Total Synthesis of a Thymidine 2-Deoxypolyoxin C Analogue

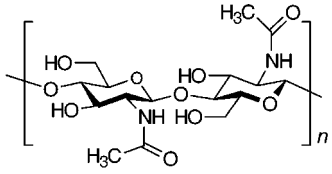
Cécile Dehoux, Evelyne Fontaine, Jean-Marc Escudier, Michel Baltas,* and Liliane Gorrichon*

Laboratoire de synthèse et physicochimie organique, ESA 5068 associé au CNRS, Université Paul Sabatier, 118 route de Narbonne, 31062 Toulouse Cedex 4, France

Received November 18, 1997

The synthesis of the thymidine 2-deoxypolyoxin C analogue **10** from a noncarbohydrate precursor was achieved in 10 steps and 9% yield starting from a chiral γ,δ-epoxy-β-hydroxy ester **11** readily available from *cis*-2-butene-1,4-diol. The main steps concern the stereo- and regioselective opening of the epoxide ring by an azide anion, the stereoselective introduction of the thymine base, and the transformation of the primary alcohol to the acid functionality of the final product. Two other approaches have also been investigated.

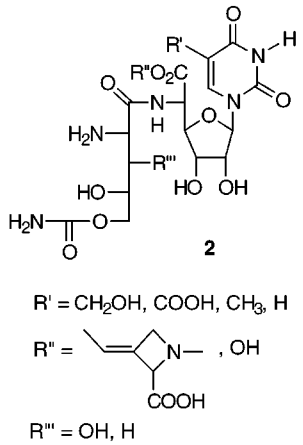
Chitin (**1**), the β-1→4-linked polymer of *N*-acetylglucosamine (GlcNAc), is one of the most common polysaccharides and one of the major structural components of the cell wall of most fungi.[1] The enzyme chitin synthase (EC 2.4.1.16)[2] catalyses the production of this linear macromolecule by polymerization of GlcNAc from the activated precursor UDP-GlcNAc.



1

Chitin is not found in green plants or vertebrates,[3] so that chitin synthase and the cellular mechanisms that regulate the activity of this enzyme can be considered excellent targets for pharmaceutical and agricultural pathogen management. Polyoxins form an important class of peptidyl nucleosides isolated from the culture broths of *Streptomyces cacaoi* var. *asoensis*[4] and were found to be potent inhibitors of chitin synthase.[5] Polyoxin D is used as an agricultural antifungal agent to treat rice sheath blight and pear black spot.[6]

Since the sugar component of the molecule is common to all members of the polyoxins as well as to related classes of compounds (nikkomycins),[7] the development of a general synthetic route to these N-glycosides and their analogues is a matter of considerable significance.

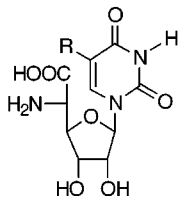


2

R' = CH_2OH, COOH, CH_3, H

R" =

R"' = OH, H



3 R = H
4 R = CH_2OH (polyoxin C)
5 R = CH_3 (deoxypolyoxin C)

These important amino acid nucleosides have been obtained either by degradation of natural polyoxins[8] or by a variety of synthetic approaches. All but one of the synthetic strategies developed have employed existing optically active natural products especially carbohydrates,[9] nucleosides[10], and cyclitols.[11] Vogel et al.[12] reported the first total asymmetric synthesis of the deoxypolyoxin C compound without using a starting material from the chiral pool; the synthesis (eq 1) begins with a Diels−Alder condensation of furan and 1-cyanovinyl (1*S*′)-camphanate. The chiral auxiliary is recovered during the third step of the reported synthesis.

* To whom correspondence should be addressed (M.B.). Tel.: 33 (0)5 61 55 62 93. Fax: 33 (0)5 61 55 60 11. E-mail: baltas@iris.ups-tlse.fr.

(1) Bartnicki-Garcia, S. *Annu. Rev. Microbiol.* **1968**, *22*, 87. Cabib, E.; Shematek, E. M. In *Biology of Carbohydrates*; Ginsburg, V., Robius, P. W., Ed.; John Wiley and Sons: New York, 1981; Vol. I, p 51. Cabib, E. *Adv. Enzymol.* **1987**, *59*, 59.

(2) Adams, D. J.; Causier, B. E.; Mellor, K. J.; Keer, V.; Milling, R.; Dada, J. In *Chitin Enzymology*; Muzzarelli, R. A. A., Ed.; European Chitin Society; Ancona, 1993; p 15.

(3) Gooday, G. W. In *Biochemistry of Cell Walls and Membranes in Fungi*; Kuhn, P. J., Trinci, A. P. J., Jung, M. J., Goosey, M. W., Copping, L. G., Eds.; Springer-Verlag: Berlin, 1990; p 61.

(4) Isono, K.; Asahi, K.; Suzuki, S. *J. Am. Chem. Soc.* **1969**, *91*, 7490. Isono, K.; Suzuki, S. *Heterocycles* **1979**, *13*, 333.

(5) Hori, M.; Kakiki, K.; Misato, T. *Agric. Biol. Chem.* **1974**, *38*, 691 and 698.

(6) Ko, K. In *Pesticide Chemistry: Human Welfare and the Environment*; Miyamoto, J., Ed.; Pergamon Press: Elmsford, NY, 1983; p 247.

(7) Konig, W. A.; Hahn, H.; Rathmann, R.; Hass, W.; Keckeisen, A.; Hagenmeier, H.; Bormann, C.; Deheler, W.; Kurt, R.; Zahner, H. *Liebigs Ann. Chem.* **1986**, 407.

(8) Isono, K. *J. Antibiot.* **1988**, *41*, 1711 and references therein.

(9) (a) Naka, T.; Hashizume, T.; Nishimura, M. *Tetrahedron Lett.* **1971**, *12*, 95. (b) Ohrui, H.; Kuzuhara, H.; Emoto, S. *Tetrahedron Lett.* **1971**, *12*, 4267. (c) Mukaiyama, T.; Suzuki, K.; Yamada, T.; Tabusa, F. *Tetrahedron* **1990**, *46*, 265. (d) Garner, P.; Park, J. M. *J. Org. Chem.* **1990**, *55*, 3772. (e) Dondoni, A.; Junquera, F.; Merchan, F. L.; Merino, P.; Tejero, T. *J. Chem. Soc., Chem. Commun.* **1995**, 2127. (f) Dondoni, A.; Franco, S.; Junquera, F.; Merchan, F. L.; Merino, P.; Tegero, T. *J. Org. Chem.* **1997**, *62*, 5497.

(10) Evina, C. M.; Guillerm, G. *Tetrahedron Lett.* **1996**, *37*, 163.

(11) Chida, N. Koizumi, K.; Kitada, Y.; Yokoyama, C.; Ogawa, S. *J. Chem. Soc., Chem. Commun.* **1994**, 111.

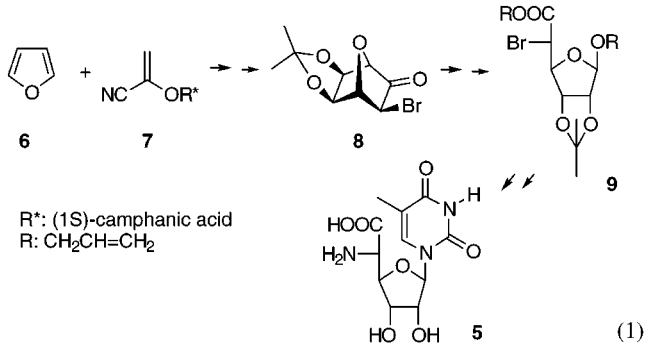
(12) Auberson, Y.; Vogel, P. *Tetrahedron* **1990**, *46*, 7019.

(13) Escudier, J. M.; Baltas, M.; Gorrichon, L. *Tetrahedron Lett.* **1992**, *33*, 1439. Nacro, K.; Baltas, M.; Escudier, J. M.; Gorrichon, L. *Tetrahedron* **1997**, *53*, 659.

(14) Nacro, K.; Baltas, M.; Escudier, J. M.; Gorrichon, L. *Tetrahedron Lett.* **1995**, *33*, 7867.

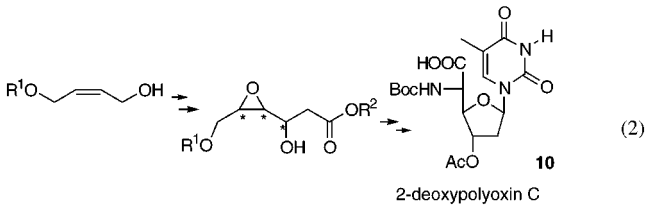
(15) Devianne, G.; Escudier, J. M.; Baltas, M.; Gorrichon, L. *J. Org. Chem.* **1995**, *60*, 7343.

S0022-3263(97)02116-6 CCC: $15.00
Published on Web 03/28/1998



(1)

We now report an efficient de novo synthesis of the *N*-*t*-Boc-2-deoxydeoxypolyoxin C derivative **10** by a strategy (eq 2) that allows stereocontrolled construction of all three contiguous asymmetric centers.



(2)

The methodology developed here is based on three key reactions, i.e., (a) the Sharpless asymmetric epoxidation of an allylic alcohol, (b) the stereocontrolled addition of a lithium ester enolate to a optically active α,*β*-epoxy aldehyde, and (c) the stereo- and regioselective opening of an epoxide ring. The usefulness of this method, which we have partly described for the synthesis of optically active butyrolactones,[13] modified nucleosides,[14] or that of the 2-deoxy-D-arabinoheptulosonic acid derivative,[15] resides in its high versatility concerning the choice of the absolute configuration of the stereocenters. In fact, the C3, C4, and C5 carbon centers of the epoxy esters can be controlled by (a) the aldolisation reaction (C3), (b) the epoxidation reaction and the ring opening of the epoxide (C4), and (c) the nature of the starting allylic alcohol, the epoxidation reaction, and the ring opening of the epoxide (C5).

Compound **10** was synthesized according to Scheme 1. Synthesis of (3*S*,4*S*,5*S*)-*tert*-butyl 6-[(*tert*-butyldiphenylsilyl)oxy]-4,5-epoxy-3-hydroxyhexanoate (**11**) was achieved as described previously by us.[16] Compound **11** was obtained in six steps starting from *cis*-2-butene-1,4-diol (total yield 34%) as the major adduct of the aldol condensation between the (2*R*,3*S*)-4-[(*tert*-butyldiphenylsilyl)oxy]-2,3-epoxybutan-1-al and the lithium enolate of *tert*-butyl acetate.

