Synthesis of (5′*S*)-5′-*C*-Alkyl-2′-deoxynucleosides

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We describe the synthesis of (5′*S*)-5′-*C*-butylthymidine (**5a**), of the (5′*S*)-5′-*C*-butyl- and the (5′*S*)-5′-*C*-isopentyl derivatives **16a** and **16b** of 2′-deoxy-5-methylcytidine, as well as of the corresponding cyanoethyl phosphoramidites **9a**,**b** and **14a**,**b**, respectively. Starting from thymidin-5′-al **1**, the alkyl chain at C(5′) is introduced *via Wittig* chemistry to selectively yield the (*Z*)-olefin derivatives **3a** and **3b** (*Scheme 2*). The secondary OH function at C(5′) is then introduced by epoxidation followed by regioselective reduction of the epoxy derivatives **4a** and **4b** with diisobutylaluminium hydride. In the latter step, a kinetic resolution of the diastereoisomer mixture **4a** and **4b** occurs, yielding the alkylated nucleoside **2a** and **2b**, respectively, with (5′*S*)-configuration in high diastereoisomer purity (de = 94%). The corresponding 2′-deoxy-5-methylcytidine derivatives are obtained from the protected 5′-alkylated thymidine derivatives **7a** and **7b** *via* known base interconversion processes in excellent yields (*Scheme 3*). Application of the same strategy to the purine nucleoside 2′-deoxyadenine to obtain 5′-*C*-butyl-2′-deoxyadenosine **25** proved to be difficult due to the sensitivity of the purine base to hydride-based reducing agents (*Scheme 4*).

1. Introduction. – With the intention to study the effects of minor-groove hydration on structure and stability of the DNA double helix, we became interested in the preparation and biophysical investigation of oligodeoxynucleotides containing 5′-*C*-butyl- and 5′-*C*-isopentyl-substituted (5′*S*)-2′-deoxynucleosides. Since these nucleoside analogues were unknown, we needed to develop a synthesis for the corresponding deoxynucleosides as well as for their phosphoramidite building blocks for standard, solid-phase oligodeoxynucleotide chemistry.

Several approaches to the preparation of 5′-*C*-alkyl deoxynucleosides are reported in the literature. The synthesis of the 5′-*C*-methyl-substituted deoxyribonucleosides, the simplest members of this class, *via* deoxygenation of the corresponding hexofuranose nucleosides thereby pioneered the field [1]. More recent and more general approaches involve the use of the corresponding nucleosid-5′-al (CH_2(5′)OH replaced by CH(5′)=O) as starting materials, to which the 5′-*C*-substituents were added either *via* organometallic reagents [2][3] or *via* aldol-type chemistry [4][5]. A radical approach has been used to prepare 5′-*C*-allylated nucleosides starting from 5′-selenonucleosides [6]. Probably the most versatile strategy, however, was developed by *Wang* and *Middelton* [7]. As a key intermediate, they prepared the 5′,6′-epoxyhexofuranose nucleosides, which could selectively be substituted at the C(6′) position with various heteronucleophiles and cyanide.

We report here the synthesis of the hitherto unknown 5′-*C*-butyl and 5′-*C*-isopentylthymidines as well as on the 5′-*C*-butyl- and 5′-*C*-isopentyl-substituted 2′-

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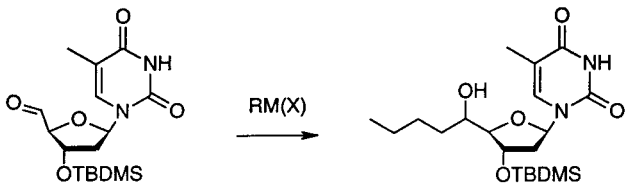
deoxy-5-methylcytidines starting from natural thymidine *via Wittig* chemistry of the nucleosid-5′-al, followed by an epoxidation/reduction pathway.

2. Results and Discussion. – 2.1. *(5′S)-5′-C-Butyl- and (5′S)-5′-C-Isopentylthymidines and the Corresponding 2′-(Cyanoethyl Phosphoramidites)*. In initial experiments, we investigated scope and limitations of direct alkylation of thymidin-5′-al **1** (*Scheme 1*) by organometallic reagents. Compound **1** is accessible in 3 steps from thymidine by oxidation of the 5′-OH group with *Dess-Martin* periodinane [8]. The results of direct addition of various butyl-derived organometallic reagents to **1** are summarized in the *Table*.

Scheme 1. *Synthesis of 5′-C-Alkylthymidines* via *Direct Addition of Organometal Reagents to Thymidin-5′-al* **1**



TBDMS = ^{t}BuMe$_2$Si

The addition of BuLi gave 5′-*C*-butyl-3′-*O*-[(*tert*-butyl)dimethylsilyl]thymidine (**2a**) in poor yields and poor diastereoselectivity (*Entry 1*). Reaction of **1** with BuMgBr in Et_2O in the presence of the *Lewis* acid $MgBr_2$ led to a small selectivity increase in favor of the desired (5′*S*) diastereoisomer of **2a** (*Entry 3*)[2].

Neither addition of Bu_4NBr nor the workup with ethylenediaminetetraacetic acid (EDTA) [10] could improve the yield significantly. As the main by-product in all experiments, the reduced 3′-*O*-[(*tert*-butyl)dimethylsilyl]thymidine was obtained, most likely as a result of a β-hydride transfer [10] of the *Grignard* reagent to the carbonyl C-atom. Also the change of the organometallic reagent to $BuCeCl_2$ [11] or $BuTi(O^iPr)_3$ did not improve the yield or the diastereoselectivity (*Entries 5* and *6*). The failure in this direct approach prompted us to change strategy.

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[2]) The assignment of the configuration at the newly formed stereocenter was achieved by comparison of the ^{1}H-NMR difference NOE spectra of the corresponding cyclic silyl ether derivatives (5′*S*)-**6a** and (5′*R*)-**6a** [9]. One diastereoisomer showed NOEs between H–C(4′) and H–C(5′), as well as between H–C(5′) and CH_2(7′)[3]), while the other isomer showed NOEs between H–C(3′) and H–C(5′), as well as between H–C(4′) and CH_2(6′). This is in agreement with the assignment of the (5′*S*)-configuration to the former and (5′*R*)-configuration to the latter isomer.

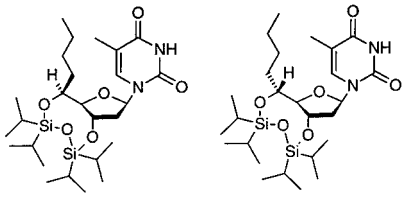


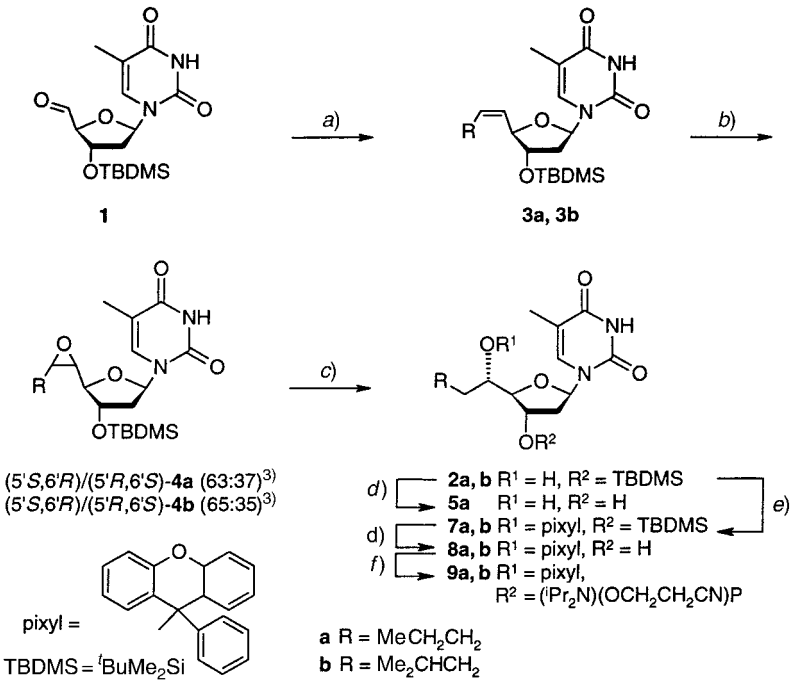
Table. *Direct Addition of Various Butylmetallic Reagents to* **1**: *Exper. Conditions and Diastereoselectivity Data*

Entry	BuMR (equiv.)	Solvent	*T* [°]	*t* [h]	Yield [%]	(5′*S*)-**2a**/5′(*R*)-**2a**
1	BuLi (2.2)	Et_2O	– 76	2.0	23	n. d.
2	BuMgBr (5)	Et_2O	– 76	3.0	37	50 : 50
3	BuMgBr (5) + $MgBr_2$ (5)	Et_2O	– 76	3.5	30	62 : 38
4	BuMgBr (4) + Bu_4NBr (4)	Et_2O	– 76	2.7	43	50 : 50
5	$BuCeCl_2$ (3)	THF	– 76	5.0	37	64 : 36
6	$BuTi(O\text{-}iPr)_3$ (3)	Et_2O	0	48.0	5[a)]	52 : 48

[a]) Besides 28% of **1**.

Wittig olefination of **1** with butyl- or isopentyltriphenylphosphonium ylide in THF at low temperature gave **3a** in 65% and **3b** in 54% from 3-*O*-[(*tert*-butyl)dimethylsilyl]thymidine (**1**) (*Scheme 2*).

Scheme 2



a) 3 equiv. of alkylphosphonium ylide, THF – 78° → r.t.; 65% (**3a**), 54% (**3b**). *b*) 1.9 equiv. of *m*CIPBA, CH_2Cl_2, – 38 → – 7°; 74% (**4a**), 77% (**4b**). *c*) 2–4 equiv. of DIBAH, THF, – 78°, 6.5 h; 40% (**2a**), 31% (**2b**). *d*) 1 equiv. of Bu_4NF, THF, r.t., 12–24 h; 95% (**5a**), 95% (**8a**), 74% (**8b**). *e*) 1.2–2.4 equiv. of pixyl chloride, pyridine, r.t., 16 h; 91% (**7a**), 87% (**7b**). *f*) 4 equiv. of $^iPr_2NEt$, 1.5 equiv. of $PCl(OCH_2CH_2CN)(iPr_2N)$, THF, r.t., 2 h; 91% (**9a**), 73% (**9b**). TBDMS = ^{t}BuMe$_2$Si

For both **3a** and **3b**, the (*E*)/(*Z*) ratio (assignment by ^{1}H-NMR NOE spectroscopy, see *Exper. Part*) was *ca.* 1:9. Epoxidation with 3-chloroperbenzoic acid (*m*CIPBA) in CH_2Cl_2 afforded **4a** and **4b**, respectively, in yields of 70–80% and in diastereoisomer

ratios (5′*S*,6′*R*)/(5′*R*,6′*S*)[3]) of *ca.* 1.8:1. Diastereoselection in this reaction was thus comparable to the best cases in the direct alkylation approach (*Table*). As expected, the reduction of the diastereoisomer mixtures **4a** and **4b** with the *Lewis* acid diisobutylaluminium hydride (DIBAH) in THF at low temperature proceeded with regiospecificity, yielding, *e.g.*, 40% of **2a** along with 33% of recovered starting material. Unexpectedly, a high diastereoisomer ratio (5′*S*)/(5′*R*) of 97:3 was observed in the product **2a**, which is due to the kinetic control of the reaction. Although *via* this kinetic resolution, **2a** (5′*S*) and **2b** (5′*S*) were obtained in acceptable diastereoisomer purity, we generally preferred to separate the diastereomer mixture of **4a** and **4b** by flash chromatography (FC) before reduction. Therefore, **2a**(5′*S*)- and **2b** (5′*S*) were usually prepared from the diastereoisomerically pure (5′*S*,6′*R*)-**4a** and -**4b**[3]) in 84 and 68% yield, respectively.

Desilylation of **2a** (5′*S*) to **5a** was achieved in 95% yield with Bu_4NF. Attempts to introduce the routinely used 4,4′-dimethoxytrityl protecting group at the 5′-OH group in satisfactory yield failed. We, therefore, switched to the sterically less-demanding 9-phenyl-9*H*-xanthen-9-yl (= pixyl) protecting group [12]. Reaction of **2a** and **2b** (both (5′*S*)) with pixyl chloride under standard conditions gave **7a** and **7b** in 91% and 87% yield, respectively. Subsequent desilylation with Bu_4NF at room temperature (→ **8a** and **8b**, resp.) and phosphitylation gave the corresponding 2′-(cyanoethyl phosphoramidites) **9a** and **9b** in good to excellent yields.

2.2. *5′-C-Butyl- and 5′-C-Isopentyl-Substituted (5′S)-2′-Deoxy-5-methylcytidines and Their Corresponding 2′-Cyanoethyl Phosphoramidites.* We planned to obtain the 5′-*C*-alkylated 2′-deoxy-5-methylcytidine phosphoramidite building blocks from **7a** and **7b** *via* a known base-interconversion process [13] (*Scheme 3*).

Thus, **7a** and **7b** were first transformed into the 1,2,4-1*H*-triazol-1-yl derivatives **10a** and **10b** with $POCl_3$ and 1,2,4-1*H*-triazole in 87 and 91% yield, respectively. Treatment of **10a** and **10b** with conc. NH_3 in dioxane gave the 5-methylcytidine derivatives **11a** and **11b** almost quantitatively. N^4-Benzoylation with benzoyl chloride in pyridine at room temperature furnished **12a** and **12b** in 87 and 70% yield, respectively. The analogous reaction sequence as applied in the thymidine series (silyl-ether cleavage (→ **13a,b**) and phosphitylation) yielded the 2′-(cyanoethyl phosphoramidites) **14a** and **14b**. The benzoate **12a** could also be directly prepared from **10a** *via* nucleophilic aromatic substitution with the benzamide anion in 87% yield. The free nucleosides **16a** and **16b** were obtained after quantitative desilylation of **11a** and **11b** with Bu_4NF and pixyl-group removal with a mild acid *via* **15a** and **15b**, respectively.

2.3. *5′-C-Butyl-2′-deoxyadenosine.* To test whether the alkylation procedure also applies to purine nucleosides, we prepared the 2′-deoxyadenosin-5′-al **17** from 2′-deoxyadenosine in 5 steps [14] (*Scheme 4*). From the reaction of **17** with butyltriphenylphosphonium ylide, the *Wittig* product **19** was obtained in more than 70% yield and a (*Z*)/(*E*) ratio of 91:9 (^{1}H-NMR). Interestingly, if the reaction was quenched at −78°, the hydroxy phosphonium intermediate **18** of the *Wittig* reaction could also be isolated and separately transformed into **19** by treatment with base. The epoxidation of **19** with *m*CIPBA gave only small amounts of the desired epoxy derivative **20**, mainly because

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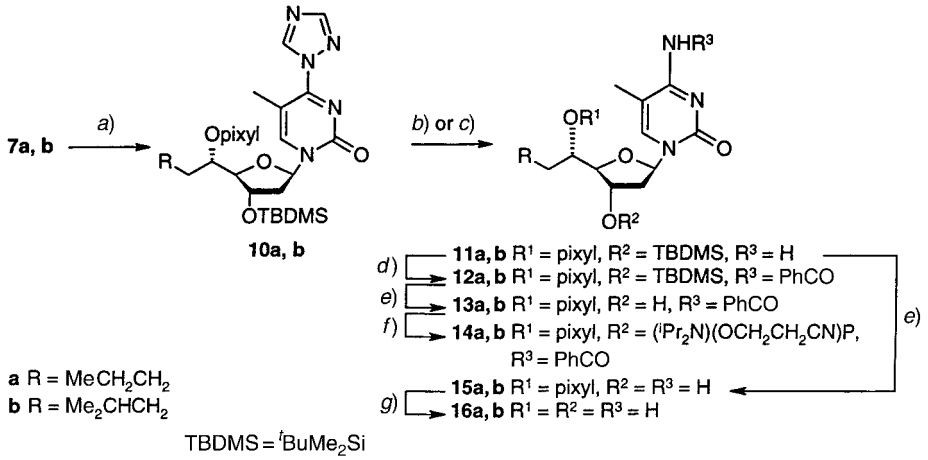
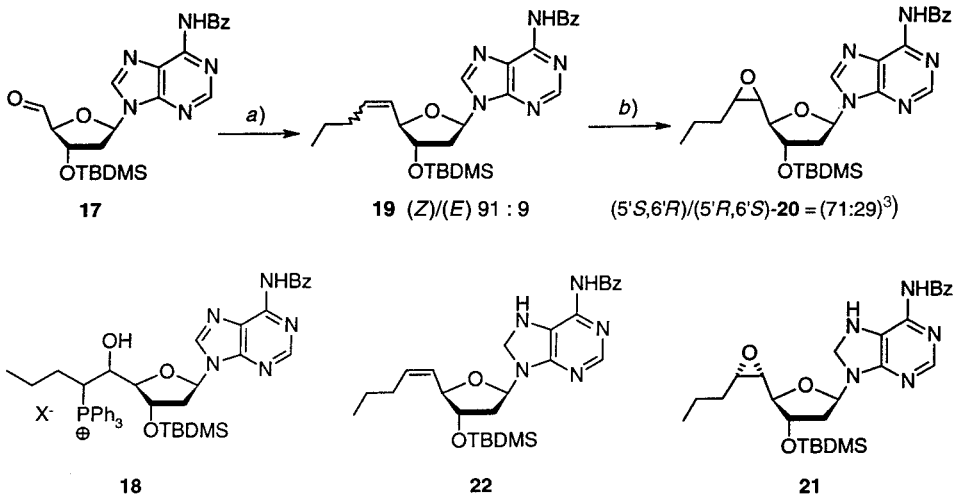
[3]) For convenience, the alkyl substituents at C(5′) are numbered by an extension of the monosaccharide numbering (C(6′), C(7′) *etc.*).

