Novel Nucleoside Analogues with Fluorophores Replacing the DNA Base

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Dedicated to Prof. Dr. *Frank Seela* on the occasion of his 60th birthday

We describe the preparation and fluorescence properties of a set of new nucleosides in which a known hydrocarbon or oligothiophene fluorophore replaces the DNA base at C(1) of the deoxyribose moiety (see **3a**–**f**). These compounds are potentially useful as probes in the study of the structure and dynamics of nucleic acids and their complexes with proteins. In addition, they may find use as fluorescent labels for nucleic-acid-based biomedical diagnostics methods. The fluorophores conjugated to deoxyribose at C(1) in the α-D-form include terphenyl, stilbene, terthiophene, benzoterthiophene, and pyrene. Also included is a non-fluorescent spacer in which cyclohexene replaces the DNA base. The nucleosides are derived from brominated fluorophore precursors and *Hoffer*'s 2-deoxy-3,5-di-*O*-(*p*-toluoyl)-D-ribofuranosyl chloride. The emission maxima of the free nucleosides range from 345 to 536 nm. Also described are the 5′-(dimethoxytrityl) 3′-*O*-phosphoramidite derivatives **5a**–**f**, suitable for incorporation into oligonucleotides by automated synthesizers.

Introduction. – Fluorescence methods are extremely widespread in chemistry and biology. They give useful information on structure, distance, orientation, complexation, and location for biomolecules [1]. In addition, time-resolved methods are increasingly used in measurements of dynamics and kinetics [2]. As a result, many strategies for fluorescence labeling of biomolecules, such as nucleic acids, have been developed [3]. In the case of DNA, one of the most convenient and useful methods for fluorescence labeling is to add a fluorescent moiety during the DNA synthesis itself; this avoids the extra steps required for post-synthesis labeling and purification. The majority of labels commonly used during DNA synthesis are attached to the DNA by tethers that are often 5 to 11 atoms long; these flexible tethers can at times be problematic, since they allow the dye to tumble independently of the DNA and make the location of the dye difficult to determine precisely [4]. There are very few examples of dye conjugates that hold the dye close to the DNA, thus avoiding these problems. Among the known dyes of this class are ethenodeoxyadenosine [5] and 9*H*-purin-2-amine deoxyriboside [6]. These latter two compounds have modified DNA bases that are themselves fluorescent, and they have found much use as probes of enzymatic activities such as DNA synthesis, editing, and repair [7–9].

We have taken a related approach to developing new fluorescent labels for DNA [10]. Rather than modifying an existing DNA base, however, we have simply replaced it by another flat aromatic structure, *i.e.*, by a hydrocarbon rather than by a heterocyclic N-containing base. This substitution is particularly attractive because it creates only a

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small perturbation to the natural DNA structure and allows for close interaction, including possible stacking, with the neighboring DNA helix. There are many known hydrocarbon-based fluorophores, many with high quantum yields and with varied excitation and emission characteristics. Moreover, their lack of functional groups makes them relatively simple to work with in preparing conjugates.

We previously reported early studies on the incorporation of 4-methyl-1*H*-indole, naphthalene, phenanthrene, and pyrene fluorophores at the C(1)-position of 2-deoxy-D-ribose [10][11]. In a similar strategy, *Coleman* and co-workers recently reported the substitution of a coumarin dye at C(1) [12]. Our 4-methyl-1*H*-indole derivative recently found use as a fluorescent reporter of DNA-repair activities [13]. In addition, the derivative with a pyrene moiety at C(1) in the α-D-form has been shown to be useful in DNA diagnostics strategies, where it efficiently forms excimers with neighboring pyrene labels [14]. We demonstrated further that the corresponding pyrene derivative in the β-D-form stabilizes DNA helices markedly (due to its low polarity) [15][16], and that it can be enzymatically incorporated into the DNA helix [17]. Thus, this new nucleic acid labeling strategy is beginning to find useful applications.

In our ongoing studies, we wished to generate a series of new nucleosides with improved fluorescence characteristics, increasing the range of emission wavelengths over those we previously studied. Such compounds might be more generally useful in biophysical and diagnostics experiments. Here we report an expanded set of new fluorescent hydrocarbons and oligothiophenes conjugated to 2-deoxy-D-ribose. These new compounds significantly broaden the range of fluorescence properties available for automated incorporation into DNA.