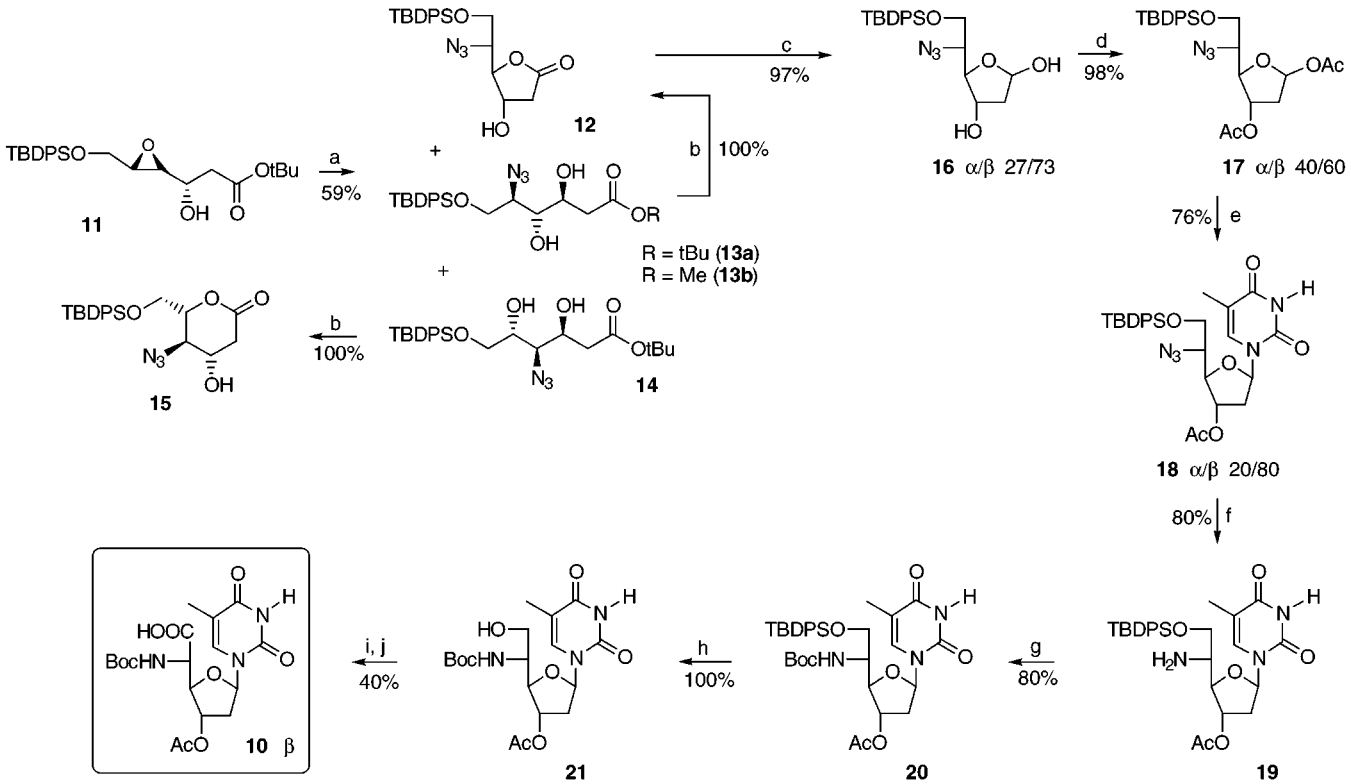
The regio- and stereospecific introduction of the azido functionality can be achieved in this step by nucleophilic oxirane ring cleavage. During the past decade, two main methods have been applied for the ring opening of epoxides, i.e., under nonchelating and chelating conditions. Results obtained by many groups, especially Sharpless,[17] Sinou,[18] or Flippin et al.,[19] showed a C3 selectivity in the ring opening of 2,3-epoxy-1-alkanol derivatives under both procedures, with an increase in regioselectivity in the presence of metal ions Li^+, Mg^{2+}, Zn^{2+}, or Ti(IV). Under chelating controlled conditions, the presence of electron-withdrawing groups at the C3 position of the epoxy alcohol dramatically decreases the C3 selectivity.[20] In all cases, introduction of the azido group takes place with inversion of configuration at the carbon center. In our hands, when the anti aldol adduct **11** was allowed to react with $Ti(O\text{-}i\text{-}Pr)_2(N_3)_2$ complex formed according to the procedure published by Choukroun and Gervais,[21] in dry benzene at 70 °C, a great number of degradation products were obtained. The major one (20% yield) has been identified as the isopropyl 5-azido-3,4-dihydroxy-6-[(*tert*-butyldiphenylsilyl)oxy]hexanoate arising from a C5 ring opening of the epoxide ring and a trans esterification reaction. When compound **11** reacted under nonchelating conditions in the presence of 5 equiv of sodium azide and 2.5 equiv of NH_4Cl in $MeOH/H_2O$ (8/1), four compounds were identified (59% total yield). Compounds **12**, **13a**, and **13b** arise from a C5 ring opening of the epoxide, while compound **14** is obtained by a nucleophilic attack at C4 of the oxirane ring. The observed regioselectivity of the reaction is 94/6 in favor of the C5 ring opening of the epoxide. The *tert*-butyl and methyl esters **13a** and **13b** were quantitatively transformed in the presence of trifluoroacetic acid to the single azido lactone **12**, which is one of our key chiral synthons in the synthetic strategy. The same reaction was also effected with an inseparable mixture of *tert*-butyl esters **13a** and **14**, leading quantitatively to the furanoazidolactone **12** and the pyranoazidolactone **15**, respectively.

Reduction of the azido lactone **12** with a 1 M hexane solution of diisobutyl aluminum hydride at −78 °C followed by acetylation (Ac_2O/pyridine) led to a mixture of the corresponding diacetyl α- and *β*-furanosides **17** in 95% yield (for the two steps) and an α/*β* ratio of 40/60. Glycosidation of 2,4-bis[(trimethylsilyl)oxy]-5-methylpyrimidine with **17** under the conditions developed by Vorbrüggen and co-workers[22] gave a mixture of the expected nucleosides **18** (76% yield) in a 20/80 α/*β* ratio. It is noteworthy that although there is no control by a C2-protected hydroxy group of the sugar moiety, the synthesis of the nucleoside proceeds with fairly good stereoselectivity. At this stage of synthesis, the two 5-azido-2,5-dideoxynucleoside anomers can be separated by silica gel column chromatography.

Catalytic hydrogenolysis of the azide function (Pd/C, EtOH, H_2O) of a mixture of α,*β*-anomers afforded the amino compound **19** in 80% yield. The two anomers were also obtained in 80% yield (α/*β* ratio 20/80) when using the PPh_3/THF, H_2O reaction conditions. The 5-amino-2,5-dideoxynucleoside was converted into the Boc-protected derivative **20**, which was then treated with 8 equiv of HF/pyridine complex in THF/pyridine to afford the monoalcohol **21** in 80% yield (two steps). The α,*β*-anomers can be also readily separated by silica gel column chromatography. The final two steps were carried out under conditions different from those described

(16) Escudier, J. M.; Baltas, M.; Gorrichon, L. *Tetrahedron* **1993**, *49*, 5253.
(17) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557.
(18) Sutovardoyo, K. I.; Sinou, D. *Bull. Soc. Chim. Fr.* **1991**, *128*, 387.
(19) Chini, M.; Crotti, P.; Flippin, L. A.; Cardelli, C.; Giovani, E.; Macchia, F.; Pineschi, M. *J. Org. Chem.* **1993**, *58*, 1221.
(20) Caron, M.; Carlier, P. R.; Sharpless, K. B. *J. Org. Chem.* **1988**, *53*, 5185.
(21) Choukroun, R.; Gervais, D. *J. Chem. Soc., Dalton Trans.* **1980**, 1800.
(22) Vorbrüggen, H.; Krolikiewicz, K.; Bennua, B. *Chem. Ber.* **1981**, *114*, 1234.

Scheme 1[a]



[a] Key: (a) 5 equiv of NaN_3, 2.5 equiv of NH_4Cl, MeOH/H_2O 8/1, reflux 48 h; (b) TFA, 5 min; (c) 1.3 equiv of DibaH, $PhCH_3$; (d) 8 equiv of Ac_2O, pyridine; (e) silylated thymine, 1.2 equiv of $CF_3SO_3SiMe_3$, $ClCH_2CH_2Cl/CH_3CN$ 1/1, 0 °C; (f) H_2, Pd/C 10%, EtOH/H_2O 9/1, 16 h; (g) 1.5 equiv of Boc_2O, CH_2Cl_2, 5 h; (h) 8 equiv of HF/Pyr, THF/Pyr; (i) 5 equiv of Pyr-SO_3, 5 equiv of Et_3N, DMSO, CH_2Cl_2; (j) 3 equiv of $NaClO_2$, 6 equiv isoamylene, 1 equiv of K_2HPO_4, THF, H_2O.

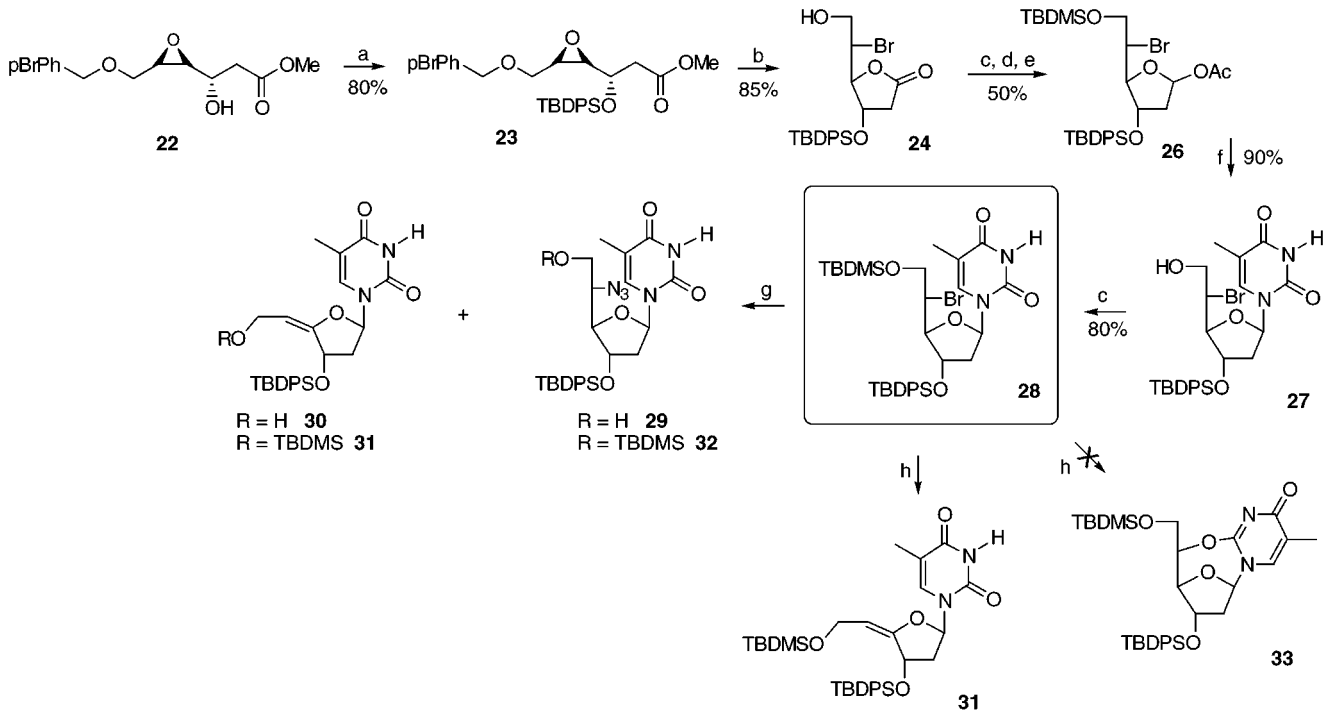
previously by Guillerm[10] and Ohrui.[9] In fact, in our case, we found better results when converting the primary hydroxy function into the acid through a two-step procedure. Selective oxidation of the alcohol to the corresponding aldehyde via the Doering procedure[23] and then oxidation of the crude product through a modified method developed by Dalcanale and Montanori.[24] By using sodium chlorite and 2-methyl-2-butene as HOCl scavenger,[25] the pure β anomer **10** was obtained in 40% yield after HPLC purification.