Scheme 3



a) 14 equiv. of 1,2,4-1*H*-triazole, 3 equiv. of $POCl_3$, 13 equiv. of Et_3N, r.t., 1 h, 87% (**10a**), 91% (**10b**). *b*) 25% aq. NH_3 soln., dioxane, r.t.; 2 h, 92% (**11a**), quant. (**11b**). *c*) 5 equiv. of KH, 4 equiv. of $PhCONH_2$, THF, r.t., 1 h; 87% (**12a**). *d*) 3.2 equiv. of PhCOCl, pyridine, 0 → r.t., 23 h, then 25% aq. NH_3 soln., 10 min.; 70% (**12b**). *e*) 1.1 equiv. of Bu_4NF, THF, r.t., 12–24 h; 99% (**13a**), quant. (**13b**), 54% (**15a**), 47% (**15b**). *f*) 4 equiv. of $^iPr_2NEt$, 1.5–2.2 equiv. of $PCl(OCH_2CH_2CN)(iPr_2N)$, THF, r.t., 2 h; 83% (**13a**), 84% (**13b**). *g*) $Cl_2CHCOOH$, THF/H_2O 9:1, r.t., 15 min; quant. (**16a**); 80% AcOH/THF 4:1, r.t., 48 h; 69% (**16b**). TBDMS = $^tBuMe_2Si$

Scheme 4.



a) 3 equiv. of $BuP(Ph)_3Br$, 3 equiv. of NaHMDS, THF, −78° → r.t. 4.75 h; 76%. *b*) 1.2 equiv. of DMDO, CH_2Cl_2, −20° → r.t., 22 h; 71%. *c*) 1 equiv. of $BH_3 \cdot$ THF, THF, −78°, 30 min, then 8 equiv. of *Oxone*®, 47% (**21**) from (5′*S*,6′*R*)-**20**; 76% (**22**) from (*Z*)-**19**.

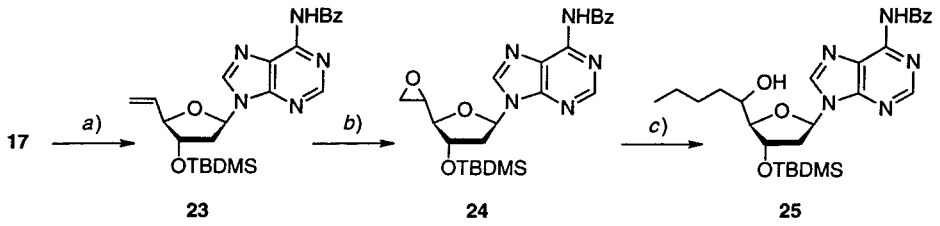
of acid-catalyzed depurination [15]. The alternative use of dimethyldioxirane (DMDO) [16] improved the yield of **20** to 71%, the by-products arising from known side reactions [17]. To our surprise, reactions of **20** directed towards epoxide ring

opening (→ **25**) failed. Instead, on treatment with DIBAH or $BH_3 \cdot THF$ complex, the nucleobase- reduced nucleoside **21** was isolated in 47 or 49% yield.

Direct hydroboration of **19** to give **25** also failed. Again the corresponding nucleobase-reduced compound **22** was obtained, this time in yields as high as 76%.

After these results, we changed to the strategy developed by *Wang* and *Middelton* [7] (*Scheme 5*). Thus, reaction of 2′-deoxyadenosin-5′-al **17** with methyltriphenylphosphonium ylide in THF at $-78°$ gave **23** in 70% yield. The following epoxidation with DMDO never gave more than a rather poor 30% of **24** as diastereoisomer mixture (77:23), along with usually 30% of starting material. Cu^I-catalyzed nucleophilic epoxide opening at the C(6′) position[3]) with PrMgBr at low temperature finally furnished **25** in 62% yield. Thus, with this reaction sequence, 5′-alkylated deoxyadenosine nucleosides can be obtained. However, yields and selectivity of the reactions deserve further improvement.

Scheme 5



a) 3 equiv. of $CH_2{=}P(Ph)_3Br$, 3 equiv. of NaHMDS, THF, $-78° \rightarrow$ r.t., 2 h; 70%; *b*) 4 equiv. of DMDO, CH_2Cl_2, $0° \rightarrow$ r.t., 2 d; 30%. *c*) 45 equiv. of PrMgBr, 0.5 equiv. of CuI, THF, -78 to $-18°$, 2 h; 62%. TBDMS = ^{t}BuMe$_2$Si

2.4. *Confirmation of the Relative Configuration at C(5′) by X-Ray Analysis.* The assignment of the configuration at C(5′), which was determined for the 5′-*C*-alkylated thymidines by ^{1}H-NMR difference NOE spetroscopy of the cyclic silyl derivative **6a**, was corroborated by the X-ray analysis of **15a** (*Fig.*)[4]).

In addition, the X-ray structure of **15a** shows the furanose ring in the 3′-*endo* conformation. This is not surprising considering the large substituent at C(4′). A second, more important feature is that the torsion angle γ lies in the $+sc$ range which corresponds to that in A- and B-DNA. This was not *a priori* to be expected after introduction of a butyl chain at C(5′). Furthermore, refinement of the structure showed that the butyl chain is flexible. It occurs in two conformations, one having two the other having only one *gauche* arrangement within the C-chain. In the crystal, one molecule of MeOH is packed between the base and sugar part of **15a**, bridging them *via* H-bonds. This gives rise to two layers in the crystal lattice: a hydrophilic layer containing the

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[4]) Crystallographic data (excluding structure factors) for the structure of **15a** have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-148358. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk.

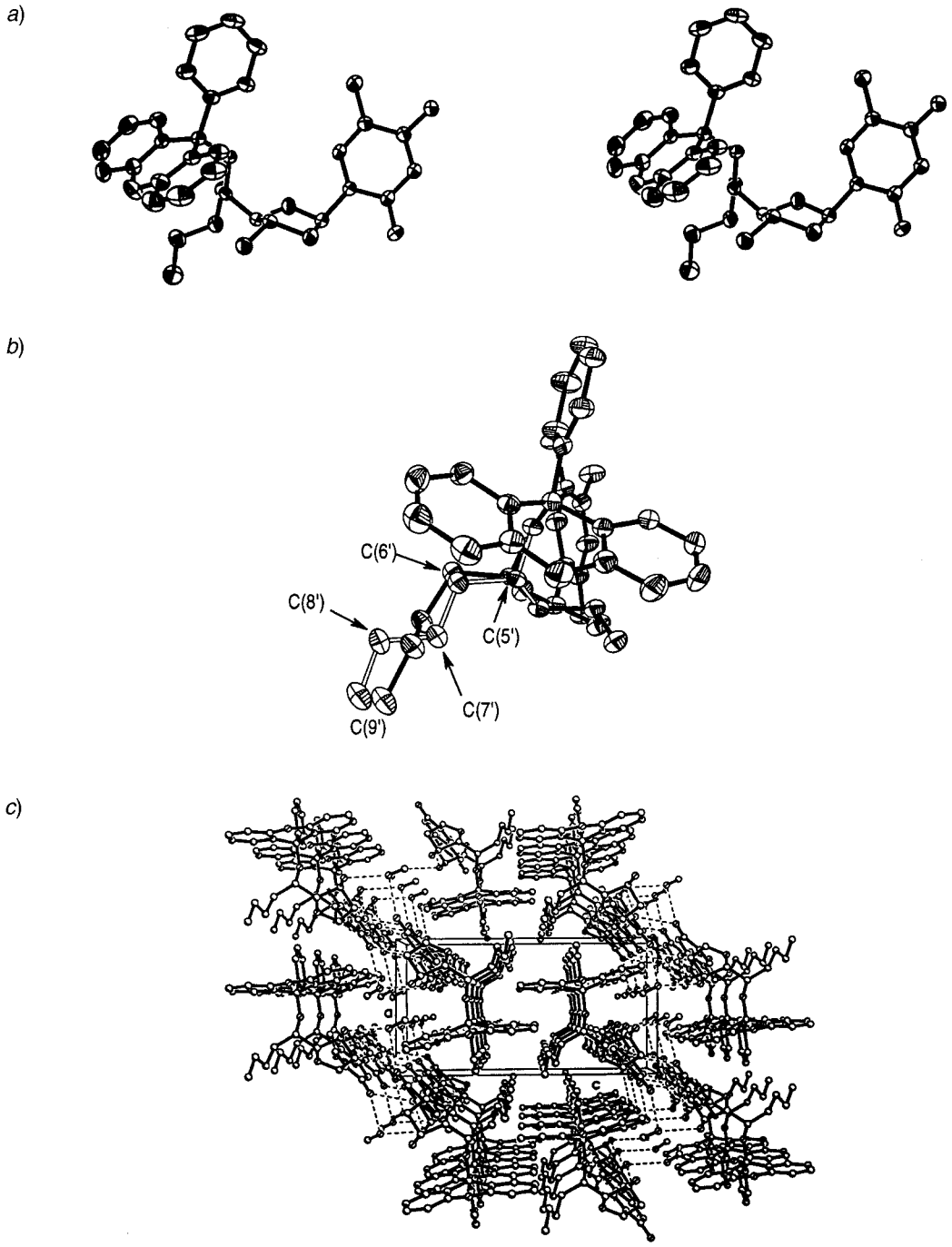

Fig. 1. *ORTEP Plot of crystals of* **15a**: a) *stereoscopic view* (25% probability thermal ellipsoids), b) *the two conformations of the butyl chain, and* c) *view along the crystallographic* a-*axis*

nucleobase, the sugar moiety, and the MeOH, and a hydrophobic layer containing the pixyl group and the butyl side chain.

3. Conclusions. – (5′*S*)-5′-*C*-Butyl- and (5′*S*)-5′-*C*-isopentylthymidine and 5′-*C*-butyl- and 5′-*C*-isopentyl-substituted (5′*S*)-2′-deoxy-5-methylcytidine as well as the corresponding 2′-(cyanoethyl phosphoramidite) building blocks for solid-phase oligonucleotide synthesis are accessible *via* the *Wittig*/epoxidation/reduction approach presented here. It is conceivable that, with this synthesis, a large variety of 5′-*C*-alkylnucleosides may be obtained. However, further improvement in the control of diastereoselectivity at C(5′) is desirable. The route described corresponds to a variation of the known 'epoxide route' [7], and thus complements the palette of synthetic methodologies towards 5′-*C*-substituted nucleosides. The synthesis of corresponding oligodeoxynucleotides as well as a structural and thermochemical analysis of duplexes containing these 5′-*C*-alkylated nucleosides by UV-spectroscopic methods and by isothermal titration calorimetry has recently been completed [9] and will be reported soon.

We thank the BENEFRI Small Molecule Crystallography Service directed by Prof. *Helen Stoeckli-Evans* for measuring the X-ray data set, and Prof. *Peter Bigler* for measuring the NOE spectra.

Experimental Part

General. All reactions were carried out under Ar starting from thymidine (*Fluka*, *purum*). Chemicals and solvents: *Dess-Martin* periodane [8], 1.1M Bu_4NF soln. in THF, 2-cyanoethyl diisopropylphosphoramidochloridite (*Aldrich*), THF, distilled over K/benzophenone, pyridine distilled over CaH_2, CH_2Cl_2, distilled over P_2O_5; all other reagents: *Fluka purum* or *puriss.* TLC: pre-coated glass plates *SIL G-25 UV$_{254}$* (*Macherey-Nagel*); visualization: UV (254 nm) and anisaldehyde stain (EtOH (180 ml), AcOH (10 ml), anisaldehyde (10 ml), conc. H_2SO_4 (2 ml)). Flash chromatography (FC): silica gel (30–60 μm) *Baker*. M.p.: uncorrected; *Büchi 510*. $[\alpha]_D$: *Perkin-Elmer* polarimeter; $l = 10$ cm, c in g/100 ml. UV Spectra: *Varian-Cary 3E*-UV/VIS photospectrometer connected to a *Compaq ProLinea-3/25-zs* personal computer. IR: *1600*-FT-IR *Perkin-Elmer* spectrometer; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR: *Bruker AC-300* (300 and 75 MHz resp.); if not otherwise stated, all spectra in $CDCl_3$; δ in ppm rel. to $CHCl_3$ (= 7.27 (^{1}H) and 77.00 (^{13}C) ppm, resp.), J in Hz; ^{13}C multiplicities from DEPT spectra; arbitrary numbering of the 5′-*O*-alkyl substituent[3]). 1D-NOE: *Bruker DRX-500* (500 MHz); δ(irradiated) → δ(observed). ^{31}P-NMR: *Bruker AMX 400* (161.92 MHz); δ in ppm rel. to 85% phosphoric acid. MS (*m/z* (%)): *Varian MAT CH-7A*, ionization energy 70 eV; only selected peaks; LSI: *AutoSpec Q VG*, matrix or DTT/DTE 2,2′,2″-nitrilotris[ethanol] (1,4-dithio-DL-threitol/1,4-dithioerythritol) 4:1. Elemental analyses: Mikroanalytisches Laboratorium, ETH-Zürich.

(5′Z)-5′-C-*Butylidene-3′*-O-*[(*tert*-butyl)dimethylsilyl]-5′-deoxythymidine* (**3a**). To a suspension of butyltriphenylphosphonium bromide (2.88 g, 7.2 mmol) in abs. THF (16 ml), 2M sodium hexamethyldisilazide (NaHMDS) in THF (3.6 ml) was added dropwise and stirred at r.t. for 30 min, and then under reflux for 1 h. To the cooled (−78°) soln., a soln. of **1** (dried by repeated co-evaporation with abs. toluene; 850 mg, 2.4 mmol) in THF (4 ml) was added. After 4 h, stirring was continued at r.t. for another 12 h. The suspension was diluted with *tert*-butyl methyl ether (^{t}BuOMe) (40 ml) and poured into sat. NH_4Cl soln. (25 ml), the aq. phase extracted with ^{t}BuOMe (3 × 40 ml), the combined org. phase dried ($MgSO_4$) and evaporated, and the residue submitted to FC (75 g, hexane/AcOEt 7:3): **3a** (619 mg, 65%). White solid. Anal. data from a crystallized (hot hexane) sample. TLC (hexane/AcOEt 1:1): R_f 0.42. M.p. 130–131°. $[\alpha]_D^{20}$ + 93.0 ($CHCl_3$, $c = 1.40$). IR (KBr): 3166*m*, 3027*m*, 2965*m*, 2857*m*, 1691*s*, 1654*s*, 1473*m*, 1426*m*, 1259*m*, 1117*m*, 1073*m*. ^{1}H-NMR: 8.75 (br., *s*, NH); 7.22 (*d*, $J = 1.1$, H–C(6)); 6.19 (*t*, J = 6.4, H–C(1′)); 5.75 (*dt*, $J = 11.0, 7.6$, H–C(6′)); 5.39 (*ddd*, $J = 10.9, 9.3, 4.4$, H–C(5′)); 4.61 (*dd*, $J = 9.3, 4.4$, H–C(4′)); 4.13 (*dt*, $J = 6.4, 4.4$, H–C(3′)); 2.37 (*ddd*, $J = 13.6, 6.4, 4.4$, H_α–C(2′)); 2.24–2.06 (*m*, H_β–C(2′)), CH_2(7′)); 1.94 (*d*, $J = 1.1$, Me–C(5)); 1.44 (*m*, CH_2(8′)); 0.89 (*s*, ^{t}BuSi); 0.07 (*s*, MeSi)); 0.06 (*s*, MeSi)). ^{13}C-NMR: 163.7 (*s*); 150.1 (*s*); 136.7 (*d*); 135.3 (*d*); 126.3 (*d*); 110.8 (*s*); 85.2 (*d*); 82.4 (*d*); 76.0 (*d*); 41.1 (*t*); 29.9 (*t*); 25.3 (*q*); 22.7 (*q*); 17.9 (*s*); 12.6 (*q*); −4.8 (*q*). NOE: 5.75 (H–C(6′)) → 1.44 (CH_2(8′), 4.6%),

2.10 (CH_2(7′), 3.0%), 2.18 (H_β–C(2′), 2.6%), 5.39 (H–C(5′), 13.5%); 5.39 (H–C(5′)) → 2.10 (CH_2(7′), 1.5%), 2.18 (H_β–C(2′), 5.9%), 4.61 (H–C(4′), 2.5%), 5.75 (H–C(6′), 10.7%), 7.22 (H–C(6), 8.2%); 4.61 (H–C(4′)) → 2.10 (CH_2(7′)), 2.18 (H_β–C(2′), 2.7%), 4.13 (H–C(3′), 2.0%), 5.39 (H–C(5′), 3.8%); 4.13 (H–C(3′)) → 2.10 (CH_2(7′), 5.0%), 4.61 (H–C(4′), 3.1%), 5.39 (H–C(5′), 5.9%), 7.22 (H–C(6), 4.5%); 2.37 (H_α–C(2′)) → 1.44 (C–H_2(8′), 5.8%), 2.18 (H_β–C(2′), 8.9%), 4.61 (H–C(4′), 8.8%), 5.75 (H–C(6′), 3.9%), 7.22 (H–C(6), 2.5%); 2.15 (H_β–C(2′)) → 1.44 (H_2C(8′), 1.7%), 2.37 (H_α–C(2′), 14.8%), 4.13 (H–C(3′), 7.2%), 4.61 (H–C(4′), 1.9%), 5.39 (H–C(5′), 1.7%), 5.75 (H–C(6′), 1.8%), 7.22 (H–C(6), 10.9%). MS: 394 (8, M^+), 183 (100). Anal. calc. for $C_{20}H_{34}N_2O_4Si$ (394.59): C 60.88, H 8.68, N 7.10; found: C 61.02, H 8.45, N 7.07.

