A Direct Synthesis of Nucleoside Analogs Homologated at the 3′- and 5′-Positions

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A new route is presented to prepare analogs of nucleosides homologated at the 3′- and 5′-positions. This route, applicable to both the D- and L-enantiomeric forms, is suitable for the preparation of monomeric bis-homonucleosides needed for the synthesis of oligonucleotide analogs. It begins with the known monobenzyl ether **3** of pent-2-yne-1,5-diol, which is reduced to alkenol **4**. *Sharpless* asymmetric epoxidation of **4**, followed by opening of the epoxide **5** with allylmagnesium bromide, gives a mixture of diols **6** and **7**. Protection of the primary alcohol as a silyl ether followed by treatment with OsO_4, $NaIO_4$, and mild acid in MeOH, followed by reduction, yields (2*R*,3*R*) {{[(*tert*-butyl)diphenylsilyl]oxy}methyl}tetrahydro-2-(2-hydroxyethyl)-5-methoxyfuran (= methyl 3-{{[(*tert*-butyl)diphenylsilyl]oxy}methyl}-2,3,5-trideoxy-α/β-D-*erythro*-hexafuranoside; **10**) (*Scheme 1*). Protected nucleobases are added to this skeleton with the aid of trimethylsilyl triflate (*Scheme 2*). The *o*-toluoyl (2-MeC_6H_4CO) and *p*-anisoyl (4-$MeOC_6H_4CO$) groups were used to protect the exocyclic amino group of cytosine. The bis-homonucleoside analogs **11** and **14a** are then converted to monothiol derivatives suitable for coupling (*Schemes 3* and *4*) to oligonucleotide analogs with bridging S-atoms. This synthesis replaces a much longer synthesis for analogous nucleoside analogs that begins with diacetoneglucose (=1,2:5,6-di-*O*-isopropylideneglucose), with the stereogenic centers in the final products derived from the *Sharpless* asymmetric epoxidation. The new route is useful for large-scale synthesis of these building blocks for the synthesis of oligonucleotide analogs.

Introduction. – While nucleosides and their analogs have long been the targets of the medicinal chemist [1], only in the past decade have the talents of synthetic organic chemists come to focus on the systematic synthesis of analogs of oligonucleotides [2–8]. Some recent work in oligonucleotide analogs has focused on a special class of nucleoside analogs homologated at both the 3′ and 5′-positions as building blocks. *Collingwood* and *Baxter*, *e.g.*, prepared phosphinate-linked dinucleotides that incorporate a 3′,5′-bishomologated sugar in a DNA analog as part of an antisense research program at *Ciba-Geigy* [9]. *Schneider* and *Benner* reported 3′,5′-bishomologated nucleoside analogs as units for uncharged DNA analogs joined by the sulfide, sulfoxide, and sulfone groups [10]. *Richert et al*. explored RNA analogs that are built from 3′,5′-bishomologated nucleoside analogs [11].

Several of these oligonucleotide analogs have interesting properties. For example, a sulfone-linked DNA analog displayed a reasonable level of bioavailability in a mouse model [12] and had intriguing biological activity in a preliminary *in vitro* cell assay [13]. A short sulfone-linked RNA dinucleotide analog formed a *Watson-Crick* duplex in a

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crystal [14]. Longer sulfone-linked RNA analogs displayed rich conformational properties, however, far broader than those allowed by simple *Watson-Crick* rules [15].

Together, these results have led some to suggest a 'second-generation' model for nucleic acid structure to guide the design of new oligonucleotide analogs [16] for the development of DNA- and RNA-like diagnostic and therapeutic agents. Further, as missions to planets and their moons (such as Titan) generate new data concerning organic chemistry there, such studies will be needed to define structural features of the 'universal genetic molecule', responsible for supporting Darwinian evolution in life that has had a genesis independent of life on Earth [17].

Central to this second-generation model is the notion that the repeating charge on oligonucleotides is an important feature for the *Watson-Crick* interaction [17] with the sugar linkage playing an important role as well in the molecular-recognition event [18]. In contrast, the nucleobases, regarded under the *Watson-Crick* model as the centers of molecular recognition, have proven to be remarkably malleable [2][19].

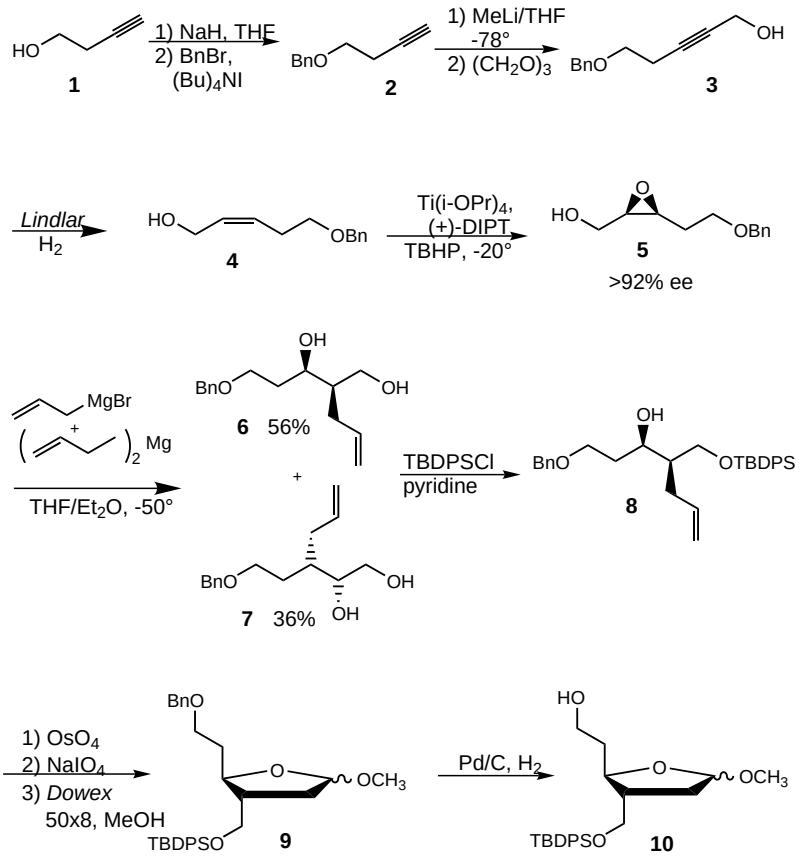
One route to 3′,5′-bishomologated nucleoside analogs developed previously began with diacetoneglucose (=1,2:5,6-di-*O*-isopropylideneglucose) [13], which provided a stereochemically reliable synthesis of the 3′,5′-bishomologated RNA nucleoside analogs. While 2′-deoxygenation was possible to generate the DNA analogs from these precursors, the synthesis is long, and a shorter synthesis leading directly to 3′,5′-bishomologated analogs of ribonucleosides would be useful.

The *Sharpless* epoxidation has long been used as an efficient way to generate enantiomerically enriched epoxides [20]. These have been used by *Jung* and co-workers to prepare nucleoside analogs [21]. Likewise, vinyl and allyl anions have been used to open epoxides in a variety of synthetic routes, including routes to nucleoside analogs [22]. We provide here a direct and efficient synthesis of 3′,5′-bishomologated analogs of deoxyribonucleosides where the *Sharpless* epoxidation is used to generate the desired configurations, and an allyl anion is used as a nucleophile to open the epoxide to assemble a skeleton that can be rapidly converted to the nucleoside analog.

Results. – The sugar analog (2*R*,3*R*)-3-{{[(*tert*-butyl)diphenylsilyl]oxy]methyl}tetrahydro-2-(2-hydroxyethyl)-5-methoxyfuran (=methyl 3-{{[(*tert*-butyl)diphenylsilyl]oxy}methyl}-2,3,5-trideoxy-α/β-D-*erythro*-hexafuranoside; **10**) was synthesized from commercially available but-3-yn-1-ol (**1**), which was deprotonated with NaH in THF and treated with benzyl bromide in the presence of tetrabutylammonium iodide [23] to yield benzyl ether **2** in 98% yield following vacuum distillation (*Scheme 1*). Alkyne **2** was deprotonated in THF with MeLi and treated with formaldehyde to yield 5-(benzyloxy)pent-2-yn-1-ol (**3**) in 93% yield following chromatography (silica gel). Alkynol **3** was hydrogenated in AcOEt to the *cis*-olefin (2*Z*)-5-(benzyloxy)pent-2-en-1-ol (**4**) with *Lindlar* catalyst in the presence of quinoline in 96% yield following chromatography [24]. The (2*Z*)-pentenol **4** was epoxidized following the procedure of *Sharpless* with tetraisopropyl orthotitanate, (+)-diisopropyl L-tartrate ((+)-DIPT), and *tert*-butyl hydroperoxide in CH_2Cl_2. The reaction temperature was maintained by means of a cryostat of $-20\pm0.2^\circ$ to ensure a high enantiomer excess (e.e.). Chromatography (silica gel) gave the oxiranemethanol **5** in 89% yield, with $\geq$92% e.e.

The oxirane ring of **5** was opened by the *Grignard* reagent allylmagnesium bromide [25] in Et_2O/THF at -50° to give 1,3-diol **6** in 56% yield after chromatography. In the

Scheme 1

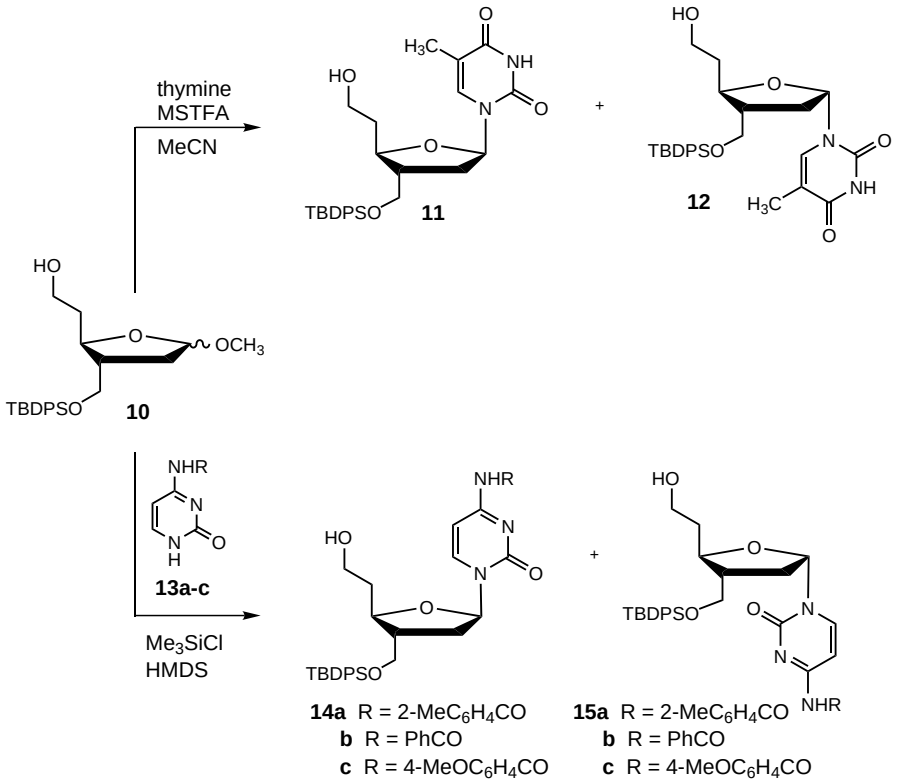


TBDPS = (*t*-Bu)Ph_2Si, DIPT = diisopropyl tartrate, TBHP = *t*-BuOOH

absence of THF, 1,2-diol **7** was the predominant product. THF may favor at equilibrium diallyl magnesium and magnesium bromide over 2 equiv. of allylmagnesium bromide [26], with altered reactivity and selectivity [27]. The primary OH function of **6** was protected with (*tert*-butyl)chlorodiphenylsilane (TBDPSCl) [28] in CH_2Cl_2/pyridine 4:1 to give **8** in 87% yield after chromatography. To generate the precursor sugar analog **10**, alkenol **8** was oxidized with osmium tetroxide (0.02 equiv.) in THF/H_2O 3:1 at 0°, and 4-methylmorpholine 4-oxide was added to regenerate OsO_4 *in situ*. The crude diol was cleaved with sodium metaperiodate in THF/H_2O 3:1 to yield the corresponding aldehyde. Subsequent cyclization *via* acetalization in the presence of *Dowex* ion exchanger in MeOH yielded methyl 6-*O*-benzyl-3-{{[(*tert*-butyl)diphenylsilyl]oxy}methyl}-2,3,5-trideoxy-α/β-D-*erythr o*-hexafuranoside (**9**) in 94% overall yield for three steps after flash chromatography. The benzyl group of **9** was cleaved with Pd/C in MeOH [29], and the product was chromatographed (silica gel) to give the methyl hexofuranoside **10** in better than 93% yield.

Thymine was prepared for coupling to the sugar building block **10** [13] by treatment with *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide (MSTFA) in MeCN. The mild *Lewis* acid trimethylsilyl triflate ($CF_3SO_3SiMe_3 = TfOSiMe_3$) was added to introduce the silylated thymine to the sugar [30][31], and the crude diastereoisomeric thymidine derivatives **11**/**12** were purified by flash chromatography (silica gel) (81% yield). Separation by prep. HPLC (silica gel; see *Exper. Part*) gave **11** and **12** in 32% and 44% yields, respectively (*Scheme 2*). The structures of the diastereoisomeric products were determined by ^{1}H-NOE experiments.

Scheme 2



TBDPS = (*t*-Bu)Ph_2Si, MSTFA = *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide, HMDS = hexamethyldisilazane

Cytosine is usually protected in DNA analogs as an N^4-benzoyl derivative [32] and similar protection has been used in the sulfone-bridged oligonucleotide analog (SNA) synthesis as well [33]. However, many authors mention the partial loss of the cytosine-protecting group on basic ester hydrolysis of the 3′-methyl thioacetate as well as of 6′-benzoylnucleosides or -nucleotides. The instability of the protecting group seemed to increase with the length of the SNA [33d,e]. A more base-stable cytosine-protecting group was therefore desirable. Several new protecting groups for cytosine have been proposed in recent years [34], mostly to obtain a protecting group *more* labile to base

than at N^4-benzoyl group. For the synthesis of SNAs, a less-labile protecting group was needed. The (benzyloxy)carbonyl (Z) protecting group, widely used in phosphate-bridged oligonucleotide analog (PNA) synthesis as well as peptide chemistry, appeared to be promising [35] but was found to be unstable during the hydrolysis of the benzoate exters [33d].

Köster et al. studied the stability of several *N*-acyl protecting groups for nucleobases [36]. The *o*-toluoyl (2-MeC_6H_4CO), 2,4-dimethylbenzoyl (2,4-$Me_2C_6H_3CO$), and *p*-anisoyl (4-$MeOC_6H_4CO$) protecting groups were found to be more stable under basic conditions than the benzoyl group. We tested several of these. For example, cytosine was protected by treatment with *o*-toluoyl chloride (anhydrous pyridine, 120 h) to give multiply acylated cytosine. Monoacylated N^4-(*o*-toluoyl)cytosine (**13a**) was obtained by partial hydrolysis in sat. NH_4OH solution (80%). The N^4-benzoyl- and N^4-(*p*-anisoyl)cytosine (**13b** and **13c**, resp.) were also prepared. These were then silylated in hexamethyldisilazane (HMDS) and Me_3SiCl [37] and glycosylated with **10** under *Vorbrüggen* conditions in the presence of the mild *Lewis* acid $TfOSiMe_3$ in 1,2-dichloroethane. For the products from the *o*-toluoyl derivative **13a**, chromatography (silica gel) gave **14a** and **15a** (37% and 41%). The structures of these diastereoisomers were determined by ^{1}H-NOE experiments. Addition of alternative *Lewis* acids in the similar glycosylation of N^4-benzoylcytosine (**13b**) did not show any advantages, however, either in selectivity or in yields of the corresponding **14b** and **15b**. Reaction of **10** with N^4-(*p*-anisoyl)cytosine (**13c**) generated an inseparable mixture of diastereoisomers. This mixture **14c**/**15c** was used directly for the stability study of the *N*-acyl protecting group.

The stability of the *N*-acyl protecting groups was tested by reaction of **14a**, **14b**, or **14c**/**15c** with 0.5N NaOH/MeOH 1:1 (*v*/*v*; 0.08 mM of the cytosine derivative) at room temperature (*Table 1*). The rate of hydrolysis was determined by UV spectroscopy (310 nm) and fitted as a first-order process. The *o*-toluoyl group is by far the most-stable protecting group for the cytosine-containing building block. It proved to be sufficiently stable throughout all steps in the SNA synthesis and is easily cleaved under standard SNA-deprotection conditions (2N NaOH/MeOH 1:1). The *p*-anisoyl group is less stable to hydrolysis. For this reason, and because the *o*-toluoyl diastereoisomers **14a** and **15a** formed in the glycosylation reaction could be separated, the *o*-toluoyl group was chosen for large-scale synthesis.