Results and Discussion. – We have previously described the preparation of *C*-nucleosides of type **3** by cadmium- or zinc-mediated reaction of *Grignard* derivatives of aromatic compounds of type **1** with *Hoffer*'s chlorosugar (= 2-deoxy-3,5-di-*O*-(*p*-toluoyl)-D-ribofuranosyl chloride) (*Scheme 1*) [18][19]. The primary product in this coupling reaction is the 1-coupled product of type **2** in the α-D-form generated with retention of configuration. Although the α-D-orientation is not the same as for natural β-D-nucleosides, α-D-nucleosides are also known to form DNA-like helices [20], and models suggest that they can still interact well with natural bases in neighboring positions. Our approach in this study was to choose a set of known fluorophores for which a bromo derivative **1** was readily available and which had varied absorption and emission characteristics.

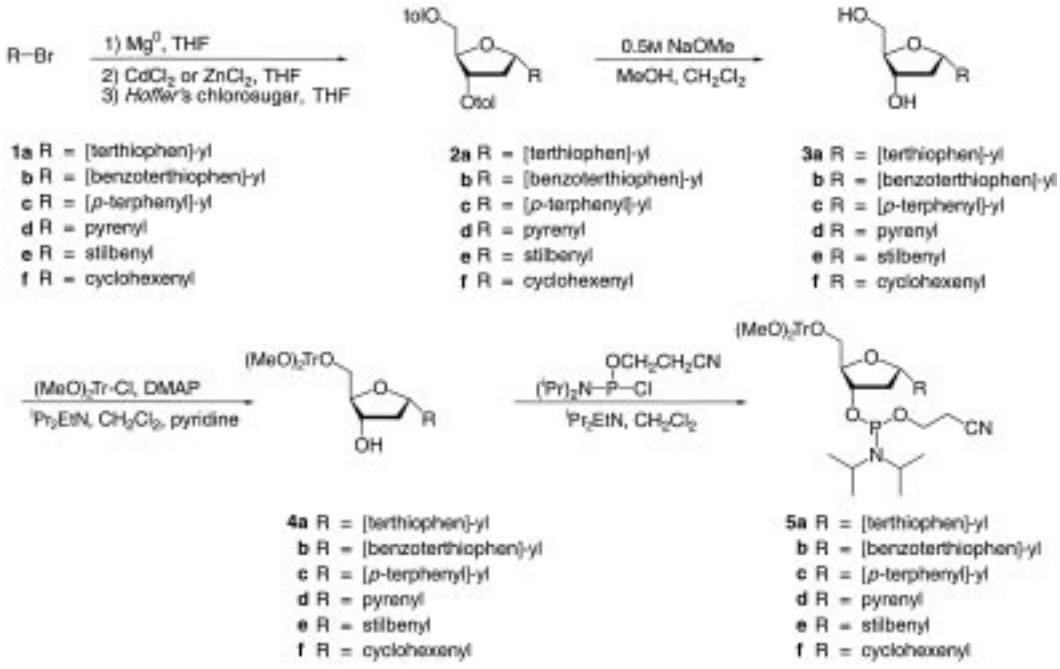
Besides this set of five fluorophores (see **3a**–**e**), we also prepared a *C*-nucleoside **3f** with cyclohexene at the 1-position as a nonfluorescent spacer. Fluorophores are usually quenched by neighboring DNA bases [21], and we observed this to be the case for the pyrene derivative **3d** as well [10]. Thus, we designed the cyclohexene compound to be inserted, if desired, between fluorophores and natural DNA bases to possibly limit any quenching that might occur. Cyclohexene was chosen rather than saturated cyclohexane because the former has sp^2 geometry at the point of attachment, the same as the other analogues and the natural bases.

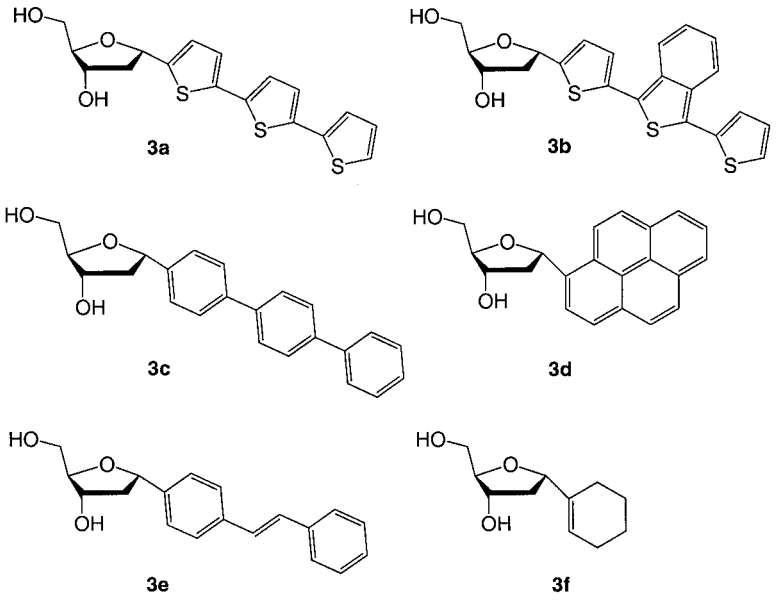
Thus, we purchased 1-bromopyrene (**1d**) and prepared bromobenzoterthiophene **1b** [22], 4-bromo-1,1′:4′,1″ terphenyl (**1c**) [23], 4-bromostilbene (= 4-bromo-1,1′-(ethene-1,2-diyl)bis[benzene]; **1e**) [24], and 1-bromocyclohexene (**1f**) [25] according

