), 2931 (w), 2873 (w), 1490 (m), 1448 (m), 1067 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.49−7.43 and 7.30−7.12 (20H, m, ArH), 4.52 (1H, d, J = 12.0 Hz, C$H_a$$H_b$Ph), 4.46 (1H, d, J = 12.0 Hz, CH_aH_bPh), 4.25 (1H, m, C*H*OH), 3.87 (1H, dd, J = 5.5, 2.5 Hz, CHOBn), 3.27 (1H, dd, J = 9.0, 7.5 Hz, C$H_a$$H_b$OTr), 3.21 (1H, dd, J = 9.0, 6.5 Hz, CH_aH_bOTr), 2.57 (1H, m, C*H*CH_2OTr), 2.11 (1H, m, C$H_a$$H_b$$CH_2$CHOH), 1.88 (1H, m,

CH_aH$_b$CHOH), 1.55−1.43 (3H, m, CH$_a$$H_bCH_2$CHOH + CH$_a$$H_b$-CHOH + OH); ^{13}C NMR (100 MHz, $CDCl_3$) 144.6 (C_{Ar} × 3), 138.8 (C_{Ar}), 128.9 (CH_{Ar} × 6), 128.4 (CH_{Ar} × 2), 127.8 (CH_{Ar} × 6), 127.6 (CH_{Ar} × 2), 127.5 (CH_{Ar}), 127.0 (CH_{Ar} × 3), 86.6 (CPh_3), 86.4 (CHOBn), 76.5 (CHOH), 72.0 (CH_2Ph), 62.8 (CH_2OTr), 41.8 (*C*HCH$_2$OTr), 31.7 (*C*H$_2$CHOH), 24.9 (*C*H$_2$CH$_2$CHOH); ES$^+$ *m*/*z* (%) 487 ((M + Na)$^+$, 100); HRMS (ES$^+$) for $C_{32}H_{32}O_3Na$ (M + Na)$^+$ calcd 487.2243, measured 487.2232.

(1*S*,2*R*,3*R*)-2-Benzyloxy-3-trityloxymethylcyclopentan-1-ol (38b). TBAF (1.0 M solution in THF, 93.0 μL, 0.0930 mmol) was added to a solution of **36b** (24.0 mg, 0.0415 mmol) in THF (0.42 mL). The mixture was stirred at rt for 4 h. The solvent was removed in vacuo, and the residue was purified by column chromatography (EtOAc/petroleum ether 3:7) to afford **38b** as a white foam (18.0 mg, 93%): [α]$_D$ +19.0 (*c* 1.7, $CHCl_3$, 24 °C); IR 3466 (w, br), 3058 (w), 3031 (w), 2968 (w), 2924 (w), 2866 (w), 1489 (w), 1448 (m), 1080 (s), 1074 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.48−7.44 and 7.36−7.24 (20H, m, ArH), 4.59 (1H, d, *J* = 11.5 Hz, CH_aH$_b$Ph), 4.54 (1H, d, *J* = 11.5 Hz, CH$_a$$H_b$Ph), 4.11 (1H, quintet, *J* = 4.5 Hz, C*H*OH), 3.73 (1H, dd, *J* = 6.5, 4.5 Hz, CHOBn), 3.17 (1H, dd, *J* = 9.0, 5.5 Hz, CH_aH$_b$OTr), 3.14 (1H, dd, *J* = 9.0, 6.0 Hz, CH$_a$$H_b$OTr), 2.54 (1H, d, *J* = 4.0 Hz, OH), 2.38 (1H, m, C*H*CH$_2$OTr), 2.01 (1H, dtd, *J* = 12.9, 9.1, 5.9 Hz, CH_aH$_b$CH$_2$CHOH), 1.88−1.73 (2H, m, CH_2CHOH), 1.42 (1H, dddd, *J* = 14.5, 9.0, 8.0, 7.0 Hz, CH$_a$$H_bCH_2$CHOH); ^{13}C NMR (100 MHz, $CDCl_3$) 144.4 (C_{Ar} × 3), 138.2 (C_{Ar}), 128.9 (CH_{Ar} × 6), 128.6 (CH_{Ar} × 2), 127.88 (CH_{Ar}), 127.87 (CH_{Ar} × 6), 127.8 (CH_{Ar} × 2), 127.1 (CH_{Ar} × 3), 86.5 (CPh_3), 83.6 (CHOBn), 72.1 (CH_2Ph), 71.7 (CHOH), 64.7 (CH_2OTr), 42.6 (*C*HCH$_2$OTr), 30.8 (*C*H$_2$CHO), 23.8 (*C*H$_2$CH$_2$CHO); ES$^+$ *m*/*z* 487 ((M + Na)$^+$, 100); HRMS (ES$^+$) for $C_{32}H_{32}O_3Na$ (M + Na)$^+$ calcd 487.2243, measured 487.2253.