Table 1. *N^4-Deacylation of Various 2′-Deoxycytidine Analogs with 0.5N NaOH/MeOH 1:1 (v/v) at Room Temperature*

N-Acylated C_d[a])	$^{bz}(\beta\text{-}C_d)$ (**14b**)	$^{an}(\alpha/\beta\text{-}C_d)$ (**14c**/**15c**)	$^{to}(\beta\text{-}C_d)$ (**14a**)
t [min]	6.1	13.3	115

[a]) C_d = 3′,5′-bishomologated 2′-deoxycytidine analog; bz = benzoyl, an = anisoyl, to = toluoyl

Alternative routes were then sought to prepare cytidine analogs. One attractive route exploited the undesired α-thymidine analog **12** prepared above. Transglycosylation of **12** with N^4-(*o*-toluoyl)cytosine (**13a**) under the conditions described above (HMDS, Me_3SiCl, $TfOSiMe_3$) yielded the toluoyl-protected analogs of β-cytidine **14a**

and α-cytidine **15a** (35 and 43%, resp.). *Ca.* 9% of the starting material was recovered as a mixture of **11** and **12** and recycled.

We then turned to preparing the building blocks for their coupling. Coupling is achieved by nucleophilic substitution of a good leaving group by a thiol (see the following paper [38]). *Huang* showed that the best mode for coupling placed the thiol at the $CH_2-C(3')$ atom, making the C(6′) atom the electrophilic center [13]. Possible leaving groups for the coupling of a thiol building block are either bromide or mesylate. These gave good yields in thioether coupling [39], and very good properties for SNA synthesis [13][33d]. Both are easy to introduce, relatively stable under storage conditions, and generate few by-products and good overall yields. Other leaving groups such as triflate, tosylate, chloride, and iodide have been investigated for SNA synthesis and showed less-favorable properties [40]. An intramolecular cyclization seen with natural nucleosides carrying a leaving group at the 5′-position with the O=C(2) in pyrimidine bases [41] was never observed with a 6′-leaving group during SNA synthesis, presumably because the formation of an eight-membered ring is less favored than the seven-membered ring that is formed with natural nucleotides.

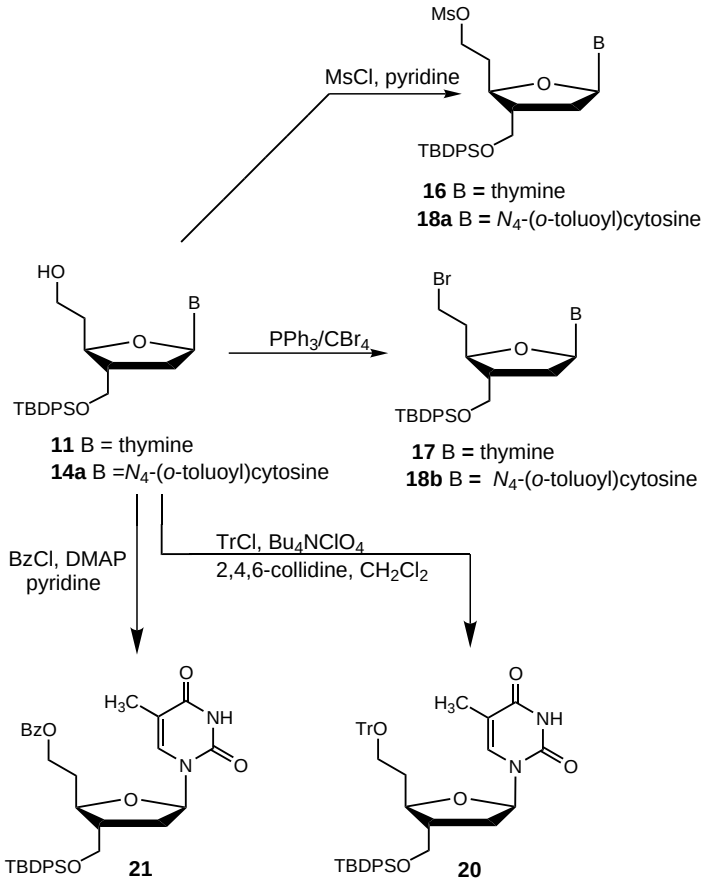
The thymidine analog **11** was mesylated with MsCl in CH_2Cl_2/pyridine at room temperature to yield **16** in 93% yield [42] (*Scheme 3*). Alternatively, **11** was brominated with PPh_3 and CBr_4 in 1,2-dichloroethane/MeCN at room temperature to yield **17** in 97% yield [43]. Bromide **17** was more stable in solution than mesylate **16**. Both compounds were stable for several months when purified and stored at $-20°$. The mesylated cytidine analog **18a** was obtained in 95% yield under similar conditions. The bromination of **14a**, however, turned out to be more difficult. Several different solvents, temperatures, and varying amounts of PPh_3 as well as CBr_4 were tested (*Table 2*). The best result was obtained when **14a** and PPh_3 (2 equiv.) were dissolved in 1,2-dichloroethane, tetrabromomethane (1.8 equiv.) was added at 0°, and stirring was continued for 2 h at room temperature. The reaction was terminated with sat. $NaHCO_3$ solution and ice, and the crude product was chromatographed (silica gel) to give **18b** in 74% yield. Higher excess of PPh_3 and CBr_4 caused an increased amount of less-polar by-products according to *Richert* [33d], presumably because of methylation and/or cyclization.

Table 2. *Overview of Bromination Reactions of Cytidine Analog* **14a**. *Yielding* **18b** (see *Scheme 3*)

Solvent	Equiv. PPh_3/CBr_4	T [°]	Quenching	Yield [%]
1,2-Dichloroethane	2.0/1.8	$0 \rightarrow 25$	$NaHCO_3$/ice	74
1,2-Dichloroethane	3/3	25	MeOH	56
1,2-Dichloroethane	5/5	25	MeOH	20
MeCN	2.2/2.2	25	MeOH	66
1,2-Dichloroethane	2.0/1.8	$-15 \rightarrow -5$	$NaHCO_3$/ice	70

Prior to modification at the $CH_2-C(3')$ atom, the 6′-OH group of nucleoside building blocks **11** and **14a** were protected, and subsequently the silylated $OCH_2-C(3')$ was deprotected. The synthesis of non-ionic SNAs (see the following paper [38]) required the use of the base-labile N^4-(*o*-toluoyl) protecting group as well as the base-labile (*t*-Bu)Ph_2Si group at the $CH_2-C(3')$ end; this suggested that an acid-labile 6′-protecting group would be most appropriate. Acid-labile protecting groups include the

Scheme 3



TBDPS = (*t*-Bu)Ph_2Si

dimethoxytrityl group ($(MeO)_2Tr$) and the more-stable trityl group (Tr) [44]. Both have the advantage of being very lipophilic and, hence, improve the solubility of SNA intermediates in organic solvents. Other useful acid-labile protecting groups are monomethoxytrityl (MeOTr) [45] and tetrahydro-2*H*-pyran-2-yl (Thp) [46]. Thp has the disadvantage of a lower lipophilicity compared to the trityl groups. The solubility of longer SNAs (tetramers to octamers) decreases with increasing length, which suggests that larger, more-lipophilic protecting groups should be used. Another advantage of the trityl groups is that their acid lability is related to the number of MeO moieties. The mesomeric effect of the MeO groups enhances the electron density of the benzene rings and, thus, stabilizes the trityl cation. Therefore, the stability of the protecting group can be fine-tuned for varying synthesis. The more-labile $(MeO)_2Tr$ and MeOTr groups are not stable enough for some steps necessary in SNA synthesis. These considerations made the Tr protecting group more-favorable for SNA synthesis. In addition, trityl

groups are cleavable with mild *Lewis* acids such as $ZnBr_2$ and $ZnCl_2$. Avoiding the use of strong acids over extended periods of time makes it possible to cleave trityl protecting groups without the formation of by-products.

Standard introduction of the Tr group at the 5′-end of natural oligonucleotide analogs with chlorotriphenylmethane in pyridine and *N*,*N*-dimethylpyridin-4-amine (DMAP) [44] proved not to be possible at the 6′-end. A method developed by *Reddy et al.* [48] for the tritylation of solid-phase oligonucleotides in the presence of tetrabutylammonium perchlorate and 2,4,6-collidine in CH_2Cl_2 was therefore used. Tetrabutylammonium perchlorate and 2,4,6-collidine activate chlorotriphenylmethane by *in situ* formation of trityl perchlorate which accelerates the substitution. Thus, tritylated thymidine analog **20** was obtained from **11** after 5 h at room temperature in 94% yield (*Scheme 3*).

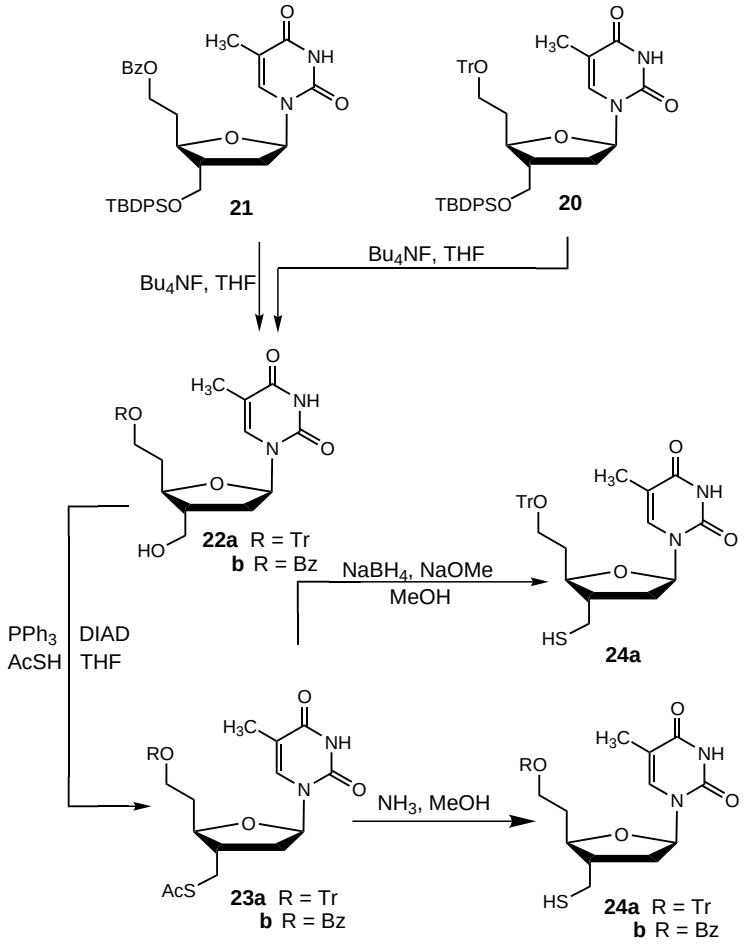
The synthesis of singly charged octameric SNAs required a different protecting-group chemistry. The designed introduction of acid-labile dimethoxytrityl thioethers at the $CH_2-C(3')$ atom implies two possibilities for the protection of the 6′-end. *Huang*'s synthesis of a singly charged all-U octamer used $(MeO)_2Tr$ protection at the 6′-end as $(MeO)_2Tr$ ether, and at the $CH_2-C(3')$ end as $(MeO)_2Tr$ thioether [13]. *Huang* found that $(MeO)_2Tr$ can be selectively cleaved from the O- and S-atom [49]: the ether can be cleaved selectively in the presence of the thioether with 80% $AcOH/H_2O$ in 95% yield, whereas the thioether is cleaved in a buffered solution of $AgNO_3$ in MeOH to give the corresponding silver salt precipitate. The thiol can be recovered with dithioerythritol (DTE) in 98% yield. Nevertheless, this strategy led to decreased yields for the deprotection of SNA $(MeO)_2Tr$ thioethers and the very labile $(MeO)_2Tr$ ether at the 6′-end.

The second strategy investigated uses a base-labile 6′-protecting group. The *O*-benzoyl protecting group was already used in SNA synthesis at the 6′, 2′, and $CH_2-C(3')$ position [33a,d]. These authors reported a partial removal of the *N*-acyl protection of cytosine during the deprotection of the *O*-benzoyl group. This problem was avoided through the use of the N^4-(*o*-toluoyl) group. The *O*-benzoyl group is also stable during ammonolysis, a saponification method successfully used for the conversion of thioacetates to thiols in SNA synthesis [50]. The introduction and removal of an *O*-benzoyl group are well established in standard organic synthesis, and the *O*-benzoyl group is very stable throughout all other reaction steps in SNA synthesis. Thus, the synthesis of **21** from **11** was achieved with benzoyl chloride and DMAP in pyridine in 83% yield (*Scheme 3*).

The synthesis of the SNAs 6′-d(TSO2T)-3″ and 6′-d(TSO2C)-3″ (T and C = 3′,5′-bishomologated analogs of unmodified nucleotides; 3″ corresponds to $CH_2-C(3')$ required the removal of the (*t*-Bu)Ph_2Si protecting group of thymidine analogs **20** and **21** at $CH_2-C(3')$. Silyl ethers are cleavable under basic and acidic conditions as well as with fluoride. The (*t*-Bu)Ph_2Si group is very stable to most acidic conditions and requires strong acids that would lead to by-products [28a]. Basic deprotection is possible for the thymine derivative, but would not be applicable for the deprotection of 6′-*O*-benzoylthymidine analog **21** as well as for the d(TC)-dimer analog due to the base-labile *N*-acyl protecting groups. In earlier studies, several fluorides cleaved the (*t*-Bu)Ph_2Si group in an SNA synthesis [33a,d]. *Richert* used Bu_4NF in THF [33d]. *Roughton* and *König* preferred HF in pyridine [50][33c], however, finding that the 2-

(4-nitrophenyl)ethyl protecting group on guanosine was partially removed with Bu_4NF [11]. The target sequence in this work did not contain guanosine in the oligomer, which made the Bu_4NF deprotection strategy preferred. Thus, compound **20** was deprotected with Bu_4NF within 3 h, and the reaction was terminated with methoxytrimethylsilane (Me_3SiOMe). It was necessary to filter the reaction solution through a layer of silica gel to remove the basic tetrabutylammonium salts and to avoid by-products. Flash chromatography gave **22a** in 95% yield (*Scheme 4*). Deprotection of **21** was achieved under similar conditions in 2.5 h to give **22b** as an amorphous solid in 94% yield. As expected, the solubility of **22a** and **22b** was reduced in organic solvents following the cleavage of the bulky silyl protecting group. This was especially true in the case of 6′-*O*-benzoylthymidine analog **22b**, which was only slightly soluble in CH_2Cl_2, $CHCl_3$, MeCN, and THF.

Scheme 4



TBDPS = (*t*-Bu)Ph_2Si, Tr = Ph_3C, DIAD = diisopropyl azodicarboxylate

The introduction of the S-atom at $CH_2-C(3')$ was performed without difficulties *via Mitsunobu* reactions with either thioacetic acid or thiobenzoic acid [53]; thioacetic acid was chosen because the resulting thioester is easier to hydrolyze to the corresponding thiol. During the *Mitsunobu* reaction, the sterically large betaine adduct that is formed between triphenylphosphine (PPh_3) and diisopropyl azodicarboxylate (DIAD) preferentially attacks primary alcohols to form the thioester. The controversial aspects of this S_N2-type-reaction mechanism are discussed in the literature [54]. Thus, compound **22a** was thioacetylated with PPh_3, DIAD, and thioacetic acid in THF to give **23a** in 97% yield (*Scheme 4*). The exact order of addition of thioacetic acid and **22a** was essential. The reagents were added subsequently and dropwise, starting with the thioacetic acid; a by-product was formed if **22a** was added first. Thioacetate **23b** was synthesized in 90% yield; the poor solubility of **22b** made it necessary to add it at once as a suspension in MeCN/THF simultaneously with thioacetic acid. The reaction time was increased to 3 h, during which the suspension turned clear as the more-soluble product **23b** was formed.

The cleavage of the thioesters **23a** and **23b** was performed in two different ways. In degassed MeOH, **23a** was hydrolyzed with $NaBH_4$ and NaOMe (*Scheme 4*). The reaction mixture was filtered through a layer of silica gel to give **24a** in 97% yield. The reductive conditions of the reaction prevented disulfide formation. The hydrolysis of **23b** was not possible under these conditions without loss of the 6′-*O*-benzoyl group. *Roughton* developed the ammonolysis of rSNA thioacetates with ammonia in degassed MeOH [11], which seemed applicable for **23a** as well as **23b**. Thus, the thioacetates **23a** and **23b** were deprotected with ammonia to give **24a** and **24b** in quantitative yields (*Scheme 4*). The acetamide produced was removed under high vacuum. The formation of disulfide was not detected. The thiols **24a** and **24b** formed disulfides if allowed to stand in solution for a prolonged time. Surprisingly, the speed of disulfide formation was dependent on the solvent. The disulfides were reduced to the corresponding thiols with either PBu_3 in THF/H_2O [55] or dithiothreitol [56] in MeOH in quantitative yields.