to literature procedures. The 5-bromo-2,2′: 4′,2″-terthiophene (**1a**) was prepared from 2-bromothiophene *via* **6** and **7** as shown in *Scheme 2*. Subsequent coupling reactions with *Hoffer*'s chlorosugar [26] were performed generally as described previously, with moderate to modest success, giving yields of 23–55% for the coupled products **2**. The pyrene nucleoside **3d** was also prepared by this approach, as previously described [10]. The toluoyl protecting groups on all the nucleosides **2a**–**f** were then removed to generate the free nucleosides **3a**–**f**. These were examined for their fluorescence characteristics (see below). For future studies, in which these fluorophores are incorporated into DNA, we carried on with the nucleosides **3a**–**f** to prepare the 5′-(dimethoxytrityl)-protected nucleosides **4a**–**f** and then the 3′-phosphoramidites **5a**–**f**.

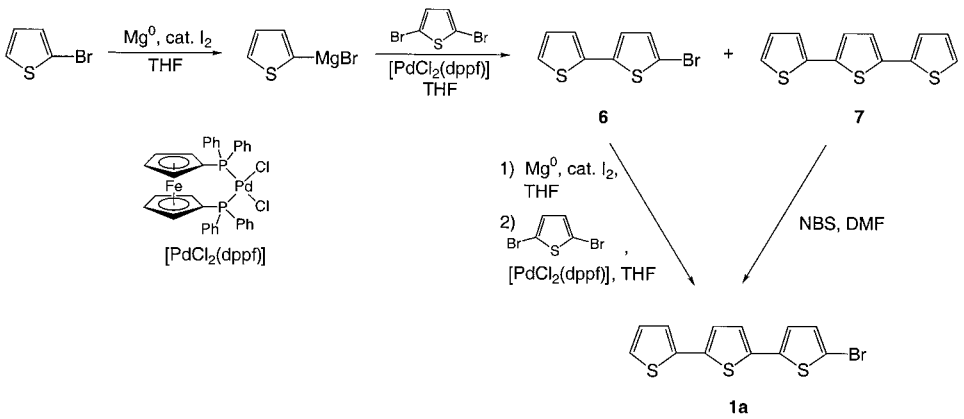
The syntheses proceeded as expected, except in the benzoterthiophene case. During the synthesis of the nucleosides **2b** and **3b**, significant decomposition was observed. To determine whether it was a thermal or a photodecomposition, an NMR sample of the di-*O*-toluoylnucleoside **2b** in $CDCl_3$ was kept exposed to fluorescent room light, and a similar sample was kept wrapped in aluminium foil. ^{1}H-NMR Spectra were measured immediately after preparation of the two samples, and then after 1 day and after 7 days. We found that the spectrum of the aluminium-foil-protected sample remained unchanged (not shown), whereas decomposition of the nucleoside **2b** could be observed in the light-exposed sample after 7 days. Subsequently, we carried out all experiments with the benzoterthiophene derivatives and limited light exposure by covering glassware with aluminium foil. The best success in coupling **1b** with *Hoffer*'s chlorosugar was observed with the debrominated form of **1b**, *i.e.*, direct deprotonation

Scheme 1





Scheme 2



formed the organolithium species which was then exchanged with $CdCl_2$ to give the analogous organocadmium-mediated reaction.