5′(Z)-3′-O-*[(*tert-*Butyl)dimethylsilyl]-2′-deoxy-5′*-C-*(3-methylbutylidene)thymidine* (**3b**). As described for **3a**; from (3-methylbutyl)triphenylphosphonium bromide (3.468 g, 8.39 mmol), 2M NaHMDS in THF (4.20 ml, 8.39 mmol), and **1** (991 mg, 2.80 mmol) in THF (5.50 ml) FC (70 g, hexane/AcOEt 2:1): **3b** (620 mg, 54%). White solid. Anal. data from a crystallized (hot hexane) sample. M.p.: 137°. TLC (hexane/AcOEt 2:1): R_f 0.30. $[\alpha]_D^{22} = +2.7$ (acetone, $c = 0.86$). IR (NaCl): 3171*s*, 3078*s*, 2953*s*, 2857*s*, 1682*s*, 1471*s*, 1271*s*, 1118*m*, 1076*m*, 1055*m*, 838*m*, 778*m*. ^{1}H-NMR: 9.32 (br., *s*, NH); 7.31 (*s*, H–C(6)); 6.20 (*t*, $J = 6.2$, H–C(1′)); 5.70–5.82 (*m*, 1 H); 5.43 (*tt*, $J = 10.9$, 1.7, 1 H); 4.60 (*ddd*, $J = 9.0$, 4.2, 1.1, 1 H); 4.13 (*m*, 1 H); 2.37 (*ddd*, $J = 13.6$, 6.6, 4.4, H_α–C(2′)); 1.96–2.15 (*m*, 3 H); 1.93 (*s*, C(5)); 1.60–1.77 (*sept.*, $J = 6.7$, 1 H); 0.96 (*s*, 3 H); 0.92 (*s*, 3 H); 0.90 (*s*, ^{t}Bu(Si)); 0.07 (*s*, MeSi); 0.06 (*s*, Si). ^{13}C-NMR: 163.9 (*s*); 150.2 (*s*); 135.7 (*d*); 135.3 (*d*); 126.8 (*d*); 110.8 (*s*); 85.2 (*d*); 82.3 (*d*); 76.0 (*d*); 75.9 (*d*); 41.1 (*t*); 36.9 (*t*); 28.5 (*d*); 25.6 (*q*); 22.4 (*q*); 22.1 (*q*); 17.9 (*s*); 12.6 (*q*); −4.8 (*q*); −4.9 (*q*). MS: 408 (6, M^+), 283 (100). Anal. calc. for $C_{21}H_{36}N_2O_4Si$ (408.61): C 61.73, H 8.88, N 6.86; found: C 61.92, H 8.99, N 6.95.

cis-*(5′S,6′*R*)- and* cis-*(5′*R*,6′*S*)-5′*-C-*Butyl-3′*-O-*[(*tert-*butyl)dimethylsilyl]-5′-deoxy-5′,6′-epoxythymidine* ((*5′S,6′R*)-**4a** and (*5′R,6′S*)-**4a**, resp.)[3]. To a soln. of **3a** (162 mg, 0.44 mmol) in dry CH_2Cl_2 (1 ml), *m*CLPBA (258 mg, 0.82 mmol) was added at −38° and stirred for 18 h. After stirring for an additional 24 h at −5°, the suspension was diluted with ^{t}BuOMe (10 ml) and quenched with 15% (*w*/*v*), aq. $Na_2S_2O_3$ soln. (5 ml). After 10 min, 1M aq. $NaHCO_3$ (15 ml) was added, the aq. phase extracted with ^{t}BuOMe (3 × 30 ml), the combined org. phase dried ($MgSO_4$) and evaporated, and the residue submitted to FC (silica gel (20 g), hexane/AcOEt 4:1 + 0.5% MeOH): 126 mg (74%) of (*5′S,6′R*)-**4a**/(*5′R,6′S*)-**4a** 63:37. White foam. Separation of the diastereoisomers could be achieved by repeated FC (CH_2Cl_2/MeCN 12:1).

*Data of (5′*S*,6′*R*)-***4a**: TLC (CH_2Cl_2/MeCN 5:1): R_f 0.24. $[\alpha]_D^{21} = +79.1$ ($CHCl_3$, $c = 1.30$). IR (KBr): 3186*w*, 3060*w*, 2958*s*, 2931*s*, 2858*m*, 1696*s*, 1466*m*, 1364*m*, 1275*s*, 1260*s*, 1202*m*, 1103*m*, 1057*s*, 837*s*, 778*m*. ^{1}H-NMR: 9.02 (br. *s*, NH); 7.55(*d*, $J = 1.3$, H–C(6)); 6.23 (*t*, $J = 6.5$, H–C(1′)); 4.45 (*dt*, $J = 6.1$, 4.0, H–C(3′)); 3.97 (*dd*, $J = 5.1$, 4.0, H–C(4′)); 3.07 (*dt*, $J = 7.5$, 4.4, H–C(6′)); 3.00 (*dd*, $J = 5.2$, 4.4, H–C(5′)); 2.31 (*ddd*, $J = 13.5$, 6.3, 4.4, 1 H–C(2′)); 2.17 (*dt*, $J = 13.6$, 6.6, 1 H–C(2′)); 1.93 (*d*, $J = 1.3$, Me–C(5)); 1.43–1.77 (*m*, 4 H); 0.97 (*t*, $J = 7.2$, Me(9′)); 0.90 (*s*, ^{t}Bu(Si)); 0.10 (*s*, 2 MeSi). ^{13}C-NMR: 163.8 (*s*); 150.2 (*s*); 136.0 (*d*); 110.8 (*s*); 85.9 (*d*); 84.1 (*d*); 74.2 (*d*); 57.5 (*d*); 56.6 (*d*); 40.6 (*t*); 29.8 (*t*); 26.9 (*q*); 20.3 (*t*); 17.9 (*s*); 13.8 (*q*); 12.5 (*q*); −4.6 (*q*); −4.9 (*q*). MS: 410 (2, M^+), 201 (100). HR-LSI-MS: 411.2317 ($C_{20}H_{34}N_2O_5Si^+$; calc. 411.2315).

*Data of (5′*R*,6′*S*)-***4a**: TLC (CH_2Cl_2/MeCN 5:1): 0.29. $[\alpha]_D^{20} = +54.9$ ($CHCl_3$, $c = 0.80$). IR (KBr): 3184*m*, 3054*m*, 2958*s*, 2931*s*, 2858*s*, 1694*s*, 1470*s*, 1404*m*, 1363*m*, 1301*m*, 1274*s*, 1192*m*, 1105*m*, 1058*s*, 837*m*, 779*m*. ^{1}H-NMR: 9.09 (br., *s*, NH); 7.15 (*d*, $J = 1.3$, H–C(6)); 6.26 (*dd*, $J = 8.6$, 5.5, H–C(1′)); 4.56 (*dt*, $J = 5.7$, 1.8, H–C(3′)); 3.70 (*dd*, $J = 8.6$, 1.8, H–C(4′)); 3.21–3.06 (*m*, H–C(6′)); 2.89 (*dd*, $J = 8.6$, 4.0, H–C(5′)); 2.32 (*ddd*, $J = 13.4$, 5.5, 2.0, 1 H–C(2′)); 2.14 (*ddd*, $J = 13.6$, 8.4, 5.5, 1 H–C(2′)); 1.94 (*d*, $J = 1.3$, Me–C(5)); 1.64–1.46 (*m*, 4 H); 0.99 (*t*, $J = 7.1$, Me(9′)); 0.90 (*s*, ^{t}Bu(Si)); 0.11 (*s*, 2 MeSi). ^{13}C-NMR: 163.6 (*s*); 150.2 (*s*); 135.1 (*d*); 111.2 (*s*); 86.2 (*d*); 84.6 (*d*); 74.8 (*d*); 57.2 (*d*); 55.9 (*d*); 39.9 (*t*); 29.6 (*t*); 25.7 (*q*); 19.7 (*t*); 18.0 (*s*); 13.9 (*q*); 12.7 (*q*); −4.9 (*q*). MS: 411 (1, $[M+1]^+$), 227 (100). Anal. calc. for $C_{20}H_{34}N_2O_5Si$ (410.59): C 58.51, H 8.35, N 6.82; found: C 58.46, H 8.24, N 6.79.

cis-*(5′*S*,6′*R*)- and* cis-*(5′*R*,6′*S*)-3′*-O-*[(*tert-*Butyl)dimethylsilyl]-5′-deoxy-5′,6′-epoxy-5′*-C-*(3-methylbutyl)thymidine* and ((*5′S,6′R*)-**4b** and (*5′R,6′S*)-**4b**, resp.)[3]. As described above; from **3b** (560 mg, 1.37 mmol) in abs. CH_2Cl_2 (14.0 ml) and *m*CLPBA (680 mg, 2.75 mmol) at −7° for 72 h. FC (60 g, hexane/AcOEt 4:1): (*5′S,6′R*)-**4b** (377 mg, 57%) and *ca.* 20% of (*5′R,6′S*)-**4b** as white foams. The diastereoisomers were purified by repeated FC (CH_2Cl_2/MeCN 12:1).

*Data of (5′*R*,6′*S*)-***4b**: TLC (CH_2Cl_2/MeCN 10:1): R_f 0.33. $[\alpha]_D^{21} = +4.9$ ($CHCl_3$, $c = 1.04$). IR (NaCl): 3424*s*, 2957*m*, 2931*s*, 2858*m*, 1696*s*, 1466*m*, 1364*m*, 1275*s*, 1260*s*, 1202*m*, 1103*m*, 1057*s*, 837*s*, 778*m*. ^{1}H-NMR: 9.02 (br. *s*, NH); 7.55 (*d*, $J = 1.3$, H–C(6)); 6.23 (*t*, $J = 6.5$, H–C(1′)); 4.45 (*dt*, $J = 6.1$, 4.0, H–C(3′)); 3.97 (*dd*, $J = 5.1$, 4.0, H–C(4′)); 3.07 (*dt*, $J = 7.5$, 4.4, H–C(6′)); 3.00 (*dd*, $J = 5.2$, 4.4, H–C(5′)); 2.31 (*ddd*, $J = 13.5$, 6.3, 4.4, 1

H–C(2′)); 2.17 (*dt*, *J* = 13.6, 6.6, 1 H–C(2′)); 1.93 (*d*, *J* = 1.3, Me–C(5)); 1.43–1.77 (*m*, 4 H); 0.97 (*t*, *J* = 7.2, 1 Me(8′)); 0.90 (*s*, *t*BuSi); 0.10 (*s*, 2 MeSi).

Data of (5′S,6′R)-**4b**: TLC (CH_2Cl_2/MeCN 10:1): 0.26. $[\alpha]_D^{20} = +3.8$ (acetone, *c* = 0.98). IR (NaCl): 3193*m*, 3057*m*, 2956*s*, 2858*s*, 1696*s*, 1471*m*, 1404*m*, 1366*w*, 1257*w*, 1193*w*, 1117*w*, 1068*w*, 836*m*. ^{1}H-NMR: 8.75 (br. *s*, NH); 7.54 (*s*, H–C(6)); 6.20 (*t*, *J* = 6.4, H–C(1′)); 4.41 (*dd*, *J* = 10.1, 4.2, 1 H); 3.94 (*t*, *J* = 4.4, 1 H); 3.09 (*q*, *J* = 4.1, 1 H); 2.90 (*t*, *J* = 4.6, 1 H); 2.26 (*m*, 1 H–C(2′)); 2.13 (*m*, 1 H–C(2′)); 1.91 (*s*, Me–C(5)); 1.82 (*sept.*, *J* = 6.6, H–C(8′)); 1.62 (*m*, 1 H); 1.49 (*m*, 1 H); 0.96, 0.94 (*d*, *J* = 2.1, 2 Me(8′)); 0.88 (*s*, *t*BuSi); 0.08 (*s*, 2 MeSi). ^{13}C-NMR: 163.51 (*s*); 150.14 (*s*); 135.15 (*d*); 111.20 (*s*); 86.21 (*d*); 84.62 (*d*); 74.80 (*d*); 56.38 (*q*); 55.71 (*d*); 39.96 (*t*); 36.29 (*t*); 26.70 (*d*); 25.71 (*q*); 22.68 (*q*); 22.63 (*q*); 17.98 (*s*); 12.65 (*q*); −4.86 (*q*). MS: 425 (2, M^+), 241 (100).

(5′S)-5′-C-*Butyl-3′*-O-*[(*tert-*butyl)dimethylsilyl]thymidine* (**2a**). To a soln. of **4a** (mixture of diastereoisomers; 125 mg, 0.30 mmol) in dry THF (1.20 ml), 1M DIBAH in hexane (1.22 ml, 1.22 mmol) was added dropwise at −78° and stirred for 6.5 h. The reaction was quenched with AcOEt (0.20 ml), diluted with additional AcOEt (9 ml), and warmed up to r.t. The soln. was treated with sat. aq. potassium sodium tartrate (4.5 ml) and 5M aq. NaOH (0.20 ml), ultrasonicated, and stored at 4° overnight to allow phase separation. The aq. phase was treated with 5M NaOH (1 ml) and extracted with AcOEt (9 × 9 ml), the combined org. layer dried ($MgSO_4$) and evaporated, and the resulting oil was applied to FC (12 g, CH_2Cl_2/MeCN 15:1): starting **4a** (41 mg, 33%; enriched in (5′*R*,6′*S*)-**4a**) and then **2a** (51 mg, 40%, (5′*S*)/(5′*R*) 97:3 by ^{1}H-NMR) as white foam. TLC (CH_2Cl_2/acetone 8:1): R_f 0.26. $[\alpha]_D^{22} = +36.1$ ($CHCl_3$, *c* = 0.92). IR (KBr): 3448*m*, 3180*m*, 3060*m*, 2956*s*, 2931*s*, 2858*s*, 1684*s*, 1472*s*, 1362*m*, 1277*s*, 1255*s*, 1198*m*, 1131*s*, 1085*s*, 1049*s*, 909*m*, 835*m*, 778*m*, 734*s*. ^{1}H-NMR: 8.64 (br. *s*, NH); 7.39 (*d*, *J* = 1.5, H–C(6)); 6.12 (*t*, *J* = 6.8, H–C(1′)); 4.47 (*dt*, *J* = 6.6, 3.3, H–C(3′)); 3.78 (*t*, *J* = 2.9, H–C(4′)); 3.68 (*qd*, *J* = 6.6, 2.2, H–C(5′)); 2.42 (*d*, *J* = 6.6, OH); 2.38 (*ddd*, *J* = 13.4, 6.8, 1 H–C(2′)); 2.16 (*ddd*, *J* = 13.4, 6.3, 3.5, 1 H–C(2′)); 1.92 (*d*, *J* = 1.5, Me–C(5)); 1.64–1.55 (*m*, 2 H); 1.51–1.29 (*m*, 4 H); 0.96–0.87 (*m*, Me(9′), *t*Bu(Si)); 0.08 (*s*, 2 MeSi). ^{13}C-NMR: 163.70 (*s*); 150.30 (*s*); 137.22 (*d*); 110.97 (*s*); 89.23 (*d*); 86.98 (*d*); 72.75 (*d*); 71.22 (*d*); 40.15 (*t*); 34.23 (*t*); 27.91 (*t*); 25.71 (*q*); 22.60 (*t*); 17.92 (*s*); 13.97 (*q*); 12.51 (*q*); −4.62 (*q*); −4.80 (*q*). MS-EI: 413 (1, $[M+1]^+$), 85 (100).

(5′S)-3′-O-*[(*tert-*Butyl)dimethylsilyl]-5′*-C-*(3-methylbutyl)thymidine* (**2b**). As described above, from pure diastereoisomer (5′*S*,6′*R*)-**4b** (467 mg, 1.10 mmol); THF (4.0 ml), and 1M DIBAH in THF (3.30 ml, 3.30 mmol). FC (CH_2Cl_2/AcOEt 7:1, 3:1): **2b** (5′*S*) (324 mg, 68%). White foam. TLC (CH_2Cl_2/AcOEt 5:1): R_f 0.15. $[\alpha]_D^{21} = +2.0$ (acetone, *c* = 1.06). IR (NaCl): 3486*w*, 2955*m*, 2858*w*, 1696*s*, 1473*m*, 1385*w*, 1254*m*, 1088*w*, 1036*w*, 972*w*, 835*m*, 779*w*. ^{1}H-NMR: 8.51 (br. *s*, NH); 7.37 (*s*, H–C(6)); 6.10 (*t*, *J* = 7.0, H–C(1′)); 4.44 (*m*, 1 H); 3.76 (*t*, *J* = 2.8, 1 H); 3.62 (br. *s*, 1 H); 2.33 (*m*, OH–C(5′); 1 H–C(2′)); 2.15 (*ddd*, *J* = 13.2, 6.2, 3.3, 1 H–C(2′)); 1.90 (*s*, Me–C(5)); 1.65 (br. *s*, 1 H); 1.66–1.51 (*m*, 4 H); 1.40–1.16 (*m*, 5 H); 0.87 (*s*, *t*BuSi); 0.06 (*s*, 2 MeSi). ^{13}C-NMR: 164.0 (*s*); 150.6 (*s*); 137.8 (*d*); 111.2 (*s*); 89.5 (*d*); 87.3 (*d*); 73.0 (*d*); 72.0 (*d*); 40.4 (*t*); 35.0 (*t*); 32.9 (*t*); 28.2 (*q*); 26.0 (*q*); 22.8 (*q*); 18.1 (*s*); 12.7 (*q*); −4.5 (*q*); −4.7 (*q*). MS: 427 (2, M^+), 201 (100).

(5′S)-5′-C-*Butylthymidine* (**5a**). A soln. of **2a** ((5′*S*); 44 mg, 0.11 mmol) in THF (1 ml) was treated with 1.1M Bu_4NF in THF (0.12 ml, 0.13 mmol) at r.t. and stirred overnight. The mixture was evaporated and the residue applied to FC (4 g, *t*BuOMe + 1% MeOH): **5a** ((5′*S*); 30 mg, 95%). Clear colorless oil. TLC (CH_2Cl_2/MeOH 10:1): R_f 0.20. $[\alpha]_D^{21} = +41.0$ (MeOH, *c* = 0.62). UV: 265 (9170 ± 240). IR (film): 3446*s*, 3061*s*, 2932*s*, 2862*s*, 1684*s*, 1472*m*, 1377*m*, 1276*m*, 1200*m*, 1133*m*, 1083*m*. ^{1}H-NMR ((D_6)acetone): 7.95 (*d*, *J* = 1.1, H–C(6)); 6.30 (*dd*, *J* = 7.5, 6.3, H–C(1′)); 4.49 (*dt*, *J* = 5.9, 2.9, H–C(3′)); 4.28 (br. *s*, OH), 3.83 (*t*, *J* = 2.6, H–C(4′)); 3.76 (*td*, *J* = 6.6, 2.4, H–C(5′)); 3.10 (br. *s*, OH), 2.27 (*ddd*, *J* = 13.2, 7.5, 5.9, 1 H–C(2′)); 2.19 (*ddd*, *J* = 13.2, 6.2, 3.3, 1 H–C(2′)); 1.79 (*d*, *J* = 1.3, Me–C(5)); 1.65–1.50 (*m*, 2 H); 1.50-1.40 (*m*, 1 H); 1.40–1.24 (*m*, 3 H); 0.87 (*t*, *J* = 7.1, Me(9′)). ^{13}C-NMR ((D_6)acetone): 164.58(*s*); 151.48(*s*); 137.70(*d*); 110.52(*s*); 90.21(*d*); 85.70(*d*); 73.07(*d*); 71.61(*d*); 40.88(*t*); 34.68(*t*); 28.74(*t*); 23.31(*t*); 14.32(*q*); 12.57(*q*). EI-MS: 299 (5, $[M+1)^+]$, 147 (100).