Discussion. – This procedure effectively required eight steps to give a common intermediate **10**, and gave an overall yield of 33%. The reactions were conveniently run on the 10-gram scale. The most-demanding step was the *Sharpless* epoxidation, due to the need to keep the temperature controlled to ensure a high e.e. The ratio of enantiomers in the product **5**, determined by the *Mosher*-ester method, was better than 96:4. This was reproducible when independently repeated by three individuals, and reflects the e.e. produced in the *Sharpless*-epoxidation step.

This route leads to less enantiomerically pure product than the route that begins with diacetoneglucose [13], and this is the principal disadvantage of this route. The advantage, in contrast, is that it generates considerably larger amounts of product in considerably greater yields in far shorter time than the route that starts with diacetoneglucose. Further, the products are the precursors for the further synthesis of analogs of di- and higher oligonucleotide analogs. Coupling of a major and minor enantiomer yields a diastereoisomer, but these proved to be easy to separate.

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Experimental Part

General. Reactions were carried out under Ar. The glassware was dried for at least 24 h at 120° and cooled under Ar prior to reactions sensitive to humidity. Molecular sieve (*Union Carbide*) was heated for 5 min in a microwave oven (500 W) and dried for 24 h under high vacuum. Oxygen-sensitive reactions were carried out in degassed solvents by either bubbling Ar through the solvents for 1 h and/or repeatedly freezing the solvent *in vacuo* with liq. N_2 and thawing under Ar at r.t. (freeze-pump cycle). Reactions at $-78°$ were accomplished in acetone/dry ice, reactions at -60 to $-20°$ in a jacketed cooling flask with a cryostat cooling system. *Dowex* (*Fluka*; *50 × 8* and *2 × 8*) was washed with MeOH, refluxed in cyclohexane for 2 h in a H_2O separator, and finally dried for 24 h under high vacuum. Osmium tetraoxide solution: crystalline osmium tetraoxide (1 g, *Fluka*) was dissolved in *t*-BuOH (76 ml) containing *tert*-butyl hydroperoxide (0.7 ml), yielding a 1.3% standard soln. (0.05M), and maintained at $-20°$ until use. The reagents used were purchased from *Fluka* or *Aldrich* at highest quality (*puriss* or *purum*), if not mentioned otherwise. THF and toluene were freshly distilled from Na, MeCN and CH_2Cl_2 from CaH_2. All other solvents were purchased from *Fluka* or *Aldrich* in the highest quality. TLC: *Merck* TLC silica gel *60 F254* ($d = 0.25$ mm) and *Waters K6F* silica gel *60* ($d = 0.25$ mm); visualization either with UV light (λ 254 nm), or by staining with either phosphomolybdic acid/ceric(IV) sulfate tetrahydrate/conc. H_2SO_4 soln. or vanillin-sulfuric acid/EtOH/conc. H_2SO_4 soln. and subsequent heating; TLCs from reactions with non-volatile solvents (pyridine, DMF) were dried for 15–30 min under high vacuum prior to staining. Flash chromatography (FC): 50- to 100-fold silica gel *60* (*Merck*, 0.040–0.063 mm, or *Fisher Davisil* 0.035–0.070 mm); 0.2–0.3 bar pressure. HPLC: semiprep. *Merck Septech-Novaprep-5000* instrument on silica gel *Merck Lichrospher-Si-60*-7-μm column, semiprep. *Waters PrepLC-4000* instrument with *Waters 486* tunable absorbance detector on *Waters Prep-Nova-Pak-HR-C_{18}* column (60 Å; 25 × 100 mm), *Waters 616* pump with *Waters 600-S* controller and *Waters 996* photodiode array detector on *Shodex RSpak-D18-613* column (6 × 150 mm) or *Waters Nova-Pak-C_{18}* column (3.9 × 150 mm). Anal. GLC: *Hewlett-Packard* gas chromatograph *5710A* combined with a mass spectrometer *571B* as detector; cross-linked-methyl-silicone-gum high-performance capillary column (*Hewlett-Packard*), He as carrier gas. UV/VIS Spectra: *Varian Cary-1-Bio-UV/VIS* spectrophotometer with a *Cary* temperature controller and a *Shimadzu UV/VIS-160* spectrophotometer; λ_{max} (ε) in nm. IR Spectra: $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Bruker AMX-500*, *Varian Unity-500*, *Varian EM-390*, *Varian XL-300*, *Varian Gemini-300*, and *Varian VXR-300* instruments; δ in ppm rel. to internal $SiMe_4$, J in Hz; multiplicity of ^{13}C-NMR signals determined with distortionless enhancement of NMR signals by polarization transfer (DEPT). MS: *VG-Tribrid* (EI spectra, 70 eV), *VG-ZAB2-SEQ* and *Finnigan MAT-95* (FAB; 3-nitrobenzyl alcohol (NOBA) matrix), *Finnigan MAT-LCQ* (ESI), and *Bruker Reflex* instruments (MALDI-TOF; for matrices, see the reaction protocols); in *m/z* (% rel. to the base peak).

4-(Benzyloxy)but-1-yne (**2**). NaH (10.56 g, 0.44 mol) was washed with hexane, suspended in anh. THF (500 ml), and Bu_4NI (14.8 g, 40 mmol) was added. But-3-yn-1-ol (**1**; 28.0 g, 0.40 mol) was slowly added dropwise within 30 min and stirred for 1 h at r.t. Benzyl bromide (71.84 g, 0.42 mol) was added dropwise and stirring continued for 8 h at r.t. Excess NaH was hydrolyzed with i-PrOH (20 ml). Crude **2** was separated from the precipitated salts by filtration, and the filtrate was evaporated. The residue was taken up in AcOEt (200 ml), the org. soln. washed with 1.6% H_2SO_4 soln. (3 × 100 ml), sat. $NaHCO_3$ soln. (3 × 100 ml), and brine (3 × 100 ml), dried ($MgSO_4$), and evaporated, and the remaining oil purified by vacuum distillation at 63°/1 Torr: **2** (62.7 g, 98%). Colorless liquid. IR ($CHCl_3$): 3410, 3060, 3010, 3005, 2900, 2865, 1960, 1720, 1700, 1600, 1480, 1360, 1200, 1050, 850, 690. ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.05 (*t*, $J = 2.2$, H–C(1)); 2.52 (*dt*, $J = 2.2$, 7, 2 H–C(3)); 3.62 (*t*, $J = 7$, 2 H–C(4)); 4.58 (*s*, PhCH_2); 7.38 (*s*, Ph). ^{13}C-NMR ($CDCl_3$, 50 MHz): 19.66 (*t*, C(3)); 67.91 (*t*, C(4)); 69.17 (*t*, PhCH_2); 72.72 (*d*, C(1)); 81.62 (*s*, C(2)); 127.44, 127.62, 128.17 (3*d*, arom. C); 137.9 (*s*, arom. C). EI-MS: 159 (16, $[M-1]^+$), 130 (7), 129 (6), 105 (23), 92 (11), 91 (100), 77 (7), 65 (12), 53 (5), 51 (7), 39 (11).

5-(Benzyloxy)pent-2-yn-1-ol (**3**). To a soln. of **2** (24.0 g, 150 mmol) in anh. THF (250 ml) at $-78°$, 1.6M MeLi in Et_2O (113 ml, 180 mmol) was added dropwise. The mixture was warmed for 30 min to $-20°$. After cooling the soln. to $-78°$, paraformaldehyde (5.4 g, 180 mmol) was added, and the mixture was allowed to warm to r.t. within 4 h. After stirring for 2 h at r.t., 1.6% H_2SO_4 soln. was added dropwise until the originally formed precipitate dissolved again. The org. phase was separated, the aq. phase extracted with AcOEt (3 × 100 ml), and the combined org. phase dried ($MgSO_4$) and concentrated to *ca*. 20% of its original volume. The crude product

was taken up in AcOEt (150 ml) and washed with 1.6% H_2SO_4 soln. (3 × 50 ml), sat. $NaHCO_3$ soln. (3 × 50 ml), and brine (3 × 50 ml). The org. phase was dried ($MgSO_4$)and evaporated. FC (silica gel, Et_2O) yielded **3** (26.5 g, 93%). Colorless liquid. IR ($CHCl_3$): 3610, 3440, 3090, 3065, 3020, 3010, 2920, 2870, 1495, 1455, 1385, 1365, 1335, 1200, 1140, 1100, 1010, 960, 820, 700. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.98 (*t*, *J* = 4.5, OH); 2.53 (*ddt*, *J* = 6.9, 2.2, 0.9, 2 H–C(4)); 4.22 (*q*, *J* = 2.3, 0.9, 2 H–C(5)); 4.54 (*s*, PhCH_2); 7.33 (*s*, 5 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 20.12 (*t*, C(4)); 51.02 (*t*, C(5)); 68.23 (*t*, PhCh$_2$); 72.93 (*t*, C(1)); 79.70 (*s*, C(3)); 82.77 (*s*, C(2)); 127.77, 128.44 (2*d*, arom. C); 137.88 (*s*, arom. C). EI-MS: 189 (1.72, $[M-1]^+$), 171 (19), 160 (11), 159 (87), 143 (6), 131 (6), 129 (16), 91 (100), 65 (8), 39 (6).

(2Z)-5-(Benzyloxy)pent-2-en-1-ol (**4**). *Lindlar* catalyst (1.0 g; Pd, Pb poisoned with $Ca(CO_3)_2$; *Aldrich*) and quinoline (5 ml) were suspended in AcOEt (140 ml, EtOH free), and the mixture was degassed several times under vacuum, and then flushed with Ar. The catalyst was activated with H_2 in a low-pressure apparatus, and a soln. of **3** (19.0 g, 100 mmol) in AcOEt (10 ml) was added. The flask was evacuated and flushed with Ar after the theoretically needed H_2 volume was consumed and TLC monitoring showed the completion of the reaction. The catalyst was filtered through *Celite*, the filtrate washed with 1.6% H_2SO_4 soln. (3 × 50 ml) and brine (3 × 50 ml), the org. phase dried ($MgSO_4$) and evaporated, and the yellow liquid chromatographed (silica gel, AcOEt/petroleum ether 1:2): **4** (18.5 g, 96%). Colorless liquid. IR ($CHCl_3$): 3520, 3450–3500, 3070, 3010, 2940, 2870, 1495, 1460, 1335, 1095, 1030, 1000, 700. ^{1}H-NMR ($CDCl_3$, 200 MHz): 2.28 (br., OH); 2.44 ('*q*', *J* = 7, 5, 2 H–C(4)); 3.52 (*t*, *J* = 5, 2 H–C(5)); 4.12 (*d*, *J* = 7, 2 H–C(1)); 4.54 (*s*, PhCH_2); 5.6 (*m*, H–C(3)); 5.8 (*m*, H–C(2)); 7.34 (*s*, 5 arom. H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 28.09 (*t*, C(4)); 57.91 (*t*, C(5)); 69.12 (*t*, PhCH_2); 73.19 (*t*, C(1)); 127.77, 128.45 (2*d*, arom. C); 129.45 (*d*, C(3)); 130.94 (*d*, C(2)); 138.03 (*s*, arom. C). EI-MS: 191 (0.1, $[M-1]^+$), 174 (2), 173 (1), 144 (1), 129 (2), 120 (4), 108 (3), 105 (2), 92 (1), 91 (100), 89 (2), 83 (3), 79 (3), 77 (3), 68 (5), 65 (14).

*(2*R*,3*S*)-3-[2-(Benzyloxy)ethyl]oxiran-2-methanol* (**5**). Activated molecular sieves (15 g; 4 Å) were suspended in CH_2Cl_2 (300 ml; free of 2-methylbut-2-ene) at −20° under Ar. Tetraisopropyl orthotitanate (5.9 ml, 17.0 mmol) was added dropwise followed by (+)-diisopropyl L-tartrate (4.3 ml, 20.4 mmol). The pale yellow soln. was stirred for 30 min, **4** (12.9 g, 67.2 mmol) in CH_2Cl_2 (100 ml) was added, and the mixture was stirred for further 4 h at −20°. Slowly, 3M *t*-BuOOH in isooctane (29 ml, 87.0 mmol) was added dropwise (1 ml/10 min), during which the temp. was carefully monitored and maintained at −20 ± 0.2°. The reaction was completed after 24 h (TLC monitoring). The cold mixture was poured to a soln. of iron(II) sulfate (30 g) and tartaric acid (13 g) in H_2O (100 ml) and stirred vigorously for 15 min. The soln. was filtered through sea sand, the org. phase separated, and the aq. phase extracted with CH_2Cl_2 (3 × 200 ml). The combined org. phase was dried (Na_2SO_4) and evaporated. FC (silica gel, Et_2O) yielded **5** (12.5 g, 89%; ≥92% e.e.). Colorless liquid. $[\alpha]_D^{20}$ = +9.38 (*c* = 1.8, $CHCl_3$). IR ($CHCl_3$): 3580–3300, 3070, 3030, 3000, 2920, 2870, 2800, 1490, 1480, 1455, 1435, 1420, 1375, 1365, 1320, 1090, 1040, 1025, 1000, 975, 960, 915, 890, 840, 700. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.79 (*ddt*, *J* = 10, 3, 5, 1 H, BnOCH$_2$CH_2); 2.08 (*ddt*, *J* = 7, 7, 3, 1 H, BnOC$_2$CH_2); 3.02–3.09 (*m*, 2 H, BnOCH_2CH$_2$, OH); 3.15–3.20 (*m*, 1 H, BnOCH_2CH$_2$); 3.52 ('*dt*', *J* = z, 5, H–C(3)); 3.60–3.70 (*m*, 2 H–C(1)); 3.85 (*ddd*, *J* = 7, 5, 2, H–C(2)); 4.54 (*s*, PhCH_2); 7.29–7.41 (*m*, Ph). ^{13}C-NMR ($CDCl_3$, 75 MHz): 28.20 (*t*, BnOCH$_2$CH_2); 54.97 (*d*, C(3)); 55.51 (*d*, C(2)); 60.15 (*t*, BnOCH$_2$CH$_2$); 66.82 (*t*, PhCH$_2$); 73.64 (*d*, C(1)); 128.05, 128.16, 128.61 (3*d*, arom. C); 137.25 (*s*, arom. C). EI-MS: 208 (<1, M^+), 207 (0.80), 160 (4), 159 (29), 149 (7), 108 (6), 107 (46), 105 (6), 92 (17), 91 (100), 79 (10), 71 (16), 65 (13), 43 (14).

*(2*R*,3*R*)-5-(Benzyloxy)-2-(prop-2-enyl)pentane-1,3-diol* (**6**). *(2*R*,3*S*)-5-(Benzyloxy)-3-(prop-2-enyl)pentane-1,2-diol* (**7**). Oxiranemethanol **5** (6 g, 28.8 mmol) was dried twice by dissolving/evaporation with toluene, and was then dissolved in Et_2O/THF 5:1 (250 ml). The soln. was cooled to −50°, and 1M allylmagnesium bromide in Et_2O (20 ml, 19.9 mmol) was added dropwise (1 ml/5 min) with vigorous stirring. The remaining 1M allylmagnesium bromide in Et_2O (110 ml, 109.7 mmol) was added within 3.5 h. The white suspension was stirred at −50° for 1 h and then allowed to warm to −20°, and stirred for 1 additional hour. The mixture was hydrolyzed with 1.6% H_2SO_4 soln. (*ca.* 50 ml) and washed with 2M HCl (4 × 100 ml); hereby the precipitate dissolved. The aq. phases were reextracted with AcOEt (2 × 100 ml). The combined org. phase was washed with 1.6% H_2SO_4 soln (3 × 50 ml) and brine (2 × 50 ml), dried ($MgSO_4$), and evaporated and the residue purified by FC (silica gel, CH_2Cl_2/Et_2O 4:1): **6** (4.0 g, 56%) and **7** (2.6 g, 36%), both as colorless oils.