Absorption and emission spectra of 10 μM solutions of the deprotected nucleosides **3a**–**c**,**e** and of the earlier described pyrene nucleoside **3d** [10] were measured in deoxygenated MeOH at room temperature. Excitation spectra were also measured (data not shown) at the emission maxima, and the spectra were identical to the absorption curves shown in the *Figure*. The quantum yields for the five compounds (*Table*) were determined with quinine sulfate and fluorescein as standards. The results show absorption maxima ranging from 285 nm for terphenyl derivative **3c** to 437 nm for

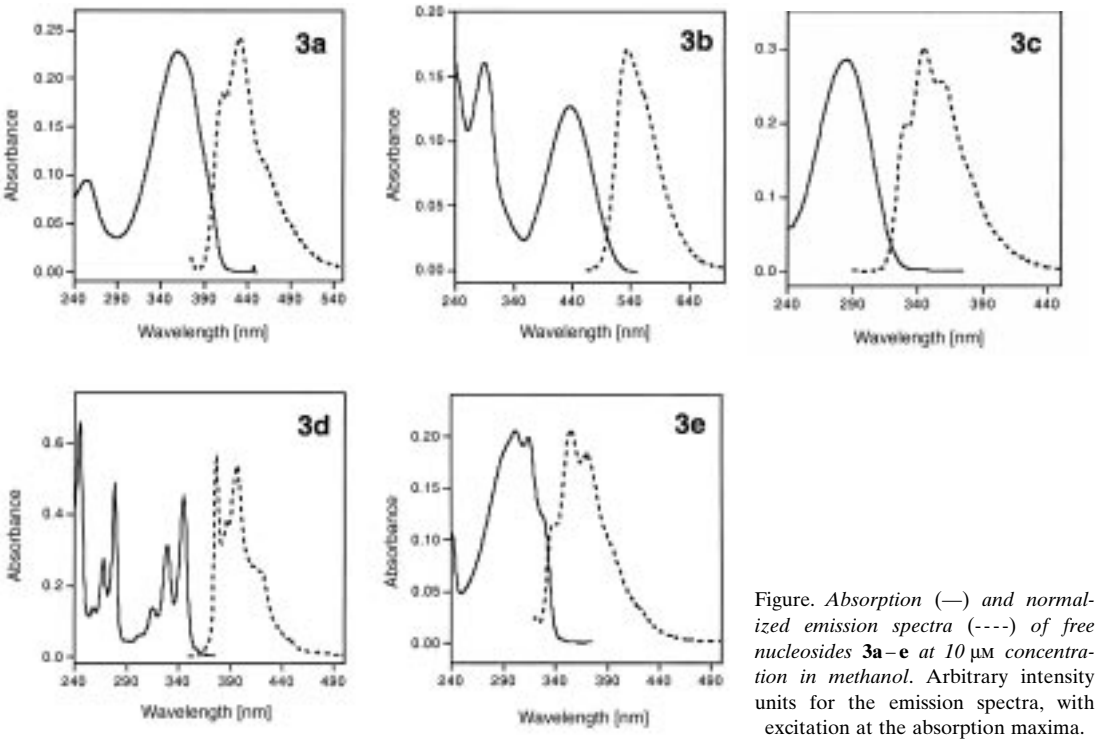


Figure. *Absorption* (—) *and normalized emission spectra* (----) *of free nucleosides* **3a**–**e** *at 10* μM *concentration in methanol*. Arbitrary intensity units for the emission spectra, with excitation at the absorption maxima.

benzoterthiophene derivative **3b**, which appears yellow-orange in solution under incandescent light. Emission maxima range from 345 nm for terphenyl derivative **3c** (a violet-blue fluorophore) to 536 nm for the benzoterthiophene derivative **3b** (which fluoresces bright yellow).

Not surprisingly, there is little difference in the absorbance and fluorescence spectra of the nucleosides **3a**–**e** and the corresponding free fluorophores. The quantum yields of the terthiophene nucleoside **3a** and the free terthiophene **7** are about the same as the reported quantum yield for free terthiophene [27], and the quantum yield of pyrene nucleoside **3d** is similar to that of pyrene-1-butanoic acid. However, the quantum yield we measured is *ca*. 20-fold smaller than the quantum yield reported by *Telser et al.* [28] for pyrenebutanoate. They used a different value for the quantum yield of quinine sulfate (0.70 instead of 0.55) and measured the quantum yield in an aqueous buffer, but those differences do not seem sufficient to explain this difference. The sharpness of the absorption and emission lines for this compound may have caused difficulties in accurately measuring a maximum value. The quantum yield we measured for the stilbene nucleoside **3e** is *ca*. 50% smaller than the quantum yield reported by *Lewis et al*. [29] for a stilbenedicarboxamide at the excitation wavelength of 330 nm, which was determined in a 4:1 aqueous EtOH solution, using a phenanthrene standard. The quantum yields for the benzoterthiophene and terphenyl nucleosides **3b** and **3c**,

Table 1. *Absorption and Emission Data and Quantum Yields (Φ_f) for Nucleosides* **3a**–**e** *in Methanol*

	Absorption maxima [nm]	Extinction coeff. [M^{-1} cm^{-1}]	Emission maxima [nm]	Φ_f (excitation) [nm]
3a	358	31400	432	0.059 (358)
3b	437	18300	536	0.67 (440)
3c	285	40100	345	0.42 (290)
3d	343	34400	377	0.025 (344)
3e	301	21100	356	0.055 (298)
Pyrene-1-butanoic acid	343	33800	377	0.027 (344)
2,2′:4′,2″-Terthiophene (**7**)[a])	355	29900	431	0.063 (358)[b])

[a]) CH_2Cl_2 solvent. [b]) The reported quantum yield is 0.055 [27].

respectively are high compared with the other nucleosides, but no literature reference could be found for comparison.