To improve the overall yield of our total synthesis we explored two other routes, starting from the major aldol adduct (anti) generated from an optically active cis α,β-epoxy alcohol. The advantage over the previously described method relies on two points: (a) the optically active cis α,β-epoxy alcohol can be obtained from *cis*-2-butene-1,4-diol in two steps instead of four for the trans isomer, and (b) during the aldolization reaction with lithium ester enolates the major anti aldol adduct can be obtained in better yields when using a *cis*-α,β-epoxy aldehyde. In fact, as we have already described,[16] in the case of *cis*-α,β-epoxy aldehyde, we obtain in 85% yield the aldol adducts with a diastereoisomeric ratio of 94/6 in favor of the anti compound, while for *trans*-α,β-epoxy aldehydes and under any of the experimental conditions we tried the diastereoisomeric ratio is always anti/syn 75/25. The following two routes were thus investigated:

(a) (3*S*,4*S*,5*R*)-Methyl 6-[(*p*-Bromobenzyl)oxy]-4,5-epoxy-3-hydroxyhexanoate (**22**) was silylated (*t*-BuPh_2SiCl, imidazole, DMF), leading to the fully protected compound **23** (Scheme 2). Catalytical hydrogenolysis gave a single product in 85% yield that has been identified as the bromohydroxy lactone **24**. Apparently, cleavage of the 4-bromobenzyl protective group leads to the simultaneous formation of hydrogen bromide that opens the oxirane ring in a stereo- and regiospecific manner to give a bromo derivative that lactonizes readily under the reaction conditions leading to compound **24**. Protection of the primary hydroxy group (*t*-BuMe_2SiCl, pyridine) and reduction of the carbonyl function with a 1 M hexane solution of diisobutyl aluminum hydride at −78 °C followed by acetylation (Ac_2O/pyridine) led to a mixture of acetyl α- and β-furanosides **26** in 50% yield (three steps). Glycosidation of compound **26** via the Vorbrüggen methodology and simultaneous cleavage of the *t*-BuMe_2-Si protective group led to an easily separable mixture of 5′-bromo-6′-hydroxy nucleoside anomers **27** (α/β ratio 24/76). After protection of the primary hydroxy function, compound **28** was allowed to react with sodium azide (1.3 equiv) in DMF (60 °C, 12 h), yielding a mixture of deprotected and protected talofuranoside **29**, **32**, and dehydrohalogenated compounds **30** and **31**. When compound **28** (5′*S* configuration) was heated in DMF in the presence of DBU, the dehydrohalogenated compound **31** was obtained in 70% yield, which upon deprotection (APTS, MeOH) led to compound **30**. During this reaction we did not observe the 2,5′-*O*-cyclonucleoside **33**. An analogous cyclonucleoside was obtained by Guillerm[10]

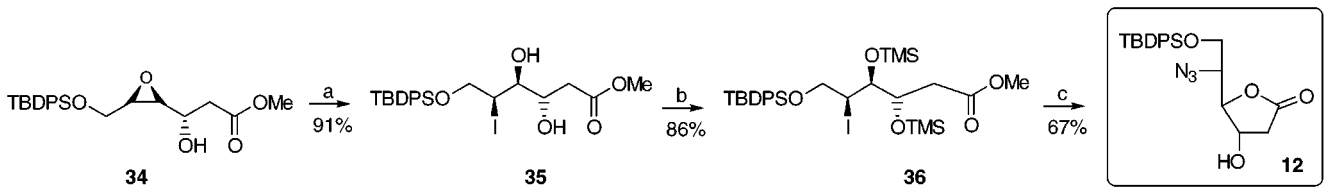
(23) Parikh, J. R.; von Doering, E. W. *J. Am. Chem. Soc.* **1967**, *89*, 5505.
(24) Dalcanale, E.; Montanari, F. *J. Org. Chem.* **1986**, *51*, 567.
(25) Bal, B. S.; Childers, W. E.; Pinnik, H. W. *Tetrahedron* **1981**, *37*, 2091.

Scheme 2[a]



[a] Key: (a) 1 equiv of *t*-$BuPh_2SiCl$, 6 equiv of imidazole, DMF; (b) H_2, Pd/C 10%, EtOH; (c) 1.5 equiv of *t*-$BuMe_2SiCl$ pyridine; (d) 1.3 equiv of DibaH, $PhCH_3$, −78 °C; (e) 8 equiv of Ac_2O, pyridine; (f) 1.2 equiv of $CF_3SO_3SiMe_3$ silylated thymine, $ClCH_2CH_2Cl/CH_3CN$ 1/1; (g) 1.3 equiv of NaN_3, DMF; (h) 1.5 equiv of DBU, DMF, reflux, 12 h.

Scheme 3[a]



[a] Key: (a) 1 equiv of MgI_2, $PhCH_3$, −78 °C, 19 h; (b) 2 equiv of HMDS, 2 equiv Me_3SiCl, pyridine, 10 h; c 5 equiv of NaN_3, 60 °C, DMF, 20 h.

when treating a (5′*R*)-mesylated nucleoside analogue under the same experimental conditions.

On the other hand, Vogel *et al.*,[12] when treating a (5′*R*)-bromo-6′-carboxylic nucleoside analogue with sodium azide in DMF, obtained a mixture of allo- and talo-azido furanosides (allo:talo ratio 1:2). They do not observe the corresponding 2,5′-*O*-cyclonucleoside, but they interpret the epimerization at the C5′ position in terms of concurrent participation by the nucleophilic nucleoside[22,26] to the displacement by an azide anion.

It seems likely that in our case we also have nucleophilic participation of the nucleoside, but the C5′-epimeric 2,5′-*O*-cyclonucleoside **33** is transformed by proton abstraction to the ethylenic compound **30** (or **31**).

(b) (3*S*,4*S*,5*R*)-Methyl 6-[(*tert*-butyldiphenylsilyl)oxy]-4,5-epoxy-3-hydroxyhexanoate (**34**) was treated with magnesium iodide in a toluene ether solution (−78 °C, 19 h) leading in 91% yield to the single product of reaction **35** issued from a C5 ring opening of the epoxide ring (Scheme 3). The iodo diol ester was then disilylated (HMDS, Me_3SiCl, pyridine) in 86% yield, and compound **36** was allowed to react with sodium azide in DMF (60 °C, 20 h). The azido lactone **12** was obtained in 67% yield; this important synthon can, therefore, now be obtained in seven steps and 30% yield starting from the *cis*-2-butene-1,4-diol, instead of eight steps and 20% yield with the previous methodology. It can then be transformed according to the same synthetic strategy described previously (Scheme 1) to the corresponding compound **10**.

Conclusion

The synthesis of the 2-deoxypolyoxin C analogue **10** was achieved in 9% (or 8%) total yield starting from epoxy hydroxy ester **11** (or **34**). The yield (5.5%) from the noncarbohydrate compound *cis*-2-butene-1,4-diol compares with that of polyoxin C obtained by two groups[9f,27] (4.4 and 5.6%, respectively) starting from D-ribose. Differently 2-substituted polyoxins can also be envisioned depending on the enolates retained in the aldolization step.

Experimental Section

Commercially available reagents were used as supplied. All solvents were distilled prior to use. Products were purified

(26) Moffatt, J. G. *Nato Adv. Study Inst. Ser.* **1979**, *A26*, 71.

(27) Barrett, A. G. M.; Lebold, S. A. *J. Org. Chem.* **1990**, *55*, 3853.

by medium-pressure liquid chromatography. NMR spectra were recorded at 250 MHz for ^{1}H and 62.9 MHz for ^{13}C using $CDCl_3$ solutions with internal tetramethylsilane as reference unless otherwise noted. Optical rotations were recorded on a digital polarimeter at 589 nm. Mass spectra were obtained at the inhouse facility of the Institute of Molecular Chemistry, while elemental analyses were performed by analytical services at the Ecole Nationale Supérieure de Chimie de Toulouse. Compound (3*S*,4*S*,5*S*)-*tert*-butyl 6-[(*tert*-butyldiphenylsilyl)oxy]-4,5-epoxy-3-hydroxyhexanoate and their precursors have been previously reported.[16]

Ring Opening of the Epoxide 11 by Sodium Azide. To a solution of (3*S*,4*S*,5*S*)-*tert*-butyl 6-[(*tert*-butyldiphenylsilyl)oxy]-4,5-epoxy-3-hydroxyhexanoate (**11**) (0.61 g, 1.35 mmol) in MeOH/H_2O (8/1 vol, 10 mL) were added ammonium chloride (0.18 g, 2.5 equiv) and sodium azide (0.439 g, 5 equiv). The mixture was stirred under reflux for 24 h, and then MeOH was evaporated. The residue was dissolved in ether, dried over $MgSO_4$, and filtered and solvent evaporated. The crude product was purified by silica gel column chromatography (eluent CCl_4/CH_3CN 9/1) to yield pure azido lactone **12** (72.5 mg) and *tert*-butyl ester **13a** (91 mg) along with inseparable mixtures of azidolactone and methyl ester **13b** (98 mg) and *tert*-butyl esters **13a** and **14** (105 mg). Compound **13a** and both mixtures were treated separately with trifluoroacetic acid (2 mL) for 5 min under stirring. Compound **13a** and the mixture containing methyl ester **13b**, after evaporation of excess trifluoroacetic acid, gave quantitatively the azido lactone **12** (76.5 and 85 mg, respectively). The crude product obtained from starting compounds **13a** and **14** gave after purification by silica gel column chromatography (eluent CH_2Cl_2/CH_3CN 9.5/0.5) furanoazido lactone **12** (93.5 mg) and pyranoazido lactone **15** (11.5 mg): total yield for azido lactone **12** (327.5 mg, 57%) and pyranoazido lactone **15** (11.5 mg, 2%).