Data of **6**: $[\alpha]_D^{20}$ = −8.65 (*c* = 1.2, $CHCl_3$). IR ($CHCl_3$): 3600–3350, 3070, 3000, 2920, 2770, 1680, 1490, 1480, 1455, 1440, 1415, 1360, 1310, 1090, 1025, 990, 715. ^{1}H-NMR ((D$_6$)DMSO, 300 MHz): 1.39–1.49 (*m*, H–C(2)); 1.54–1.62 (*m*, 1 H–C(4)); 1.63–1.75 (*m*, 1 H–C(4)); 1.92–2.01 ('*quin.*', 1 H, CH$_2$=CHCH_2); 2.08–2.16 ('*quint.*', 1 H–C(4)); 3.31–3.47 (*m*, 2 H–C(1)); 3.52 ('*q*', *J* = 1, 6, 2 H–C(5)); 3.68–3.76 ('*dt*', *J* = 6, 4, H–C(3)); 4.35 (*t*, *J* = 5, OH); 4.37 (*t*, *J* = 5, OH); 4.45 (*s*, PhCH_2); 4.82–4.86, 4.92–4.98, 5.01–5.03 (3*m*, CH_2=CHCH$_2$); 5.73–5.86 (*m*, CH$_2$=C*H*CH$_2$); 7.24–7.46 (*m*, Ph). ^{13}C-NMR ((D$_6$)DMSO, 100 MHz): 30.55

(*t*, C(4)); 34.05 (*t*, CH_2=CH*C*H_2); 45.92 (*d*, C(2)); 60.69 (*t*, C(5)); 66.91 (*d*, C(3)); 67.49 (*t*, Ph*C*H_2); 71.79 (*t*, C(1)); 115.27 (*t*, *C*H_2=CHCH$_2$); 127.16, 127.28, 128.09 (*d*, 3 arom. C); 138.22 (*d*, CH_2=*C*HCH$_2$); 138.71 (*s*, arom. C). EI-MS: 251 (0.4, $[M+1]^+$), 201 (65), 189 (2), 165 (4), 163 (4), 159 (8), 146 (6), 141 (4), 108 (7), 107 (22), 92 (13), 91 (100), 89 (5), 79 (16), 77 (12), 65 (13).

Data of **7**. $[\alpha]_D^{20} = -14.2$ ($c = 1.2$, $CHCl_3$). IR ($CHCl_3$): 3600–3540, 3420–3160, 3060, 3000, 2920, 2860, 1680, 1490, 1470, 1450, 1440, 1415, 1360, 1090, 1070, 1050, 1030, 995, 825, 640. ^{1}H-NMR ((D_6)DMSO, 300 MHz): 1.44–1.57 (*m*, H–C(3)); 1.59–1.76 (*m*, 1 H–C(4)); 1.91–2.00 (*m*, 1 H–C(4)); 2.09–2.18 (*m*, CH_2=CHCH_2); 3.28–3.38 (*m*, H–C(2), 2 OH); 3.41–3.47 ('*dd*', $J = 10, 4$, 2 H–C(5)); 4.44 (*m*, PhCH_2, 2 H–C(1)); 4.93–5.02 (*m*, CH_2=CHCH$_2$); 5.70–5.85 (*m*, CH_2=C*H*CH$_2$); 7.24–7.38 (*m*, Ph). ^{13}C-NMR ((D_6)DMSO, 75 MHz): 29.62 (*t*, C(4)); 33.00 (*t*, CH_2=CH*C*H_2); 36.67 (*d*, C(3)); 63.51 (*t*, C(5)); 68.02 (*t*, Ph*C*H_2); 71.70 (*t*, C(1)); 72.28 (*d*, C(2)); 115.50 (*t*, *C*H_2=CHCH$_2$); 127.18, 127.28, 128.09 (3*d*, arom. C); 138.05 (*d*, CH_2=*C*HCH$_2$); 138.67 (*s*, arom. C). EI-MS: 250 (0.4, M^+), 220 (6), 205.19 (17), 201 (8), 189 (10), 159 (2), 157 (2), 143 (2), 141 (3), 131 (3), 111 (5), 108 (5), 107 (11), 105 (5), 92 (13), 91 (100), 81 (5), 79 (10), 77 (7), 65 (10).

*(2*R*,3*R*)-5-(Benzyloxy)-1-{[(*tert*-butyl)diphenylsilyl]oxy}-2-(prop-2-enyl)pentan-3-ol* (**8**). Diol **6** (1.0 g, 4.0 mmol) was dried twice by dissolving/evaporation with toluene, and was then dissolved in anh. CH_2Cl_2/pyridine 4:1 (25 ml) at 0°. (*t*-Bu)Ph_2SiCl (1.1 ml, 4.4 mmol) was added and the soln. allowed to warm to r.t. and stirred overnight. CH_2Cl_2 (100 ml) was added, the soln. washed with 1.6% H_2SO_4 soln. (3 × 20 ml) and brine (3 × 20 ml), dried ($MgSO_4$) and evaporated, and the residue submitted to FC (silica gel, CH_2Cl_2): **8** (1.7 g, 87%). Colorless oil. $[\alpha]_D^{20} = +4.88$ ($c = 1.1$, $CHCl_3$). IR ($CHCl_3$): 3600–3440, 3070, 3010, 2960, 2930, 2840, 1680, 1605, 1590, 1470, 1460, 1450, 1430, 1390, 1360, 1110, 1010, 1000, 920, 840, 700. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.05 (*s*, *t*-Bu); 1.65–1.79 (*m*, 2 H–C(4)); 1.67–1.91 (*m*, CH_2=CHCH_2); 2.17 (*tt*, $J = 13, 7$, H–C(2)); 3.33 (*d*, $J = 4$, OH); 3.64 ('*dt*', $J = 2, 4$, 2 H–C(5)); 3.72 (*s*, 1 H–C(1)); 3.73 (*d*, $J = 1$, 1 H–C(1)); 4.05 (*dt*, $J = 9, 4$, H–C(3)); 4.52 (*s*, PhCH_2); 4.98 ('*dt*', $J = 9, 3$, CH_2=CHCH$_2$); 5.64–5.66 (2*m*, CH_2=C*H*CH$_2$); 7.28–7.35 (*m*, *P*HCH$_2$); 7.37–7.46 (*m*, 6 H, Ph_2Si); 7.60–7.68 (*m*, 4 H, Ph_2Si). ^{13}C-NMR ($CDCl_3$, 75 MHz): 19.16 (*s*, Me_3C); 26.89 (*q*, *Me*$_3$C); 30.27 (*t*, C(4)); 33.91 (*t*, CH_2=CH*C*H_2); 45.13 (*d*, C(2)); 65.01 (*t*, Ph*C*H_2); 68.80 (*t*, C(5)); 71.95 (*d*, C(3)); 73.21 (*t*, C(1)); 116.09 (*t*, *C*H_2=CHCH$_2$); 127.61, 127.63 (*d*, Ph_2Si); 127.72, 128.40 (*d*, *Ph*CH_2); 129.78, 129.80 (*d*, Ph_2Si); 133.02, 133.14 (*s*, Ph_2Si); 135.59, 135.67 (*d*, Ph_2Si); 137.21 (*d*, CH_2=*C*HCH$_2$); 138.27 (*s*, *Ph*CH_2): EI-MS: 470 ($[M - H_2O]^+$), 353 (3), 289 (4), 263 (4), 261 (4), 229 (8), 221 (5), 201 (7), 200 (13), 199 (71), 197 (8), 195 (9), 183 (6), 181 (7), 169 (4), 139 (16), 135 (8), 107 (8), 105 (5), 92 (9), 91 (100), 79 (5), 77 (5). Anal. calc. for $C_{31}H_{40}O_3Si$: C 76.18, H 8.25; found: C 75.95, H 8.20.

*Methyl 6-*O*-Benzyl-3-{[(*tert*-butyl)diphenylsilyl]oxy}methyl}-2,3,5-trideoxy-α/β-*D*-erythro-hexofuranoside* (**9**). To a soln. of 4-methylmorpholine 4-oxide (3.9 g, 28.8 mmol) in THF/H_2O 3:1 (90 ml), a soln. of **8** (6.4 g, 13.1 mmol) in THF (30 ml) was added and cooled to 0°. Then, 0.05M osmium tetraoxide in *t*-BuOH (5.2 ml, 260 μmol) was added dropwise. The pale yellow soln. was stirred for 10 min at 0°, warmed to r.t., and stirred overnight. $Na_2S_2O_3$ (2.0 g, 29.6 mmol) was added to reduce excess osmium tetraoxide. Stirring was continued for a further 20 min, and THF was evaporated. The remaining soln. was taken up in AcOEt (200 ml) and washed successively with sat. $Na_2S_2O_3$ soln. (3 × 20 ml), 0.5M HCl (3 × 20 ml), and brine (1 × 20 ml). The aq. phases were carefully reextracted with AcOEt. The combined org. phase was evaporated, the residue taken up in THF/H_2O 3:1 (300 ml), and sodium metaperiodate (6.16 g, 28.8 mmol) added in portions of *ca.* 1.5 g (turbid soln. within 2 min). The salts were filtered off after 30 min, THF was evaporated, and the remaining emulsion was taken up in Et_2O (100 ml). The org. phase was washed with brine (3 × 150 ml), dried ($MgSO_4$), and evaporated at max. 30° and co-evaporated twice with cyclohexane (2 × 50 ml). The remaining oil was taken up in MeOH (150 ml), and *Dowex 50* × *8* (1.3 g, dried) was added. The suspension was stirred for 1.5 h at r.t. and then the *Dowex* resin removed by filtration. The filtrate was evaporated and the residue chromatographed (silica gel, CH_2Cl_2): α- and β-D-isomers **9** (6.2 g, 94%). Colorless liquid. $[\alpha]_D^{20} = -18.70$ ($c = 1.8$, $CHCl_3$). IR ($CHCl_3$): 3070, 3040, 3020, 3000, 2960, 2930, 2900, 2860, 1470, 1465, 1450, 1430, 1390, 1360, 1120, 1025, 1000, 820, 700. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.04, 1.05 (2*s*, 9 H, *t*-Bu); 1.64–1.70, 1.73–1.79 (2*m*, 1 H, H–C(3)); 1.72–1.91 (*m*, 1 H, H–C(5)); 1.95–2.08 (*m*, 1 H, H–C(5)); 2.04–2.18 (*m*, 1 H, H–C(2)); 2.34–2.42 (*m*, 1 H, H–C(2)); 3.27, 3.30 (2*s*, 3 H, MeO); 3.52–3.60 (*m*, 2 H, H–C(6)); 3.62, 3.68 (2*d*, $J = 7$, 2 H, CH_2–C(3)); 3.93–3.99, 4.01–4.07 (2*m*, 1 H, H–C(4)); 4.48, 4.49 (2*s*, 2 H, PhCH_2); 4.92 (*d*, $J = 5$, 0.5 H, H–C(1)); 4.96 (*dd*, $J = 5, 2$, 0.5 H, H–C(1)); 7.30–7.44 (*m*, 11 arom. H); 7.59–7.67 (*m*, 4 H, Ph_2Si). ^{13}C-NMR ($CDCl_3$, 75 MHz): 19.29 (*s*, Me_3C); 26.90 (*q*, *Me*$_3$C); 35.50, 35.87 (2*t*, C(5)); 36.58, 37.58 (2*t*, C(2)); 45.22, 45.87 (2*d*, C(3)); 54.40 (*q*, MeO); 65.23, 65.94 (2*t*, *C*H_2–C(3)); 67.69, 67.88 (2*t*, C(6)); 72.96 (*t*, PhCH_2); 78.11, 79.76 (2*d*, C(4)); 104.62, 105.04 (2*d*, C(1)); 127.42, 127.58, 127.74, 128.32 (4*d*, Ph_2Si); 129.65 (*d*, *Ph*CH_2); 133.57, 133.74 (2*s*, Ph_2Si); 135.57 (*d*, Ph_2Si); 138.74 (*s*, *Ph*CH_2). EI-MS: 503 ($[M - 1^+$), 473, 447, 415 (3), 339 (4), 293 (4), 279 (4), 249 (16), 247 (19), 225 (5), 219 (6), 218 (6), 217 (36), 216 (19), 213 (15), 200 (7), 199 (39), 197 (12), 187 (4), 183 (14), 181 (12), 173 (5), 169

(8), 153 (5), 139 (7), 135 (19), 125 (7), 105 (7), 95 (7), 92 (8), 91 (100). Anal. calc. for $C_{31}H_{40}O_4Si$: C 73.77, H 7.99; found: C 73.64, H 8.02.

Methyl 3-tert-*{[[(Butyl)diphenylsilyl]oxy}methyl}-2,3,5-trideoxy-α/β*-D-erythro-*hexofuranoside* (**10**). Pd/C (1.0 g; 10% Pd) was suspended in MeOH under Ar, and the catalyst was activated with H_2 for 30 min. A soln. of **9** (1.0 g, 2.0 mmol) in MeOH (5 ml) was added to the suspension and stirred rapidly for 4 h under H_2. The flask was flushed with Ar, the suspension filtered through *Celite*, and washed with AcOEt (100 ml). The filtrate was evaporated and the crude product chromatographed (silica gel, CH_2Cl_2/Et_2O 4:1): **10** (818 mg, 98%) as β/α-D-mixture 1:2. Colorless oil. $[\alpha]_D^{20} = \pm 0.2$ ($c = 1.9$, $CHCl_3$).

Data of β-D-**10**: $[\alpha]_D^{20} = +62.2$ ($c = 1.9$, $CHCl_3$). IR ($CHCl_3$): 3600–3350, 3070, 3050, 3000, 2960, 2930, 2860, 1920, 1890, 1830, 1580, 1470, 1460, 1440, 1430, 1390, 1360, 1260, 1240, 1050, 1030, 1020, 1005, 1000, 990, 970, 900, 820. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.05 (*s*, *t*-Bu); 1.59 (*ddt*, $J = 2$, 4, 7, H–C(3)); 1.72–1.83 (*m*, 1 H–C(5)); 1.92–2.01 (*m*, 1 H–C(5)); 2.08–2.21 (*m*, 2 H–C(2)); 2.67 (*t*, $J = 6$, OH); 3.29 (*s*, MeO); 3.70 (*dd*, $J = 5$, 2.5, CH_2–C(3)); 3.78 (*q*, $J = 5$, 2 H–C(6)); 4.00–4.07 (*m*, H–C(4)); 4.99 (*dd*, $J = 2$, 5, H–C(3)); 7.35–7.46 (*m*, 6 H, Ph_2Si); 7.61–7.67 (*m*, 4 H, Ph_2Si). ^{13}C-NMR ($CDCl_3$, 75 MHz): 19.22 (*s*, Me_3C); 26.85 (*q*, Me_3C); 35.47 (*t*, C(5)); 37.05 (*t*, C(2)); 45.70 (*d*, C(3)); 54.65 (*q*, MeO); 61.58 (*t*, CH_2–C(3)); 65.83 (*t*, C(6)); 81.39 (*d*, C(4)); 104.65 (*d*, C(1)); 127.72, 129.74 (2*d*, Ph_2Si); 133.43, 133.46 (2*s*, Ph_2Si); 135.60 (*d*, Ph_2Si). EI-MS: 413 ($[M-1]^+$), 383, 357 (2), 327 (2), 326 (8), 325 (30), 307 (7), 297 (8), 296 (6), 295 (25), 255 (7), 249 (6), 247 (19), 229 (14), 225 (6), 219 (10), 217 (6), 213 (34), 211 (6), 201 (7), 200 (18), 199 (100), 197 (20), 195 (8), 183 (28), 181 (21), 169 (9), 161 (7), 141 (8), 139 (15), 135 (16), 127 (8), 123 (8), 105 (13), 91 (10), 83 (9), 81 (10), 77 (8). Anal. calc. for $C_{24}H_{34}O_4Si$ (414.62): C 69.53, H 8.27; found: C 69.51, H 8.42.