We expect that some of these nucleoside analogues will have a range of uses. There are several colors to choose from, which allows for possible multiplex use in diagnostics studies. In addition, some of the free fluorophores incorporated here are known to undergo excimer formation when two are present at high local concentrations. We expect that excimer, exciplex, and other forms of energy transfer might be observed for some of these nucleosides when placed in proximity with one another. Such studies are currently underway.

We thank the *U.S. Army Research Office* for support, and the *Swiss National Science Foundation* for a 'Stipendium für angehende Forschende' to *C.S.* We also thank *Joseph Langenhan* for early work with the cyclohexene derivative.

Experimental Part

General. Solvents used as reaction media were purified and dried by distillation over CaH_2 (pyridine, MeCN, and CH_2Cl_2), Na (THF), or MeONa (MeOH) before use. Chemicals were purchased from *Acros*, *Aldrich*, *Alfa-Aesar*, *Lancaster*, *Fisher*, or *J. T. Baker*. Flash chromatography (FC): silica gel *Merck 60*, 0.040–0.063 mm. ^{1}H-NMR (400 MHz) and ^{13}C-NMR (100 MHz): in $CDCl_3$ unless otherwise stated; *Bruker-Avance-400* spectrometer; chemical shifts in ppm rel. to $SiMe_4$, coupling constants *J* in Hz. High resolution mass spectral analyses (HR-MS) were performed by the University of California-Riverside mass spectrometry facility. EI-MS: *HP 5973* mass selective detector. Abbreviations: DMAP = 4-(dimethylamino)pyridine. $(MeO)_2Tr$ = 4,4′-dimethoxytrityl.

General Procedure A (*G.P. A*). A soln. of the aryl bromide **1** in dry THF was slowly added to Mg turnings in dry THF. To start the *Grignard* reaction, a few drops of 1,2-dibromoethane were added, and the mixture was slightly heated. Afer complete addition of the aryl bromide soln., the mixture was stirred for 2 h at 50°. $CdCl_2$ was then added and the mixture stirred for 2 h under reflux. The mixture was cooled to r.t., and a soln. of 2-deoxy-3,5-di-*O*-(*p*-toluoyl)-D-ribofuranosyl chloride [22] in THF was added. After stirring for 16 h at r.t., the solvent was evaporated and the residue suspended in CH_2Cl_2 and washed twice with 10% NH_4Cl soln. The aq. layers were extracted with CH_2Cl_2 and the org. layers dried ($MgSO_4$) and evaporated. Purification by FC (hexanes/AcOEt 6:1) gave the pure α-D-anomers **2** (the β-D-anomers as minor products were not isolated).

General Procedure B (*G.P. B*). Freshly prepared 0.5M NaOMe in MeOH was added to a soln. of the protected nucleoside **2** in MeOH/CH_2Cl_2 1:1. After stirring for 4 h at r.t., crystalline NH_4Cl was added, and the solvent was evaporated. Purification by FC (AcOEt) gave the pure deprotected nucleosides.

General Procedure C (*G.P. C*). The deprotected nucleoside **3** was co-evaporated twice with pyridine and then dissolved in pyridine/CH_2Cl_2. Then, 4,4′-dimethoxytrityl chloride ($(MeO)_2$Tr-Cl), ^{i}Pr$_2$EtN, and a catalytic amount of 4-(dimethylamino)pyridine (DMAP) were added, and the mixture was stirred for 4–8 h at r.t. Then

the solvents were evaporated, and the residue was purified by FC (hexanes/AcOEt 4:1 → 1.5:1, preequilibrated with hexanes containing 5% Et_3N): **4**.

General Procedure D (*G.P. D*). To a soln. of the $(MeO)_2$Tr-protected nucleoside **4** in CH_2Cl_2, 2-cyanoethyl diisopropylphosphoramidochloridite and $^iPr_2EtN$ were added, and the mixture was stirred for 5 h at r.t. The solvent was evaporated and the residue purified by FC (hexanes/AcOEt 3:1, preequilibrated with hexanes/AcOEt 3:1 containing 5% Et_3N): **5**.