(3*S*,4*R*,5*R*)-*tert*-Butyl [5-azido-6-[(*tert*-butyldiphenylsilyl)oxy]-3,4-dihydroxyhexanoate (13a): R_f = 0.26 (eluent CCl_4/CH_3CN 9/1); $[\alpha]_D$ −21.8° (*c* 1.16, $CHCl_3$); IR (film) ν cm^{-1} 3474 (OH), 3073, 3038 (CH arom), 2934, 2861 (CH), 2103 (N_3), 1710 (C=O), 1258 (CO), 1154 (CO + SiC), 1110 (SiO); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.73−7.69 (m, 4H), 7.46−7.39 (m, 6H), 4.04 and 3.97 (AB part of an ABX system, 2H, J = 3.2, 6.1, 10.9 Hz), 4.00 (m, 1H), 3.74 (m, 1H), 3.66 (d, 1H, J = 3.65 Hz), 3.58 (ddd, 1H, J = 3.2, 6.1, 6.0 Hz), 2.88 (d, 1H, J = 4.83 Hz), 2.60 and 2.48 (AB part of an ABX system, 2H, J = 2.9, 9.3, 16.8 Hz), 1.48 (s, 9 H), 1.09 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 172.9, 135.7, 135.6, 132.7, 132.6, 130.0, 127.9, 81.8, 73.1, 68.6, 64.4, 63.2, 37.2, 28.1, 26.8, 19.1; MS (DCI, NH_3) 517 (66.57, M + 18), 500 (100, M + 1). Anal. Calcd for $C_{26}H_{37}N_3O_5Si$: C, 62.50; H, 7.46; N, 8.41. Found: C, 62.99; H, 7.52; N, 7.88.

(4*S*,5*R*,1′*R*)-5-[1′-Azido-2′-[(*tert*-butyldiphenylsilyl)oxy]-ethyl]-4-hydroxy-2-oxo-1-oxacyclopentane (12): R_f = 0.14 (eluent CCl_4/CH_3CN 9/1); $[\alpha]_D$ −11.0° (*c* 1.6, $CHCl_3$); IR (film) ν cm^{-1} 3452 (OH), 3073, 3037 (CH arom), 2935, 2861 (CH), 2108 (N_3), 1787 (C=O), 1269 (CO), 1188 (CO + SiC), 1111 (SiO); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.71−7.66 (m, 4H), 7.48−7.42 (m, 6H), 4.52 (ddd, 1H, J = 3.7, 7.5, 4.9 Hz), 4.39 (dd, 1H, J = 3.7, 5.1 Hz), 3.86 and 3.91 (AB part of an ABX system, 2H, J = 4.8, 5.5, 10.8 Hz), 3.74 (ddd, 1H, J = 5.1, 4., 5.5 Hz), 2.90 and 2.52 (AB part of an ABX system, 2H, J = 4.9, 7.6, 18.0 Hz), 2.73 (br.s., 1H), 1.09 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 174.0, 135.6, 135.5, 132.3, 132.2, 130.2, 128.0, 85.0, 68.3, 63.9, 63.7, 37.4, 26.8, 19.2; MS (DCI, NH_3) 443 (100, M + 18), 400 (4.93), 274 (13.19). Anal. Calcd for $C_{22}H_{27}N_3O_4Si$: C, 62.09; H, 6.40; N, 9.87. Found: C, 62.52; H, 6.93; N, 8.95.

(4*S*,5*R*,6*R*)-5-Azido-6-[[(*tert*-butyldiphenylsilyl)oxy]-methyl]-4-hydroxy-2-oxacyclohexane (15): R_f = 0.32 (eluent CH_2Cl_2/CH_3CN 9.5/0.5); $[\alpha]_D$ −18.1° (*c* 0.74, $CHCl_3$); IR (film) ν cm^{-1} 3439 (OH), 3073 (CH arom), 2934, 2860 (CH), 2114 (N_3), 1733 (C=O), 1249 (CO), 1150 (CO + SiC), 1110 (SiO); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.72−7.67 (m, 4H), 7.47−7.38 (m, 6H), 3.93 (m, 5H), 3.04 and 2.64 (AB part of an ABX system, 2H, J = 5.1, 9.2, 17.7 Hz), 2.81 (m, 1H), 1.08 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 168.1, 135.8, 135.6, 132.6, 132.1, 130.1, 127.9, 79.3, 67.6, 62.5, 61.6, 37.3, 26.8, 19.3; MS (DCI, NH_3) 443 (100, M + 18). Anal. Calcd for $C_{22}H_{27}N_3O_4Si$: C, 62.09; H, 6.40; N, 9.87. Found: C, 62.41; H, 6.84; N, 9.05.

(4*S*,5*R*,1′*R*)-5-[1′-Azido-2′-[(*tert*-butyldiphenylsilyl)oxy]-ethyl]-2,4-dihydroxy-1-oxacyclopentane (16). To a solution of diisobutylaluminum hydride (1 M in hexane, 0.77 mL) was added dropwise under N_2 and at −78 °C a solution of azidolactone **12** (0.250, 0.59 mmol) in toluene (2 mL). The reaction mixture was stirred for 15 min and then hydrolyzed with a 0.25 N aqueous HCl solution (3 mL) and diluted with ether (8 mL). After 1 h of stirring, the aqueous phase was extracted with ether; the organic phases were washed with H_2O and then dried over $MgSO_4$ and evaporated. The crude product was purified by silica gel column chromatography (eluent petroleum ether/Et_2O/EtOAc 1/1.2/0.3), yielding compound **16** (0.245 g, 97% yield) as a mixture of anomers (α:β 27:73): R_f = 0.33; $[\alpha]_D$ +8.0° (*c* 1.2, $CHCl_3$); IR (film) ν cm^{-1} 3408 (OH), 3073 (CH arom.), 2935, 2861 (CH), 2103 (N_3), 1272 (CO), 1110 (CO + SiO); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.71−7.67 (m, 8H), 7.44−7.41 (m, 12H), 5.49 (m, 2H), 4.61 (m, 1H), 4.28 (m, 1H), 4.13 (dd, 1H, J = 1.8, 6.1 Hz), 3.84 (m, 4H), 3.87 and 3.77 (AB part of an ABX system, 2H, J = 7.4, 4.2, 10.7 Hz), 3.46 (m, 1H, J = 7.4, 4.2, 6.7, 1.2 Hz), 3.30 (m, 1H), 2.72 (m, 2H), 2.43 (m, 1H), 2.13 (m, 4H), 1.09 (s, 18H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 135.8, 135.6, 132.8, 132.7, 130.0, 127.9, 99.2, 98.7, 86.0, 84.6, 72.8, 72.4, 65.7, 64.8, 64.7, 64.4, 41.8, 41.4, 26.8, 19.2; MS (DCI, NH_3) 445 (100, M + 18), 428 (9.71, M + 1), 427 (28.94, M). Anal. Calcd for $C_{22}H_{29}N_3O_4Si$: C, 61.80; H, 6.84; N, 9.83. Found: C, 61.42; H, 6.94; N, 9.54.

(4*S*,5*R*,1′*R*)-5-[1′-Azido-2′-[(*tert*-butyldiphenylsilyl)oxy]-ethyl]-2,4-diacetoxy-1-oxacyclopentane (17). To a solution of **16** (0.138 g, 0.32 mmol) in pyridine (0.5 mL) was added acetic anhydride (0.24 mL, 2.56 mmol). The reaction mixture was stirred at room temperature for 12 h. The pyridine was evaporated, and the crude product was purified by silica gel column chromatography (eluent petroleum ether/Et_2O/EtOAc 5/4/1) to yield the desired compound (0.160 g, 98%) as a mixture of anomers (α:β 40/60): R_f = 0.40; $[\alpha]_D$ +6.5° (*c* 1.7, $CHCl_3$); IR (film) ν cm^{-1} 3074 (CH arom), 2935, 2860 (CH), 2105 (N_3), 1745 (C=O), 1227 (CO), 1184 (CO + SiC), 1110 (SiO); ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.37 (m, 2H), 5.39 (m, 1H, J = 3.4, 4.6, 6.9 Hz), 5.21 (m, 1H, J = 2.7, 5.1 Hz), 4.37 (dd, 1H, J = 2.7, 4.9 Hz), 4.20 (dd, 1H, J = 3.4, 6.8 Hz), 3.78 and 3.86 (AB part of an ABX system, 2H, J = 4.0, 6.6 Hz), 3.80 (d, 2H, J = 5.6 Hz), 3.65 (m, 1H, J = 5.6, 4.9 Hz), 3.56 (m, 1H, J = 4.0, 6.6, 6.8 Hz), 2.52 (m, 2H), 2.29 (dd, 1H, J = 4.6, 5.5 Hz), 2.23 (dd, 1H, J = 5.1, 5.6 Hz), 2.12 (2s, 6H), 2.02 (2s, 6H), 1.05 (2s, 18H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 170.2, 169.9, 135.6, 132.8, 132.7, 132.6, 129.9, 127.9, 98.1, 98.0, 83.8, 82.8, 74.2, 73.3, 64.8, 64.4, 64.0, 63.9, 38.9, 38.6, 26.7, 21.3, 21.1, 21.0, 20.9, 19.2; MS (DCI, NH_3) 529 (100, M + 18). Anal. Calcd for $C_{26}H_{33}N_3O_6Si$: C, 61.04; H, 6.50; N, 8.21. Found: C, 61.77; H, 6.63; N, 8.10.

(3*S*,4*R*,5*R*)-1-[5-Azido-2,5-dideoxy-6-(*O*-*tert*-butyldiphenylsilyl)hexofuranosyl]-5-methyluracil (18). Trimethylsilyl trifluoromethanesulfonate (3.0 mL, 1.2 equiv) was added to a stirred solution of **17** (660 mg, 1.2 mmol) and freshly distilled 2,4-bis[(trimethylsilyl)oxy]-5-methylpyrimidine (0.680 mL) in $ClCH_2CH_2Cl$/CH_3CN 1/1 (20 mL) under N_2 atmosphere. After being stirred at room temperature for 3 h, the mixture was hydrolyzed with a saturated aqueous solution of $NaHCO_3$. The organic extract was washed with water and dried over $MgSO_4$. After concentration, 750 mg (100%) was obtained. A total of 120 mg of anomers was separated by column chromatography on silica gel (eluent 2-propanol/petroleum ether 1/9) to give 85 mg of anomer α and 17 mg of anomer β along with 16 mg of a mixture of α and β anomers.