Data of α-D-**10**: $[\alpha]_D^{20} = -35.6$ ($c = 2.1$, $CHCl_3$). IR ($CHCl_3$): 3600–3400, 3060, 3040, 3000, 2950, 2920, 2860, 1920, 1580, 1470, 1460, 1440, 1430, 1390, 1360, 1260, 1240, 1050, 1030, 1020, 1000, 990, 970, 900, 820, 715. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.05 (*s*, *t*-Bu); 1.71–1.77 (*m*, H–C(3)); 1.78–1.86 (*m*, 1 H–C(5)); 1.87–1.92 (*m*, 1 H–C(5)); 1.98 (*dd*, $J = 12$, 7, 1 H–C(2)); 2.40 ('*q*', 1 H–C(2)); 2.58 (*t*, $J = 5$, OH); 3.35 (*s*, MeO); 3.58–3.69 (*m*, CH_2–C(3)); 3.79 (*q*, $J = 6$, 2 H–C(6)); 4.01–4.08 (*m*, H–C(4)); 4.94 (*d*, $J = 6$, H–C(1)); 7.36–7.47 (*m*, 6 H, Ph_2Si); 7.62–7.68 (*m*, 4 H, Ph_2Si). ^{13}C-NMR ($CDCl_3$, 75 MHz): 19.26 (*s*, Me_3C); 26.87 (*q*, Me_3C); 36.07 (*t*, C(5)); 38.98 (*t*, C(2)); 45.13 (*d*, C(3)); 54.77 (*q*, MeO); 61.70 (*t*, CH_2–C(3)); 64.97 (*t*, C(6)); 82.68 (*d*, C(4)); 105.27 (*d*, C(1)); 127.75, 129.72, 129.80 (3*d*, Ph_2Si); 133.36, 133.56 (2*s*, Ph_2Si); 135.61 (*d*, Ph_2Si). EI-MS: 413 ($[M-1]^+$), 383, 357 (1), 327 (2), 326 (9), 325 (29), 307 (7), 297 (8), 296 (6), 295 (24), 255 (7), 249 (6), 247 (18), 229 (14), 225 (6), 219 (10), 217 (6), 213 (35), 211 (6), 201 (7), 200 (18), 199 (100), 197 (21), 195 (8), 183 (24), 181 (17), 169 (9), 141 (8), 139 (15), 135 (16), 127 (8), 123 (7), 105 (13), 91 (10), 83 (9), 81 (10), 77 (8), 57 (6). Anal. calc. for $C_{24}H_{34}O_4Si$ (414.62): C 69.53, H 8.27; found: C 69.46, H 8.31.

*1-{3′-{[[(*tert-*Butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-β*-D-erythro-*hexofuranosyl}thymine* (**11**) *and 1-{3′-{[[(*tert-*Butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-α*-D-erythro-*hexofuranosyl}thymine* (**12**). Thymine (946 mg, 7.5 mmol) and **10** (1.24 g, 3.0 mmol) were suspended in MeCN (25 ml), and MSTFA (3.33 ml, 18 mmol) was added dropwise. The initially turbid suspension turned clear after stirring for 1 h at r.t. The mixture was cooled to 0°, and $TfOSiMe_3$ (1.6 ml, 9.0 mmol) was added dropwise. The mixture was allowed to warm to r.t., stirred for 8 h, cooled to 0°, and hydrolyzed with sat. $NaHCO_3$ soln. (20 ml). The precipitate was filtered through sea sand which was washed with CH_2Cl_2 (100 ml). The org. phase was washed with brine (3 × 20 ml), dried (Na_2SO_4), and evaporated and the crude product chromatographed (silica gel, AcOEt): **11**/**12** (1.24 g, 81%). Colorless foam. The diastereoisomers were separated by HPLC (*Merck Lichrospher-Si-60*-7-μm column; 500 mg of **11**/**12** per injection; AcOEt/CH_2Cl_2 1:1, flow 30 ml/min for 60 min; elution of **11** after 23.5–28 min and of **12** after 29–35 min): **11** (494 mg, 32%) and **12** (674 mg, 44%) as colorless foams.

Data of **11**: $[\alpha]_D^{20} = +26.65$ ($c = 2.4$, $CHCl_3$). UV: 212 (37000), 265 (12000). IR ($CHCl_3$): 3600–3360, 3080, 3050, 3010, 2960, 2940, 2900, 2880, 1750–1630, 1590, 1470, 1430, 1405, 1390, 1360, 1310, 1270, 1110, 1040, 1010, 980, 940, 820. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.07 (*s*, *t*-Bu); 1.79–1.89 (*m*, H–C(3′)); 1.94, 1.95 (2*s*, Me–C(5)); 1.90–2.08 (*m*, 2 H–C(5′)); 2.10–2.24 (*m*, 1 H–C(2′)); 2.25–2.37 (*m*, 1 H–C(2′)); 3.68 (*d*, $J = 5$, CH_2–C(3′)); 3.73–3.85 ('*t*', 2 H–C(5′)); 4.01 (*dt*, $J = 3$, 8, H–C(4′)); 6.08 (*dd*, $J = 4$, 7, H–C(1′)); 7.19 (2*s*, H–C(6)); 7.37–7.48 (*m*, 6 H, Ph_2Si); 7.62–7.65 (*m*, 4 H, Ph_2Si); 9.09 (br., NH). ^{13}C-NMR ($CDCl_3$, 125 MHz): 12.72 (*q*, *Me*–C(5)); 19.22 (*s*, Me_3C); 26.88 (*q*, Me_3C); 34.96 (*t*, C(5′)); 37.02 (*t*, C(2′)); 45.24 (*d*, C(3′)); 60.79 (*t*, CH_2–C(3′)); 63.44 (*t*, C(6′)); 81.86 (*d*, C(4′)); 85.05 (*d*, C(1′)); 110.96 (*s*, C(5)); 127.86, 129.95, 129.96 (3*d*, Ph_2Si); 132.95, 132.98 (2*s*, Ph_2Si); 135.26 (*d*, C(6)); 135.56, 135.60 (2*d*, Ph_2Si); 150.29 (*s*, C(2)); 163.77 (*s*, C(4)). FAB-MS (NOBA; pos.): 1017.8 ($2M^+$), 531 ($[M+Na]^+$), 507 ($[M-1]^+$), 383 (14), 325 (15), 269 (18), 239 (22), 227 (17), 200 (26), 199 (95), 198 (26), 197 (92), 183 (34), 181 (35), 165 (28), 154 (22), 139 (36), 138 (15), 137 (64), 136 (50), 135 (100), 127 (92), 123 (17), 121 (30), 109 (17); 107 (24); 105 (52); 91 (31); 89 (20); 81

(30); 79 (18); 77 (35); 57 (18). Anal. calc. for $C_{28}H_{36}N_2O_5Si$: C 66.11, H 7.13, N 5.51; found: C 66.00, H 7.19, N 5.48.

Data of **12**: $[\alpha]_D^{20} = -5.4$ ($c = 2.7$, $CHCl_3$). UV: 215 (38000), 266 (12500). IR ($CHCl_3$): 3600–3400, 3080, 3060, 3050, 3010, 2960, 2940, 2900, 2880, 1750–1630, 1580, 1470, 1430, 1410, 1390, 1360, 1310, 1270, 1120, 1040, 1010, 980, 940, 820, 715. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.06 (*s*, *t*-Bu); 1.67–1.77 (*m*, H–C(3′)); 1.79–1.98 (*m*, 2 H–C(5′)); 1.91 (2*s*, Me–C(5)); 2.20–2.33 (*m*, 1 H–C(2′)); 2.48–2.57 (*m*, 1 H–C(2′)); 3.71 (*dd*, $J = 5$, 1, CH_2–C(3′)); 3.76 (*t*, $J = 6$, 2 H–C(6′)); 4.31 (*dt*, $J = 3$, 8.5, H–C(4′)); 6.16 (*dd*, $J = 6$. 7.5, H–C(1′)); 7.16, 7.17 (2*s*, H–C(6)); 7.36–7.48 (*m*, 6 H, Ph_2Si); 7.60–7.65 (*m*, 4 H, Ph_2Si); 9.04 (br., NH). ^{13}C-NMR ($CDCl_3$, 125 MHz): 12.65 (*q*, *Me*–C(5)); 19.26 (*s*, Me_3C); 26.87 (*q*, Me_3C); 35.24 (*t*, C(5′)); 37.16 (*t*, C(2′)); 46.60 (*d*, C(3′)); 60.49 (*t*, CH_2–C(3′)); 62.71 (*t*, C(6′)); 81.26 (*d*, C(4′)); 85.49 (*d*, C(1′)); 111.15 (*s*, C(5)); 127.87, 127.88 (2*d*, Ph_2Si); 133.00, 130.01 (2*d*, Ph_2Si); 132.92, 132.93 (*s*, Ph_2Si); 134.86 (*d*, C(6)); 135.52, 135.55 (2*d*, Ph_2Si); 150.37 (*s*, C(2)); 163.79 (*s*, C(4)). FAB-MS (NOBA; pos.): 1018 ($2M^+$), 531 ($[M + Na]^+$), 507 ($[M - 1]^+$), 383 (6), 247 (4), 227 (4), 200 (4), 199 (19), 198 (4), 197 (20), 195 (4), 187 (6), 183 (7), 181 (10), 175 (5), 169 (25), 167 (6), 165 (8), 163 (5), 155 (5), 154 (5), 143 (8), 139 (9), 137 (12), 136 (10), 135 (31), 129 (7), 128 (9), 127 (100), 123 (6), 121 (8), 117 (25), 115 (7), 109 (14), 107 (9), 105 (20), 95 (6), 91 (16), 89 (8), 83 (14), 81 (15), 79 (11), 77 (22), 57 (11). Anal. calc. for $C_{28}H_{36}N_2O_5Si$: C 66.11, H 7.13, N 5.51; found: C 65.83, H 7.09, N 5.52.

N^4-*(*o*-Toluoyl)cytosine* (= N-*(1,2-Dihydro-2-oxopyrimidin-4-yl)-2-methylbenzamide*; **13a**). Cytosine (7.5 g, 67.5 mmol) was suspended in anh. pyridine (150 ml) and *o*-toluoyl chloride (29 ml, 222 mmol, 3.3 equiv.) was added in 20 min at r.t. The milky suspension was stirred for 5 d at r.t. (→ ochre). The suspension was cooled to 0°, and 1M HCl (200 l) was added dropwise; the cytosine derivative was initially dissolved and then precipitated as the hydrochloride. The mixture was stirred for 2 h at r.t. The precipitate was filtered and washed with warm 50% aq. EtOH soln. (50°, 3 × 100 ml) and EtOH (2 × 100 ml). The residue was suspended in sat. NH_4OH soln. (100 ml) and stirred overnight at 0°. The mixture was neutralized with conc. HCl soln. The precipitate was filtered and washed with H_2O (2 × 50 ml) and EtOH (2 × 50 ml). The colorless residue **13a** (12.1 g, 80%) was dried for 2 days in a desiccator over P_2O_5. ^{1}H-NMR ((D_6)DMSO, 300 MHz): 2.38 (*s*, Me(to)); 7.22 (*d*, $J = 7.0$, H–C(5)); 7.28 (*m*, H–C(3)(to), H–C(5)(to)); 7.39 (*m*, H–C(4)(to)); 7.47 (*d*, $J = 7.6$, H–C(6)(to)); 7.88 (*d*, $J = 7.0$, H–C(6)). EI-MS: 229 (1, M^+), 214 (1, $[M - Me]^+$), 119 (2, $MeC_6H_4CO^+$); 91 (3, $MeC_6H_4^+$).

N^4-*Benzoylcytosine* (= N-*(1,2-Dihydro-2-oxopyrimidin-4-yl)benzamide*; **13b**). As described by *Brown et al.* [32]. ^{1}H-NMR ((D_6)DMSO, 300 MHz): 7.11 (*m*, H–C(5)); 7.50 (*m*, 2 H, bz)); 7.61 (*m*, 1 H (bz)); 7.87 (*d*, $J =$ 7.0, H–C(6)); 7.99 (*m*, 2 H (bz)).

N^4-*(*p*-Anisoyl)cytosine* (= N-*(1,2-Dihydro-2-oxopyrimidin-4-yl)-4-methoxybenzamide*; **13c**). As described for **13a**, with cytosine (3 g, 27 mmol), pyridine (150 ml), and *p*-anisoyl chloride (29 ml, 216 mmol, 8 equiv.); the yellowish suspension was stirred overnight at r.t. After treatment with 1M HCl (150 ml) and washing with warm 50% aq. EtOH soln. (50°, 3 × 100 ml) and EtOH (2 × 100 ml) (no NH_4OH treatment), the colorless residue **13c** (6.3 g, 95%) was dried for two days in a desiccator over P_2O_5. ^{1}H-NMR ((D_6)DMSO, 300 MHz): 3.89 (*s*, MeO); 7.06 (*m*, H–C(5)); 7.15 (*d*, $J = 8.9$, H–C(3)(an), H–C(5)(an)); 8.08 (*m*, H–C(6), H–C(2)(an), H–C(6)(an)).

*1-{3′-{{[(*tert*-Butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-β-*D*-*erythro*-hexofuranosyl}-*N^4*-(*o*-toluoyl)-cytosine* (**14a**), *and 1-{3′-{{[(*tert*-Butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-α-*D*-*erythro*-hexofuranosyl}-*N^4*-(*o*-toluoyl)cytosine* (**15a**). *Method 1:* To a suspension of **13a** (400 mg, 1.75 mmol) in HMDS (10 ml), Me_3SiCl (1.0 ml, 7.6 mmol) was added dropwise, and the mixture was refluxed for 6 h. The solvent was evaporated and the residue dried for 24 h under high vacuum. The remaining pale yellow oil was dissolved in 1,2-dichloroethane (5 ml), and **10** (250 mg, 0.60 mmol) was added as a soln. in 1,2-dichloroethane (5 ml). The mixture was cooled to 0°, and $TfOSiMe_3$ (0.40 ml, 2.06 mmol) was added dropwise. The mixture was stirred for 30 min at 0°, and then for 6 h at r.t., cooled again to 0°, and hydrolyzed with sat. $NaHCO_3$ soln. (20 ml). Stirring continued for 10 min. The precipitate was then removed by filtration through sea sand, which was washed in CH_2Cl_2 (100 ml). The combined org. phase was washed with brine (3 × 20 ml), dried (Na_2SO_4), and evaporated and the remaining yellow foam chromatographed (silica gel, AcOEt/petroleum ether 2:1): **14a** (226 mg, 37%) and **15a** (251 mg, 41%) as colorless foams.

Method 2: To a suspension of **13a** (2.0 g, 8.7 mmol) in HMDS (20 ml), Me_3SiCl (3.6 ml, 27.4 mmol) was added dropwise, and the mixture was refluxed for 6 h. The solvent was evaporated and the residue dried for 24 h under high vacuum. The remaining pale yellow oil was dissolved in 1,2-dichloroethane (10 ml), and **12** (1.45 g, 2.85 mmol) was added as a soln. in 1,2-dichloroethane (5 ml). The mixture was cooled to 0°, and $TfOSiMe_3$ (2.5 ml, 12.5 mmol) was added dropwise. The mixture was allowed to warm to r.t., stirred for 48 h, cooled again to 0°, and hydrolyzed with sat. $NaHCO_3$ soln. (50 ml). Stirring was continued for 10 min. The precipitate was then removed by filtration through sea sand, which was washed with CH_2Cl_2 (100 ml) and AcOEt (100 ml). The

combined org. phase was washed with sat. $NaHCO_3$ soln. (3×50 ml) and brine (3×50 ml), dried (Na_2SO_4), and evaporated and the remaining yellow foam chromatographed (silica gel, Et_2O/AcOEt 1:0, 4:1, 1:1, 0:1): **14a** (605 mg, 35%), **15a** (746 mg, 43%), and starting **12** (132 mg, 9%) as colorless foams. The products of the two methods were identical according to TLC and ^{1}H-NMR.

Data of **14a**: UV (MeCN): 252 (15500), 309 (6800). ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.06 (*s*, *t*-Bu); 1.76–1.88 (*m*, 1 H–C(5′)); 1.97–2.12 (*m*, 1 H–C(5′), H–C(3′)); 2.14–2.22 (*m*, 1 H–C(2′)); 2.51 (*s*, Me (to)); 2.51–2.63 (*m*, 1 H–C(2′)); 3.69 (*d*, $J = 5.0$, CH_2–C(3′)); 3.74–3.85 ('*dt*', $J = 2.0$, 6.0, 2 H–C(6′)); 4.15 (*dt*, $J = 3.5$, 9.0, H–C(4′)); 6.07 (*dd*, $J = 2.5$, 7.0, H–C(1′)); 7.28 (*m*, H–C(3)(to), H–C(5)(to)); 7.34–7.48 (*m*, 6 H, Ph_2Si); 7.48–7.58 (*m*, H–C(4)(to), H–C(6)(to), H–C(5)); 7.62–7.64 (*m*, 4 H, Ph_2Si); 8.04 (*d*, $J = 7.4$, H–C(6)); 8.32 (br., NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 19.23 (*s*, Me_3C); 20.10 (*q*, Me (to)); 26.07 (*q*, Me_3C); 36.15 (*t*, C(5′)); 37.13 (*t*, C(2′)); 44.51 (*d*, C(3′)); 60.89 (*t*, C(6′)); 62.90 (*t*, CH_2–C(3′)); 83.19 (*d*, C(4′)); 87.89 (*d*, C(1′)); 95.91 (*d*, C(5)); 126.16, 126.98 (2*d*, to); 127.87, 129.96 (2*d*, Ph_2Si); 131.58, 131.81 (2*d*, to); 132.82 (*s*, Ph_2Si); 134.11 (*s*, C_{ipso} (to)); 135.55 (*d*, Ph_2Si); 137.47 (*s*, C_o (to)); 144.00 (*d*, C(6)); 162.11 (*s*, C=O). FAB-MS (NOBA; pos.): 634 (15, $[M + Na]^+$), 613 (15, $[M + H]^+$), 612 (34, M^+), 611 (20, $[M - H]^+$), 610 (31, $[M - 2H]^+$), 556 (15, $[M - t\text{-Bu} + 2H]^+$); 555 (41, $[M^+ - (t\text{-Bu}) + H]^+$), 554 (100, $[M - (t\text{-Bu})]^+$), 534 (24), 509 (15), 468 (14), 428 (27), 411 (18), 410 (29), 404 (14), 230 ($[MeC_6H_4CONHC_4H_3N_2O + H]^+$); 135 (only $m/z > 130$ were considered).