(1*S*,2*R*,3*R*)-2-Benzyloxy-3-trityloxymethylcyclopent-1-yl Methanesulfonate (42). MsCl (5.3 μL, 0.0678 mmol) was added to a solution of **38b** (21.0 mg, 0.0452 mmol) and Et_3N (9.5 μL, 0.0678 mmol) in CH_2Cl_2 (0.45 mL). The mixture was stirred at rt for 45 min. The solvent was evaporated in vacuo, and the crude was purified by column chromatography (acetone/petroleum ether 25:75) to afford **42** as white crystals (24 mg, 98%): mp 139−140 °C (CH_2Cl_2/petroleum ether); [α]$_D$ +54.1 (*c* 0.61, $CHCl_3$, 26 °C); IR 3058 (w), 3031 (w), 2937 (w), 2871 (w), 1490 (m), 1449 (m), 1354 (s), 1176 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.44−7.40 and 7.32−7.22 (20H, m, ArH), 5.19 (1H, m, CHOS), 4.65 (1H, d, *J* = 11.5 Hz, CH_aH$_b$Ph), 4.43 (1H, d, *J* = 11.5 Hz, CH$_a$$H_b$Ph), 3.81 (1H, dd, *J* = 9.0, 4.0 Hz, CHOBn), 3.23 (1H, dd, *J* = 9.0, 4.5 Hz, CH_aH$_b$OTr), 3.16 (1H, dd, *J* = 9.0, 5.5 Hz, CH$_a$$H_b$OTr), 2.97 (3H, s, SO_2CH_3), 2.38 (1H, m, C*H*CH$_2$OTr), 2.11−1.94 (3H, m, CH_2CHOS + CH_aH$_b$CH$_2$CHOS), 1.63 (1H, m, CH$_a$$H_bCH_2$CHOS); ^{13}C NMR (100 MHz, $CDCl_3$) 144.2 (C_{Ar} × 3), 137.9 (C_{Ar}), 128.9 (CH_{Ar} × 6), 128.5 (CH_{Ar} × 2), 128.1 (CH_{Ar} × 2), 127.9 (CH_{Ar} × 7), 127.1 (CH_{Ar} × 3), 86.6 (CPh_3), 81.9 (CHOBn + CHOS), 72.6 (CH_2Ph), 63.5 (CH_2OTr), 42.0 (*C*HCH$_2$OAc), 39.0 (SO_2CH_3), 28.9 (*C*H$_2$CHOS), 22.9 (*C*H$_2$CH$_2$CHOS); ES$^+$ *m*/*z* 565 ((M + Na)$^+$, 100); HRMS (ES$^+$) for $C_{33}H_{34}O_5S$ (M + Na)$^+$ calcd 565.2019, measured 565.2032.