Anomer β: $[\alpha]_{Hg}$ +5.7 (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) ν cm^{-1} 3395 (NH), 2997 (CH), 2401 (N_3), 1740 (CH_3C=O), 1696 (C=O thym), 1288 (CO), 1119 (SiO); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.71 (bs, 1H, NH), 7.70−7.64 (m, 4H), 7.49−7.36 (m, 6H), 7.31 (s, 1H), 6.30 (dd, 1H, J = 6.0, 8.6 Hz), 5.21 (td, 1H, J = 2.6, 6.0 Hz), 4.05 (t, 1H, J = 2.6 Hz), 3.88 (m, 3H), 2.28 (m, 2H, CH_2CH anom), 2.01 (s, 3H), 1.94 (s, 3H), 1.09 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.9, 163.3, 150.3, 135.5, 134.7, 132.6, 132.5, 130.0, 127.9, 111.8, 84.0, 82.5, 73.3, 65.1, 64.0, 35.7, 26.7,

20.9, 19.1, 12.8; MS (DCI, NH_3) 595 (MNH_4^+, 100), 578 (MH^+, 13). Anal. Calcd for $C_{29}H_{35}N_5O_6Si$: C, 60.29; H, 6.11; N, 12.12. Found: C, 59.67; H, 6.03; N, 11.56.

Mixture of α and β anomers: α/β = 20/80; IR ($CHCl_3$) ν cm^{-1} 3395 (NH), 3076−3032 (CH arom), 2935−2862 (CH), 2108 (N_3), 1740 (CH_3C=O), 1695 (C=O thym), 1271 (CO), 1111 (SiO). ^1H NMR (250 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.93 (s, 1H), 7.70−7.65 (m, 4H), 7.26−7.47 (m, 12H), 7.32 (2s, 2H), 6.31 (dd, 1H, J = 6.1, 8.5 Hz), 6.21 (dd, 1H, J = 2.3, 7.5 Hz), 5.29 (ddd, 1H, J = 1.3, 2.8, 5.2 Hz), 5.22 (ddd, 1H, J = 2.1, 2.3, 5.8 Hz), 4.38 (dd, 1H, J = 1.3, 5.0 Hz), 4.05 (t, 1H, J = 2.3 Hz), 3.87 (m, 5H), 3.54 (m, 1H, J = 5.0, 6.4, 7.6 Hz), 2.29 (m, 4H), 2.02 (s, 3H), 1.99 (s, 3H), 1.95 (s, 6H), 1.08 (s, 18H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 170.0, 163.4, 150.4, 135.5, 134.8, 132.6, 132.5, 130.1, 127.9, 111.9, 110.3, 84.0, 82.5, 73.9, 73.4, 65.1, 64.4, 64.1, 37.5, 26.7, 20.9, 19.1, 12.8; MS (DCI, NH_3) 595 (MNH_4^+, 100), 578 (M + 1, 14). Anal. Calcd for $C_{29}H_{35}N_5O_6Si$: C, 60.29; H, 6.11; N, 12.12. Found: C, 60.41; H, 6.45; N, 11.21.

(3*S*,4*R*,5*R*)-1-[5-Amino-2,5-dideoxy-6-(*O*-*tert*-butyldiphenylsilyl)hexofuranosyl]-5-methyluracil (19). A mixture of **18** (380 mg, 0.7 mmol), EtOH (16.6 mL), and 10% Pd/C (75 mg) was degassed and then pressurized with H_2. After being shaken at 20 °C for 6 h, the mixture was filtered on Celite and then concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent Et_2O/EtOAc 3/2, R_f = 0.17) to yield 215 mg (60%) of the desired compound.

Anomer β: $[\alpha]_{Hg}$ +5.7 (c 0.5, $CHCl_3$); IR ($CHCl_3$) ν cm^{-1} 3392 (NH_2 + NH), 2933 (CH), 1693 (C=O thym), 1265 (CO), 1112 (SiO); ^1H NMR (250 MHz, $CDCl_3$) δ 7.66−7.64 (m, 4H), 7.46−7.26 (m, 8H), 6.26 (dd, 1H, J = 5.8, 8.5 Hz), 5.40 (ddd, 1H, J = 6.0, 2.1, 2.6 Hz), 4.00 (dd, 1H, J = 2.6, 5.7 Hz), 3.74 and 3.72 (AB part of an ABX system, 2H, J = 4.6, 5.9, 10.2), 3.10 (ddd, 1H, J = 4.6, 5.7, 5.9 Hz), 2.35−2.16 (m, 2H), 2.05 (s, 3H), 1.87 (s, 3H), 1.06 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm 170.2, 163.5, 150.4, 135.6, 135.5, 135.2, 133.1, 133.0, 129.9, 127.8, 111.5, 84.9, 84.0, 78.8, 65.6, 54.7, 37.6, 26.8, 21.0, 19.3, 12.6; MS (DCI, NH_3) 553 (MH^+, 100).

Mixture of α and β anomers: mixture = 20/80; IR ($CHCl_3$) ν cm^{-1} 3394 (NH_2 + NH), 3030 (CH arom), 2935−2862 (CH), 1740 (CH_3C=O), 1686 (C=O thym), 1247 (CO), 1202−1110 (SiO); ^1H NMR (250 MHz, $CDCl_3$) δ 7.67−7.64 (8H, m), 7.43−7.34 (14H, m), 6.27 (dd, 1H, J = 5.8, 8.0 Hz), 6.11 (1H, dd, J = 1.4, 7.2 Hz), 5.52 (m, 1H), 5.40 (m, 1H), 4.26 (t, 1H, J = 2.8 Hz), 4.01 (dd, 1H, J = 2.6, 5.7 Hz), 3.67 and 3.74 (AB part of an ABX system, 2H, J = 4.8, 5.8, 10.3 Hz), 3.71 (m, 2H), 3.11 (m, 1H, J = 4.8, 5.8, 5.7 Hz), 2.82 (m, 1H), 2.21 and 2.33 (AB part of an ABX(Y) system, 2H, J = 1.7, 5.8, 8.0, 14.2 Hz), 2.23 (2H, m), 2.06 (3H, s), 2.02 (s, 3H), 1.90 (s, 3H), 1.87 (s, 3H), 1.06 (s, 18H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm 170.4, 163.9, 150.7, 135.6, 135.3, 133.1, 133.0, 129.9, 127.6, 111.6, 84.9, 84.0, 73.8, 73.8, 65.6, 54.7, 37.6, 26.7, 21.1, 19.3, 12.7; MS (DCI, NH_3) 552 (MH^+, 100). Anal. Calcd for $C_{29}H_{37}N_3O_6Si$: C, 63.13; H, 6.76; N, 7.62. Found: C, 61.78; H, 6.83; N, 7.11.

(3*S*,4*R*,5*R*)-1-[5-[*N*-(*tert*-Butyloxycarbonyl)amino]-2,5-dideoxy-6-(*O*-*tert*-butyldiphenylsilyl)hexofuranosyl]-5-methyluracil (20). A mixture of **19** (56 mg, 0.10 mmol) and Boc_2O (33 mg, 1.5 equiv) in CH_2Cl_2 (1.0 mL) was stirred for 12 h. The reaction mixture was diluted with CH_2Cl_2 and washed with a saturated aqueous solution of $NaHCO_3$ and then with brine. After drying over $MgSO_4$ and concentration, the crude product was purified by column chromatography on silica gel (eluent Et_2O/EtOAc 3/2, R_f = 0.48) leading to 51 mg (80%) of compound **20**.

Anomer β: $[\alpha]_{Hg}$ −9.1 (c 0.4, $CHCl_3$). IR ($CHCl_3$) ν cm^{-1} 3449, 3394 (NH), 2936, 2861 (CH), 1696 (C=O), 1499 (C=C), 1112 (SiO); ^1H NMR (250 MHz, $CDCl_3$) δ 7.65−7.61 (m, 4H), 7.44−7.33 (m, 4H), 7.03 (s, 1H), 6.31 (m, 1H, J = 5.5−8.8 Hz), 5.42 (ddd, 1H, J = 1.2, 1.8, 5.8 Hz), 5.14 (d, 1H, J = 8.9 Hz), 4.11 (dd, 1H, J = 1.8, 8.6 Hz), 3.83 (m, 3H), 2.20 (m, 2H), 2.10 (s, 3H), 1.84 (s, 3H), 1.46 (s, 9H), 1.07 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 170.1, 163.5, 155.8, 150.4, 111.7, 84.5, 82.7, 74.7, 62.9, 53.7, 36.6, 28.4, 26.9, 21.1, 19.3, 12.6; MS (DCI, NH_3); 652 (MH^+, 100), 669 (MNH_4^+, 21).

Mixture of α and β anomers: mixture = 22/78; IR ($CHCl_3$) ν cm^{-1} 3454, 3397 (NH), 3009 (CH arom), 2936, 2862 (CH), 1740 (C=O Boc), 1734 (CH_3C=O), 1694 (C=O thym), 1198, 1169 (CO + SiC), 1110 (CO + SiC); ^1H NMR (400 MHz, $CDCl_3$) δ 9.17 (m, 1H), 7.62−7.59 (m, 4H), 7.38−7.32 (m, 6H), 7.00 (m, 1H), 6.31 (m, 1H), 6.10 (m, 1H), 5.40 (m, 1H), 5.00 (m, 1H), 4.10 (m, 1H), 3.75 (m, 3H), 2.35 et 2.25 (m, 2H), 2.07 (m, 3H), 1.82 (m, 3H), 1.43 (m, 9H), 1.09 (m, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 170.1, 163.5, 156.0, 150.5, 135.6, 134.5, 132.9−132.6, 129.9, 127.9, 127.8, 111.8, 84.5, 82.8, 80.2, 74.7, 62.9, 53.6, 36.5, 28.3, 26.9, 21.1, 19.3, 12.7; MS (DCI, NH_3) 652 (MH^+, 100). Anal. Calcd for $C_{34}H_{45}N_3O_8Si$: C, 62.65; H, 6.96; N, 6.45. Found: C, 62.41; H, 7.15; N, 5.79.

(3*S*,4*R*,5*R*)-1-[5-[*N*-(*tert*-Butyloxycarbonyl)amino]-2,5-dideoxy-6-hydroxy)hexofuranosyl]-5-methyluracil (21). To a mixture of **20** (84 mg, 0.13 mmol) in THF (1.2 mL) and pyridine (0.64 mL) was added HF/pyridine 70% (0.133 mL). After being stirred for 1 h 30 min, the reaction mixture was diluted with ethyl acetate and then hydrolyzed with a saturated aqueous solution of $NaHCO_3$. The organic extract was washed with water and dried over $MgSO_4$. The solvents were evaporated, and the product was purified by column chromatography on silica gel (eluent Et_2O/EtOAc 3/2, $R_f(\beta)$ = 0.26, $R_f(\alpha)$ = 0.20) to give 31 mg of β anomer and 4 mg of a β,α mixture (global yield: 70%).