Data of **15a**: UV (MeCN): 253 (16100), 309 (7200). ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.05 (*s*, *t*-Bu); 1.76–1.98 (*m*, H–C(3′)), 2 H–C(5′)); 2.27–2.38 (*m*, 1 H–C(2′)); 2.86 (*dt*, $J = 6.0$, 9.0, 1 H–C(2′)); 3.56–3.69 (*m*, CH_2–C(3′)); 3.81 (*dd*, $J = 5.0$, 10.3, 2 H–C(6′)); 4.36 (*dt*, $J = 3.5$, 8.0, H–C(4′)); 6.08 (*t*, $J = 4.0$, H–C(1′)); 7.26–7.32 (*m*, 2 H, to); 7.37–7.47 (*m*, 7 H, Ph_2Si, H–C(5)); 7.48–7.52 (*m*, 2 H, to); 7.58–7.63 (*m*, 4 H, Ph_2Si); 7.89 (*d*, $J = 7.4$, H–C(6)); 8.33 (br., NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 19.21 (*s*, Me_3C), 20.41 (*q*, Me (to)); 26.82 (*q*, Me_3C); 36.18 (*t*, C(5′)); 37.15 (*t*, C(2′)); 44.61 (*d*, C(3′)); 61.29 (*t*, C(6′)); 62.90 (*t*, CH_2–C(3′)); 83.15 (*d*, C(4′)); 88.65 (*d*, C(1′)); 95.93 (*d*, C(5)); 126.21, 126.90 (2*d*, to); 127.88, 129.82 (2*d*, Ph_2Si); 131.51, 131.93 (2*d*, to); 132.62 (*s*, Ph_2Si); 134.13 (*s*, C_{ipso} (to)); 135.53 (*d*, Ph_2Si); 137.81 (*s*, C_o (to)); 144.11 (*d*, C(6)); 162.12 (*s*, C=O). FAB-MS (NOBA; pos.): 634 (21, $[M + Na]^+$), 613 (44, $[M + H]^+$), 612 (100, M^+), 554 (59, $[M - (t\text{-Bu})]^+$), 510 (14), 509 (31), 491 (29), 451 (20), 433 (15), 428 (18), 413 (16), 411 (19), 410 (17), 269, 230 ($[MeC_6H_4CONHC_4H_3N_2O + H]^+$); 197, 135 (only $m/z > 130$ were considered).

*N^4-Benzoyl-1-{3′-{{[(*tert*-butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-β*-D-erythro-*hexofuranosyl}cytosine* (**14b**) *and N^4-Benzoyl-1-{3′-{{[(*tert*-butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-α*-D-erythro-*hexofuranosyl}cytosine* (**15b**). As described for **14a**/**15a** (*Method 2*), with **13b** (1.94 g, 9 mmol) in HMDS (20 ml), and Me_3SiCl (3.8 ml, 30 mmol) for 8 h. Then with the pale yellow oil in 1,2-dichloroethane (15 ml), **10** (1.24 g, 3 mmol), 1,2-dichloroethane (10 ml), and $TfOSiMe_3$ (1.64 ml, 9 mmol) for 4 h. After hydrolyzation with sat. $NaHCO_3$ soln. (20 ml), filtration through sea sand, and washing with CH_2Cl_2 (100 ml), the org. filtrate was washed with brine (3×20 ml), dried (Na_2SO_4), and evaporated and the remaining yellow foam chromatographed (silica gel, AcOEt/petroleum ether 2:1): **14b** (681 mg, 38%) and **15b** (792 mg, 44%). Colorless foams.

Data of **14b**: $[\alpha]_D^{20} = +66.73$ ($c = 1.6$, $CHCl_3$). UV: 259 (24800), 308 (8000). IR ($CHCl_3$): 3450–3360, 3070, 3030, 3000, 2960, 2930, 2890, 2860, 1710, 1660, 1620, 1550, 1480, 1430, 1390, 1360, 1310, 1300, 1260, 1110, 1070, 1040, 1000, 980, 940, 910–890, 820. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.06 (*s*, *t*-Bu); 1.83–1.88 (*m*, H–C(3′)); 1.89–2.16 (*m*, 2 H–C(5′)); 2.16–2.19 (*m*, OH); 2.17–2.22 (*m*, 1 H–C(2′)); 2.45–2.55 (*m*, 1 H–C(3′)); 3.68 (*d*, $J = 5$, CH_2–C(3′)); 3.82–3.86 ('*dt*, $J = 2$, 7, 2 H–C(6′)); 4.15 (*dt*, $J = 3$, 9, H–C(4′)); 6.04 (*dd*, $J = 2$, 7, H–C(1′)); 7.37–7.47 (*m*, 7 arom. H); 7.48–7.54 (*m*, 2 H, bz); 7.58–7.65 (*m*, 5 H, Ph_2Si, H–C(5)); 7.88–7.92 (*m*, 2 H, bz); 8.03 (*d*, $J = 7$, H–C(6)); 8.79 (br., NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 19.23 (*s*, Me_3C); 26.87 (*q*, Me_3C); 36.15 (*t*, C(5′)); 37.16 (*t*, C(2′)); 44.57 (*d*, C(3′)); 60.86 (*t*, C(5′)); 62.96 (*t*, C(6′)); 83.09 (*d*, C(4′)); 87.63 (*d*, C(1′)); 96.19 (*d*, C(5)); 127.54, 129.06 (2*d*, bz); 127.86, 129.94 (2*d*, Ph_2Si); 132.95, 133.17 (2*s*, Ph_2Si); 135.55 (*d*, Ph_2Si); 143.87 (*d*, C(6)); 162.18 (*s*, C=O). FAB-MS (NOBA; pos.): 620 ($[M + Na]^+$); 598 (M^+), 540, 302, 295, 269 (3), 239 (5), 238 (9), 217 (27), 216 (100), 215 (6), 199 (23), 198 (5), 197 (19), 183 (6), 165 (6), 154 (8), 139 (9), 137 (17), 136 (15), 135 (45), 127 (27), 121 (7), 112 (6), 109 (8), 107 (7), 106 (6), 105 (52), 97 (7), 95 (8), 91 (11), 83 (9), 81 (14), 79 (8), 77 (15), 69 (8). Anal. calc. for $C_{34}H_{39}N_3O_5Si$: C 68.31, H 6.58, N 7.03; found: C 68.05, H 6.74, N 6.80.

Data of **15b**: $[\alpha]_D^{20} = -41.32$ ($c = 1.7$, $CHCl_3$). UV: 207 (45000), 260 (20500), 304 (7500). IR ($CHCl_3$). 3450–3380, 3050, 3000, 2960, 2930, 2860, 1700, 1660, 1640, 1550, 1480, 1430, 1390, 1360, 1300, 1260, 1110, 1070, 1050, 1000, 970, 890, 820. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.03 (*s*, *t*-Bu); 1.76–1.83 (*m*, H–C(3′)); 1.83–1.97 (*m*, 2 H–C(5′)); 2.05 (*m*, OH); 2.26–2.38 (*m*, 1 H–C(2′)); 2.85 (*dt*, $J = 6$, 9, 1 H–C(2′)); 3.57–3.69 (*m*, CH_2–C(3′)); 3.80 (*t*, $J = 5$, 2 H–C(6′)); 4.35 (*dt*, $J = 3.5$, 8, H–C(4′)); 6.04 (*t*, $J = 4$, H–C(1′)); 7.36–7.46 (*m*, 6 H, Ph_2Si); 7.49–7.52 (*m*, 3 H, bz, H–C(5)); 7.58–7.64 (*m*, 4 H, Ph_2Si); 7.87–7.90 (*m*, 3 H, bz, H–C(6)); 8.76 (br., NH). ^{13}C-NMR ($CDCl_3$, 100 MHz): 19.21 (*s*, Me_3C); 26.86 (*q*, Me_3C); 36.56 (*t*, C(5′)); 37.19 (*t*, C(2′)); 46.38 (*d*, C(3′)); 60.32 (*t*, CH_2–C(3′)); 63.19 (*t*, C(6′)); 81.94 (*d*, C(4′)); 88.03 (*d*, C(1′)); 96.33 (*d*, C(5)); 127.55

(*d*, bz); 127.55, 127.87 (2*d*, Ph_2Si); 128.23 (*d*, bz); 129.06 (*d*, bz); 129.97, 129.99 (2*d*, Ph_2Si); 132.92, 132.95 (2*s*, Ph_2Si); 133.18 (*s*, bz); 135.55 (*d*, Ph_2Si); 143.29 (*d*, C(6)); 155.2 (*s*, C(2)); 162.18 (*s*, C=O). FAB-MS (NOBA; pos.): 620 ($[M+Na]^+$), 598 (M^+), 540, 302, 282, 239 (6), 238 (10), 217 (27), 216 (100), 199 (23), 198 (6), 197 (21), 183 (6), 165 (6), 154 (5), 139 (9), 137 (15), 136 (13), 135 (46), 127 (24), 121 (8), 112 (7), 109 (8), 107 (7), 106 (6), 105 (56), 97 (8), 95 (9), 91 (12), 83 (12), 81 (16), 79 (9), 77 (16), 69 (11), 67 (8), 57 (11). Anal. calc. for $C_{34}H_{39}N_3O_5Si$: C 68.31, H 6.58, N 7.03; found: C 68.11, H 6.67, 6.99.

N^4-*(*p-*Anisoyl)-1-{3′-{{[(*tert-*butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-β-*D-erythro-*hexofuranosyl}-cytosine* (**14c**) *and* N^4-*(*p-*Anisoyl)-1-{3′-{{[(*tert-*butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-α-*D-erythro-*hexofuranosyl}cytosine* (**15c**). As described for **14a**/**15a**, with **13c** (1.35 g, 5.5 mmol), HMDS (20 ml), and Me_3SiCl (2.1 ml, 16.5 mmol) 11 h, then, with the pale yellow oil, in 1,2-dichloroethane (5 ml), **10** (740 mg, 1.8 mmol), 1,2-dichloroethane (5 ml), and $OSiMe_3$ (1.0 ml, 5.5 mmol) for 30 min at 0° and 4 h at r.t. After hydrolyzation with sat. $NaHCO_3$ soln. (10 ml) at 0°, the precipitate was worked up as described in *Method 1:* **14c**/**15c** (883 mg, 78%). Colorless foam. The diastereoisomers could not be separated with FC because of their identical R_f values. TLC (AcOEt): R_f 0.28.

*Configuration Analysis: (*αS*)-α-Methoxy-α-(trifluoromethyl)benzeneacetic Acid {(2*R,*3*S*)-3-[2-(Benzyloxy)ethyl]oxiran-2-yl}methyl Ester.* Et_3N (200 µl) and **5** (0.05 mmol) were mixed at 0° in CH_2Cl_2 (5 ml) with DMAP (7.4 mg, 0.06 mmol). (−)-(αR)-α-Methoxy-α-(trifluoromethyl)benzeneacetyl chloride (14 µl; *Fluka Chira Select* > 99.5) was then added dropwise. The soln. was warmed to r.t. The reaction was essentially complete after 30 min (TLC monitoring). Then 3-(dimethylamino)propylamine (50 µl) was added dropwise, the crude mixture evaporated under high vacuum, the residue taken up in Et_2O/petroleum ether 2:1, and the soln. passed through a short silica gel column, which was washed with 50 ml of Et_2O/petroleum ether 2:1. After evaporation and drying under vacuum for 24 h, the crude product (*ca.* 20–30 mg) was analyzed by ^{19}F-NMR to assess its enantiomer purity.

*1-{3′-{{[(*tert-*Butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-6′-*O*-(methylsulfonyl)-β-*D-erythro-*hexofuranosyl}thymine* (**16**). Compound **11** (278 mg, 0.546 mmol) was co-evaporated 3× with pyridine and dissolved in pyridine/CH_2Cl_2 4:1 (5 ml). The soln. was cooled to 0°, and methanesulfonyl chloride (65 µl, 0.84 mmol) was added dropwise. The mixture was allowed to warm to r.t., stirred for 3 h, and hydrolyzed with 1.6% H_2SO_4 soln. (2 ml). CH_2Cl_2 (50 ml) was added, the soln. washed with 1.6% H_2SO_4 soln. (3 × 10 ml) and brine (3 × 10 ml), dried (Na_2SO_4), and evaporated, and the crude product chromatographed (silica gel, AcOEt/petroleum ether 1:1, 3:1): **16** (299 mg, 93%). Colorless foam. UV (MeCN): 203 (26700), 266 (8900). ^1H-NMR ($CDCl_3$, 300 MHz): 1.07 (*s*, Me_3C); 1.96 (*s*, Me−C(5)); 1.99–2.08 (*m*, 2 H−C(5′)); 2.17–2.36 (*m*, H−C(3′), 2 H−C(2′)); 2.99 (*s*, $MeSO_2$); 3.63–3.73 (*m*, CH_2−C(3′)); 3.98 (*dt*, *J* = 2.6, 8.8, H−C(4′)); 4.27–4.37 (*m*, 1 H−C(6′)); 4.38–4.47 (*m*, 1 H−C(6′)); 6.05 (*dd*, *J* = 4.1, 7.1, H−C(1′)); 7.14 (2*s*, H−C(6)); 7.39–7.47 (*m*, 6 H, Ph_2Si); 7.62–7.66 (*m*, 4 H, Ph_2Si); 9.26 (br., NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 12.62 (*q*, *Me*−C(5)); 19.61 (*s*, Me_3C); 26.84 (*q*, Me_3C); 34.34 (*t*, C(5′)); 34.69 (*t*, C(2′)); 37.31 (*q*, $MeSO_2$); 45.05 (*d*, C(3′)); 63.43 (*t*, CH_2−C(3′)); 66.92 (*t*, C(6′)); 78.79 (*d*, C(4′)); 84.94 (*d*, C(1′)); 111.21 (*s*, C(5)); 127.90, 130.01 (2*d*, Ph_2Si); 132.80 (*s*, Ph_2Si); 135.20 (*d*, C(6)); 135.55 (*d*, Ph_2Si); 150.20 (*d*, C(2)); 163.74 (*s*, C(2)). ESI-MS (pos.): 1194.8 ($[2M+Na]^+$), 1172.7 ($[2M+H]^+$), 609.2 ($[M+Na]^+$), 586.9 ($[M+H]^+$).

*1-{6′-Bromo-3′-{{[(*tert-*butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-β-*D-erythro-*hexofuranosyl}thymine* (**17**). Compound **11** (50 mg, 98 µmol) and PPh_3 (51 mg, 196 µmol) were co-evaporated 3× with toluene, then dried overnight under high vacuum at r.t., and dissolved in 1,2-dichloroethane/MeCN 4:1 (10 ml). A soln. of tetrabromomethane (65 mg, 196 µmol) in 1,2-dichloroethane (2 ml) was added, and the mixture was stirred for 1.5 h at r.t. MeOH (1 ml) was added to quench the reaction. The solvents were evaporated and FC (silica gel, CH_2Cl_2/AcOEt 1:1) yielded **17** (54 mg, 97%). Colorless foam. UV (MeCN): 215 (17000), 265 (10400). ^1H-NMR ($CDCl_3$, 300 MHz): 1.08 (*s*, *t*-Bu); 1.95 (*s*, Me−C(5)); 1.98–2.09 (*m*, 1 H−C(5′)); 2.10–2.23 (*m*, 1 H−C(5′), H−C(3′)); 2.25–2.38 (*m*, 2 H−C(2′)); 3.41–3.59 (*m*, 2 H−C(6′)); 3.67 (*d*, *J* = 4.0, CH_2−C(3′)); 4.03 (*dt*, *J* = 2.5, 9.0, H−C(4′)); 6.06 (*dd*, *J* = 4.4, 7.1, H−C(1′)); 7.11, 7.12 (2*s*, H−C(6)); 7.26–7.44 (*m*, 6 H, Ph_2Si); 7.64–7.66 (*m*, 4 H, Ph_2Si); 9.17 (br., NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 12.70 (*q*, *Me*−C(5)); 19.15 (*s*, Me_3C); 26.83 (*q*, Me_3C); 29.48 (*t*, C(6′)); 34.87 (*t*, C(5′)); 38.07 (*t*, C(2′)); 44.87 (*d*, C(3′)); 63.40 (*t*, CH_2−C(3′)); 80.63 (*d*, C(4′)); 87.89 (*d*, C(1′)); 110.89 (*s*, C(5)); 127.82, 129.92 (2*d*, Ph_2Si); 132.85 (*s*, Ph_2Si); 135.20 (*d*, C(6)); 135.55 (*d*, Ph_2Si); 150.22 (*d*, C(2)); 163.76 (*s*, C(4)). FAB-MS (NOBA; pos.): 573 (24, $[M_1+H]^+$), 572 (10, $[M_2+2H]^+$), 571 (25, $[M_2+H]^+$), 559 (14), 515 (23), 513 (21), 492 (37, $[M-Br+H]^+$), 491 (100, $[M-Br]^+$), 433 (17), 289 (20), 287 (22), 269 (32), 263 (20), 261 (29), 251 (22), 247 (31), 244 (21), 243 (74), 239 (44), 237 (18), 235 (60), 233 (19), 229 (18), 227 (35), 225 (34), 223 (24), 213 (28), 211 (19), 209 (21), 207 (22), 203 (24), 201 (31), 200 (33), 190, 189, 136, 135.