(1′*R*,2′*R*,3′*R*)-(2′-Benzyloxy-3′-trityloxymethylcyclopent-1′-yl)-4-nitrobenzoate (43). DIAD (21.0 μL, 0.0980 mmol) was added to a solution of PPh_3 (25.5 mg, 0.0972 mmol) in THF (0.65 mL) at 0 °C, and the mixture was stirred for 1 h. A solution of 4-nitrobenzoic acid (16.2 mg, 0.0972 mmol) and alcohol **38b** (30.1 mg, 0.0648 mmol) in THF (0.65 mL) was then added at 0 °C, and the mixture was stirred at rt for 1 h. The solvent was evaporated in vacuo, and the crude was purified by column chromatography (acetone/petroleum ether 15:85) to afford **43** as a white foam (38.5 mg, 97%): [α]$_D$ −30.4 (*c* 1.35, $CHCl_3$, 27 °C); IR 3085 (w), 3057 (w), 3031 (w), 2869 (w), 1723 (s), 1607 (m), 1527 (s), 1271 (s), 1102 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 8.24 (2H, d, *J* = 9.0 Hz, CH_{Ar}), 8.02 (2H, d, *J* = 9.0 Hz, CH_{Ar}), 7.46−7.41 and 7.29−7.19 (20H, m, ArH), 5.40 (1H, quintet, *J* = 3.0 Hz, CHOC=O), 4.67 (1H, d, *J* = 12.0 Hz, CH_aH$_b$Ph), 4.60 (1H, d, *J* = 12.0 Hz, CH$_a$$H_b$Ph), 3.93 (1H, ddd, *J* = 5.0, 2.5, 1.0 Hz, CHOBn), 3.24 (1H, dd, *J* = 9.0, 6.0 Hz, CH_aH$_b$OTr), 3.17 (1H, dd, *J* = 9.0, 6.5 Hz, CH$_a$$H_b$OTr), 2.41 (1H, m, C*H*CH$_2$OTr), 2.20 (1H, dddd, *J* = 14.0, 10.0, 8.0, 6.0 Hz, CH_aH$_b$CHO), 2.03 (1H, m, CH_aH$_b$CH$_2$CH), 1.85 (1H, m, CH$_a$$H_b$CHO), 1.68 (1H, dddd, *J* = 13.0, 10.0, 9.0, 7.0 Hz, CH$_a$$H_bCH_2$CH); ^{13}C NMR (100 MHz, $CDCl_3$) 164.0 (C=O), 150.6 (C_{Ar}), 144.2 (C_{Ar} × 3), 138.4 (C_{Ar}), 135.8 (C_{Ar}), 130.8 (CH_{Ar} × 2), 128.9 (CH_{Ar} × 6), 128.5 (CH_{Ar} × 2), 127.9 (CH_{Ar} × 6), 127.8 (CH_{Ar} × 2), 127.7 (CH_{Ar}), 127.1 (CH_{Ar} × 3), 123.6 (CH_{Ar} × 2), 86.6 (CPh_3), 86.2 (CHOBn), 81.5 (CHOC=O), 72.1 (CH_2Ph), 64.8 (CH_2OTr), 45.6 (*C*HCH$_2$OTr), 30.3 (*C*H$_2$CHO), 26.0 (*C*H$_2$CH$_2$CH); ES$^+$ *m*/*z* 636 ((M + Na)$^+$, 5), 243 (100); HRMS (ES$^+$) for $C_{39}H_{35}NO_6Na$ (M + Na)$^+$ calcd 636.2357, measured 636.2365.