1. *Terthiophene Nucleoside. 5-Bromo-2,2′-bithiophene* (**6**). A soln. of 2-bromothiophene (4.967 g, 24.92 mmol) in dry THF (5 ml) was added dropwise to Mg turnings (752 mg, 30.94 mmol) and a small I_2 crystal in dry THF (25 ml). When *ca.* 1 ml of the bromothiophene soln. was added, the reaction started, and the mixture was kept under reflux. After the addition, the mixture was stirred for 1 h under reflux. The mixture was then transferred with a syringe to an addition funnel and added slowly during 3 h to an ice-cooled mixture of 2,5-dibromothiophene (8.206 g, 33.91 mmol) and [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) ([$PdCl_2$(dppf)$_2$]; 250 mg, 0.306 mmol; 1:1 complex with CH_2Cl_2 in dry THF (50 ml). This mixture was stirred for 2 h at 0° and for 16 h at r.t. The solvent was evaporated and the residue suspended in AcOEt and washed with sat. $NaHCO_3$ soln. and brine. The aq. layers were extracted with AcOEt and the org. layers dried ($MgSO_4$) and evaporated. Purification by FC (hexanes) gave 4.229 g (57%) of **6** and 1.216 g (16%) of *2,2′:5′,2″-terthiophene* (**7**) as yellow solids.

Data of **6**: ^{1}H-NMR: 7.22 (*dd*, *J* = 5.2, 0.8, 1 H); 7.11 (*dd*, *J* = 3.6, 0.8, 1 H); 7.00 (*dd*, *J* = 5.2, 3.6, 1 H); 6.96 (*d*, *J* = 3.9, 1 H); 6.91 (*d*, *J* = 3.9, 1 H). ^{13}C-NMR: 138.9, 136.4 (2*s*); 130.6, 127.8, 124.8 (3*d*); 124.3 (*s*); 124.0, 123.8 (2*d*). EI-MS: 246 (100, M^+ (^{81}Br)), 244 (88, M^+ (^{79}Br)), 165 (39), 121 (53).

5-Bromo-2,2′:5′,2″-terthiophene [23] (**1a**). *From* **6**: A soln. of **6** (3.052 g, 12.45 mmol) in dry THF (20 ml) was added dropwise to Mg turnings (332 mg, 13.66 mmol) and a small I_2 crystal in dry THF (10 ml). To start the *Grignard* reaction, the mixture had to be heated under reflux. After the addition, the mixture was stirred for 2 h under reflux. Then it was cooled to r.t., transferred with a syringe to an addition funnel, and added dropwise during 2 h to a mixture of 2,5-dibromothiophene (3.031 g, 12.53 mmol) and [$PdCl_2$(dppf)$_2$] (113 mg, 0.138 mmol; 1:1 complex with CH_2Cl_2) in dry THF (50 ml) at −20°. This mixture was stirred for 2 h at −20° and then for 14 h at r.t. The solvent was evaporated and the residue dissolved in CH_2Cl_2 and washed with 5% HCl soln. and brine. The aq. layers were extracted with CH_2Cl_2 and the org. layers dried ($MgSO_4$) and evaporated. Purification by FC (hexane) gave 1.597 g (39%) of **1a**.

From **7**: *N*-Bromosuccinimide (3.147 mg, 17.681 mmol) was added in portions during 5 h to a soln. of **7** (4.315 g, 17.373 mmol) in DMF (10 ml) at −20°. After *ca.* 90 min, a precipitate was formed. After stirring for 14 h at r.t., the mixture was dissolved in CH_2Cl_2 (300 ml) and washed with 1N HCl (2 × 100 ml). The aq. layers were extracted with CH_2Cl_2 and the org. layers dried ($MgSO_4$) and evaporated. Purification by FC (hexanes) gave 5.222 g (92%) of **1a**. Yellow solid. ^{1}H-NMR: 7.23 (*dd*, *J* = 5.2, 1.0, 1 H); 7.17 (*dd*, *J* = 3.6, 1.0, 1 H); 7.07 (*d*, *J* = 3.7, 1 H); 7.02 (*dd*, *J* = 5.3, 3.6, 1 H); 7.01 (*d*, *J* = 3.6, 1 H); 6.98 (*d*, *J* = 3.9, 1 H); 6.91 (*d*, *J* = 3.8, 1 H). ^{13}C-NMR ($CDCl_3$): 138.6; 136.8; 136.7; 135.0; 130.7; 127.9; 124.7; 124.5; 124.3; 123.9; 123.7; 111.0. EI-MS: 328 (100, M^+ (^{81}Br)), 326 (88, M^+, (^{79}Br)), 247 (15), 203 (32).