*1-{3′-{{[(*tert*-Butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-6′*-O-*(methylsulfonyl)-β*-D-erythro-*hexofuranosyl}*-N^4-(o-*toluoyl)cytosine* (**18a**). Compound **14a** (380 mg, 0.62 mmol) was co-evaporated 3 × with pyridine and dissolved in pyridine/CH_2Cl_2 1:2 (6 ml). The soln. was cooled to 0°, and methanesulfonyl chloride (67 µl, 0.86 mmol) was added dropwise. The mixture was allowed to warm to r.t., stirred for 3 h, and hydrolyzed with 1.6% H_2SO_4 soln. (2 ml). CH_2Cl_2 (50 ml) was added, the soln. washed with 1.6% H_2SO_4 soln. (3 × 10 ml) and brine (3 × 10 ml), dried (Na_2SO_4), and evaporated and the crude product chromatographed (silica gel, AcOEt): **18a** (321 mg, 95%). Colorless foam. UV (MeCN): 253 (19700), 309 (8600). ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.08 (*s*, ^{t}Bu); 1.98–2.15 (*m*, 2 H–C(5′)); 2.16–2.23 (*m*, H–C(3′)); 2.28–2.40 (*m*, 1 H–C(2′)); 2.46–2.58 (*m*, 1 H–C(2′)); 2.52 (*s*, Me (to)); 3.02 (*s*, $MeSO_2$); 3.65–3.74 (*m*, CH_2–C(3′)); 4.13 (*dt*, *J* = 2.0, 9.0, H–C(4′)); 4.35–4.50 (*m*, H–C(6′)); 6.06 (*dd*, *J* = 3.0, 7.0, H–C(2)); 7.26–7.32 (*m*, 2 H, to); 7.37–7.46 (*m*, 7 H, Ph_2Si, H–C(5)); 7.48–7.53 (*m*, 1 H, to); 7.55–7.60 (*m*, 1 H, to); 7.60–7.67 (*m*, 4 H, Ph_2Si); 7.95 (*d*, *J* = 7.0, H–C(6)); 8.34 (br., NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 19.23 (*s*, Me_3C); 20.12 (*q*, Me (to)); 26.04 (*q*, Me_3C); 36.16 (*t*, C(5′)); 37.18 (*t*, C(2′)); 37.53 (*q*, $MeSO_2$);44.61 (*d*, C(3′)); 62.67 (*t*, C(6′)); 62.92 (*t*, CH_2–C(3′)); 83.12 (*d*, C(4′)); 87.65 (*d*, C(1′)); 95.95 (*d*, C(5)); 126.17, 126.98 (2*d*, to); 127.87, 129.94 (2*d*, Ph_2Si); 131.57, 131.80 (2*d*, to); 132.83 (*s*, Ph_2Si); 134.15 (*s*, C_{ipso} (to)); 135.55 (*d*, Ph_2Si); 137.45 (*s*, C_o (to)); 144.04 (*d*, C(6)); 162.10 (*s*, C=O). FAB-MS (NOBA; pos.): 1380 (27, 2M^+), 692 (18, $[M+2H]^+$), 691 (42, $[M+H]^+$), 690 (100, M^+), 632 (28), 594 (13), 365 (15), 277, 230 ($[MeC_6H_4CONHC_4H_3NO_2+H]^+$).

*1-{6′-Bromo-3′-{{[(*tert*-butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-β*-D-erythro-*hexofuranosyl}*-N^4-*(*o-*toluoyl)cytosine* (**18b**). Compound **14a** (50 mg, 82 µmol) and PPh_3 (43 mg, 163 µmol) were co-evaporated 3 × with toluene, then dried overnight under high vacuum at r.t., and dissolved in 1,2-dichloroethane (10 ml). The soln. was cooled to 0°, and tetrabromomethane (49 mg, 147 µmol) in 1,2-dichloroethane (2 ml) was added. The mixture was allowed to warm to r.t. and stirred for 2 h. The soln. was poured into sat. $NaHCO_3$ soln. (15 ml) containing ice (10 g). CH_2Cl_2 (60 ml) was added, the aq. phase extracted with CH_2Cl_2 (4 × 20 ml), the combined org. phase dried ($MgSO_4$) and evaporated at 30° (water-bath temp.) and the residue submitted to FC (silica gel, CH_2Cl_2 (100 ml), CH_2Cl_2/AcOEt 3:1 (200 ml)): **18b** (41 mg, 74%). Colorless foam. UV (MeCN): 254 (15400), 308 (7500). ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.06 (*s*, ^{t}Bu); 1.98–2.28 (*m*, 2 H–C(5′), H–C(3′)); 2.28–2.42 (*m*, 1 H–C(2′)); 2.43–2.61 (*m*, 1 H–C(2′)); 2.52 (*s*, Me (to)); 3.48–3.67 (*m*, 2 H–C(6′)); 3.68–3.74 (*d*, CH_2–C(3′)); 4.19 (*dt*, H–C(4′)); 6.04 (*dd*, H–C(1′)); 7.25–7.31 (*m*, 2 H, to); 7.36–7.52 (*m*, 7 H, Ph_2Si, to); 7.52–7.61 (*m*, 3 H, to, H–C(5)); 7.61–7.70 (*m*, 4 H, Ph_2Si, to); 7.94 (*d*, *J* = 7.0, H–C(6)); 8.38 (br., NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 19.18 (*s*, Me_3C); 20.14 (*q*, Me (to)); 26.84 (*q*, Me_3C); 29.41 (*t*, C(6′)); 36.18 (*t*, C(5′)); 38.09 (*t*, C(2′)); 44.16 (*d*, C(3′)); 62.90 (*t*, CH_2–C(3′)); 82.04 (*d*, C(4′)); 87.46 (*d*, C(1′)); 95.77 (*d*, C(5)); 126.19, 126.91 (2*d*, to); 127.86, 129.95 (2*d*, Ph_2Si); 131.60, 131.83 (2*d*, to); 132.82 (*s*, Ph_2Si); 134.16 (*s*, C_{ipso} (to)); 135.55 (*d*, Ph_2Si); 137.48 (*s*, C_o (to)); 143.72 (*d*, C(6)); 162.03 (*s*, C=O). FAB-MS (NOBA; pos.): 677 (38, $[M_1+2H]^+$); 676 (50, $[M_1+H]^+$), 675 (77, $[M_2+2H]^+$), 674 (95, $[M_2+H]^+$), 663 (25), 618 (23, $[M_1-(t\text{-Bu})+H]^+$), 616 (23, $[M_2-(t\text{-Bu})+H]^+$), 573 (35), 572 (30), 571 (50), 561 (20), 515 (70), 513 (63), 448 (21), 447 (62), 446 (23), 445 (66), 389 (55), 387 (47), 383 (25), 369 (25), 365 (29), 341 (25), 339 (32), 337 (24), 335 (21), 329 (23), 327 (32), 326 (20), 325 (50), 323 (20), 319 (29), 317 (35), 316 (29), 315 (34), 313 (22), 230 ($[MeC_6H_4CONHC_4H_3NO_2+H^+]$), 190, 189, 136, 135.

*1-{3′-{{[(*tert*-Butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-6′*-O-*(triphenylmethyl)-β*-D-erythro-*hexofuranosyl}thymine* (**20**). Compound **11** (300 mg, 590 µmol) was co-evaporated 3 × with pyridine. Tetrabutylammonium perchlorate (202 mg, 590 µmol), 2,4,6-collidine (=2,4,6-trimethylpyridine; 156 µl, 1.18 mmol), and **11** (300 mg, 590 µmol) were dissolved in CH_2Cl_2 (10 ml) at r.t., and chlorotriphenylmethane (247 mg, 885 µmol) in CH_2Cl_2 (5 ml) was added dropwise. The reaction was terminated after 5 h with MeOH (3 ml). The mixture was stirred for another 10 min, filtered through a layer of silica gel, and evaporated. FC (silica gel, Et_2O) yielded **20** (417 mg, 94%). Pale yellow foam. IR ($CHCl_3$): 3060, 3020, 3000, 2950, 2930, 2860, 1750–1640, 1600, 1490, 1470, 1450, 1430, 1390, 1360, 1310, 1270, 1110, 1090, 1070, 1000, 980, 940, 890, 825. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.07 (*s*, ^{t}Bu); 1.78–1.87 (*m*, H–C(3′)); 1.88, 1.89 (2*s*, Me–C(5)); 1.92–1.99 (*m*, 1 H–C(5′)); 2.03–2.06 (*m*, 1 H–C(5′)); 2.04–2.14 (*m*, 1 H–C(2′)); 2.26–2.40 (*m*, 1 H–C(2′)); 3.25 (*t*, *J* = 6, 2 H–C(6′)); 3.64 (*d*, *J* = 5, CH_2–C(3′)); 4.05 (*dt*, *J* = 3, 8, H–C(4′)); 5.99 (*dd*, *J* = 5, 6.5, H–C(1′)); 7.10, 7.11 (2*s*, H–C(6)); 7.18–7.31 (*m*, 9 H, Tr); 7.33–7.38 (*m*, 4 H, Ph_2Si); 7.40–7.45 (*m*, 8 H, Tr, Ph_2Si); 7.62–7.64 (*m*, 4 H, Ph_2Si); 8.38 (br., NH). ^{13}C-NMR ($CDCl_3$, 100 MHz): 12.73 (*q*, *Me*–C(5)); 19.24 (*s*, Me_3C); 26.89 (*q*, Me_3C); 35.49 (2*t*, C(2′), C(5′)); 45.18 (*d*, C(3′)); 60.79 (*t*, CH_2–C(3′)); 63.65 (*t*, C(6′)); 80.17 (*d*, C(4′)); 85.05 (*d*, C(1′)); 86.79 (*s*, Tr); 110.40 (*s*, C(5)); 126.98 (*d*, Tr); 127.78, 129.84 (*d*, Ph_2Si); 128.63 (*d*, Tr); 129.89 (*d*, Ph_2Si); 133.03, 133.06 (2*s*, Ph_2Si); 135.24 (*d*, C(6)); 135.57, 135.58 (2*d*, Ph_2Si); 144.17 (*s*, Tr); 150.04 (*s*, C(2)); 163.56 (*s*, C(4)). FAB-MS (NOBA; pos.): 750 ($[M-1]^+$); 673, 605, 516, 307 (7), 259 (11), 257 (7), 255 (8), 254 (7), 253 (10), 252 (12), 245 (17), 244 (83), 243 (100), 242 (22), 241 (39), 240 (12), 239 (42), 229 (15), 228 (38), 227 (13), 226 (16), 216 (10),

215 (36), 213 (11), 203 (10), 202 (20), 200 (15), 199 (47), 198 (17), 197 (59), 195 (11), 189 (17), 183 (25), 182 (10), 181 (41), 178 (15), 167 (21), 166 (38), 165 (86), 163 (10), 152 (13), 137 (10), 135 (27), 105 (11). Anal. calc. for $C_{47}H_{50}N_2O_5Si$: C 75.17, H 6.71, N 3.73; found: C 75.12, H 6.99, N 3.67.

*1-{6′-*O*-Benzoyl-3′-{{[(*tert*-butyl)diphenylsilyl]oxy}methyl}-2′,3′,5′-trideoxy-β-*D*-*erythro*-hexofuranosyl}thymine* (**21**). Compound **11** (259 mg, 491 μmol) was co-evaporated 3 × with pyridine and suspended in pyridine (30 ml). DMAP (2 mg) was added and the mixture cooled to 0°. Benzoyl chloride (91.3 μl, 786 μmol) was slowly added dropwise within 10 min. The clear soln. was allowed to warm to r.t., stirred for 5 h, and cooled again to 0°. Sat. $NaHCO_3$ soln. (20 ml) was added slowly to terminate the reaction. The soln. was evaporated to *ca.* 10 ml, CH_2Cl_2 (150 ml) and deionized H_2O (20 ml) were added, and the org. phase was separated. The aq. phase was extracted with CH_2Cl_2 (2 × 50 ml, 2 × 25 ml), the combined org. phase washed with 5% HCl soln. (2 × 15 ml), sat. $NaHCO_3$ soln. (15 ml), and brine (20 ml) and evaporated and the residue submitted to FC (silica gel, Et_2O): **21** (250 mg, 83%). Colorless foam. UV (MeCN): 220 (17800), 265 (14500). ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.05 (*s*, ^{t}Bu); 1.93 (2*s*, Me–C(5)); 1.99–2.11 (*m*, 2 H–C(5′)); 2.14–2.39 (*m*, H–C(3′), 2 H–C(2′)); 3.68–3.72 (*m*, CH_2–C(3′)); 4.10 (*dt*, *J* = 3.0, 8.5, H–C(4′)); 4.38–4.47 (*m*, 1 H–C(6′)); 4.53–4.61 (*m*, 1 H–C(6′)); 6.06 (*dd*, *J* = 4.4, 6.8, H–C(1′)); 7.22 (2*s*, H–C(6)); 7.34–7.46 (*m*, 2 H of Bz, 6 H of Ph_2Si); 7.52–7.58 (*m*, 1 H, Bz); 7.61–7.64 (*m*, 4 H, Ph_2Si); 8.01–8.04 (*m*, 2 H, Bz); 8.99 (br., NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 12.63 (*q*, Me–C(5)); 19.16 (*s*, Me_3C); 26.77 (*q*, Me_3C); 34.07 (*t*, C(5′)); 35.02 (*t*, C(2′)); 45.14 (*d*, C(3′)); 61.99 (*t*, C(6′)); 63.42 (*t*, CH_2–C(3′)); 79.77 (*d*, C(4′)); 85.12 (*d*, C(1′)); 110.76 (*s*, C(5)); 127.81 (*d*, Ph_2Si); 128.33, 129.41 (2*d*, Bz); 129.86 (*d*, Ph_2Si); 130.10 (*s*, Bz); 132.85 (*s*, Ph_2Si); 132.97 (*d*, Bz); 135.17 (*d*, C(6)); 135.48 (*d*, Ph_2Si); 150.21 (*d*, C(2)); 163.74 (*s*, C(4)); 166.41 (*s*, C=O). ESI-MS (pos.): 1246.6 ([2*M* + Na]$^+$), 635.2 ([*M* + Na]$^+$), 612.7 ([*M* + H]$^+$), 486.9 ([*M* – (thymine) · H + H]$^+$).