(5′S)-5′-C-*Butyl-3′*-O-*[(*tert-*butyl)dimethylsilyl]-5′*-O-*(9-phenyl-9*H-*xanthen-9-yl)thymidine* (**7a**). To a soln. of dry (co-evaporated with dry pyridine, 3 × 8 ml) **2a** (359 mg, 0.87 mmol) in dry pyridine (9.5 ml), 9-chloro-9-phenyl-9*H*-xanthene (509 mg, 1.74 mmol) was added in one portion at r.t. The initially green soln. slowly turned yellow, and, after 5 h, additional 9-chloro-9-phenyl-9*H*-xanthene (125 mg, 0.43 mmol) was added and stirred overnight. The solvent was evaporated, the residue dissolved in CH_2Cl_2 (30 ml) and mixed with sat. $NaHCO_3$ soln. (30 ml), the mixture extracted with CH_2Cl_2 (3 × 30 ml), the combined org. layer dried ($NaSO_4$) and evaporated, and the residue applied to FC (60 g, hexane/AcOEt 4:1 + 0.5% Et_3N): **7a** as white foam (535 mg, 91%) and educt (34 mg, 9%). TLC (hexane/AcOEt 3:2): R_f 0.39. $[\alpha]_D^{22} = +33.2$ ($CHCl_3$, *c* = 1.25). IR (KBr): 3178*m* (br.), 3024*m*, 2955*s*, 2930*s*, 1696*s* (br.), 1602*m*, 1476*s*, 1447*s*, 1364*m*, 1318*m*, 1292*m*, 1276*m*, 1242*m*, 1133*m*, 1101*m*, 1055*m*, 756*s*. ^{1}H-NMR: 8.80 (br. *s*, NH); 7.87 (*d*, *J* = 1.3, H–C(6)); 7.47–7.33 (*m*, 4 H); 7.32–7.23 (*m*, 6 H); 7.09–6.91 (*m*, 4 H); 6.24 (*dd*, *J* = 9.3, 5.1, H–C(1′)); 3.75 (*d*, *J* = 1.1, 1 H); 3.41 (*d*, *J* = 2.0, 1

H); 3.25–3.18 (*m*, 1 H); 2.08–1.98 (*m*, 4 H, Me–C(5) and 1 H–C(2′)); 1.81 (*ddd*, *J* = 12.7, 9.3, 5.0, 1 H–C(2′); 1.47–1.33 (*m*, 1 H); 1.13–0.99 (*m*, 1 H); 0.98–0.85 (*m*, 2 H); 0.81 (*s*, ^{t}BuSi); 0.77–0.73 (*m*, 1 H); 0.69 (*t*, *J* = 7.5, Me(9′)); −0.11 (*s*, ^{t}BuSi); −0.18 (*s*, 2 MeSi). ^{13}C-NMR: 163.90 (*s*); 151.87 (*s*); 150.18 (*s*); 147.18 (*s*); 136.18 (*d*); 131.76 (*d*); 130.78 (*d*); 129.81 (*d*); 129.77 (*d*); 127.73 (*d*); 127.67 (*d*); 127.13 (*d*); 124.22 (*s*); 123.56 (*d*); 123.39 (*s*); 123.28 (*d*); 116.61 (*d*); 116.57 (*d*); 110.43 (*s*); 88.96 (*d*); 85.28 (*d*); 74.37 (*d*); 74.23 (*d*); 41.22 (*t*); 31.83 (*t*); 27.87 (*t*); 25.65 (*q*); 22.41 (*t*); 17.73 (*s*); 13.84 (*q*); 12.65 (*q*); −4.76 (*q*); −4.92 (*q*). LSI-MS: 669.3 (0.2, [*M* + 1)$^+$], 257 (100).

*(5′*S*)-3′*-O-*[(*tert*-*Butyl)dimethylsilyl]-5′*-C-*(3-methylbutyl)-5′*-O-*(9-phenyl-9*H-*xanthen-9-yl)thymidine* (**7b**). As described above, from **2b** (308 mg, 0.80 mmol); pyridine (4.3 ml), and 9-chloro-9-phenyl-9*H*-xanthene (314 mg, 1.07 mmol). FC (30 g, hexane/AcOEt 3:1): **7b** (319 mg, 87%). White foam. TLC (hexane/AcOEt 7:2): R_f 0.33. $[\alpha]_D^{21} = +27$ (acetone, *c* = 0.84). IR (NaCl): 3441*s*, 2954*m*, 2930*m*, 2857*w*, 1696*s*, 1575*w*, 1473*m*, 1445*m*, 1365*w*, 1317*w*, 1274*w*, 1242*w*, 1132*w*, 1088*w*, 1061*w*, 1040*w*, 964*w*, 944*w*, 833*w*, 757*m*. ^{1}H-NMR: 8.20 (br. *s*, NH); 7.80 (*s*, 1 H); 7.40–7.15 (*m*, 8 H); 7.04–6.85 (*m*, 5 H); 6.20 (*t*, *J* = 5.1, H–C(1′)); 3.71 (*s*, 1 H); 3.37 (*m*, 1 H); 3.19 (*m*, 1 H); 2.11–1.95 (*m*, 1 H); 1.88–1.72 (*m*, 1 H); 1.17 (*s*, 3 H); 1.12–1.02 (*m*, 1 H); 1.00–0.72 (*m*, 3 H); 0.68 (*s*, ^{t}BuSi); 0.64, 0.58 (2 *d*, *J* = 6.6, 2 Me–C(8′)); −0.14 (*s*, MeSi); −0.20 (*s*, MeSi). ^{13}C-NMR: 151.95 (*s*); 151.86 (*s*); 147.27 (*s*); 136.19 (*d*); 131.75 (*d*); 130.79 (*d*); 129.86 (*d*); 129.81 (*d*); 127.74 (*d*); 127.70 (*d*); 127.16 (*d*); 124.20 (*s*); 123.60 (*d*); 123.47 (*s*); 123.37 (*d*); 116.68 (*d*); 116.65 (*d*) 110.41 (*s*); 89.02 (*d*); 85.30 (*d*); 77.20 (*d*); 74.91 (*d*); 74.64 (*d*); 74.39 (*d*); 41.27 (*s*); 34.93 (*t*); 30.13 (*t*); 27.99 (*t*); 26.98 (*q*); 25.67 (*q*); 22.55 (*q*); 22.26 (*q*); 17.76 (*s*); 12.66 (*q*); −4.74 (*q*); −4.86 (*q*).

*(5′*S*)-5′*-C-*Butyl-5′*-O-*(9-phenyl-9*H-*xanthen-9-yl)thymidine* (**8a**). As described for **5a**, from **7a** (510 mg, 0.76 mmol), 1.1M Bu_4NF in THF (0.76 ml, 0.84 mmol), and THF (11 ml). FC (20 g, CH_2Cl_2 + 1% Et_3N) and crystallization ($CHCl_3$) yielded **8a** (400 mg, 95%). White needles. M.p.: 142–144°. TLC (AcOEt/hexane 2:1): R_f 0.18. $[\alpha]_D^{22} = +26.2$ ($CHCl_3$, *c* = 1.17). IR (KBr): 3448*m*, 3180*m*, 3060*m*, 2956*s*, 2931*s*, 2858*s*, 1684*s*, 1472*s*, 1362*m*, 1277*s*, 1255*s*, 1198*m*, 1131*s*, 1085*s*, 1049*s*, 836*s*, 734*s*. ^{1}H-NMR: 8.85 (br. *s*, NH); 7.63 (*d*, *J* = 1.1, H–C(6)); 7.51–7.43 (*m*, 2 H); 7.42–7.22 (*m*, 7 H); 7.11–6.98 (*m*, 4 H); 6.15 (*t*, *J* = 6.4, H–C(1′)); 3.67–3.57 (*m*, H–C(3′), H–C(4′)); 3.30 (*m*, H–C(5′)); 2.19 (*ddd*, *J* = 4.7, 6.3, 13.6, 1 H–C(2′)); 2.05–1.95 (*m*, 1 H–C(2′), Me–C(5)); 1.50–1.33 (*m*, 2 H, OH); 1.11–0.98 (*m*, 1 H); 0.92 (*q*, *J* = 6.9, 2 H); 0.85–0.72 (*m*, 2 H); 0.67 (*t*, *J* = 7.2). ^{13}C-NMR: 163.73 (*s*); 152.16 (*s*); 151.74 (*s*); 150.17 (*s*); 147.08 (*s*); 135.63 (*d*); 131.79 (*d*); 130.76 (*d*); 129.80 (*d*); 127.77 (*d*); 127.73 (*d*); 127.16 (*d*); 124.06 (*s*); 123.35 (*d*); 123.21 (*s*); 116.76 (*d*); 116.52 (*d*); 110.75 (*s*); 86.47 (*d*); 83.93 (*d*); 72.37 (*d*); 70.67 (*d*); 40.42 (*t*); 31.70 (*t*); 27.78 (*t*); 22.44 (*t*); 13.82 (*q*); 12.74 (*q*). MS: 467 (7), 257 (100). Anal. calc. for $C_{33}H_{34}N_2O_6$: C 71.46, H 6.18, N 5.05; found: C 71.51, H 6.26, N 5.20%.

*(5′*S*)-5′*-C-*(3-Methylbutyl)-5′*-O-*(9-phenyl-9*H-*xanthen-9-yl)thymidine* (**8b**). As described for **5a**, from **7b** (231 mg, 0.34 mmol), 1M Bu_4NF in THF (0.4 ml, 0.40 mmol), and THF (4.6 ml). FC (20 g, hexane/AcOEt 1:2, gradient): **8b** (142 mg, 74%). White crystals. TLC (hexane/AcOEt 1:2): R_f 0.48. $[\alpha]_D^{21} = +4.4$ (acetone, *c* = 1.04). IR (NaCl): 3443*w*, 3166*w*, 3052*w*, 2950*w*, 1696*m*, 1681*s*, 1666*s*, 1599*m*, 1574*w*, 1473*m*, 1442*m*, 1366*w*, 1313*m*, 1288*w*, 1266*m*, 1236*w*, 1199*w*, 1126*w*, 1088*w*, 1050*w*, 1018*w*, 949*w*, 907*w*, 871*w*, 814*w*, 756*m*. ^{1}H-NMR: 8.67 (br. *s*, NH); 8.44 (*s*, 1 H); 7.50–6.91 (*m*, 13 H); 6.17 (*dd*, *J* = 6.3, 2.2, H–C(1′)); 3.93 (*dd*, 1 H); 3.83 (*dd*, 1 H); 3.69 (*dd*, 1 H); 2.71 (*d*, 1 H); 2.53 (br. *s*, OH–C(3′)); 2.38 (*m*, 1 H–C(2′)); 2.24 (*m*, 1 H–C(2′)); 1.82 (*s*, Me–C(5)); 1.69–1.52 (*m*, 3 H); 1.45–1.12 (*m*, 1 H); 1.08–0.93 (*m*, 2 H); 0.89–0.78 (*m*, 6 H). ^{13}C-NMR: 152.20 (*s*); 151.70 (*s*); 150.03 (*s*); 147.09 (*s*); 135.60 (*d*); 131.78 (*d*); 130.76 (*d*); 129.83 (*d*); 129.81 (*d*); 127.78 (*d*); 127.79 (*d*); 127.17 (*d*); 124.02 (*s*); 123.43 (*d*); 123.34 (*d*); 123.20 (*s*); 116.79 (*d*); 116.56 (*d*); 110.74 (*s*); 86.27 (*d*); 83.80 (*d*); 77.20 (*d*); 72.70 (*d*); 70.39 (*d*); 40.35 (*t*); 34.88 (*t*); 29.92 (*t*); 27.98 (*d*); 22.52 (*q*); 22.19 (*q*); 21.04 (*d*); 14.18 (*d*); 13.67 (*d*); 12.74 (*q*).

*(5′*S*)-5′*-C-*Butyl-5′*-O-*(9-phenyl-9*H-*xanthen-9-yl)thymidine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**9a**). To a soln. of **8a** (352 mg, 0.64 mmol) and ^{i}Pr$_2$NEt (0.44 ml, 2.60 mmol) in dry THF (7 ml), $PCl(OCH_2CH_2CN)(N^iPr_2)$ (0.22 ml, 0.97 mmol) was added at r.t. After 2 h, the soln. was diluted with CH_2Cl_2 (30 ml) and poured into ice-cold sat. aq. $NaHCO_3$ soln. (20 ml). The mixture was extracted with CH_2Cl_2 (3 × 30 ml), the combined org. layer dried (Na_2SO_4) and evaporated, and the residue applied to FC (30 g, hexane/AcOEt 1:1 + 1% Et_3N): **9a** (431 mg, 91%). Colorless foam. TLC (hexane/AcOEt 1:2 + 1% Et_3N): R_f 0.58, 0.42. ^{1}H-NMR: 8.67 (br. *s*, NH); 7.78, 7.72 (2 *d*, *J* = 1.1, H–C(6)); 7.47–7.21 (*m*, 10 H); 7.10–6.97 (*m*, 4 H); 6.21 (*dt*, *J* = 4.7, 4.7, H–C(1′)); 3.91 (*s*, 1 H); 3.84 (*s*, 1 H); 3.78–3.46 (*m*, 5 H); 3.27 (*dt*, *J* = 2.6, 9.2, 1 H); 2.62 (*t*, *J* = 6.3, 1 H); 2.49 (*t*, *J* = 6.5, 1 H); 2.27 (*td*, *J* = 6.1, 12.5, 1 H–C(2′)); 2.02 (*d*, *J* = 1.1, Me–C(5)); 1.98–1.86 (*m*, 1 H–C(2′)); 1.45–1.20 (*m*, 2 H); 1.16, 1.06 (*d*, *J* = 6.8, 12 H, 2 *Me*$_2$CHN); 0.98–0.89 (*m*, 2 H); 0.88–0.73 (*m*, 2 H); 0.69 (*t*, *J* = 7.2, Me(9′)). ^{13}C-NMR: 163.74 (*s*); 151.83 (*s*); 151.72 (*s*); 151.87 (*s*); 147.39 (*s*); 135.83 (*d*); 131.69 (*d*); 130.96 (*d*); 130.86 (*d*); 129.80 (*d*); 129.71 (*d*); 127.70 (*d*); 127.65 (*d*); 127.10 (*d*); 127.06 (*d*); 123.87 (*s*); 123.81(*s*); 123.60 (*d*); 123.53 (*d*); 123.32 (*d*); 123.22 (*d*); 116.56 (*d*); 116.50 (*d*); 110.76 (*s*); 110.64 (*s*); 87.46 (*d*); 87.39 (*d*);

87.11 (*d*); 87.02 (*d*); 84.84 (*d*); 84.67 (*d*); 77.20 (*d*); 75.88 (*d*); 75.66 (*d*); 75.61 (*d*); 75.41 (*d*); 74.00 (*d*); 73.94 (*d*); 58.15 (*t*); 58.10 (*t*); 57.92 (*t*); 57.85 (*t*); 43.41 (*d*); 43.25 (*d*); 40.17 (*t*); 40.09 (*t*); 40.00 (*t*); 31.74 (*t*); 31.69 (*t*); 27.78 (*t*); 24.62 (*q*); 24.53 (*q*); 24.48 (*q*); 24.37 (*q*); 22.48 (*t*); 22.43 (*t*); 20.36 (*t*); 20.26 (*t*); 20.15 (*t*); 20.05 (*t*); 13.80 (*q*); 12.63 (*q*). ^{31}P-NMR: 155.96; 155.44. MALDI-TOF-MS (pos.-ion mode, matrix salicylamide): 755.4 $(M+H)^+$; calc. 755.8).

*(5′*S*)-5′*-C-*Butyl-3′*-O-*[(*tert*-butyl)dimethylsilyl]-4-dehydroxy-5′*-O-*(9-phenyl-9*H*-xanthen-9-yl)-4-(1*H*-1,2,4-triazol-1-yl)thymidine* (**10a**). To an ice-cold soln. of 1,2,4-1*H*-triazole (469 mg, 6.78 mmol) and $POCl_3$ (0.13 ml, 1.43 mmol) in abs. MeCN (3.90 ml), Et_3N (0.90 ml, 6.47 mmol) was added and stirred for 15 min. Then a soln. of **7a** (325 mg, 0.49 mmol) in abs. MeCN (2.00 ml) was added during 5 min, and after 20 min, stirring was continued at r.t. After 1 h, the reaction was quenched with Et_3N (0.54 ml) and H_2O (0.20 ml), and the solvent was removed. The solid was redissolved in CH_2Cl_2 (15 ml) and washed with 0.5M aq. $NaHCO_3$. The aq. layer was extracted with CH_2Cl_2 (3×10 ml) and the combined org. layer dried ($NaSO_4$) and evaporated. FC (25 g, CH_2Cl_2/MeOH 100:1 → 100:3): **10a** (306 mg, 87%) as white foam and **7a** (25 mg, 7%). TLC ($MeCl_2$/MeOH 20:1): R_f 0.51. $[\alpha]_D^{26} = +100.0$ (acetone, $c = 0.89$). IR (KBr): 3060*w*, 2955*s*, 2930*s*, 1684*s*, 1602*m*, 1521*s*, 1502*s*, 1476*s*, 1446*s*, 1430*s*, 1379*m*, 1319*m*, 1293*m*, 1241*m*, 1123*m*, 1100*m*, 1056*m*, 972*s*, 949*m*, 834*m*, 757*m*. ^{1}H-NMR: 9.36 (*s*, 1 H); 8.59 (*s*, 1 H); 8.17 (*s*, 1 H); 7.41–7.34 (*m*, 2 H); 7.32–7.21 (*m*, 4 H); 7.21–7.06 (*m*, 3 H); 7.06–6.95 (*m*, 3 H); 6.87 (*dd*, *J* = 7.9, 1.7, 1 H); 6.24 (*dd*, *J* = 8.6, 5.2, H–C(1′)); 3.90 (*s*, H–C(3′)); 3.35 (*d*, *J* = 4.8, H–C(4′)); 3.29–3.22 (*m*, H–C(5′)); 2.57 (*s*, Me–C(5)); 2.52 (*dd*, *J* = 13.2, 5.3, 1 H–C(2′)): 1.90 (*ddd*, *J* = 13.1, 8.5, 4.8, 1 H–C(2′)); 1.50–1.44 (*m*, 1 H); 1.19–1.03 (*m*, 1 H); 1.02–0.88 (*m*, 2 H); 0.80 (*s*, ^{t}BuSi, 1 H of Bu); 0.70 (*t*, *J* = 7.1, Me(9′)). ^{13}C-NMR: 158.06 (*s*); 153.93 (*s*); 153.44 (*d*); 152.08 (*s*); 151.86 (*s*); 147.39 (*d*); 147.07 (*s*); 145.10 (*d*); 131.69 (*d*); 130.84 (*d*); 129.94 (*d*); 129.86 (*d*); 127.55 (*d*); 127.50 (*d*); 127.14 (*d*); 123.67 (*d*); 123.37 (*d*); 116.64 (*d*); 104.95 (*s*); 90.46 (*d*); 88.69 (*d*); 74.75 (*d*); 74.01 (*d*); 42.57 (*t*); 32.14 (*t*); 28.04 (*t*); 25.70 (*q*); 22.42 (*s*); 17.80 (*s*); 17.34 (*d*); 13.84 (*q*); −4.72 (*q*); −4.96 (*q*). LSI-MS: 720.5 (0.4, $[M+H]^+$), 257 (100).