(1*R*,2*R*,3*R*)-2-Benzyloxy-3-trityloxymethylcyclopentan-1-ol (44). A mixture of **43** (22.9 mg, 0.0373 mmol) and NH_3 (7 N solution in MeOH; 0.74 mL, 5.18 mmol) was stirred at rt for 16 h. The solvent was evaporated in vacuo, and the crude was purified by column chromatography (acetone/petroleum ether 2:8) to afford **44** as a white foam (12.2 mg, 70%) and starting material **43** (5.2 mg, 23%): [α]$_D$ +25.3 (*c* 0.48, $CHCl_3$, 27 °C); IR 3458 (m, br), 3058 (w), 3030 (w), 2868 (w), 1490 (m), 1449 (m), 1069 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.47−7.42 and 7.32−7.21 (20H, m, ArH), 4.54 (2H, s, CH_2Ph), 4.16 (1H, m, C*H*OH), 3.58 (1H, dd, *J* = 5.0, 4.0, Hz, CHOBn), 3.22 (1H, dd, *J* = 9.0, 5.5 Hz, CH_aH$_b$OTr), 3.19 (1H, dd, *J* = 9.0, 5.5 Hz, CH$_a$$H_b$OTr), 2.22 (1H, m, C*H*CH$_2$OTr), 1.97−1.83 (2H, m, CH_aH$_b$CH$_2$CH + CH_aH$_b$CHOH), 1.74−1.60 (3H, m, CH$_a$$H_b$CHOH + CH$_a$$H_bCH_2$CH + OH); ^{13}C NMR (100 MHz, $CDCl_3$) 144.3 (C_{Ar} × 3), 138.8 (C_{Ar}), 128.9 × 6 (CH_{Ar} × 6), 128.5 (CH_{Ar} × 2), 127.9 (CH_{Ar} × 6), 127.73 (CH_{Ar} × 2), 127.65 (CH_{Ar}), 127.1 (CH_{Ar} × 3), 89.1 (CHOBn), 86.9 (CPh_3), 77.8 (CHOH), 72.0 (CH_2Ph), 65.2 (CH_2OTr), 44.7 (*C*HCH$_2$OTr), 32.2 (*C*H$_2$CHOH), 24.7 (*C*H$_2$CH$_2$CH); ES$^+$ *m*/*z* 487 ((M + Na)$^+$, 18), 243 (100); HRMS (ES$^+$) for $C_{32}H_{32}O_3Na$ (M + Na)$^+$ calcd 487.2244, measured 487.2250.

(1*R*,2*R*,3*R*)-*N*-(2-Benzyloxy-3-trityloxymethylcyclopent-1-yl)-phthalimide (45). DIAD (70.0 μL, 0.333 mmol) was added to a solution of PPh_3 (87.3 mg, 0.333 mmol) in THF (2.2 mL) at 0 °C, and the mixture was stirred for 0.5 h. Alcohol **38b** (103 mg, 0.222 mmol) in THF (2.2 mL) was then added, followed by phthalimide (98.0 mg, 0.666 mmol), and the mixture was stirred at rt for 2 d. The solvent was evaporated in vacuo, and the crude was purified by column chromatography (EtOAC/petroleum ether 2:8) to afford **45** as a white solid (124 mg, 94%): mp 52−55 °C; [α]$_D$ −13.6 (*c* 0.54, $CHCl_3$, 27 °C); IR 3059 (w), 3031 (w), 2946 (w), 2915 (w), 2872 (w), 1770 (m), 1708 (vs), 1387 m, 1072 (m) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.79−7.74 (2H, m, ArH), 7.71−7.66 (2H, m, ArH), 7.53−7.48 (6H, m, ArH), 7.35−7.22 (10H, m, ArH), 7.02−6.91 (4H, m, ArH), 4.60 (1H, dt, *J* = 9.5, 8.0 Hz, CHN), 4.44 (1H, t, *J* = 8.0 Hz, CHOBn), 4.39 (1H, d, *J* = 12.0 Hz, CH_aH$_b$Ph), 4.23 (1H, d, *J* = 12.0 Hz, CH$_a$$H_b$Ph), 3.35 (1H, dd, *J* = 9.0, 5.0 Hz, CH_aH$_b$OTr), 3.24 (1H, dd, *J* = 9.0, 6.0 Hz, CH$_a$$H_b$OTr), 2.31 (1H, m, C*H*CH$_2$OTr), 2.11−1.94 (4H, m, CH_2 × 2); ^{13}C NMR (100 MHz, $CDCl_3$) 168.2 (C=O × 2), 144.4 (C_{Ar} × 3), 138.7 (C_{Ar}), 133.8 (CH_{Ar} × 2), 132.2 (C_{Ar} × 2), 129.0 (CH_{Ar} × 6), 128.2 (CH_{Ar} × 2), 127.9 (CH_{Ar} × 8), 127.3 (CH_{Ar}), 127.1 (CH_{Ar} × 3), 123.2 (CH_{Ar} × 2), 86.6 (CPh_3), 82.8 (CHOBn), 72.4 (CH_2Ph), 64.5 (CH_2OTr), 56.5 (CHN), 45.1 (*C*HCH$_2$OTr), 26.1 (CH_2), 25.1 (CH_2); ES$^+$ *m*/*z* 616 ((M + Na)$^+$, 100); HRMS (ES$^+$) for $C_{40}H_{35}NO_4Na$ (M + Na)$^+$ calcd 616.2458, measured 616.2466.