Anomer β: $[\alpha]_{Hg}$ +38.9 (c 0.5, $CHCl_3$); IR ($CHCl_3$) ν cm^{-1} 3628 (OH), 3440−3396 (NH), 2979 (CH), 1740 (CH_3C=O), 1697 (C=O thym), 1166 (CO); ^1H NMR (250 MHz, $CDCl_3$) δ 9.05 (bs, 1H), 7.28 (s, 1H), 6.24 (dd, 1H, J = 5.3, 9.1 Hz), 5.38 (m, 1H), 4.04 (dd, 1H, J = 1.8, 6.7 Hz), 3.85 (m, 3H), 2.96 (m, 1H), 2.35 and 2.20 (m, 2H), 2.10 (s, 3H), 1.92 (s, 1H), 1.44 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 170.9, 163.9, 156.2, 150.6, 135.3, 111.7, 85.0, 84.1, 80.3, 74.9, 62.0, 53.6, 36.3, 28.3, 21.1, 12.5; MS (DCI, NH_3) 431 (MNH_4^+, 86), 414 (MH^+, 100).

Mixture of α and β anomers: mixture = 20/80; IR ($CHCl_3$) ν cm^{-1} 3640 (OH), 3446, 3396 (NH), 3030 (CH arom), 2932 (CH), 1740 (CH_3C=O), 1691 (C=O thym), 1200 (CO), 1666 (CO + SiO); ^1H NMR (400 MHz, $CDCl_3$) δ 9.10 (m, 1H), 7.33 (m, 1H), 7.26 (1H, m), 6.21 (m, 1H), 5.40 (m, 1H), 5.33 (m, 1H), 4.02 (m, 1H), 3.80 (m, 2H), 3.72 (m, 1H), 3.00 (m, 1H), 2.20 and 2.38 (m, 2H), 2.08 (s, 3H), 1.89 (s, 3H), 1.42 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ ppm 171.0, 163.7, 156.2, 150.5, 135.2, 111.7, 84.9, 84.3, 80.3, 75.0, 62.2, 53.6, 36.4, 28.3, 21.1, 12.6; MS (DCI, NH_3) 431 (MNH_4^+, 100), 414 (MH^+, 97).

(3*S*,4*R*,5*R*)-1-[5-[*N*-(*tert*-Butyloxycarbonyl)amino]-2,5-dideoxy-6-(*O*-*tert*-butyldiphenylsilyl)uronic acid]-5-methyluracil (10). A mixture of **21** (37 mg, 0.09 mmol), DMSO (0.180 mL), Et_3N (0.063 mL, 5 equiv), and pyr/SO_3 (71 mg, 5 equiv) in CH_2Cl_2 was stirred for 25 min. After dilution with CH_2Cl_2, the organic layer was washed with water and brine. After drying and concentration, 34 mg was obtained and then dissolved with THF (0.222 mL), KH_2PO_4 (8 mg, 1 equiv) in H_2O (0.09 mL), 2-methyl-2-butene (0.041 mL), t-BuOH (0.390 mL), and $NaClO_2$ (6 mg) in 0.180 mL. After being stirred for 2 h 15 min, the reaction mixture was acidified with HCl (1 N) and extracted with EtOAc. The product was dried and concentrated: $[\alpha]_{Hg}$ +20.1 (c 0.5, $CHCl_3$); IR (CH_3CN) ν cm^{-1} 3283−3075 (OH acid), 3470, 3419 (NH), 1741 (C=O Boc), 1710 (C=O acid), 1698 (C=O thym), 1355 (CO acid), 1169 (CO); ^1H NMR (250 MHz, CD_3OD) δ 7.70 (s, 1H), 6.17 (dd, 1H, J = 6.6 Hz), 5.54 (m, 1H), 4.34 (1H, bd, J = 4.7 Hz), 4.28 (m, 1H), 2.60 (m, 2H), 2.09 (s, 3H), 1.90 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (62.9 MHz, CD_3OD) δ 173.9, 172.1, 157.8, 152.4, 137.9, 111.9, 86.7, 86.0, 80.8, 76.0, 58.6, 37.9, 28.8, 30.8, 12.6; MS (DCI, NH_3) 445 (MNH_4^+, 4), 428 (MH^+, 3).

(3*S*,4*S*,5*R*)-Methyl [6-(*p*-Bromobenzyloxy)-4,5-epoxy-3-hydroxy]hexanoate (22). The aldolization reaction was performed as previously described.[16] Starting from (2*R*,3*R*)-4-[(*p*-bromobenzyl)oxy]-2,3-epoxybutan-1-al (1 g, 3.69 mmol), we obtained after purification by silica gel column chromatography (eluent petroleum ether/CH_2Cl_2/EtOAc 1/3.2/0.8) the desired compound **22** (895 mg, 70% yield): R_f = 0.25; $[\alpha]_D$ −23.2° (c 0.4, $CHCl_3$); IR ($CHCl_3$) ν cm^{-1} 3625 and 3471 (OH), 3007 (=CH), 1731 (C=O), 1047 (CO); ^1H NMR (250 MHz, $CDCl_3$) δ 7.50−7.45 (m, 2H), 7.23−7.20 (m, 2H), 4.56 and 4.51 (AB system, 2H, J = 12 Hz), 3.86 (td, 1H, J = 3.5, 8.3 Hz), 3.78 and 3.70 (AB part of an ABX(Y), 2H, J = 4.8, 5.9, 10.8

Hz), 3.73 (s, 3H), 3.28 (ddd, 1H, J = 4.6, 4.8, 5.9 Hz), 3.18 (m, 1H), 3.02 (dd, 1H, J = 4.6, 8.1 Hz), 2.74 and 2.63 (A′B′ part of an A′B′X′(Y) system, 2H, J = 3.6, 8.5, 16.3 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ 172.3, 136.4, 131.7, 129.5, 121.9, 72.7, 68.3, 66.5, 57.1, 55.1, 52.0, 38.9. Anal. Calcd for $C_{14}H_{17}BrO_5$: C, 48.71; H, 4.96. Found: C, 48.75; H, 4.93.

(3*S*,4*R*,5*R*)-Methyl [6-[(*p*-Bromobenzyl)oxy]-3-[(*tert*-butyldiphenylsilyl)oxy]-4,5-epoxy]hexanoate (23). To a solution of epoxy ester **22** (516 mg, 1.5 mmol) in anhydrous DMF (6 mL) were added imidazole (637 mg, 10 mmol) and then *tert*-butyldiphenylsilyl chloride (0.582 mL, 2.25 mmol). The mixture was stirred at room temperature for 12 h and then hydrolyzed with an aqueous saturated NH_4Cl solution (3 mL) and extracted with ether (3 × 10 mL). The organic phases were washed with an aqueous saturated NaCl solution and then dried over $MgSO_4$ and solvent evaporated. The crude product was purified by silica gel column chromatography (eluent petroleum ether/Et_2O 8/2) to yield compound **23** (811 mg, 93%): R_f = 0.16; $[\alpha]_D$ +7.4° (*c* 0.6, $CHCl_3$); IR ($CHCl_3$) ν cm^{-1} 3029 (=CH), 1736 (C=O), 1593 (C=C), 1109 (CO); ^{1}H NMR (250 MHz, C_6D_6) δ 7.74−7.68 (m, 4H), 7.24 and 6.77 (A_2B_2 system, 4H, J = 8.4 Hz), 7.17−7.14 (m, 6H), 4.18 (m, 1H), 3.98 and 3.86 (AB system, 2H, J = 12 Hz), 3.29 (s, 3H), 2.95 (m, 2H), 2.84 (m, 1H), 2.78−2.70 (m, 3H), 1.09 (s, 9H); ^{13}C NMR (63 MHz, C_6D_6) δ 170.8, 137.6, 136.3, 136.2, 133.7, 133.4, 131.6, 130.3, 129.4, 128.0, 72.0, 68.4, 68.1, 57.8, 57.2, 51.3, 41.3, 26.9, 19.5. Anal. Calcd for $C_{30}H_{35}BrO_5Si$: C, 61.74; H, 6.04. Found: C, 61.88; H, 6.03.

(4*S*,5*S*,1′*S*)-5-(1′-Bromo-2′-hydroxyethyl)-4-[(*tert*-butyldiphenylsilyl)oxy]-2-oxo-1-oxacyclopentane (24). A mixture of **23** (2.6 g, 3.2 mmol), EtOH (25 mL), and 10% Pd/C (200 mg) was degassed and then pressurized with H_2. After being shaken at 20 °C for 3 h, the mixture was filtered on Celite and then concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent petroleum ether/CH_2Cl_2/EtOAc 5/4/1) to give 1.7 g (85%) of the desired compound: R_f = 0.33; $[\alpha]_{Hg}$ +40.16° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) ν cm^{-1} 3615 (OH), 3074 (CH arom.), 2934 (CH), 1786 (C=O), 1590, 1471 (CH= arom), 1111 (SiO); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.68−7.59 (m, 4H), 7.50−7.40 (m, 6H), 4.55 (dd, 1H, J = 1.8, 2.2 Hz), 4.43 (ddd, 1H, J = 2.2, 3.3, 7.5 Hz), 3.69 (m, 2H), 3.32 (td, 1H, J = 1.8, 7.0 Hz), 2.55 and 2.85 (AB part of an ABX system, 2H, J = 3.3, 7.5, 18.4 Hz), 1.08 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ: 174.9, 135.7−135.6, 132.7, 132.3, 130.5, 130.4, 128.2, 128.1, 85.4, 72.3, 63.8, 54.5, 38.4, 26.8, 18.9; MS (DCI, NH_3) 480 (MNH_4^+, 93). Anal. Calcd for $C_{22}H_{27}BrO_4Si$: C, 57.02; H, 5.87. Found: C, 56.96; H, 6.21.