*(5′*S*)-3′*-O-*[(*tert*-Butyl)dimethylsilyl]-4-dehydroxy-5′*-C-*(3-methylbutyl)-5′*-O-*(9-phenyl-9*H*-xanthen-9-yl)-4-(1*H*-1,2,4-triazol-1-yl)thymidine* (**10b**). As described for **10a**, from 1,2,4-1*H*-triazole (580 mg, 8.52 mmol), $POCl_3$ (0.16 ml, 1.83 mmol), Et_3N (1.15 ml, 8.27 mmol), MeCN (5.00 ml), **7b** (430 mg, 0.63 mmol), and MeCN (2.00 ml). FC (30 g, hexane/AcOEt 2:1, gradient to AcOEt): **10b** (421 mg, 91%). White foam. TLC (hexane/AcOEt 3:2): R_f 0.31. $[\alpha]_D^{21} = +113.7$ (acetone, $c = 1.00$). IR (KBr): 3144*w*, 3059*w*, 2954*s*, 2930*s*, 2857*m*, 1684*s*, 1602*m*, 1572*w*, 1522*s*, 1502*s*, 1477*s*, 1459*s*, 1446*s*, 1430*s*, 1380*m*, 1320*s*, 1293*m*, 1242*s*, 1205*m*, 1188*m*, 1117*m*, 1090*m*, 1063*m*, 1042*m*, 1004(*w*), 973*s*, 949*m*, 872*w*, 834*m*, 779*m*, 758*s*, 734*m*, 701*m*, 670*m*. ^{1}H-NMR: 9.36 (*s*, 1 H); 8.61 (*s*, 1 H); 8.17 (*s*, 1 H); 7.42–7.33 (*m*, 2 H); 7.31–7.22 (*m*, 4 H); 7.21–7.11 (*m*, 3 H); 7.09–6.97 (*m*, 3 H); 6.86 (*dd*, *J* = 7.9, 1.7, 1 H); 6.24 (*dd*, *J* = 8.6, 5.2, H–C(1′)); 3.89 (*s*, 1 H); 3.35 (*d*, *J* = 4.6, 1 H); 3.27–3.20 (*m*, H–C(5′)); 2.57 (*d*, *J* = 0.4, Me–C(5)); 2.52 (*dd*, *J* = 13.1, 5.3, 1 H–C(2′)); 1.91 (*ddd*, *J* = 13.0, 8.6, 4.8, 1 H–C(2′)); 1.49–1.32 (*m*, 1 H); 1.21–1.07 (*m*, 1 H); 1.07–0.85 (*m*, 2 H); 0.80 (*s*, ^{t}BuSi); 0.81–0.75 (*m*, 1 H); 0.68 (*d*, *J* = 6.4, 1 Me(8′)); 0.62 (*d*, *J* = 6.4, 1 Me(8′)); −0.11 (*s*, MeSi); −0.18 (*s*, MeSi). ^{13}C-NMR: 158.04 (*s*); 153.93 (*s*); 153.43 (*d*); 152.09 (*s*); 151.81 (*s*); 147.39 (*d*); 147.11 (*s*); 145.08 (*d*); 131.65 (*d*); 130.83 (*d*); 129.95 (*d*); 129.89 (*d*); 127.55 (*d*); 127.47 (*d*); 127.13 (*d*); 123.67 (*d*); 123.63 (*s*); 123.58 (*s*); 123.43 (*d*); 116.68 (*d*); 104.95 (*s*); 90.45 (*d*); 88.70 (*d*); 77.31 (*s*); 74.74 (*d*); 74.35 (*d*); 42.57 (*t*); 35.04 (*t*); 30.43 (*t*); 28.00 (*d*); 25.70 (*q*); 22.55 (*q*); 22.25 (*q*); 17.80 (*s*); 17.36 (*q*); −4.72 (*q*); −4.94 (*q*). LSI-MS: 734.1 (0.1, $[M+H]^+$), 257 (100).

*(5′*S*)-5′*-C-*Butyl-3′*-O-*[(*tert*-butyldimethylsilyl]-2′-deoxy-5-methyl-5′*-O-*(9-phenyl-9*H*-xanthen-9-yl)cytidine* (**11a**). To a soln. of **10a** (100 mg, 0.14 mmol) in dioxane (0.56 ml) 25% aq. NH_3 soln (0.14 ml) was added and stirred at r.t. After 2 h, the solvent was removed and the residue applied to FC (10 g, AcOEt, AcOEt/MeOH 19:1): **11a** (85 mg, 92%). White foam. TLC (AcOEt): R_f 0.15. $[\alpha]_D^{26} = +48.6$ (acetone, $c = 0.94$). IR (KBr): 3342*m*, 3073*m*, 2955*s*, 2929*s*, 2857*s*, 1668*s*, 1603*s*, 1573*m*, 1515*s*, 1478*s*, 1446*s*, 1352*m*, 1318*s*, 1293*s*, 1259*m*, 1240*m*, 1128*m*, 1101*m*, 1087*s*, 1054*s*, 1002*m*, 959*m*, 834*m*, 778*m*, 757*s*, 700*m*. ^{1}H-NMR: 8.20 (*s*, NH); 7.96 (*d*, *J* = 0.7, H–C(6)); 7.42–7.31 (*m*, 4 H); 7.30–7.21 (*m*, 6 H); 7.09–6.98 (*m*, 3 H); 6.91 (*dd*, *J* = 7.9, 1.7, 1 H); 6.26 (*dd*, *J* = 8.9, 5.1, H–C(1′)); 3.79 (br. *s*, 1 H); 3.38 (*d*, *J* = 4.6, 1 H); 3.28–3.20 (*m*, H–C(5′)); 2.27 (*dd*, *J* = 12.9, 5.3, 1 H–C(2′)); 2.05 (*s*, Me–C(5)); 1.82 (*ddd*, *J* = 12.9, 8.6, 4.7, 1 H–C(2′)); 1.50–1.34 (*m*, 1 H); 1.16–1.01 (*m*,1 H); 1.01–0.85 (*m*, 2 H); 0.85–0.65 (*m*, 2 H); 0.79 (*s*, ^{t}BuSi); 0.68 (*t*, *J* = 7.1, Me(9′)); −0.12 (*s*, MeSi); −0.19 (*s*, MeSi). ^{13}C-NMR: 165.67 (*s*); 156.14 (*s*); 151.98 (*s*); 151.83 (*s*); 147.51 (*s*); 138.93 (*d*); 131.75 (*d*); 130.97 (*d*); 129.76 (*d*); 129.68 (*s*); 127.70 (*d*); 127.57 (*d*); 126.97 (*d*); 123.89 (*d*); 123.81 (*s*); 123.58 (*d*); 123.22 (*d*); 116.53 (*d*); 101.12 (*s*); 89.16 (*d*); 86.74 (*d*); 77.19 (*s*); 74.61 (*d*); 74.19 (*d*); 42.25 (*t*); 31.93 (*t*); 27.96 (*t*); 25.68 (*q*); 22.45 (*t*); 17.77 (*s*); 13.85 (*q*); 13.42(*q*); −4.69 (*q*); −4.93 (*q*). LSI-MS: 1334.4 (8, $[2M-2H]^+$), 690.3 (2.6, $[M+Na]^+$), 668.3 (1.3, $[M+H]^+$), 257 (100).

*(5′*S*)-3′*-O-*[(*tert*-Butyl)dimethylsilyl]-2′-deoxy-5-methyl-5′*-C-*(3-methylbutyl)-5′*-O-*(9-phenyl-9*H*-xanthen-9-yl)cytidine* (**11b**). As described for **11a**, from dioxane/25% aq. NH_3 soln. 4:1 (2.86 ml) and **10b** (420 mg,

0.57 mmol). FC (21 g, AcOEt/MeOH 20:1, gradient): **11b** (415 mg, quant.). White foam. TLC (AcOEt): R_f 0.13. $[\alpha]_D^{23} = +56.4$ (acetone, $c = 0.92$). IR (KBr): 3342*m*, 3131*m*, 2954*s*, 2929*s*, 2858*m*, 1670*s*, 1657*s*, 1604*s*, 1511*m*, 1478*s*, 1447*s*, 1317*m*, 1293*m*, 1241*m*, 1133*m*, 1087*m*, 1061*m*, 1040*m*, 834*m*, 757*m*. ^{1}H-NMR: 8.19 (*s*, NH_2–C(4)); 7.99 (*s*, H–C(6)); 7.43–7.31 (*m*, 4 H); 7.31–7.20 (*m*, 5 H); 7.08–6.98 (*m*, 3 H); 6.91 (*dd*, J = 7.9, 1.7, 1 H); 6.28 (*dd*, *J* = 9.0, 5.0, H–C(1′)); 3.79 (*s*, 1 H); 3.38 (*d*, *J* = 4.6, 1 H); 3.5–3.18 (*m*, H–C(5′)); 2.27 (*dd*, *J* = 12.6, 5.1, 1 H–C(2′)); 2.09 (*s*, Me–C(5)); 1.84 (*ddd*, *J* = 12.8, 8.7, 4.6, 1 H–C(2′)); 1.14 (*sept.*, *J* = 6.6, 1 H); 1.06–0.92 (*m*, 1 H); 0.92–0.83 (*m*, 1 H); 0.82–0.58 (*m*, 2 H); 0.80 (*s*, ^{t}BuSi); 0.67 (*d*, *J* = 6.4, 1 Me–C(8′)); 0.60 (*d*, *J* = 6.6, Me–C(8′)); −0.11 (*s*, MeSi); −0.18 (*s*, MeSi). ^{13}C-NMR: 165.81 (*s*); 156.31 (*s*); 152.01 (*s*); 151.80 (*s*); 147.50 (*s*); 138.78 (*d*); 131.72 (*d*); 130.94 (*d*); 129.78 (*d*); 129.74 (*d*); 127.68 (*d*); 127.59 (*d*); 127.00 (*d*); 123.85 (*s*); 123.80 (*s*); 123.59 (*d*); 123.30 (*d*); 116.58 (*d*); 101.61 (*s*); 89.19 (*d*); 86.70 (*d*); 74.60 (*d*); 74.53 (*d*); 42.23 (*t*); 34.99 (*t*); 30.23 (*t*); 28.00 (*d*); 25.67 (*q*); 22.57 (*q*); 22.24 (*q*); 17.77 (*s*); 13.47 (*q*); −4.68 (*q*); −4.89 (*q*). LSI-MS: 682.2 (0.2, $[M+H]^+$), 257 (100).

*(5′*S*)-*N*^{4}*-Benzoyl-5′*-C*-butyl-3′*-O*-[(*tert*-butyl)dimethylsilyl]-2′-deoxy-5-methyl-5′*-O*-(9-phenyl-9*H*-xanthen-9-yl)cytidine* (**12a**). To a suspension of oil-free KH (75 mg, 1.87 mmol) in dry THF (3.50 ml), $PhCONH_2$ (170 mg, 1.39 mmol) was added. After the gas evolution had ceased, this suspension was quickly added to a soln. of **10a** (250 mg, 0.35 mmol) in dry THF (3.50 ml) and stirred at r.t. After 1 h, the reaction was quenched with AcOH (0.12 ml, 1.50 mmol) and 0.5M aq. $NaHCO_3$ (10 ml). The mixture was extracted with CH_2Cl_2 (3 × 10 ml) and the combined org. layer dried ($NaSO_4$) and evaporated. FC (25 g, hexane/AcOEt 4:1) gave **12a** (232 mg, 87%). White foam. TLC (hexane/AcOEt 3:1): R_f 0.67. $[\alpha]_D^{23} = +72.9$ ($CHCl_3$, $c = 1.03$). IR (KBr): 3068*w*, 2955*m*, 2929*m*, 2857*w*, 1712*s*, 1652*m*, 1601*s*, 1568*s*, 1478*s*, 1447*s*, 1362*m*, 1328*s*, 1275*s*, 1261*s*, 1238*s*, 1207*m*, 1124*m*, 1092*m*, 1055*m*, 959*m*, 834*m*, 756*m*, 712*m*. ^{1}H-NMR: 13.36 (br. *s*, NH); 8.40–8.36 (*m*, 2 H, Ph); 8.08 (*d*, *J* = 1.1, H–C(6)); 7.62–7.32 (*m*, 7 H); 7.31–7.22 (*m*, 5 H); 7.11–7.01 (*m*, 3 H); 6.94 (*dd*, *J* = 7.9, 1.7, 1 H); 6.25 (*dd*, *J* = 9.1, 5.1, H–C(1′)); 3.80 (br. *s*, H–C(4′)); 3.40 (*d*, *J* = 4.6, H–C(3′)); 3.28–3.19 (*m*, H–C(5′)); 2.24 (*d*, *J* = 0.9, Me–C(5)); 2.14 (*dd*, *J* = 12.9, 5.2, 1 H–C(2′)); 1.84 (*ddd*, *J* = 12.7, 9.2, 4.9, 1 H–C(2′)); 1.49–1.38 (*m*, 1 H); 1.16–1.06 (*m*, 1 H); 1.06–0.88 (*m*, 2 H); 0.87–0.67 (*m*, 2 H); 0.80 (*s*, ^{t}BuSi); 0.70 (*t*, *J* = 7.2, Me(9′)); −0.11 (*s*, MeSi); −0.18 (*s*, MeSi). ^{13}C-NMR: 179.56 (*s*); 160.02 (*s*); 151.95 (*s*); 151.89 (*s*); 147.87 (*s*); 147.19 (*s*); 137.56 (*d*); 137.36 (*s*); 132.23 (*d*); 131.78 (*d*); 130.82 (*t*); 129.90 (*d*); 129.85 (*d*); 128.11 (*d*); 127.74 (*d*); 127.70 (*d*); 127.15 (*d*); 124.13 (*s*); 123.62 (*d*); 123.45 (*d*); 123.32 (*s*); 116.65 (*d*); 116.62 (*d*); 111.32 (*s*); 89.36 (*d*); 86.07 (*d*); 77.20 (*s*); 74.49 (*d*); 74.20 (*d*); 41.60 (*t*); 31.93 (*t*); 27.92 (*t*); 25.67 (*q*); 22.43 (*t*); 17.76 (*s*); 13.86 (*q*); 13.79 (*q*); −4.76 (*q*); −4.93 (*q*). LSI-MS: 772.5 (4, $[M+H]^+$), 257 (100).