(1*R*,2*R*,3*R*)-2-Benzyloxy-3-trityloxymethylcyclopentamine (54). Hydrazine (28.0 μL, 0.570 mmol) and **45** (84.7 mg, 0.143 mmol) in EtOH (1.4 mL) were stirred at reflux for 4 h. The mixture was cooled, filtered, and concentrated in vacuo. The crude was purified by column chromatography (acetone/petroleum ether 2:8) to afford a mixture of compounds that was purified by HPLC (MeOH/CH_2Cl_2 5:95) to afford amine **54** as a clear oil (26.1 mg, 44%): [α]$_D$ = +5.7 (*c* = 1.1, $CHCl_3$, 27 °C); IR 3059 (w), 3030 (w), 2948 (w),

2867 (w), 1662 (w), 1597 (w), 1491 (m), 1449 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.49−7.44 and 7.33−7.22 (20H, m, ArH), 4.55 (1H, d, J = 12.0 Hz, CH_aH$_b$Ph), 4.48 (1H, d, J = 12.0 Hz, CH_aH$_b$Ph), 3.36 (1H, t, J = 6.0 Hz, CHOBn), 3.27 (1H, m, CHN), 3.22 (1H, dd, J = 9.0, 6.0 Hz, CH_aH$_b$OTr), 3.16 (1H, dd, J = 9.0, 6.5 Hz, CH$_a$$H_b$OTr), 2.26 (1H, m, C$HCH_2$OTr), 1.97−1.85 (2H, m, CH_aH$_b$CH$_2$CHN + CH_aH$_b$CHN), 1.60 (1H, m, CH$_a$$H_bCH_2$CHN), 1.41−1.28 (3H, m, CH$_a$$H_b$CHN + NH$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) 144.4 (C_{Ar} × 3), 139.0 (C_{Ar}), 128.9 (CH_{Ar} × 6), 128.5 (CH_{Ar} × 2), 127.9 (CH_{Ar} × 6), 127.7 (CH_{Ar} × 2), 127.6 (CH_{Ar}), 127.1 (CH_{Ar} × 3), 90.6 (CHOBn), 86.7 (CPh_3), 72.3 (CH_2Ph), 65.5 (CH_2OTr), 58.7 (CHN), 45.1 (*C*HCH$_2$OTr), 32.2 (*C*H$_2$CHN), 25.2 (*C*H$_2$CH$_2$CH); ES^+ *m*/*z* 504 ((M + MeCN)$^+$, 25); HRMS (ES^+) for $C_{32}H_{34}NO_2$ (M + H)$^+$ calcd 464.2584, measured 464.2577.