(4*S*,5*S*,1′*S*)-5-[1′-Bromo-2′-[(*tert*-butyldimethylsilyl)oxy]-ethyl]-4-[(*tert*-butyldiphenylsilyl)oxy]-2-oxo-1-oxacyclopentane (25). A mixture of **24** (446 mg, 0.96 mmol) and *tert*-butyldimethylsilyl chloride (220 mg, 1.5 equiv) in anhydrous pyridine (6 mL) was stirred for 22 h. After dilution with ethyl acetate, the mixture was washed with a saturated aqueous solution of NH_4Cl and with brine and dried over $MgSO_4$. After concentration in vacuo and filtration on silica gel (eluent petroleum ether/CH_2Cl_2/EtOAc 5/4/1), 580 mg (100%) was obtained: IR ($CHCl_3$) ν cm^{-1} 3072 (CH arom), 2956−2932 (CH), 1796 (C=O), 1590, 1471 (CH= arom), 1112 (SiO); $[\alpha]_{Hg}$ +28.1° (*c* 1.3, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.65−7.58 (m, 4H), 7.48−7.39 (m, 6H), 4.73 (dd, 1H, J = 1.5, 2.0 Hz), 4.40 (ddd, 1H, J = 2.0, 3.3, 7.7 Hz), 3.69 (m, 2H), 3.33 (ddd, 1H, J = 1.5, 6.1, 8.8 Hz), 2.55 and 2.87 (AB part of an ABX system, 2H, J = 3.3, 7.7, 18.3 Hz), 1.07 (s, 9H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 174.9, 135.7, 135.6, 132.6, 130.4, 130.3, 127.7, 127.6, 84.6, 72.2, 63.6, 52.8, 38.6, 26.8, 25.7, 18.9, 18.1, −5.4; MS (DCI, NH_3) 594 (MNH_4^+, 89). Anal. Calcd for $C_{28}H_{41}BrO_4Si_2$: C, 58.21; H, 7.15. Found: C, 57.71; H, 7.15.

(4*S*,5*S*,1′*S*)-5-[1′-Bromo-2′-[(*tert*-butyldimethylsilyl)oxy]-ethyl]-4-[(*tert*-butyldiphenylsilyl)oxy]-2-acetoxy-1-oxacyclopentane (26). Diisobutylaluminum hydride (1.8 mL, 1.2 equiv) was added dropwise to a solution of **25** (800 mg, 1.4 mmol) in toluene (3.6 mL) at −78 °C under N_2 atmosphere. The mixture was stirred for 1 h and then hydrolyzed with HCl (0.25 M). The mixture was extracted with Et_2O, washed with water, and dried over $MgSO_4$. The solvents were evaporated. The crude product obtained (772 mg) was dissolved in pyridine (1.8 mL). Acetic anhydride (620 mL, 4.5 equiv) was added. After the mixture was stirred for 12 h at 20 °C, pyridine was evaporated. The residue was purified by column chromatography on silica gel (eluent petroleum ether/CH_2Cl_2/EtOAc 2/4/1) to yield 720 mg (80%). α/β: 48/52; R_f = 0.33; IR (film) ν cm^{-1} 3072 (CH arom), 2932, 2858 (CH), 1755 (C=O), 1590−1471 (CH arom), 1111 (SiO); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.76−7.64 (m, 4H), 7.46−7.26 (m, 6H), 6.33 (bd, 1H, J = 5.0 Hz), 6.22 (dd, 1H, J = 1.4, 5.5 Hz), 4.60 (ddd, 1H, J = 6.0, 8.0, 14.0 Hz), 4.42 (dd, 1H, J = 1.8, 2.8 Hz), 4.34 (ddd, 1H, J = 2.0, 2.8, 7.0 Hz), 4.20 (bd, 1H, J = 6.0 Hz), 3,66 (m, 5H), 3.36 (ddd, 1H, J = 1.8, 6.0, 8.5 Hz), 2.38−2.02 (m, 4H), 2.10 (s, 6H), 1.07 (s, 18H), 0.88 (s, 18H), 0.03 (s, 12H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ: 170.4, 170.2, 135.8, 135.7, 133.4, 133.0, 130.1, 130.0, 127.9, 127.8, 99.1, 96.9, 85.7, 84.1, 75.2, 73.3, 54.2, 54.0, 41.4, 40.5, 26.9, 26.8, 25.8, 25.7, 21.4, 21.2, 19.1, 19.0, 18.2, −5.4, −5.3; MS (DCI, NH_3) 638 (MNH_4^+, 83). Anal. Calcd for $C_{30}H_{45}BrO_5Si_2$: C, 57.95; H, 7.30. Found: C, 57.67; H, 7.38.

(3*S*,4*S*,5*S*)-1-[5-Bromo-2,5-dideoxy-3-*O*-(*tert*-butyldiphenylsilyl)hexofurasonyl]-5-methyluracil (27). Trimethylsilyl trifluoromethanesulfonate (4.6 mL, 1.2 equiv) was added to a stirred solution of **26** (1.2 g, 1.9 mmol) and freshly distilled 2,4-bis[(trimethylsilyl)oxy]-5-methylpyrimidine (1.1 mL) in $ClCH_2CH_2Cl/CH_3CN$ 1/1 (30 mL) under N_2 atmosphere. After being stirred at 0 °C for 2 h, the mixture was hydrolyzed with a saturated aqueous solution of $NaHCO_3$. The organic extract was washed with water and dried over $MgSO_4$. After concentration, the residue was purified by column chromatography on silica gel (eluent petroleum ether/CH_2Cl_2/EtOAc 15/28/7, $R_f(\beta)$ = 0.31, $R_f(\alpha)$ = 0.25). The isomer β weighed 750 mg (70%). $[\alpha]_{Hg}$ +43.2 (*c* 0.6, $CHCl_3$); IR (KBr) ν cm^{-1} 3429 (OH), 2932 (CH arom), 1693 (C=O thym), 1471 (CH= arom), 1111 (SiO); ^{1}H NMR (250 MHz, $CDCl_3$) δ: 8.75 (bs, 1H), 7.69−7.39 (11H, m), 6.45 (dd, 1H, J = 5.8, 8.5 Hz), 4.37 (ddd, 1H, J = 2.4, 2.8, 7.0 Hz), 4.02 (dd, 1H, J = 1.9, 2.8 Hz), 3.69 (m, 2H), 3.36 (td, 1H, J = 1.9, 6.4 Hz), 2.30 (ddd, 1H, J = 2.4, 5.8, 13.6 Hz), 2.10 (m, 1H), 2.02 (ddd, 1H, J = 7.0, 8.5, 13.6 Hz), 1.74 (s, 3H), 1.09 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ: 163.7, 150.4, 135.8, 135.7, 135.4, 133.0, 132.7, 130.4, 130.3, 128.1, 128.0, 111.5, 85.2, 83.7, 75.3, 64.8, 56.5, 40.1, 26.9, 19.0, 12.7; MS (DCI, NH_3) 590 (MNH_4^+, 90), 573 (MH^+, 12).

The isomer α weighed 218 mg (20%): $[\alpha]_{Hg}$ +19.5 (*c* 0.3, $CHCl_3$); IR (KBr) ν cm^{-1} 3430 (OH), 2932 (CH), 1687 (C=O thym), 1471 (CH arom), 1112 (SiO); ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.68−7.38 (m, 11H), 6.39 (dd, 1H, J = 2.6, 7.8 Hz), 4.50 (dd, 1H, J = 1.8, 2.3 Hz), 4.38 (td, 1H, J = 6.8, 1.8 Hz), 4.63 (m, 2H), 3.20 (td, 1H, J = 2.3, 6.5 Hz), 2.20 (m, 2H), 1.97 (s, 3H), 1.09 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 164.3, 150.6, 136.3, 135.8, 135.6, 132.6, 132.1, 130.5, 130.4, 128.2−128.1, 110.8, 88.7, 87.6, 76.5, 64.2, 55.4, 41.5, 26.9, 19.0, 12.7; MS (DCI, NH_3) 590 (MNH_4^+, 97), 573 (MH^+, 17).

(3*S*,4*S*,5*S*)-1-[5-Bromo-2,5-dideoxy-6-*O*-(*tert*-butyldimethylsilyl)-3-*O*-(*tert*-butyldiphenylsilyl)hexofurasonyl]-5-methyluracil (28). A mixture of **27** (400 mg, 0.96 mmol) and *tert*-butyldimethylsilyl chloride (161 mg, 1.5 equiv) in anhydrous pyridine (4 mL) was stirred for 20 h under N_2 atmosphere. After dilution with ethyl acetate, the organic extract was washed with a saturated aqueous solution of NH_4Cl and with brine and dried over $MgSO_4$. After concentration in vacuo, the crude product was purified by column chromatography on silica gel (eluent petroleum ether/Et_2O/EtOAc 5/4/1). We obtained 285 mg (80%) of **28** along with 90 mg of starting product: $[\alpha]_{Hg}$ +49.0 (*c* 0.6, $CHCl_3$); IR ($CHCl_3$) ν cm^{-1} 3392 (NH), 2984−2957 (CH), 1691 (C=O), 1111 (SiO); ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.72 (bs, 1H), 7.67−7.38 (m, 11H), 7.45 (dd, 1H, J = 5.7, 8.4 Hz), 4.33 (ddd, 1H, J = 2.4, 3.2, 7.2 Hz), 4.16 (dd, 1H, J = 1.5, 3.2 Hz), 3.71 (m, 2H), 3.43 (ddd, 1H, J = 1.5, 6.2, 8.0 Hz), 2.32 (ddd, 1H, J = 2.4, 5.7, 13.6 Hz), 1.94 (ddd, 1H, J = 7.2, 8.4, 13.6 Hz), 1.87 (s, 3H), 1.09 (s, 9H), 0.90 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 163.9, 150.5, 135.8, 135.7, 135.6, 133.0, 132.9, 130.2, 130.1, 128.0, 127.9, 111.3, 83.8, 83.5, 75.1, 64.3, 55.0, 40.6, 26.9, 25.8, 19.0, 18.2, 12.7, −5.37, − 5.44; MS (DCI, NH_3) 704 (MNH_4^+, 85),

687 (MH^+, 15). Anal. Calcd for $C_{33}H_{47}BrO_5Si$: C, 57.63; H, 6.89; N, 4.07. Found: C, 57.64; H, 7.05; N, 4.05.

Synthesis of 29−32. Reaction of Compound 28 with Sodium Azide. A mixture of **28** (145 mg, 0.21 mmol) in DMF (2 mL) and NaN_3 (18 mg, 1.3 equiv) was stirred at 60 °C under N_2. After 24 h, the reaction was not complete. NaN_3 (15 mg) was added. The mixture was stirred for 12 h. DMF was evaporated, and the crude product was diluted with water and washed with a saturated aqueous solution of NaCl. After drying and concentration, the residue was purified by column chromatography on C18 silica gel (eluent CH_3CN/H_2O 3/2) to give 27 mg of **30** (26%), 29 mg of **29** (26%), and 26 mg of a **31** and **32** mixture (3 and 17%, respectively).