*(5′*S*)-*N*^{4}*-Benzoyl-3′*-O*-[(*tert*-butyl)dimethylsilyl]-2′-deoxy-5-methyl-5′*-C*-(3-methylbutyl)-5′*-O*-(9-phenyl-9*H*-xanthen-9-yl)cytidine* (**12b**). Dried (co-evaporation with pyridine) **11b** (300 mg, 0.44 mmol) was dissolved in dry pyridine (5.0 ml), cooled to 0°, and treated with PhCOCl (65 µl, 0.53 mmol). The mixture was warmed to r.t. overnight, and after 12 h, additional PhCOCl (0.100 ml, 0.87 mmol) was added. After 23 h, the mixture was quenched with H_2O (1.0 ml), stirred for 5 min, treated with cold conc. aq. NH_3 soln. (1.0 ml), and stirred for another 10 min. The solvent was evaporated, the solid redissolved in 0.5M aq. $NaHCO_3$ soln. (10 ml), the soln. extracted with CH_2Cl_2 (4 × 10 ml), the combined org. layer dried ($NaSO_4$) and evaporated, and residual pyridine co-evaporated with toluene. FC (28 g, hexane/AcOEt 3:1) gave **12b** (243 mg, 70%). White foam. TLC (hexane/AcOEt 3:1): R_f 0.69. $[\alpha]_D^{22} = +86.7$ (acetone, $c = 1.15$). IR (KBr): 3068*m*, 3029*m*, 2954*s*, 2929*s*, 2900*m*, 2857*m*, 1709*s*, 1654*s*, 1600*s*, 1568*s*, 1477*s*, 1447*s*, 1364*s*, 1318*s*, 1275*s*, 1261*s*, 1238*s*, 1207*m*, 1093*m*, 1062*m*, 1041*m*, 962*m*, 834*m*, 778*m*, 757*s*, 712*m*, 681*m*. ^{1}H-NMR: 13.68 (br. *s*, NH); 8.41–8.35 (*m*, 2 H, Ph); 8.10 (*d*, *J* = 0.9, H–C(6)); 7.60–7.52 (*m*, 1 H); 7.52–7.36 (*m*, 6 H); 7.36–7.23 (*m*; 5 H); 7.10–7.01 (*m*, 3 H); 6.94 (*dd*, *J* = 8.0, 1.6, 1 H); 6.25 (*dd*, *J* = 9.2, 5.0, H–C(1′)); 3.78 (br. *s*, 1 H); 3.40 (*d*, *J* = 4.8, 1 H); 3.25–3.18 (*m*, H–C(5′)); 2.24 (*d*, *J* = 0.7, Me–C(5)); 2.14 (*dd*, *J* = 12.7, 5.5, 1 H–C(2′)); 1.86 (*ddd*, *J* = 12.7, 8.8, 4.8, 1 H–C(2′)); 1.49–1.34 (*m*, 1 H); 1.22–1.11 (*m*, 1 H); 1.06–0.90 (*m*, 1 H); 0.89–0.73 (*m*, 1 H); 0.80 (*s*, ^{t}BuSi); 0.72–0.55 (*m*, 1 H); 0.68 (*d*, *J* = 6.6, 1 Me–C(8′)); 0.62 (*d*, *J* = 6.6, 1 Me–C(8′)); −0.11 (*s*, MeSi); −0.18 (*s*, MeSi). ^{13}C-NMR: 160.02 (*s*); 151.98 (*s*); 151.85 (*s*); 147.87 (*s*); 147.25 (*s*); 137.56 (*d*); 137.35 (*s*); 132.24 (*d*); 131.75 (*d*); 130.82 (*d*); 129.90 (*d*); 129.88 (*s*); 128.11 (*d*); 127.70 (*d*); 127.14 (*d*); 124.06 (*s*); 123.64 (*d*); 123.50 (*s*); 123.38 (*d*); 116.67 (*d*); 111.32 (*s*); 89.49 (*d*); 86.07 (*d*); 77.20 (*s*); 74.57 (*d*); 74.49 (*d*); 41.63 (*t*); 34.94 (*t*); 30.20 (*t*); 28.00 (*d*); 25.67 (*q*); 22.56 (*q*); 22.26 (*q*); 17.76 (*s*); 13.79 (*q*); −4.74 (*q*); −4.90 (*q*). LSI-MS: 786.4 (1, $[M+H]^+$), 150 (100).

*(5′*S*)-*N*^{4}*-Benzoyl-5′*-C*-butyl-2′-deoxy-5-methyl-5′*-O*-(9-phenyl-9*H*-xanthen-9-yl)cytidine* (**13a**). As described for **5a**, from **12a** (230 mg, 0.30 mmol), 1.0M Bu_4NF in THF (0.33 ml, 0.33 mmol), and THF (4.30 ml). FC (hexane/AcOEt 1:1, gradient): **13a** (193 mg, 99%). TLC (hexane/AcOEt 1:1): R_f 0.48. $[\alpha]_D^{24} = +91.5$ (acetone, $c = 0.93$). IR (KBr): 3448*m*, 3068*w*, 2956*m*, 2929*m*, 2870*m*, 1706*s*, 1654*s*, 1600*s*, 1571*s*, 1477*s*, 1447*s*, 1364*m*, 1317*s*, 1276*s*, 1243*s*, 1210*m*, 1024*m*, 955*m*, 757*m*, 713*m*. ^{1}H-NMR: 13.37 (br. *s*, NH); 8.39–8.33 (*m*, 2 H, Ph); 7.85 (*d*, *J* = 1.1, H–C(6)); 7.61–7.42 (*m*, 5 H); 7.32–7.23 (*m*, 5 H); 7.14–7.01 (*m*, 4 H); 6.14 (*t*, *J* = 6.1,

H–C(1′)); 3.68 (*q*, *J* = 5.4, H–C(3′)); 3.62 (*dd*, *J* = 4.6, 2.2, H–C(4′)); 3.35–3.29 (*m*, H–C(5′)); 2.25 (*ddd*, *J* = 13.6, 6.5, 5.1, 1 H–C(2′)); 2.20 (*d*, *J* = 0.9, Me–C(5)); 2.05 (*dt*, *J* = 13.6, 6.5, 1 H–C(2′)); 1.52–1.38 (*m*, 1 H); 1.13–1.02 (*m*, 1 H); 0.95 (*m*, 2 H); 0.89–0.76 (*m*, 2 H); 0.69 (*t*, *J* = 7.1, Me(9′)). ^{13}C-NMR: 159.86 (*s*); 152.21 (*s*); 151.76 (*s*); 147.83 (*s*); 147.02 (*s*); 137.24 (*s*); 136.93 (*d*); 132.39 (*d*); 131.80 (*d*); 130.77 (*d*); 129.90 (*d*); 129.85 (*d*); 128.11 (*d*); 127.80 (*d*); 127.76 (*d*); 127.18 (*d*); 124.04 (*s*); 123.38 (*d*); 123.17 (*s*); 116.79 (*d*); 116.56 (*d*); 111.53 (*s*); 86.62 (*d*); 84.59(*d*); 72.19 (*d*); 70.40 (*d*); 40.71 (*t*); 31.82 (*t*); 27.78 (*t*); 22.45 (*t*); 13.87 (*q*); 13.83 (*q*). LSI-MS: 658.2 (8, $[M+H]^+$), 257 (100).

*(5′*S*)-*N*^{4}*-Benzoyl-2′-deoxy-5-methyl-5′*-C*-(3-methylbutyl)-5′*-O*-(9-phenyl-9*H*-xanthen-9-yl)cytidine* (**13b**). As for **5a**, from **12b** (238 mg, 0.30 mmol), and 1.0M Bu_4NF in THF (0.33 ml, 0.33 mmol), and THF (4.40 ml). FC (20 g, AcOEt/hexane 1:1, AcOEt): **13b** (203 mg, quant.). White foam. TLC (hexane/AcOEt 2:1): R_f 0.17. $[\alpha]_D^{23} = +100.4$ (acetone, *c* = 0.99). IR (KBr): 3447*m*, 3069*m*, 3030*w*, 2955*s*, 2928*s*, 2869*m*, 1701*s*, 1652*s*, 1600*s*, 1570*s*, 1477*s*, 1447*s*, 1365*s*, 1317*s*, 1275*s*, 1244*s*, 1209*m*, 1171*m*, 1124*m*, 1100*m*, 1066*m*, 1024*m*, 964*m*, 909*m*, 757*m*, 733*m*, 713*m*, 680*m*. ^{1}H-NMR: 13.36 (br. *s*, NH); 8.41–8.34 (*m*, 2 H, Ph); 7.86 (*d*, *J* = 0.9, H–C(6)); 7.61–7.44 (*m*, 5 H); 7.44–7.31 (*m*, 5 H); 7.31–7.23 (*m*, 2 H); 7.12–7.01 (*m*, 4 H); 6.14 (*t*, *J* = 6.2, H–C(1′)); 3.70 (*q*, *J* = 5.5, H–C(3′)); 3.61 (*dd*, *J* = 4.6, 2.2, H–C(4′)); 3.30 (*ddd*, *J* = 9.6, 3.6, 2.2, H–C(5′)); 2.26 (*ddd*, *J* = 13.6, 6.5, 5.2, 1 H–C(2′)); 2.20 (*d*, *J* = 0.9, Me–C(5)); 2.09 (*dt*, *J* = 13.8, 6.3, 1 H–C(2′)); 1.50–1.35 (*m*, 1 H); 1.16 (*m*, 2 H); 1.15–0.76 (*m*, 2 H); 0.67 (*d*, *J* = 6.6, 1 Me–C(8′)); 0.61 (*d*, *J* = 6.6, 1 Me–C(8′)). ^{13}C-NMR: 159.86 (*s*); 152.25 (*s*); 151.74 (*s*); 147.83 (*s*); 147.08 (*s*); 137.26 (*s*); 136.92 (*d*); 132.39 (*d*); 131.80 (*t*); 130.78 (*d*); 129.91 (*d*); 129.86 (*d*); 128.11 (*d*); 127.82 (*d*); 127.75 (*d*); 127.19 (*d*); 124.00 (*s*); 123.45 (*d*); 123.38 (*d*); 123.22 (*s*); 116.81 (*d*); 116.60 (*t*); 111.53 (*s*); 86.54 (*d*); 84.54 (*d*); 77.20 (*s*); 72.59 (*d*); 70.33 (*d*); 40.72 (*s*); 34.88 (*d*); 30.06 (*t*); 28.01 (*d*); 22.54 (*q*); 22.21 (*q*); 13.87 (*q*). HR-LSIMS: 672.3074 ($C_{41}H_{42}N_3O_6^+$; calc. 672.3089).

*(5′*S*)-*N*^{4}*-Benzoyl-5′*-C*-butyl-2′-deoxy-5-methyl-5′*-O*-(9-phenyl-9*H*-xanthen-9-yl)cytidine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**14a**). As described for **9a**, from **13a** (188 mg, 0.29 mmol), ^{i}Pr$_2$NEt (0.20 ml, 1.15 mmol), dry THF (3.20 ml), $PCl(OCH_2CH_2CN)(N^iPr_2)$ (150 µl, 0.64 mmol). FC (18 g, hexane/AcOEt 3:1, gradient): **14a** (204 mg, 83%) as a diastereoisomeric mixture. TLC (hexane/AcOEt 2:1): R_f 0.62, 0.37. ^{1}H-NMR: 13.35 (br. *s*, NH); 8.40–8.33 (*m*, 2 H, Ph); 7.99, 7.92 (2 *d*, *J* = 1.1, H–C(6)); 7.61–7.22 (*m*, 12 H); 7.14–6.97 (*m*, 4 H); 6.23 (*m*, H–C(1′)); 3.97, 3.88 (2 br. *s*, 1 H); 3.80–3.45 (*m*, 5 H); 3.30 (*dt*, *J* = 9.0, 2.5, 1 H); 2.62, 2.49 (2 *t*, *J* = 6.5, 2 H); 2.43–2.30 (*m*, 1 H–C(2′)); 2.22–2.20 (*m*, Me–C(5)); 1.94 (*ddd*, *J* = 13.4, 8.6, 5.3, 1 H–C(2′)); 1.48–1.31 (*m*, 1 H); 1.24–1.19 (*m*, 1 H); 1.15, 1.06 (2 *d*, *J* = 6.8, 2 *Me*$_2$CH); 1.02–0.74 (*m*, 4 H); 0.74–0.63 (*m*, Me(9′)). ^{13}C-NMR: 159.91 (*s*); 151.91 (*s*); 151.86 (*s*); 151.69 (*s*); 147.82 (*s*); 147.39 (*s*); 137.29 (*s*); 137.16 (*d*); 132.36 (*d*); 131.69 (*d*); 130.98 (*d*); 130.86 (*d*); 129.91 (*d*); 129.86 (*s*); 129.82 (*d*); 129.73 (*d*); 128.10 (*d*); 127.72 (*d*); 127.65 (*d*); 127.11 (*d*); 127.06 (*d*); 123.81 (*s*); 123.75 (*s*); 123.64 (*d*); 123.58 (*d*); 123.34 (*d*); 123.24 (*d*); 116.58 (*d*); 116.53 (*d*); 111.51 (*s*); 87.86 (*d*); 87.80 (*d*); 87.47 (*d*); 87.39 (*d*); 85.69 (*d*); 85.39 (*d*); 77.23 (*s*); 75.93 (*d*); 75.71 (*d*); 75.46 (*d*); 73.98 (*d*); 73.93 (*d*); 58.17 (*t*); 58.08 (*t*); 57.93 (*t*); 57.83 (*t*); 43.43 (*d*); 43.39 (*d*); 43.26 (*d*); 43.22 (*d*); 40.56 (*t*); 40.48 (*t*); 40.34 (*t*); 31.82 (*t*); 31.77 (*t*); 27.80 (*t*); 24.63 (*q*); 24.54 (*q*); 24.50 (*q*); 24.40 (*q*); 22.50 (*t*); 22.45 (*t*); 20.36 (*t*); 20.26 (*t*); 20.16 (*t*); 20.06 (*t*); 13.80 (*q*); 13.75 (*q*); 8.34 (*t*); 8.09 (*t*). ^{31}P-NMR ($CDCl_3$): 151.23, 150.59. LSI-MS 858 (1.4, $[M+H]^+$), 150 (100).

*(5′*S*)-*N*^{4}*-Benzoyl-2′-deoxy-5-methyl-5′*-C*-(3-methylbutyl)-5′*-O*-(9-phenyl-9*H*-xanthen-9-yl)cytidine 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**14b**). As described for **9a**, from **13b** (185 mg, 0.27 mmol), THF (3.0 ml) iPr_2NEt (0.19 ml, 1.10 mmol), and $PCl(OCH_2CH_2CN)(N^iPr_2)$ (0.09 ml, 0.41 mmol). FC (23 g, hexane/AcOEt 3:1, gradient): **14b** (203 mg, 84%) as diastereoisomer mixture. Light yellow foam. TLC (hexane/AcOEt 2:1): R_f 0.58, 0.50. IR (KBr): 3068*w*, 2964*m*, 2930*m*, 2879*m*, 1708*s*, 1654*m*, 1600*s*, 1570*s*, 1477*m*, 1447*s*, 1365*m*, 1318*m*, 1275*s*, 1239*s*, 1205*m*, 1123*m*, 1099*m*, 1080*m*, 1053*m*, 1024*m*, 976*m*, 757*m*, 713*m*. ^{1}H-NMR: 13.35 (br. *s*, NH); 8.41–8.33 (*m*, 2 H, Ph); 8.01, 7.96 (2 *d*, *J* = 1.1, H–C(6)); 7.58–7.52 (*m*, 1 H); 7.51–7.34 (*m*, 6 H); 7.34–7.22 (*m*, 5 H); 7.11–6.96 (*m*, 4 H); 6.23 (*dt*, *J* = 4.7, H–C(1′)); 3.96, 3.88 (br. *s*, 1 H); 3.80–3.46 (*m*, 5 H); 3.32–3.24 (*m*, 1 H); 2.62, 2.49 (2 *t*, *J* = 6.5, 2 H); 2.37 (*td*, *J* = 12.4, 5.2, 1 H–C(2′)); 2.22 (2 *d*, *J* = 1.0, Me–C(5)); 1.97 (*ddd*, *J* = 13.2, 8.4, 5.2, 1 H–C(2′)); 1.47–1.33 (*m*, 1 H); 1.30–1.10 (*m*, 2 H); 1.16, 1.07 (2 *d*, *J* = 6.8, Me_2CH); 1.04–0.79 (*m*, 3 H); 0.70–0.59 (*m*, 2 Me–C(8′)). ^{13}C-NMR: 157.74 (*s*); 149.76 (*s*); 149.70 (*s*); 149.52 (*s*); 149.48 (*s*); 145.79 (*s*); 145.27 (*s*); 135.12 (*d*); 134.97 (*d*); 130.19 (*d*); 129.49 (*d*); 128.79 (*d*); 128.66 (*d*); 127.73 (*d*); 127.67 (*d*); 127.59 (*d*); 125.93 (*d*); 125.55 (*d*); 125.45 (*d*); 124.93 (*d*); 121.57 (*d*); 121.48 (*s*); 121.42 (*s*); 121.24 (*d*); 121.14 (*d*); 114.45 (*d*); 114.40 (*d*); 109.43 (*s*); 109.34 (*s*); 85.66 (*d*); 85.60 (*d*); 85.33 (*d*); 85.25 (*d*); 83.41 (*d*); 83.22 (*d*); 75.04 (*s*); 73.77 (*d*); 73.49 (*d*); 73.28 (*d*); 72.14 (*d*); 56.01 (*t*); 55.91 (*t*); 55.77 (*t*); 55.66 (*t*); 41.25 (*d*); 41.09 (*d*); 41.05 (*d*); 38.41 (*d*); 38.33 (*t*); 38.22 (*t*); 32.74 (*t*); 32.66 (*t*); 27.90 (*t*); 25.85 (*d*); 25.78 (*d*); 22.46 (*q*); 22.37 (*q*); 22.33 (*q*); 22.22 (*q*); 20.34 (*q*); 20.01 (*q*); 18.19 (*t*); 18.09 (*t*); 17.98 (*t*); 17.88 (*t*); 11.57 (*q*). ^{31}P-NMR: 167.72, 167.04. LSI-MS: 872 (0.8, $[M+H]^+$), 150 (100).

(5′S)-5′-C-*Butyl-2′-deoxy-5-methyl-5′*-O-*(9-phenyl-9*H-*xanthen-9-yl)cytidine* (=*4-Amino-5-methyl-1-[2′,6′,7′8′,9′-pentadeoxy-5′*-O-*(9-phenyl-9*H-*xanthen-9-yl)-α*-L-lyxo-*nonafuranosyl]pyrimidin-2(1*H)-*one*; **15a**). As described for **5a**, from **11a** (81 mg, 0.12 mmol), 1.0M Bu_4NF in THF (0.14 ml, 0.14 mmol), and THF (1.75 ml). Crystallization from hot acetone (10 ml) and recrystallization from hot MeOH (5 ml) gave **15a** (36 mg, 54%). Colorless blocks. M.p. 212° (dec.). TLC (AcOEt/MeOH 20:1): R_f 0.33. $[\alpha]_D^{23} = +76.0$ (MeOH, $c = 0.55$). IR (KBr): 3492*m*, 3311*m*, 3209*m*, 3059*w*, 2957*m*, 2929*m*, 2867*w*, 1659*s*, 1602*s*, 1514*s*, 1477*s*, 1447*s*, 1318*s*, 1292*s*, 1238*m*, 1128*m*, 1102*m*, 1065*s*, 1025*m*, 965*m*, 758*s*, 702*m*. ^{1}H-NMR ((D_6)DMSO): 7.54 (br. *s*, H–C(6)); 7.44–7.20 (*m*, 1 NH, 9 H (pixyl)); 7.12–7.01 (*m*, 2 H (pixyl)); 6.97 (*dd*, $J = 8.0, 1.6$, 1 H (pixyl)); 6.92 (*dd*, J = 7.9, 1.7, 1 H (pixyl)); 6.85 (br. *s*, NH); 6.04 (*dd*, $J = 7.9, 5.7$, H–C(1′)); 4.91 (*d*, $J = 4.1$, OH–C(3′)); 3.58 (*t*, $J = 2.5$, 1 H); 3.56–3.50 (*m*, 1 H); 3.24–3.18 (*m*, H–C(5′)); 2.00 (*ddd*, $J = 12.9, 5.7, 2.2$, 1 H–C(2′)); 1.85 (*s*, Me–C(5)); 1.88–1.76 (*m*, 1 H–C(2′)); 1.25–1.11 (*m*, 1 H); 1.02–0.88 (*m*, 1 H); 0.88–0.65 (*m*, 4 H); 0.59 (*t*, $J =$ 7.0, Me(9′)). ^{13}C-NMR ((D_6)DMSO): 165.49 (*s*); 155.15 (*s*); 151.28 (*s*); 150.98 (*s*); 148.35 (*s*); 137.66 (*d*); 131.36 (*d*); 131.09 (*d*); 130.03 (*d*); 127.89 (*d*); 127.27 (*d*); 127.02 (*d*); 124.24 (*s*); 123.71 (*d*); 123.54 (*d*); 122.89 (*s*); 116.45 (*d*); 116.36 (*d*); 101.33 (*s*); 87.15 (*d*); 84.51 (*d*); 76.11 (*s*); 73.63 (*d*); 71.10 (*d*); 41.00 (*t*); 31.09 (*t*); 27.30 (*t*); 22.12 (*t*); 13.84 (*q*); 13.72 (*q*). LSI-MS: 554.0 (1.1, $[M+H]^+$), 118 (100).