(1*R*,2*R*,3*R*)-*N*^{1}-(2-Benzyloxy-3-trityloxymethylcyclopentyl)-*N*^{3}-((*E*)-3-methoxyacryloyl)urea (56). A mixture of amine **54** (36.9 mg, 0.0796 mmol), Et_3N (13.3 μL, 0.0955 mmol), and carbamate **55** (14.3 mg, 0.0955 mmol) in dioxane (0.8 mL) was stirred at 100 °C for 36 h. The solvent was evaporated in vacuo, and the residue was purified by column chromatography (acetone/petroleum ether 3:7) to afford carbanucleoside precursor **56** as a white foam (22.3 mg, 47%): $[\alpha]_D$ −5.9 (*c* 0.67, $CHCl_3$, 27 °C); IR 3233 (m,br), 3087 (w), 3061 (w), 2958 (m,br), 2868 (w), 1701 (m), 1677 (s), 1616 (m), 1549 (s), 1491 (m), 1449 (m), 1152 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 9.96 (1H, s, NH), 8.81 (1H, d, J = 12.5 Hz, NH), 7.65 (1H, d, J = 12.5 Hz, CH=CH), 7.46−7.41 and 7.31−7.19 (20H, m, ArH), 5.39 (1H, d, J = 12.5 Hz, CH=CH), 4.66 (1H, d, J = 11.5 Hz, CH_aH$_b$Ph), 4.54 (1H, d, J = 11.5 Hz, CH$_a$$H_b$Ph), 4.24 (1H, tt, J = 7.5, 5.0 Hz, CHN), 3.71 (1H, m, CHOBn), 3.61 (3H, s, OMe), 3.15 (2H, app. d, J = 6.0 Hz, CH_2OTr), 2.29 (1H, tq, J = 8.5, 6.0 Hz, CHCH$_2$OTr), 2.11 (1H, m, CH_aH$_b$CHN), 1.96 (1H, m, CH_aH$_b$CH$_2$CH), 1.66−1.54 (2H, m, CH$_a$$H_b$CHN + CH$_a$$H_bCH_2$CH); ^{13}C NMR (100 MHz, $CDCl_3$) 168.1 (C=O), 163.4 (C=O), 155.1 (*C*H=CH), 144.3 (C_{Ar} × 3), 138.7 (C_{Ar}), 128.9 (CH_{Ar} × 6), 128.4 (CH_{Ar} × 2), 127.9 (CH_{Ar} × 6), 127.7 (CH_{Ar} × 2), 127.5 (CH_{Ar}), 127.0 (CH_{Ar} × 3), 97.8 (CH=*C*H), 87.6 (CHOBn), 86.6 (CPh_3), 72.1 (CH_2Ph), 65.0 (CH_2OTr), 57.8 (OCH_3), 56.5 (CHN), 45.6 (*C*HCH$_2$OTr), 30.3 (*C*H$_2$CHN), 25.8 (*C*H$_2$CH$_2$CH); ES^+ *m*/*z* 613 ((M + Na)$^+$, 12); HRMS (ES^+) for $C_{37}H_{38}N_2O_5Na$ (M + Na)$^+$ calcd 613.2673, measured 613.2684.

(1*R*,2*R*,3*R*)-1-(2-Benzyloxy-3-hydroymethylcyclopentyl)uracil (57). A solution of urea **56** (53.2 mg, 0.0901 mmol) in 2 M H_2SO_4/dioxane (1:1; 1.8 mL) was stirred at reflux for 4 h. NaOH (2 M, 0.9 mL) was added, and neutralization was completed by the addition of satd $NaHCO_3$. The solvent was evaporated in vacuo, and the residue was suspended in EtOH (5 mL) and sonicated (or vigorously stirred) for 5 min. The ethanolic suspension was filtered, concentrated in vacuo, and purified by column chromatography (MeOH/CH_2Cl_2 4:96) to afford **57** as a white solid (19.7 mg, 69%): mp 115−116 °C; $[\alpha]_D$ −5.1 (*c* 0.87, $CHCl_3$, 27 °C); IR 3412 (m, br), 3197 (m, br), 3059 (w), 2947 (w), 2876 (w), 1678 (vs), 1464 (m), 1380 (m), 1072 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) 7.31−7.22 (5H, m, ArH), 7.11 (1H, d, J = 8.0 Hz, CH=CH), 5.62 (1H, d, J = 8.0 Hz, CH=CH), 4.57 (1H, d, J = 12.0 Hz, CH_aH$_b$Ph), 4.56 (1H, td, J = 9.5, 7.5 Hz, CHN), 4.50 (1H, d, J = 12.0 Hz, CH$_a$$H_b$Ph), 4.17 (1H, t, J = 7.0 Hz, CHOBn), 3.77 (1H, dd, J = 10.5, 5.5 Hz, CH_aH$_b$OH), 3.74 (1H, dd, J = 10.5, 6.0 Hz, CH$_a$$H_b$OH), 2.26 (1H, m, C$HCH_2$OH), 2.08 (1H, m, C$H_aH_b$CHN), 1.99−1.87 (2H, m, CH_aH$_b$CH$_2$CH + CH$_a$$H_b$CHN), 1.71 (1H, m, CH$_a$$H_bCH_2$CH); ^{13}C NMR (100 MHz, $CDCl_3$) 163.6 (C=O), 151.1 (C=O), 143.1 (*C*=C), 138.1 (C_{Ar}), 128.6 (CH_{Ar} × 2), 128.1 (CH_{Ar} × 3), 102.7 (*C*=*C*), 83.2 (CHOBn), 72.2 (CH_2Ph), 66.4 (CHN), 64.1 (CH_2OH), 45.8 (*C*HCH$_2$OH), 27.7 (*C*H$_2$CHN), 24.3 (*C*H$_2$CH$_2$CH); ES^+ *m*/*z* 317 ((M + H)$^+$, 100); HRMS (ES^+) for $C_{17}H_{20}N_2O_4Na$ (M + Na)$^+$ calcd 339.1315, measured 339.1323.