(1S)-1,4-Anhydro-1,2-dideoxy-([2,2′:5′,2″-terthiophen]-5-yl)-3,5-di-O-(p-*toluoyl)*-D-erythro-*pentitol* (**2a**). According to *G.P. A* with **1a** (1.809 g, 5.528 mmol) in THF (15 ml), Mg turnings (141 mg, 5.802 mmol) in THF (2 ml), $CdCl_2$ (1.021 g, 5.569 mmol) and *Hoffer*'s chlorosugar (2.144 g, 5.514 mmol) in THF (10 ml); 1.816 g (55%) of **2a**. Yellow foam. ^{1}H-NMR: 7.97, 7.83 (2*d*, *J* = 8.2, 4 arom. H); 7.24–7.16 (*m*, 6 arom. H); 7.07 (*d*, *J* = 3.8, 1 arom. H); 7.03–7.01 (*m*, 3 arom. H); 6.91 (*d*, *J* = 3.5, 1 arom. H); 5.62 (*m*, H−C(3)); 5.57 (*dd*, *J* = 7.5, 4.9, H−C(1)); 4.70 (*m*, H−C(4)); 4.58 (*m*, 2 H−C(5)); 2.96, 2.47 (2*m*, 2 H−C(2)); 2.41, 2.39 (2*s*, 2 *Me*C_6H_4). ^{13}C-NMR: 166.3, 166.1 (2 C=O); 145.5, 144.0, 143.9, 137.1, 136.7, 136.1 (6*s*, 7 arom. C); 129.73, 129.71, 129.1, 129.0, 127.9 (5*d*, 9 arom. CH); 127.0, 126.8 (2*s*, 2 arom. C); 125.0, 124.5, 124.3, 124.1, 123.6, 123.2 (6*d*, 6 arom. CH); 82.1, 76.8, 76.2 (3*d*, CH(1), CH(3), CH(4)); 64.4, 40.3 (2*t*, CH(5), CH_2(2)); 21.7 (*q*, *C*$H_3C_6H_4$). HR-MS: 600.1109 ($C_{33}H_{28}O_5S_3^+$, M^+; calc. 600.1099).

(1S)-1,4-Anhydro-1,2-dideoxy-1-([2,2′:5′,2″-terthiophen]-5-yl)-D-erythro-*pentitol* (**3a**). According to *G.P. B* with **2a** (535 mg, 0.891 mmol) and 0.5M NaOMe in MeOH (1 ml, 0.5 mmol) in MeOH/CH_2Cl_2 1:1 (5 ml): 235 mg (72%) of **3a**. Yellow crystals. ^{1}H-NMR: 7.25–6.93 (*m*, 7 arom. H); 5.35 (*m*, H−C(1)); 4.49, 4.10 (2*m*, H−C(3), H−C(4)); 3.86, 3.76 (2*m*, 2 H−C(5)); 2.75, 2.26 (2*m*, 2 H−C(2)). ^{13}C-NMR (D_5)pyridine): 148.2, 137.4, 136.9, 136.3 (4*s*); 128.6, 125.4, 125.1, 124.7, 124.4, 123.9 (6*d*, 7 arom. CH); 87.7, 76.1, 72.8 (3*d*, CH(1), CH(3), CH(4)); 63.0, 44.8 (2*t*, CH(5), CH(2)). HR-MS: 364.0273 ($C_{17}H_{16}O_3S_3^+$, M^+; calc. 364.0262).

(1S)-1,4-Anhydro-1,2-dideoxy-5-O-(4,4′-dimethoxytrityl)-1([2,2′:5′,2″-terthiophen]-5-yl)-D-erythro-*pentitol* (**4a**). According to *G.P.* with *C*, $(MeO)_2$Tr-Cl (269 mg, 0.794 mmol), $^iPr_2EtN$ (115 µl, 0.672 mmol), a spatula tip of DMAP, **3a** (161 mg, 0.442 mmol), and pyridine/CH_2Cl_2 1:1 (8 ml) 6 h. Purification gave 268 mg (91%) of **9a**.