X-Ray Analysis of **15a**: Colorless transparent block ($0.55 \times 0.35 \times 0.10$ mm); monoclinic space group *P*2(1). Intensities were collected at 223 K with a *Stoe Image Plate* diffractometer (MoK_α, λ 0.71073 Å). Of the 5908 independent reflections ($\theta = 2.09–25.96°$), 4720 with $F > 4\sigma(I)$ were used in the refinement. The structure was solved by direct methods with SHELX-86 [18] and refined by full-matrix least-square procedures SHELX-97. Non-H-atoms were refined anisotropically. The refinement converged at $R = 0.0736$, $R_w = 0.1781$.

(5′S)-2′-Deoxy-5-methyl-5′-C-*(3-methylbutyl)-5′*-O-*(9-phenyl-9*H-*xanthen-9-yl)cytidine* (**15b**). As described for **5a**, from **11b** (96 mg, 0.14 mmol), 1.0M Bu_4NF in THF (0.15 ml, 0.15 mmol), and THF (2.0 ml). Crystallization from hot MeOH (4 ml) gave **15b** (38 mg, 47%). Colorless plates. M.p. 211–214° (dec.). TLC (AcOEt/MeOH 20:1): R_f 0.12. $[\alpha]_D^{22} = +98.4$ (MeOH, $c = 0.56$). IR (KBr): 3396*m*, 3337*m*, 3214*m*, 3064*w*, 2952*m*, 2925*m*, 2867*w*, 1661*s*, 1600*s*, 1573*m*, 1514*m*, 1477*s*, 1445*s*, 1317*m*, 1292*m*, 1239*m*, 1101*m*, 1080*m*, 1038*m*, 1019*m*, 968*m*, 950*m*, 787*m*, 755*m*. ^{1}H-NMR ((D_6)DMSO): 7.56 (*s*, H–C(6)); 7.43–7.18 (*m*, 10 H, including 1 NH); 7.13–7.01 (*m*, 2 H); 6.97 (*dd*, $J = 12.5, 1.7$, 1 H); 6.94 (*dd*, $J = 12.7, 1.7$, 1 H); 6.86 (br. *s*, 1 NH); 6.05 (*dd*, $J =$ 7.9, 5.7, H–C(1′)); 4.92 (*d*, $J = 3.9$, OH–C(3′)); 3.58 (br. *s*, H–C(3′), H–C(4′)); 3.24–3.16 (*m*, H–C(5′)); 2.07–1.96 (*m*, 1 H–C(2′)); 1.90–1.79 (*m*, 1 H–C(2′)); 1.84 (*s*, Me–C(5)); 1.23–1.09 (*m*, 1 H); 1.01 (*d*, $J = 6.5$, 1 H); 0.97–0.71 (*m*, 2 H); 0.57–0.51 (*m*, 1 H); 0.56 (*d*, $J = 6.4$, 1 Me–C(8′)); 0.53 (*d*, $J = 6.4$, 1 Me–C(8′)). ^{13}C-NMR ((D_6)DMSO): 165.50 (*s*); 155.15 (*s*); 151.28 (*s*); 150.93 (*s*); 148.44 (*s*); 137.64 (*d*); 131.32 (*d*); 131.08 (*d*); 130.07 (*d*); 127.89 (*d*); 127.24 (*d*); 127.01 (*d*); 124.27 (*s*); 123.71 (*d*); 123.57 (*d*); 122.81 (*s*); 116.47 (*d*); 116.39 (*d*); 101.33 (*s*); 87.12 (*d*); 84.49 (*d*); 76.08 (*s*); 73.98 (*d*); 71.02 (*d*); 41.03 (*t*); 34.46 (*t*); 29.33 (*t*); 27.60 (*d*); 22.50 (*q*); 22.26 (*q*); 13.70 (*q*). LSI-MS: 568.2 (0.2, $[M+H]^+$), 257 (100).

(5′S)-5′-C-*Butyl-2′-deoxy-5-methylcytidine* (**16a**). At r.t., **15a** (80 mg, 0.14 mmol) was dissolved in THF/H_2O 9:1 (4.0 ml) and then $Cl_2CHCOOH$ (0.12 ml) was added. After 15 min, the solvent was removed and the yellow residue adsorbed on silica gel and purified by FC (3 g, CH_2Cl_2/MeOH 7:1, gradient): **16a** (43 mg, quant.). White solid. TLC (CH_2Cl_2/MeOH 5:1): R_f 0.16. $[\alpha]_D^{21} = +64.8$ (MeOH, $c = 0.42$). UV (H_2O): 208 (10850), 277 (7050). IR (KBr): 3359*s*, 3212*s*, 2956*m*, 2931*m*, 2870*m*, 1664*s*, 1603*s*, 1522*m*, 1485*s*, 1358*m*, 1297*m*, 1135*m*, 1082*m*, 1050*m*, 1025*m*, 1006*m*, 786*m*. ^{1}H-NMR ((D_6)DMSO): 7.83 (*d*, $J = 0.9$, H–C(6)); 7.59 (br. *s*, 1 NH); 6.99 (br. *s*, 1 NH); 6.13 (*t*, $J = 6.7$, H–C(1′)); 4.93 (br. *s*, OH–C(3′), OH–C(5′)); 4.21 (*dt*, $J = 5.7, 3.0$, H–C(3′)); 3.62 (*t*, $J = 2.8$, H–C(4′)); 3.58–3.51 (*m*, H–C(5′)); 2.08–1.91 (*m*, 2 H–C(2′)); 1.81 (*d*, $J = 0.7$, Me–C(5)); 1.51–1.36 (*m*, 3 H); 1.36–1.19 (*m*, 3 H); 0.86 (*t*, $J = 7.0$, Me(9′)). ^{13}C-NMR ((D_6)DMSO): 164.95 (C(2)); 154.64 (C(4)); 139.23 (C(6)); 101.34 (C(5)); 89.09; 84.98 (C(1′), C(2′)); 71.35, 69.90 (C(4′), C(5′)); 40.71 (C(2′)); 33.77 (C(6′)); 27.92 (C(7′)); 22.43 (C(8′)); 14.21, 13.54 (C(9′), *Me*–C(5)). HR-MS: 298.17668 ($C_{14}H_{24}N_3O_4^+$; calc. 298.17667).

(5′S)-2′-Deoxy-5-methyl-5′-C-*(3-methylbutyl)cytidine* (**16b**). To a soln. of 80% AcOH/THF 4:1 (4.0 ml), **15b** (42 mg, 0.074 mmol) was added and the mixture stirred at r.t. for 48 h. The solvent was removed and the solid partitioned between H_2O (3 ml) and ^{t}BuOMe (3 ml). The aq. layer extracted with ^{t}BuOMe (2×3 ml), the combined org. phase evaporated, and the residue dissolved in 1M aq. NH_3 (1 ml), adsorbed on silica gel and submitted to FC ($MeCl_2$/MeOH 7:1): **16b** (16 mg, 69%). TLC ($MeCl_2$/MeOH 5:1): R_f 0.27. $[\alpha]_D^{20} = +59.2$ (MeOH, $c = 0.47$). UV (H_2O): 210 (10980), 276 (7460). IR (KBr): 3456*m*, 3100*m*, 2954*s*, 2932*s*, 2868*m*, 1674*s*, 1610*s*, 1516*m*, 1489*s*, 1453*m*, 1411*m*, 1345*m*, 1319*m*, 1298*m*, 1261*m*, 1191*m*, 1139*m*, 1096*s*, 1076*m*, 786*m*. ^{1}H-NMR ((D_6)DMSO): 7.80 (*d*, $J = 0.9$, H–C(6)); 7.25 (br. *s*, 1 NH); 6.78 (br. *s*, 1 NH); 6.13 (*t*, $J = 6.7$, H–C(1′)); 5.03 (very br. *s*, OH–C(5′), OH–C(3′)); 4.22 (*dt*, $J = 5.7, 3.0$, H–C(3′)); 3.62 (*t*, $J = 2.8$, H–C(4′)); 3.52 (*td*, $J = 6.5, 2.2$, H–C(5′)); 2.08–1.89 (*m*, 2 H–C(2′)); 1.80 (*d*, $J = 0.7$, Me–C(5)); 1.62–1.38 (*m*, 3 H);

1.38–1.00 (*m*, 3 H); 0.85 (*d*, *J* = 6.4, 1 Me–C(8′)); 0.84 (*d*, *J* = 6.6, 1 Me–C(8′)). ^{13}C-NMR ((D$_6$)DMSO): 165.48 (*s*); 155.37 (*s*); 138.99 (*d*); 101.29 (*s*); 89.02 (*d*); 84.93 (*d*); 71.31 (*d*); 70.21 (*d*); 40.72 (*t*); 34.99 (*t*); 31.86 (*t*); 27.74 (*d*); 22.81 (*q*); 22.69 (*q*); 13.61 (*q*). HR-LSI-MS: 312.12233 ($C_{15}H_{26}N_3O_4^+$; calc. 312.12296).

N^6-*Benzoyl-5′*-C-*butylidene-3′*-O-*[(*tert-*butyl)dimethylsilyl]-2,5′-dideoxyadenosine* (**19**). To a suspension of butyltriphenylphosphonium bromide (1.005 g, 2.52 mmol) in dry THF (3.80 ml), 1.8M NaHMDS in THF (1.40 ml, 2.52 mmol) was added, and after 0.5 h at r.t., the mixture was refluxed for 1 h. To the cooled (−78°) orange suspension, a soln. of **17** (392 mg, 0.84 mmol) was added within 15 min. The mixture was slowly warmed, and after 2.25 h (0°), additional NaHMDS (0.20 ml, 0.36 mmol) was added and stirred for another 2.5 h. The mixture was diluted with CH_2Cl_2 (10 ml) and subsequently washed with 1M aq. NH_4Cl (7 ml) and sat. aq. $NaHCO_3$ soln. (10 ml). The aq. layer was extracted with CH_2Cl_2 (3 × 10 ml), the combined org. phase dried ($MgSO_4$) and evaporated, and the brown residue submitted to FC (40 g, CH_2Cl_2/AcOEt 4:1, gradient): **19** (324 mg, 76%), (*Z*)/(*E*) 9:1 (by ^{1}H-NMR). White foam. TLC (AcOEt): 0.73. IR (KBr): 3313*m*, 3148*s*, 3014*w*, 2956*m*, 2929*m*, 2856*m*, 1664*s*, 1601*s*, 1565*m*, 1474*m*, 1438*m*, 1417*m*, 1347*m*, 1324*m*, 1309*m*, 1248*s*, 1193*s*, 1129*m*, 857*m*, 842*m*, 782*m*. ^{1}H-NMR: 9.12 (br. *s*, NH); 8.80 (*s*, 1 H); 8.16 (*s*, 1 H); 8.05–8.00 (*m*, 2 H, Ph); 7.65–7.57 (*m*, 1 H, Ph); 7.57–7.48 (*m*, 2 H, benzoyl); 6.42 (*t*, *J* = 6.2, H–C(1′)); 5.72 (*dt*, *J* = 10.8, 7.7, 1 H); 5.55–5.46 (*m*, 1 H); 4.76 (*ddd*, *J* = 9.3, 4.3, 0.9, H–C(4′)); 4.45 (*dd*, *J* = 10.5, 4.6, H–C(3′)); 2.85 (*dt*, *J* = 13.4, 5.9, 1 H–C(2′)); 2.54 (*ddd*, *J* = 13.3, 6.6, 5.1, 1 H–C(2′)); 2.24–2.08 (*m*, 2 H–C(7′)); 1.50–1.37 (*m*, 2 H–C(8′)); 0.96–0.90 (*m*, Me(9′)); 0.92 (*s*, ^{t}BuSi); 0.11 (*s*, MeSi); 0.10 (*s*, MeSi). ^{13}C-NMR: 152.46 (*d*); 151.31 (*d*); 149.46 (*s*); 141.63 (*d*); 136.02 (*d*); 135.89 (*s*); 133.66 (*s*); 132.72 (*d*); 128.83 (*d*); 127.84 (*d*); 127.13 (*s*); 126.75 (*d*); 123.99 (*s*); 123.76 (*s*); 88.39 (*d*); 84.77 (*d*); 84.59 (*d*); 83.00 (*d*); 76.21 (*d*); 40.80 (*t*); 29.88 (*t*); 25.70 (*q*); 22.72 (*t*); 17.98 (*s*); 13.71 (*q*); −4.77 (*q*); −4.80 (*q*). HR-LSI-MS: 507.2649 ($C_{27}H_{38}N_5O_3Si^+$, calc. 507.2666).

N^6-*Benzoyl-5′*-C-*butyl-3′*-O-*[(*tert-*butyl)dimethylsilyl]-2′,5′-dideoxy-5′,6′-epoxyadenosine*[3]) (**20**). To a cold (−20°) soln. of **19** (191 mg, 0.38 mmol) in CH_2Cl_2 (4.50 ml), 0.10M DMDO in acetone (4.50 ml, 0.45 mmol) [16] was added and stirred at 0° for 4 h. Then additional DMDO (3.80 ml, 0.38 mmol) was added and the mixture warmed to r.t. After 22 h, evaporation and FC (15 g, CH_2Cl_2/MeOH 75:1, 50:1) gave (5′*R*,6′*S*)/(5′*S*,6′*R*)-**20** (141 mg, 71%). A further FC (14 g, AcOEt/hexane 1:1, gradient) provided first (5′*R*,6′*S*)-**20** (26 mg, 13%), and after mixed fractions, (5′*S*,6′*R*)-**20** (70 mg, 35%).

Data of (5′*R*,6′*S*)-**20**: TLC (AcOEt/hexane 2:1): R_f 0.28. $[\alpha]_D^{20} = +18.1$ ($CHCl_3$, *c* = 0.99). IR (KBr): 3244*w*, 3186*w*, 3088*w*, 3064*w*, 2956*s*, 2929*s*, 2857*m*, 1696*s*, 1608*s*, 1577*s*, 1508*m*, 1458*s*, 1252*s*, 1102*m*, 1057*s*, 836*m*, 778*m*. ^{1}H-NMR: 8.79 (*s*, 1 H); 8.16 (*s*, 1 H); 8.06–8-01 (*m*, 2 H, Ph); 7.65–7.59 (*m*, 1 H, Ph); 7.59–7.50 (*m*, 2 H, Ph); 6.47 (*dd*, *J* = 8.6, 5.7, H–C(1′)); 4.83–4.79 (*m*, H–C(3′)); 3.83 (*dd*, *J* = 8.9, 1.4, H–C(4′)); 3.24–3.13 (*m*, 1 H–C(2′)); 3.19 (*dd*, *J* = 8.5, 3.7, H–C(5′)); 3.10–3.03 (*m*, H–C(6′)); 2.49 (*ddd*, *J* = 13.2, 5.7, 1.8, 1 H–C(2′)); 1.62–1.44 (*m*, 2 H–C(7′), 2 H–C(8′)); 1.03–0.92 (*m*, Me(9′)); 0.95 (*s*, ^{t}BuSi); 0.16 (*s*, MeSi); 0.15 (*s*, MeSi). ^{13}C-NMR: 164.68 (*s*); 152.42 (*d*); 151.64 (*s*); 149.63 (*s*); 141.98 (*d*); 133.60 (*s*); 132.76 (*d*); 128.83 (*d*); 127.86 (*d*); 123.97 (*s*); 86.17 (*d*); 85.35 (*d*); 75.28 (*d*); 57.29 (*d*); 55.62 (*d*); 39.33 (*t*); 29.64 (*t*); 25.74 (*q*); 19.65 (*t*); 18.01 (*s*); 13.92 (*q*); −4.80 (*q*); −4.88 (*q*). HR-LSI-MS: 524.2693 ($C_{27}H_{38}N_5O_4Si^+$; calc. 524.2671).

Data for (5′*S*,6′*R*)-**20**. TLC (AcOEt/hexane 2:1): R_f 0.22. $[\alpha]_D^{19} = +16.3$ ($CHCl_3$, *c* = 0.99). IR (KBr): 3254*w*, 3184*w*, 3094*w*, 3065*w*, 2958*s*, 2930*s*, 2858*m*, 1700*s*, 1611*s*, 1582*s*, 1512*m*, 1457*s*, 1253*s*, 1223*m*, 1112*m*, 1061*m*, 838*m*. ^{1}H-NMR: 8.80 (*s*, 1 H); 8.36 (*s*, 1 H); 8.07–8.00 (*m*, 2 H, Ph); 7.65–7.57 (*m*, 1 H, Ph); 7.57–7.49 (*m*, 2 H, Ph); 6.47 (*t*, *J* = 6.3, H–C(1′)); 4.79 (*q*, *J* = 5.0, H–C(3′)); 4.03 (*dd*, *J* = 6.2, 4.3, H–C(4′)); 3.15–3.04 (*m*, H–C(5′), H–C(6′)); 2.93 (*dt*, *J* = 13.2, 6.0, 1 H–C(2′)); 2.52 (*ddd*, *J* = 13.2, 6.7, 5.0, 1 H–C(2′)); 1.78–1.65 (*m*, 1 H); 1.62–1.45 (*m*, 3 H); 0.99–0.91 (*m*, Me(9′)); 0.15 (*s*, MeSi); 0.14 (*s*, MeSi). ^{13}C-NMR: 164.65 (*s*); 152.43 (*d*); 151.24 (*s*); 149.51 (*s*); 142.16 (*d*); 133.64 (*s*); 132.71 (*d*); 128.80 (*d*); 127.83 (*d*); 123.63 (*s*); 85.10 (*d*); 85.05 (*d*); 73.98 (*d*); 57.10 (*d*); 56.64 (*d*); 40.61 (*t*); 30.21 (*t*); 25.67 (*q*); 20.23 (*q*); 17.90 (*s*); 13.85 (*q*); −4.64 (*q*); −4.86 (*q*). HR-LSI-MS: 524.2693 ($C_{27}H_{38}N_5O_4Si^+$; calc. 524.2671).