(6′*R*)-6′-Carba-2′,3′-dideoxy-6′-hydroxy-L-uridine (58). A mixture of $Pd(OH)_2$ on carbon (20% Pd; 10.0 mg, 0.0142 mmol) and **57** (22.4 mg, 0.0709 mmol) in MeOH (0.7 mL) was stirred under a hydrogen atmosphere (balloon) at rt for 30 min. The mixture was then filtered through Celite, concentrated in vacuo, and purified by HPLC (MeOH/CH_2Cl_2 2:8) to afford **58** (13.8 mg, 86%) as a white waxy solid: $[\alpha]_D$ −6.0 (*c* 0.47, $CHCl_3$, 27 °C); IR 3367 (m, br), 3052 (w), 2952 (w), 2879 (w), 1662 (vs), 1468 (m), 1383 (m), 1259 (m) cm^{-1}; ^1H NMR (400 MHz, CD_3OD) 7.63 (1H, d, J = 8.0 Hz, CH=CH), 5.69 (1H, d, J = 8.0 Hz, CH=CH), 4.59 (1H, q, J = 9.0 Hz, CHN), 4.04 (1H, t, J = 9.0 Hz, CHOH), 3.73 (1H, dd, J = 11.0, 4.5 Hz, CH_aH$_b$OH), 3.60 (1H, dd, J = 11.0, 6.5 Hz, CH$_a$$H_b$OH), 2.12−1.89 (3H, m, C$HCH_2$OH + C$H_aH_b$CHN + C$H_aH_bCH_2$CH), 1.83−1.66 (2H, m, CH$_a$$H_b$CHN + CH$_a$$H_bCH_2$CH); ^{13}C NMR (100 MHz, CD_3OD) 166.5 (C=O), 153.3 (C=O), 144.5 (*C*=C), 102.6 (*C*=*C*), 76.6 (CHOH), 65.7 (CHN), 64.2 (CH_2OH), 47.1 (*C*HCH$_2$OH), 26.6 (*C*H$_2$CHN), 23.8 (*C*H$_2$CH$_2$CH); ES^+ *m*/*z* 227 ((M + H)$^+$, 100); HRMS (ES^+) for $C_{10}H_{15}N_2O_4$ (M + H)$^+$ calcd 227.1026, measured 227.1028.

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Supporting Information Available: Experimental details and compound characterization data from (1) the carbacyclization (Scheme 2), (2) the monofunctionalization of **15** and the Brook rearrangement on **25** with structural correlation of the monoaddition products with **12b**, (3) optimization of the tritylation of **12**, (4) the Mukayiama reaction investigations (Scheme 8), (5) unsuccessful Mitsunobu attempts with **44a** and derivatives, and (6) reaction of **36a** with H_2, Pd/C. Copies of ^1H and ^{13}C NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(43) The United Kingdom Database Service: Fletcher, D. A., McMeeking, R. F., Parkin, D. *J. Chem. Inf. Comput. Sci.* **1996**, *36*, 746−749.