*1-[2′,3′,5′-Trideoxy-6′-*O*-(triphenylmethyl)-β-*D*-*erythro*-hexofuranosyl]thymine* (**22a**). To a soln. of **20** (1.0 g, 1.33 mmol) in THF (20 ml) at r.t., 1M Bu_4NF in THF (4 ml, 4 mmol) was added, and the soln. was stirred for 3 h. The reaction was terminated with Me_3SiOMe (0.46 ml, 3.3 mmol). The mixture was filtered through a layer of silica gel, the solvent evaporated, and the residue chromatographed (silica gel, Et_2O/AcOEt 1:1, AcOEt): **22a** (649 mg, 95%). Colorless foam. M.p. 77–78°. $[\alpha]_D^{20} = +49.1$ (*c* = 1.5, $CHCl_3$). IR ($CHCl_3$): 3080, 3060, 3010, 2930, 2880, 1750–1630, 1600, 1490, 1470, 1450, 1405, 1390, 1375, 1320, 1270, 1180, 1115, 1090, 1070, 1040, 1020, 1000, 900, 810, 660, 650, 630. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.89 (2*s*, Me–C(5)); 1.93–2.08 (*m*, H–C(3′), 2 H–C(5′)); 2.18 (*qt*, *J* = 3, 8, 1 H–C(2′)); 2.26–2.33 (*m*, 1 H–C(2′)); 3.30 (*t*, *J* = 6, 2 H–C(6′)); 3.63 (*d*, *J* = 5, CH_2–C(3′)); 4.00 (*dt*, *J* = 4, 8, H–C(4′)); 5.99 (*dd*, *J* = 5, 6.5, H–C(1′)); 7.14, 7.15 (2*s*, H–C(6)); 7.21–7.32 (*m*, 9 H, Tr); 7.42–7.44 (*m*, 6 H, Tr); 8.68 (br., NH). ^{13}C-NMR ($CDCl_3$, 100 MHz): 12.71 (*q*, *Me*–C(5)); 35.47 (*t*, C(5′)); 35.67 (*t*, C(2′)); 45.15 (*d*, C(3′)); 60.78 (*t*, CH_2–C(3′)); 62.99 (*t*, C(6′)); 80.22 (*d*, C(4′)); 85.02 (*d*, C(1′)); 86.97 (*s*, Tr); 110.59 (*s*, C(5)); 127.08, 127.85, 128.61 (3*d*, Tr); 135.18 (*d*, C(6)); 144.03 (*s*, Tr); 150.20 (*s*, C(2)); 163.66 (*s*, C(4)). FAB-MS (NOBA; pos.): 535 ([*M* + Na]$^+$), 289 (1), 265, 259 (2), 244 (25), 243 (100), 242 (5), 241 (8), 239 (9), 228 (7), 215 (7), 202 (5), 166 (7), 165 (41), 152 (5), 133 (5), 127 (6), 115 (5), 105 (7), 91 (5), 89 (6), 77 (11), 63 (5). Anal. calc. for $C_{31}H_{32}N_2O_5$: C 72.64, H 6.29, N 5.46; found: C 72.47, H 6.41, N 5.39.

*1-{6′-*O*-Benzoyl-2′,3′,5′-trideoxy-β-*D*-*erythro*-hexofuranosyl}thymine* (**22b**). As described for **22a**, with **21** (240 mg, 392 μmol), THF (10 ml), and 1M Bu_4NF in THF (1.18 ml, 1.18 mmol) for 2.5 h (termination with Me_3SiOMe (0.14 ml, 0.98 mmol)). Chromatography (silica gel, AcOEt) gave **22b** (138 mg, 94%). Colorless amorphous solid. UV (MeCN): 221 (17300), 265 (16400). ^{1}H-NMR ((D$_6$)DMSO, 300 MHz): 1.80 (*s*, Me–C(5)); 2.00–2.33 (*m*, 2 H–C(5′), H–C(3′), 2 H–C(2′)); 3.46–3.53 (*m*, CH_2–C(3′)); 3.90 (*dt*, *J* = 3.8, 7.6, H–C(4′)); 4.31–4.48 (*m*, 2 H–C(6′)); 4.81 (*t*, *J* = 5.0, OH); 6.00 (*dd*, *J* = 5.6, 6.3, H–C(1′)); 7.46 (2*s*, H–C(6)); 7.49–7.55 (*m*, 2 H, Bz); 7.63–7.68 (*m*, 1 H, Bz); 7.95–7.98 (*m*, 2 H, Bz). ^{13}C-NMR ((D$_6$)DMSO, 75 MHz): 12.29 (*q*, *Me*–C(5)); 33.67, 33.95 (2*t*, C(5′), C(2′)); 45.06 (*d*, C(3′)); 61.57 (*t*, C(6′)); 62.43 (*t*, CH_2–C(3′)); 79.34 (*d*, C(4′)); 83.91 (*d*, C(1′)); 109.84 (*s*, C(5)); 128.87, 129.28 (*d*, Bz); 130.00 (*s*, Bz); 133.45 (*d*, Bz); 136.17 (*d*, C(6)); 150.60 (*d*, C(2)); 163.92 (*s*, C(4)); 165.90 (*s*, C=O). FAB-MS (NOBA; pos.): 375 (5, [*M* + H]$^+$), 249 (23), 165 (11), 147 (22), 123 (38), 121 (29), 111 (28), 109 (55), 107 (52), 105 (41), 97 (60), 95 (87), 93 (35), 91 (48), 85 (31), 83 (78), 81 (94).

*1-{3′-[(Acetylthio)methyl]-2′,3′,5-trideoxy-6′-*O*-(triphenylmethyl)-β-*D*-*erythro*-hexofuranosyl}thymine* (**23a**). PPh_3 (925 mg, 1.8 mmol) was dried under high vacuum at 45° for 3 h and then dissolved in THF (10 ml). The soln. was cooled to 0°, and diisopropyl azodicarboxylate (DIAD; 0.78 ml, 4.0 mmol) in THF (2 ml) was added dropwise. The soln. was stirred for 30 min at 0°. A white precipitate was formed after 10 min. Thioacetic acid (0.29 ml, 4.0 mmol) and **22a** (256 mg, 0.5 mmol; dried overnight under high vacuum at r.t.) were dissolved separately in THF (each 2 ml) and alternately added dropwise, beginning with thioacetic acid. The mixture was allowed to warm to r.t., stirred for 2 h, and quenched with Et_3N/MeOH 2:1 (2 ml). The soln. was evaporated

and chromatographed (silica gel, AcOEt/petroleum ether 1:1): **23a** (960 mg, 94%). Colorless foam. M.p. 67–68°. $[\alpha]_D^{20} = +63.1$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3060, 3020, 2930, 2890, 1750–1630, 1600, 1490, 1470, 1450, 1410, 1385, 1350, 1320, 1310, 1180, 1140, 1115, 1070, 1030, 1000, 980, 965, 900, 695, 630. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.88, 1.89 (2*s*, Me–C(5)); 2.03–2.08 (*m*, H–C(3′)); 2.09–2.20 (*m*, 1 H–C(2′), 2 H–C(5′)); 2.35 (*s*, MeCO); 2.32–2.38 (*m*, 1 H–C(2′)); 2.81–2.88 (*m*, 1 H, CH_2–C(3′)); 3.03–3.09 (*m*, 1 H, CH_2–C(3′)); 3.30 (*t*, $J = 6$, 2 H–C(6′)); 3.83–3.89 (*m*, H–C(4′)); 5.96, 6.00 (2 '*d*', H–C(1′)); 7.08, 7.09 (2*s*, H–C(6)); 7.18–7.32 (*m*, 9 H, Tr); 7.42–7.46 (*m*, 6 H, Tr); 8.55 (br., NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 12.69 (*q*, *Me*–C(5)); 30.15 (*t*, C(5′)); 30.59 (*q*, *Me*CO); 34.75 (*t*, C(2′)); 38.23 (*t*, *C*H_2–C(3′)); 42.83 (*d*, C(3′)); 60.57 (*t*, C(6′)); 81.93 (*d*, C(4′)); 84.78 (*d*, C(1′)); 86.92 (*s*, Tr); 110.55 (*s*, C(5)); 127.04, 128.83, 128.22, 128.64 (4*d*, Tr); 135.05 (*d*, C(6)); 144.08 (*s*, Tr); 150.03 (*s*, C(2)); 163.51 (*s*, C(4)); 194.81 (*s*, Me*C*O). FAB-MS (NOBA; pos.): 593 ($[M + Na]^+$), 571 ($[M + 1]^+$), 447, 399 (4), 245 (5), 244 (35), 243 (100), 166 (5), 165 (16), 155 (7), 154 (22), 152 (4), 149 (4), 139 (6), 138 (10), 137 (17), 136 (19), 127 (10), 125 (4), 123 (4), 121 (4), 120 (4), 115 (4), 109 (4), 107 (9), 105 (8), 97 (4), 95 (6), 91 (8), 90 (5), 89 (7), 83 (5), 81 (7), 79 (5), 78 (4), 77 (10), 71 (4), 69 (9), 67 (5), 57 (10). Anal. calc. for $C_{33}H_{34}N_2O_5S$: C 69.45, H 6.00, N 4.91; found: C 69.59, H 6.18, N 4.84.

1-[3′-[(Acetylthio)methyl]-6′-O-*benzoyl-2′,3′,5′-trideoxy-β-*D-erythro-*hexofuranosyl]thymine* (**23b**). PPh_3 (282 mg, 1.07 mmol) was dried under high vacuum at 50° for 1 h and then dissolved in THF (5 ml). The soln. was cooled to 0°, and DIAD (152 µl, 787 µmol) was added dropwise. The soln. was stirred for 30 min at 0°. A white precipitate was formed after 5 min. Thioacetic acid (56 µl, 787 µmol) and **22b** (134 mg, 358 µmol; dried overnight under high vacuum at r.t.) were dissolved/suspended separately in THF (each 1 ml) and alternately added dropwise, beginning with thioacetic acid (**22b** was added in a suspension, because it could not be dissolved in an aprotic solvent). The mixture was allowed to warm to r.t., stirred for 3 h, quenched with Et_3N/MeOH 2:1 (2 ml) and then evaporated. The crude product was chromatographed (silica gel, AcOEt/petroleum ether 1:1): **23b** (139 mg, 90%). Colorless foam. UV (MeCN): 225 (14100), 266 (9800). ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.93 (*s*, Me–C(5)); 2.03–2.15 (*m*, 1 H–C(5′)); 2.18–2.28 (*m*, 1 H–C(5′), H–C(3′)); 2.29–2.40 (*m*, 2 H–C(2′)); 2.33 (*s*, MeCO); 2.94 (*dd*, $J = 6.6$, 13.7, 1 H, CH_2–C(3′)); 3.08 (*dd*, $J = 5.1$, 13.7, 1 H, CH_2–C(3′)); 3.85 (*dt*, $J =$ 3.0, 8.5, H–C(4′)); 4.41–4.46 (*m*, 1 H–C(6′)); 4.56–4.64 (*m*, 1 H, H–C(6′)); 6.05 ('*t*', $J = 5.2$, H–C(1′)); 7.20 (2*s*, H–C(6)); 7.42–7.47 (*m*, 2 H, Bz); 7.55–7.60 (*m*, 1 H, Bz); 8.03–8.05 (*m*, 2 H, Bz); 9.51 (br., NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 12.59 (*q*, *Me*–C(5)); 29.98 (*t*, *C*H_2–C(3′)); 30.48 (*q*, *Me*CO); 33.33 (*t*, C(5′)); 37.92 (*t*, C(2′)); 42.76 (*d*, C(3′)); 61.77 (*t*, C(6′)); 81.24 (*d*, C(4′)); 84.88 (*d*, C(1′)); 110.87 (*s*, C(5)); 128.32, 129.49 (2*d*, Bz); 130.00 (*s*, Bz); 132.99 (*d*, Bz); 135.03 (*d*, C(6)); 150.31 (*d*, C(2)); 163.87 (*s*, C(4)); 166.35 (*s*, Ph*C*O); 194.83 (*s*, Me*C*O). FAB-MS (NOBA; pos.): 433 (6, M^+), 289 (3), 280 (27), 279 (100), 247 (11), 201 (9), 127 (16), 125 (10), 124 (3), 108 (4), 107 (10), 106 (4), 105 (26), 95 (3), 91 (6), 90 (5).

1-[2′,3′,5′-Trideoxy-3′-(mercaptomethyl)-6′-O-*(triphenylmethyl)-β-*D-erythro-*hexofuranosyl]thymine* (**24a**). *Method 1:* To a soln. of $NaBH_4$ (77 mg, 2.0 mmol) in degassed MeOH (5 ml; 1 h Ar), a soln. of NaOMe (30 mg) in degassed MeOH (1 ml) was added, and the soln. was cooled to 0°. A soln. of **23a** (464 mg, 813 µmol) in degassed MeOH (15 ml; 1 h Ar) was slowly added dropwise. The mixture was allowed to warm to r.t., stirred for 4 h, and cooled again to 0°. AcOH was added until pH 5 was reached. AcOEt (20 ml) was added and the soln. filtered through alox *B* as well as silica gel. The solvent was evaporated and the residue dried under high vacuum: **24a** (417 mg, 97%). Colorless foam.

Method 2: Through a soln. of **23a** (325 mg, 566 µmol) in degassed MeOH (10 ml; 1 h Ar) cooled to 0° ammonia was bubbled for 15 min, and stirring was continued for 2 h. The mixture was carefully evaporated at a water-bath temperature of 0°. The acetamide was removed under high vacuum at r.t. overnight: **24a** (300 mg, quant.). Colorless foam. $[\alpha]_D^{20} = +48.88$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 3090, 3060, 3030, 3005, 2960, 2930, 2880, 1760–1630, 1600, 1490, 1470, 1450, 1365, 1320, 1260, 1180, 1170, 1115, 1090, 1075, 1030, 1000, 900, 705, 650, 630. ^{1}H-NMR ($CDCl_3$, 400 MHz): 1.36 (*t*, $J = 8$, SH); 1.90 (2*s*, Me–C(5)); 2.00–2.03 (*m*, H–C(3′)); 2.11–2.20 (*m*, 2 H–C(5′)); 2.22–2.30 (*m*, 1 H–C(2′)); 2.32–2.40 (*m*, 1 H–C(2′)); 2.44–2.52 (*m*, 1 H, CH_2–C(3′)); 2.57–2.72 (*m*, 1 H, CH_2–C(3′)); 3.30 (*t*, $J = 6$, 2 H–C(6′)); 3.91 (*dt*, $J = 4.5$, 8, H–C(4′)); 6.00 (*dd*, $J = 4$, 7, H–C(1′)); 7.11 (2*s*, H–C(6)); 7.22–7.32 (*m*, 9 H, Tr); 7.42–7.51 (*m*, 6 H, Tr); 8.40 (br., NH). ^{13}C-NMR ($CDCl_3$, 100 MHz): 12.73 (*q*, *Me*–C(5)); 26.11 (*t*, C(5′)); 34.97 (*t*, C(2′)); 37.94 (*t*, *C*H_2–C(3′)); 45.88 (*d*, C(3′)); 60.53 (*t*, C(6′)); 81.55 (*d*, C(4′)); 84.69 (*d*, C(1′)); 86.95 (*s*, Tr); 110.64 (*s*, C(5)); 127.10, 127.86, 128.61 (3*d*, Tr); 136.06 (*d*, C(6)); 144.02 (*s*, Tr); 150.04 (*s*, C(2)); 163.46 (*s*, C(4)). FAB-MS (NOBA; pos.): 535, 505, 461, 429, 415, 401, 327 (5), 244 (24), 243 (100), 166 (9), 165 (42), 154 (9), 147 (31), 137 (10), 136 (26), 127 (14), 115 (10), 107 (12), 106 (9), 105 (18), 95 (9), 91 (26), 90 (16), 89 (13), 85 (9), 81 (11), 79 (11), 77 (22), 75 (12), 73 (81), 69 (13), 67 (11), 57 (13).

1-[6′-O-*Benzoyl-2′,3′,5′-trideoxy-3′-(mercaptomethyl)-β-*D-erythro-*hexofuranosyl]thymine* (**24b**). As described for **24a** (*Method 2*), with **23b** (136 mg, 314 µmol), MeOH (5 ml) and ammonia (15 min and 1.5 h).

FC (silica gel, AcOEt) yielded **24b** (123 mg, quant.). Colorless foam. UV (MeCN): 227 (17500), 266 (10100). ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.44 (*t*, *J* = 8.2, SH); 1.93 (2*s*, Me–C(5)); 2.03–2.38 (*m*, 2 H–C(5′), H–C(3′), 2 H–C(2′)); 2.55–2.65 (*m*, 1 H, CH_2–C(3′)); 2.67–2.77 (*m*, 1 H, CH_2–C(3′)); 3.90–3.98 (*m*, H–C(4′)); 4.41–4.50 (*m*, 1 H–C(6′)); 4.55–4.64 (*m*, 1 H–C(6′)); 6.04–6.08 (*m*, H–C(1′)); 7.23 (2*s*, H–C(6)); 7.39–7.47 (*t*, 2 H, Bz); 7.51–7.60 (*t*, 1 H, Bz); 7.99–8.06 (*d*, 2 H, Bz); 9.55 (br., NH). ^{13}C-NMR ($CDCl_3$, 75 MHz): 12.63 (*q*, Me–C(5)); 26.02 (*t*, CH_2–C(3′)); 33.63 (*t*, C(5′)); 37.66 (*t*, C(2′)); 45.89 (*d*, C(3′)); 61.79 (*t*, C(6′)); 81.05 (*d*, C(4′)); 84.86 (*d*, C(1′)); 110.98 (*s*, C(5)); 128.39, 129.48 (2*d*, Bz); 129.93 (*s*, Bz); 133.08 (*d*, Bz); 135.03 (*d*, C(6)); 150.32 (*d*, C(2)); 163.82 (*s*, C(4)); 166.38 (*s*, Ph*C*O).

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