N^6-*Benzoyl-5′*-C-*butyl-3′*-O-*[(*tert-*butyl)dimethylsilyl]-2′,5′-dideoxy-5′,6′-epoxy-7,8-dihydroadenosine*[3]) (**21**). To a soln. of (5′*S*,6′*R*)-**20** (63 mg, 0.12 mmol) in dry THF (1.15 ml), 1M BH_3·THF complex in THF (0.12 ml, 0.12 mmol) was added at −78° and stirred for 30 min. The reaction was quenched with sat. aq. $NaHCO_3$ soln. (0.57 ml), and the resulting yellow soln. treated with *Oxone*® (560 mg, 0.96 mmol) in sat. aq. $NaHCO_3$ soln. (2.9 ml), warmed to r.t., and stirred for 40 min. The mixture was diluted with CH_2Cl_2 (4 ml), the org. phase separated, and the aq. layer extracted with CH_2Cl_2 (3 × 3 ml). The combined org. layer was dried ($MgSO_4$) and the crude product was submitted to FC (6 g, AcOEt/hexane 1:2): **21** (29 mg, 47%) and **20** (22 mg, 35%). TLC (AcOEt/hexane 2:1): R_f 0.28. $[\alpha]_D^{19} = +55.8$ ($CHCl_3$, *c* = 1.16). IR: 3309*m*, 3210*m*, 3126*w*, 2957*s*, 2926*s*, 2858*s*, 1664*s*, 1629*m*, 1578*s*, 1518*s*, 1491*s*, 1405*s*, 1345*m*, 1314*s*, 1260*s*, 1116*s*, 1045*s*, 1005*m*, 894*m*, 836*m*, 777*m*, 757*m*. ^{1}H-NMR: 9.16 (br. *s*, NH); 7.91–7.88 (*m*, 2 H); 7.82 (*s*, H–C(2)); 7.58–7.53 (*m*, 1 H); 7.49–7.43 (*m*, 2 H); 6.15 (*t*, *J* = 6.9, H–C(1′)); 5.31 (br. *s*, H–N(7), H–C(8)); 5.15 (*m*, H–C(8)); 4.38 (*dt*, *J* = 6.2, 4.1, H–C(3′)); 3.78 (*dd*,

$J = 7.0, 4.1$, H–C(4′)); 3.01 (*dt*, $J = 7.5, 3.9$, H–C(6′)); 2.88 (*dd*, $J = 7.0, 4.2$, H–C(5′)); 2.35 (*dt*, $J = 13.2, 6.7$, 1 H–C(2′)); 2.10 (*ddd*, $J = 13.2, 6.6, 4.2$, 1 H–C(2′)); 1.80–1.62 (*m*, 1 H); 1.61–1.43 (*m*, 3 H); 0.97 (*t*, $J = 7.3$, Me(9′)); 0.92 (*s*, ^{t}BuSi); 0.12 (*s*, MeSi); 0.10 (*s*, MeSi). ^{13}C-NMR: 165.35 (*s*); 160.96 (*s*); 148.91 (*d*); 133.55 (*d*); 133.18 (*s*); 132.46 (*d*); 128.79 (*d*); 127.60 (*d*); 122.26 (*s*); 83.34 (*d*); 82.94 (*d*); 74.05 (*d*); 63.45 (*t*); 57.09 (*d*); 56.85 (*d*); 37.38 (*t*); 30.49 (*t*); 25.71 (*q*); 20.29 (*t*); 17.94 (*s*); 13.89 (*q*); −4.56 (*q*); −4.87 (*q*). HR-LSI-MS 526.2850 ($C_{27}H_{40}N_5O_4Si^+$; calc. 526.2791).

N^6-*Benzoyl-3′*-O-*[(*tert-*butyl)dimethylsilyl]-5′-butylidene-2′,5′-deoxyadenosine* (**22**). To a soln. of **19** (40 mg, 0.08 mmol) in dry THF (0.80 ml), 1M $BH_3 \cdot$THF complex soln. in THF (80 µl, 0.08 mmol) was slowly added at −40°. After 40 min, additional $BH_3 \cdot$THF complex soln. (8 µl, 0.008 mmol) was added and warmed to −20°. After 1.5 h, the reaction was quenched with sat. aq. $NaHCO_3$ soln. (0.40 ml), and a soln. of *Oxone*® (338 mg, 0.64 mmol) in sat. aq. $NaHCO_3$ soln. (2.0 ml) was added and stirred at r.t. for 30 min. The mixture was diluted with CH_2Cl_2 (3 ml), the aq. phase extracted with CH_2Cl_2 (3 × 3 ml), the combined org. phase dried ($MgSO_4$) and evaporated, and the residue submitted to FC (5 g, AcOEt/hexane 1:2, gradient): **22** (31 mg, 76%) and **19** (4 mg, 10%). TLC (AcOEt/hexane 1:1): R_f 0.48. $[\alpha]_D^{19} = +91.3$ ($CHCl_3$, $c = 0.38$). UV: 241, 274, 336. IR (film): 3300*w*, 3219*w*, 3137*w*, 2956*s*, 2929*s*, 2891*m*, 2857*s*, 1665*s*, 1636*m*, 1581*s*, 1514*s*, 1490*s*, 1402*s*, 1343*m*, 1310*m*, 1259*s*, 1112*s*, 1064*s*, 1027*s*, 889*m*, 837*s*, 777*m*, 708*m*. ^{1}H-NMR: 9.42 (br. *s*, NH–C(6)); 7.94–7.83 (*m*, 3 H); 7.62–7.54 (*m*, 1 H, Ph); 7.54–7.44 (*m*, 2 H, Ph); 6.19 (*t*, $J = 6.8$, H–C(1′)); 5.62 (*dt*, $J = 10.9, 7.4$, H–C(6′)); 5.38–5.29 (*m*, H–N(7), H–C(5′)); 5.29–5.25 (*m*, 1 H–C(8)); 5.12 (*t*, $J = 4.0$, 1 H–C(8)); 4.54 (*dd*, $J = 9.2, 4.0$, H–C(4′)); 4.07 (*dt*, $J = 6.1, 4.1$, H–C(3′)); 2.30–2.17 (*m*, 1 H–C(2′)): 2.17–1.99 (*m*, 2 H–C(7′), 1 H–C(2′)); 1.39 (*sext.*, $J = 7.4$, 2 H–C(8′)); 0.95–0.87 (*m*, Me(9′)); 0.90 (*s*, ^{t}BuSi); 0.07 (*s*, MeSi); 0.06 (*s*, MeSi). ^{13}C-NMR: 165.43 (*s*); 161.15 (*s*); 148.97 (*d*); 134.87 (*d*); 133.51 (*s*); 133.18 (*s*) 132.43 (*d*); 128.75 (*d*); 127.62 (*d*); 127.40 (*d*); 122.29 (*s*); 86.35 (*d*); 82.05 (*d*); 76.47 (*d*); 63.06 (*t*); 37.26 (*t*); 29.91 (*t*); 25.72 (*q*); 22.78 (*t*); 17.99 (*s*); 13.71 (*q*); −4.77 (*q*); −4.84 (*q*). HR-LSI-MS: 509.2822 ($C_{27}H_{39}N_5O_3Si^+$; calc. 509.2808).

N^6-*Benzoyl-3′*-O-*[(*tert-*butyl)dimethylsilyl]-2′,5′-dideoxy-5′-methylideneadenosine* (**23**). As described for **3a**, from methyltriphenylphosphonium bromide (688 mg, 1.92 mmol), 2M NaHMDS in THF (0.96 ml, 1.92 mmol) in THF (4.80 ml), and **17** (300 mg, 0.64 mmol) in THF (3.50 ml). FC (40 g, CH_2Cl_2/AcOEt 4:1, gradient): **23** (209 mg, 70%). White foam. TLC (AcOEt): R_f 0.82. $[\alpha]_D^{24} = +21.7$ ($CHCl_3$, $c = 1.07$). IR (KBr): 3261*w*, 3066*w*, 2955*s*, 2929*s*, 2886*m*, 2857*s*, 1701*s*, 1611*s*, 1578*s*, 1508*m*, 1458*s*, 1329*m*, 1297*m*, 1255*s*, 1096*m*, 1053*m*, 837*s*, 779*m*, 708*m*. ^{1}H-NMR: 9.20 (br. *s*, NH); 8.79 (*s*, 1 H); 8.16 (*s*, 1 H); 8.06–7.99 (*m*, 2 H, Ph); 7.63–7.57 (*m*, 1 H, Ph); 7.55–7.47 (*m*, 2 H, Ph); 6.47 (*t*, $J = 6.3$, H–C(1′)); 5.97 (*ddd*, $J = 17.2, 10.4, 6.7$, H–C(5′)); 5.36 (*dt*, $J = 17.1, 1.3$, 1 H–C(6′)); 5.27 (*dt*, $J = 10.5, 1.3$, H–C(6′)); 4.49 (*dt*, $J = 5.7, 4.2$, 1 H); 4.43–4.38 (*m*, 1 H); 2.84 (*dt*, $J = 13.2, 6.1$, 1 H–C(2′)); 2.50 (*ddd*, $J = 13.2, 6.4, 4.5$, 1 H–C(2′)); 0.92 (*s*, ^{t}BuSi); 0.11 (*s*, 2 MeSi). ^{13}C-NMR: 164.70 (*s*); 152.52 (*d*); 149.54 (*s*); 141.53 (*d*); 135.37 (*d*); 133.65 (*s*); 132.71 (*d*); 128.79 (*d*); 128.53 (*s*); 128.37 (*s*); 127.86 (*d*); 123.69 (*s*); 117.99 (*t*); 88.35 (*d*); 84.74 (*d*); 75.63 (*d*); 40.10 (*t*); 25.70 (*q*); 17.99 (*s*); −4.73 (*q*). HR-LSI-MS: 466.2274 ($C_{24}H_{32}N_5O_3Si^+$; calc. 466.2275).

N^6-*Benzoyl-3′*-O-*[(*tert-*butyl)dimethylsilyl]-2′,5′-dideoxy-5′,6′-epoxy-5′-methyladenosine*[3]) (**24**). To an ice-cold soln. of **23** (142 mg, 0.31 mmol) in dry CH_2Cl_2 (4.00 ml), was added 0.14M DMDO in acetone (4.35 ml, 0.61 mmol) and stirred overnight at r.t. After evaporation, CH_2Cl_2 (1.00 ml) and DMDO soln. (4.35 ml, 0.61 mmol) were added and stirred for 2 d at r.t. Then 1 g of deactivated silica gel (MeOH) was added, the solvent evaporated, and the residue submitted to FC (AcOEt/hexane 1:1, gradient): **24** (45 mg, 30%; dr. 77:23 by ^{1}H-NMR) as white foam and **23** (45 mg, 31%). **24** TLC (AcOEt/hexane 2:1): R_f 0.32. IR (KBr): 3385*m*, 3058*m*, 2955*s*, 2929*s*, 2856*s*, 1717*s*, 1608*s*, 1583*s*, 1516*s*, 1489*m*, 1456*s*, 1352*m*, 1330*m*, 1299*m*, 1255*s*, 1223*m*, 1184*m*, 1120*m*, 1084*m*, 1027*m*, 837*m*, 780*m*, 721*m*, 695*m*. ^{1}H-NMR: 9.12 (br. *s*, NH); 8.80 (*s*, 1 H); 8.46, 8.23 (2 *s*, 1 H); 8.07–8.00 (*m*, 2 H, Ph); 7.71–7.43 (*m*, 3 H, Ph); 6.62 (*dd*, $J = 7.5, 6.0$, H–C(1′)); 6.49 (*dd*, $J = 7.4, 6.3$, H–C(1′)); 4.74 (*dt*, $J = 5.2, 2.8$, H–C(3′)); 4.59 (*dt*, $J = 5.3, 2.8$, H–C(3′)); 4.20 (*t*, $J = 2.3$, H–C(4′)); 3.97 (*dd*, $J = 5.1, 2.5$, H–C(4′)); 3.29 (*ddd*, $J = 5.0, 4.0, 2.6$, 1 H); 3.22–3.18 (*m*, 1 H); 3.08–2.98 (*m*, 1 H); 2.89 (*t*, $J = 4.4$, 1 H); 2.82–2.75 (*m*, 2 H); 2.72–2.61 (*m*, 1 H); 2.53–2.40 (*m*, 1 H–C(2′)); 0.95, 0.93 (2 *s*, ^{t}BuSi); 0.15, 0.13 (2 *s*, 2 MeSi). ^{13}C-NMR: 164.55 (*s*); 152.66 (*d*); 151.80 (*s*); 149.38 (*s*); 141.76 (*d*); 141.47 (*d*); 133.65 (*s*); 132.71 (*d*); 132.13 (*d*); 132.01 (*d*); 131.90 (*d*); 131.86 (*d*); 128.83 (*d*); 128.54 (*d*); 128.37 (*d*); 127.83 (*d*); 123.13 (*s*); 87.66 (*d*); 85.24 (*d*); 84.52 (*d*); 84.11 (*d*); 74.25 (*d*); 72.61 (*d*); 51.79 (*d*); 51.18 (*d*); 45.75 (*t*); 43.75 (*t*); 41.03 (*t*); 40.12 (*t*); 25.71 (*q*); 17.99 (*s*); −4.69 (*q*); −4.88 (*q*). HR-MS: 482.2224 ($C_{24}H_{32}N_5O_4Si^+$; calc. 482.2212).

N^6-*Benzoyl-5′-butyl-3′*-O-*[(*tert-*butyl)dimethylsilyl]-2′-deoxydenosine* (**25**). A soln. of 0.61M PrMgBr (1.20 ml, 7.29 mmol) in THF was added dropwise to a suspension of anh. CuI (15.8 mg, 0.08 mmol) in dry THF (7.50 ml). Then, the mixture was cooled to −78°, reheated to −40°, and slowly treated with a soln. of **24** (78 mg, 0.16 mmol) in dry THF (1.80 ml). The suspension turned immediately yellow, and after 30 min, the mixture was slowly warmed to −18°. After 2 h, the reaction was quenched with sat. aq. NH_4Cl soln. (4.50 ml),

warmed to r.t., and diluted with CH_2Cl_2 (6 ml). The aq. phase was extracted with CH_2Cl_2 (2×4 ml), the combined org. phase concentrated and washed with 0.5M EDTA soln. (3 ml), dried ($MgSO_4$), and evaporated, and the residue submitted to FC (8 g, AcOEt/hexane 1:1): **25** (53 mg, 62%; d.r. 84:16 by ^{1}H-NMR). Light green foam. TLC (AcOEt/hexane 2:1): R_f 0.47. IR (KBr): 3284*m*, 2955*s*, 2928*s*, 2857*s*, 1700*s*, 1611*s*, 1582*s*, 1517*m*, 1459*s*, 1331*m*, 1255*s*, 1105*m*, 1086*m*, 1051*m*, 835*m*, 777*m*. ^{1}H-NMR: 9.11 (br. *s*, NH); 8.79, 8.77 (2 *s*, 1 H); 8.10, 8.09 (2 *s*, 1 H); 8.07–7.98 (*m*, 2 H, Ph); 7.72–7.58 (*m*, 1 H, Ph); 7.56–7.42 (*m*, 2 H, Ph); 6.36 (*dd*, $J = 9.6$, 5.3, H–C(1′)); 6.32 (*dd*, $J = 9.8$, 5.2, H–C(1′)); 6.07 (br. *s*, OH); 5.39 (*d*, $J = 11.2$, OH); 4.68 (*d*, $J = 5.0$, 1 H); 4.06 (br. *s*, 1 H); 3.94–3.88 (*m*, H–C(5′)); 3.74–3.64 (*m*, H–C(5′)); 3.11–2.99 (*m*, 1 H–C(2′)); 2.21 (*ddd*, $J = 12.9$, 8.0, 5.4, 1 H–C(2′)); 1.68–1.23 (*m*, 2 H–C(6′), 2 H–C(7′), 2 H–C(8′)); 1.00–0.86 (*m*, Me(9′)); 0.94 (*s*, ^{t}BuSi); 0.13 (*s*, MeSi); 0.12 (*s*, MeSi). ^{13}C-NMR: 164.42 (*s*); 152.10 (*d*); 151.95 (*d*); 150.73 (*s*); 150.22 (*s*); 142.62 (*d*); 133.49 (*s*); 132.88 (*d*); 132.14 (*s*); 132.01 (*d*); 131.87 (*s*); 128.88 (*d*); 128.54 (*d*); 128.38 (*d*); 127.86 (*d*); 124.65 (*s*); 93.37 (*d*); 91.65 (*d*); 87.77 (*d*); 87.44 (*d*); 74.98 (*d*); 72.13 (*d*); 71.83 (*d*); 71.77 (*d*); 41.50 (*t*); 40.77 (*t*); 34.05 (*t*); 32.74 (*t*); 28.44 (*t*); 28.08 (*t*); 25.78 (*q*); 25.70 (*q*); 22.72 (*t*); 22.64 (*t*); 17.98 (*s*); 17.85 (*s*); 13.98 (*q*); 13.95 (*q*); 2 – 4.56 (*q*); –4.71 (*q*); –4.80 (*q*). HR-MS: 526.2850 ($C_{27}H_{40}N_5O_4Si^+$; calc. 526.2831).

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