(3*S*,4*R*,5*S*)-1-[5-Azido-2,5-dideoxy-6-hydroxy-4-*O*-(*tert*-butyldiphenylsilyl)hexofuranosyl)-5-methyluracil (29): $[\alpha]_{Hg}$ +20.8 (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) ν cm^{-1} 3694 (OH), 3390 (NH), 3074 (CH arom), 2971, 2962, 2933 (CH), 1693 (C═O), 1590, 1507 (C═C), 1113 (SiO), 1043 (CO); ^1H NMR (250 MHz, $CDCl_3$) δ 8.91 (bs, 1H), 7.69−7.62 (m, 4H), 7.51−7.31 (m, 6H), 7.13 (d, 1H, J = 1.2 Hz), 6.26 (dd, 1H, J = 5.7, 8.6 Hz), 4.42 (ddd, 1H, J = 2.2, 2.3, 6.0 Hz), 4.02 (dd, 1H, J = 2.3, 4.4 Hz), 3.70−3.55 (m, 2H), 3.40 (m, 1H), 2.20 and 2.24 (AB part of an ABXY system + bs, 3H, J = 2.2, 5.7, 6.0, 8.6, 13.4 Hz), 1.88 (s, 3H, J = 1.2), 1.08 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 163.5, 150.4, 135.9, 135.8, 135.7, 132.9, 132.7, 130.3, 130.2, 111.5, 86.2, 85.9, 73.3, 64.5, 62.3, 39.4, 26.9, 19.1, 12.5; MS (DCI, NH_3) 553 (MNH_4^+, 100), 536 (MH^+, 38).

(3*S*)-1-[4-(2-Hydroxyethylidene)-3-*O*-(*tert*-butyldiphenylsilyl)-2,5-dideoxyhexofuranosyl]-5-methyluracil (30): $[\alpha]_{Hg}$ +13.5 (*c* 2.8, $CHCl_3$); IR ($CHCl_3$) ν cm^{-1} 3612 (OH), 3390 (NH), 2997, 2961, 2934, 2893 (CH), 1695 (C═O thym), 1429 (C═C), 1111 (SiO), 1086, 1046 (CO); ^1H NMR (250 MHz, $CDCl_3$) δ 8.95 (bs, 1H), 7.70−7.65 (m, 4H), 7.46−7.37 (m, 6H), 6.84 (d, 1H, J = 1.2 Hz), 6.67 (dd, 1H, J = 6.0, 7.4 Hz), 4.68 (dd, 1H, J = 2.3, 5.6 Hz), 4.47 (t, 1H, J = 6.9 Hz), 4.09 (m, 2H), 2.44 and 1.95 (AB part of an ABXY system, 2H, J = 2.3, 5.6, 6.0, 7.4, 13.5 Hz), 1.86 (d, 3H, J = 1.2 Hz), 1.06 (s, 9H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ: 163.4, 156.3, 150.1, 135.9, 135.8, 134.4, 133.0, 132.8, 130.2, 130.1, 128.0, 127.7, 112.0, 101.4, 86.1, 71.9, 56.9, 39.9, 26.8, 19.1, 12.6; MS (DCI, NH_3) 510 (MNH_4^+, 100), 492 (MH^+, 6).

(3*S*)-1-[4-[2-[(*tert*-Butyldiphenylsilyl)oxy]ethylidene]-3-*O*-(*tert*-butyldiphenylsilyl)-2,5-dideoxy-hexofuranosyl]-5-methyluracil (31). A solution of **28** (60 mg, 0.096 mmol) and diazabicycloundecene (15 μL, 1.1 equiv) in anhydrous DMF (1 mL) was stirred for 12 h at 60 °C. The temperature was raised to room temperature. Then, a saturated Na_2SO_3 solution was added. After extraction with EtOAc, the organic layer was washed with water, dried over $MgSO_4$, and concentrated. The crude product was purified on silica gel (eluent petroleum ether/Et_2O/EtOAc 5/4/1) to give 37 mg (67%) of the compound **31**: R_f = 0.28; $[\alpha]_{Hg}$ +14.2 (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) ν cm^{-1} 3393 (NH), 2958, 2859 (CH), 1694 (C═O thym), 1110 (O−Si); ^1H NMR (250 MHz, $CDCl_3$) δ 8.63 (bs, 1H), 7.69−7.64 (m, 4H), 7.45−7.36 (m, 6H), 6.84 (d, 1H), 6.70 (dd, 1H, J = 5.9, 7.4 Hz), 4.66 (dd, 1H, J = 2.1, 5.5 Hz), 4.46 (dd, 1H, J = 5.5, 7.6 Hz), 4.28 and 4.25 (AB part of an ABX system, 2H, J = 5.5, 7.6, 12.5 Hz), 2.37 (m, 1H), 1.86 (m, 1H), 1.86 (d, 3H), 1.07 (s, 9H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 163.3, 154.6, 150.0, 135.9−135.8, 134.1, 133.0−132.9, 130.1−130.0, 127.9−127.7, 111.9, 102.6, 85.5, 71.8, 57.6, 40.2, 26.8, 25.6, 19.1, 18.4, 12.5, 5.2, 5.1; MS (DCI, NH_3) 624 (MNH_4^+, 100), 607 (MH^+, 2.2).

(3*S*,4*S*,5*R*)-Methyl [6-[(*tert*-butyldiphenylsilyl)oxy]-4,5-epoxy-3-hydroxy]hexanoate (34). The aldolization reaction was performed as previously described.[16] Starting from (2*R*,3*R*)-4-[(*tert*-butyldiphenylsilyl)oxy]-2,3-epoxybutan-1-al (1 g, 2.94 mmol), we obtained after purification by silica gel column chromatography (eluent petroleum ether/CH_2Cl_2/EtOAc 5/4/1) the desired compound **34** (960 mg, 79% yield): R_f = 0.27; $[\alpha]_D$ −6.3° (*c* 0.7, $CHCl_3$); IR ($CHCl_3$) ν cm^{-1} 3599 (OH), 3007 (═CH), 1732 (C═O), 1200, 1110 (CO); ^1H NMR (250 MHz, C_6D_6) δ 7.78−7.72 (m, 4H), 7.24−7.20 (m, 6H), 3.90 and 3.84 (AB part of an ABX(Y) system, 2H, J = 4.9, 6.2, 12 Hz), 3.80 (m, 1H), 3.22 (s, 3H), 3.07 (ddd, 1H, J = 4.2, 4.9, 6.2 Hz), 2.95 (d, 1H, J = 4 Hz), 2.79 (dd, 1H, J = 4.2, 7.9 Hz), 2.46 and 2.38 (A′B′ part of an A′B′X′(Y) system, 2H, J = 4, 8.1, 16.1 Hz), 1.13 (s, 9H); ^{13}C NMR (63 MHz, C_6D_6) δ 172.0, 136.0, 133.5, 130.1, 128.3, 66.6, 62.9, 57.5, 57.0, 51.3, 39.3, 27.0, 19.4; MS (DCI, NH_3) 560 (MNH_4^+, 100). Anal. Calcd for $C_{23}H_{30}O_5Si$: C, 66.63; H, 7.29. Found: C, 66.62; H, 7.39.

(3*S*,4*S*,5*S*)-Methyl [5-Iodo-6-(*tert*-butyldiphenylsilyl)-oxy]hexanoate (35). A solution of **34** (2.1 g, 5.3 mmol) in toluene (50 mL) was added at −78 °C to a suspension of MgI_2 (1.4 g, 1 equiv) in Et_2O. After being stirred for 19 h at −78 °C, a saturated aqueous solution of Na_2SO_3 was added. The resulting mixture was extracted with Et_2O. The organic layers were washed with water and brine and dried over $MgSO_4$. After concentration, column chromatography on silica gel (petroleum ether/Et_2O/EtOAc 15/6/4, R_f = 0.31) gave 2.2 g (80%) of the desired compound: $[\alpha]_{Hg}$ −12.4 (*c* 0.7, $CHCl_3$); IR (KBr) ν cm^{-1} 3472 (OH), 3071 (CH arom), 2931, 2858 (CH), 1725 (C═O), 1173 (CO), 1110 (SiO); ^1H NMR (250 MHz, $CDCl_3$) δ 7.73−7.64 (m, 4H), 7.46−7.37 (m, 6H), 4.74 (td, 1H, J = 1.3−5.0 Hz), 4.05 (d, 2H), 3.85 (dddd, 1H, J = 2.8, 5.6, 8.7 Hz), 3.72 (s, 3H), 3.29 (d, 1H, J = 5 Hz), 2.94 and 2.57 (AB part of an ABX(Y) system, 2H, J = 2.8, 8.7, 16.9 Hz), 2.86 (ddd, 1H, J = 1.3, 5.0, 8.7 Hz), 2.74 (d, 1H, J = 5.6 Hz), 1.08 (s, 9H); ^{13}C NMR (62.9 MHz, C_6D_6) δ 173.7, 135.7, 135.5, 132.6, 132.2, 130.0, 127.9, 73.8, 71.6, 68.6, 51.8, 40.7, 37.0, 26.8, 19.2; MS (DCI, NH_3) 560 (MNH_4^+, 100).

(3*S*,4*S*,5*S*)-Methyl [5-Iodo-6-[(*tert*-butyldiphenylsilyl)-oxy]-3,4-bis[(trimethylsilyl)oxy]hexanoate (36). To a solution of **35** (500 mg, 0.92 mmol) in pyridine (5 mL) at −78 °C under N_2 atmosphere were added distilled hexamethyldisilazane (0.430 mL) and trimethylsilyl chloride (0.260 mL). The mixture was stirred for 12 h. A saturated aqueous solution NH_4Cl was added. The aqueous layer was extracted with Et_2O. The organic extract was washed with water and brine and dried over $MgSO_4$. After concentration, 620 mg (98%) of the desired compound was obtained: $[\alpha]_{Hg}$ −2.7 (*c* 0.7, $CHCl_3$); IR (KBr) ν cm^{-1} 3078 (CH arom), 2955, 2859 (CH), 1744 (C═O), 1253 (CO + SiO), 1113 (COSi); ^1H NMR (250 MHz, $CDCl_3$) δ 7.66−7.62 (m, 4H), 7.47−7.34 (m, 6H), 4.38 (ddd, 1H, J = 1.6, 6.5, 8.5 Hz), 4.04 (td, 1H, J = 3.6, 7.2 Hz), 3.88−3.85 (m, 2H), 3.69 (s, 3H), 3.35 (dd, 1H, J = 1.6, 7.2 Hz), 2.70 and 2.51 (AB part of an ABX(Y) system, 2H, J = 3.6, 7.2, 14.9 Hz), 1.07 (s, 9H), 0.16−0.14 (9H, s); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ: 172.0, 135.8, 135.7, 133.4, 133.2, 130.2, 130.1, 128.1, 128.0, 73.6, 72.9, 66.7, 51.6, 41.5, 39.3, 27.1, 19.4, 1.0−0.8; MS (DCI, NH_3) 704 (MNH_4^+, 100).

Acknowledgment. We thank Chantal Zedde for liquid chromatography assistance. Financial support by MESR and CNRS is gratefully acknowledged.

JO972116S