Yellowish foam. ^{1}H-NMR: 7.50 (*d*, *J* = 7.5, 2 arom. H); 7.41–7.19, 7.10–7.04 (2*m*, 13 arom. H); 6.95 (*d*, *J* = 3.5, 1 arom. H); 6.88 (*d*, *J* = 8.8, 4 arom. H); 5.36 (*t*, *J* = 7.0, H–C(1)); 4.45 (*m*, H–C(3)); 4.21 (*m*, H–C(4)); 3.82 (*s*, 2 MeO); 3.38, 3.27 (2*m*, 2 H–C(5)); 2.75, 2.21 (2*m*, 2 H–C(2)). ^{13}C-NMR: 158.5, 145.9, 144.7, 137.1, 136.7, 136.2, 136.1, 135.9 (8*s*, 10 arom. C); 130.0, 128.1, 127.9, 126.9, 125.0, 124.5, 124.3, 124.2, 123.7, 123.3, 113.2 (11*d*, 20 arom. CH); 86.4 (*s*, 1 C); 84.4, 75.9, 74.8 (3*d*, CH(1), CH(3), CH(4)); 64.5 (*t*, CH_2(5)); 55.2 (*q*, 2 MeO); 42.9 (*t*, CH_2(2′)). HR-MS: 689.1430 ($C_{38}H_{34}NaO_5S_3^+$, $[M+Na]^+$; calc. 689.1466).

*(1*S*)-1,4-Anhydro-1,2-dideoxy-5-*O*-(4,4′-dimethoxytrityl)-1-([2,2′:5′,2″-terthiophen]-5-yl)-*D-erythro-*pentitol 3-(2-(Cyanoethyl Diisopropylphosphoramidite)* (**5a**). According to *G.P. D*, with 2-cyanoethyl diisopropylphosphoramidochloridite (172 mg, 0.726 mmol), ^{i}Pr$_2$EtN (350 µl, 2.044 mmol), **4a** (313 mg, 0.469 mmol), and CH_2Cl_2 (5 ml). Purification gave 321 mg (79%) of **5a**. Yellowish foam. ^{1}H-NMR (mixture of 2 diastereoisomers): 7.53–7.50, 7.42–7.17, 7.09–7.01, 6.93–6.91, 6.86–6.82 (5*m*, 20 arom. H); 5.43 (*m*, H–C(1)); 4.57, 4.34 (2*m*, H–C(3), H–C(4)); 3.81, 3.80 (2*s*, 2 MeO); 3.72–3.48, 3.38–3.27, 3.17–3.13 (3*m*, 2 Me$_2$C*H*N), O*CH*$_2$CH$_2$CN, 2 H–C(5)); 2.75 (*m*, 1 H–C(2)); 2.56–2.51 (*m*, OCH$_2$*CH*$_2$CN); 2.37 (*m*, 1 H–C(2)); 1.17–1.03 (*m*, 2 *Me*$_2$CHN). ^{13}C-NMR: 158.4; 146.1; 144.9, 137.1, 136.4, 136.1, 136.0 (7*s*, 10 arom. C); 130.1, 128.2, 127.9, 127.8, 126.7, 124.9, 124.4, 124.3, 124.0, 123.6, 123.2 (11*d*, 16 arom. CH); 117.5 (*s*, CN); 113.1 (*d*, 4 arom. CH); 86.1 (*s*, 1 C); 84.7, 76.3 (2*d*, CH(1), CH(4)); 75.0, 74.8 (2*d*, CH(3)); 63.8 (*t*, CH_2(5)); 58.2, 58.1 (2*t*, O*C*H$_2$CH$_2$CN); 55.2 (*q*, 2 MeO); 43.2, 43.1 (2*d*, 2 Me$_2$*C*HN); 42.4 (*t*, CH_2(2)); 24.6, 24.5, 24.4, 24.3 (4*q*, 2 *Me*$_2$CHN); 20.1, 20.0 (2*t*, OCH$_2$*C*H$_2$CN). HR-MS: 889.2532 ($C_{47}H_{51}N_2NaO_6PS_3^+$, $[M+Na]^+$; calc. 889.2545).

2. *Benzoterthiophene Nucleoside. (1*S*)-1,4-Anhydro-1,2-dideoxy-1-{5-[3-(thiophen-2-yl)benzo[*c*]thiophen-1-yl]thiophen-2-yl}-3,5-di-*O-(p-*toluoyl)-*D-erythro-*pentitol* (**2b**). The reaction was performed in the absence of light (flasks wrapped in Al-foil). To a soln. of 1,3-di(thiophen-2-yl)benzo[*c*]thiophene [22] in THF (40 ml) at −68°, 2.5M BuLi in hexane (1 ml, 2.5 mmol) was slowly added and stirred for 90 min. $CdCl_2$ (281 mg, 1.533 mmol) was added at −68° and the mixture allowed to warm up to r.t. and stirred for 2 h at r.t. A soln. of *Hoffer*'s chlorosugar (831 mg, 2.137 mmol) in THF (20 ml) was added and stirred for 16 h. Then the solvent was evaporated, the residue dissolved in CH_2Cl_2, the soln. washed twice with 10% NH_4Cl soln. The aq. layers were extracted with CH_2Cl_2 and the org. layers dried ($MgSO_4$) and evaporated. Purification by FC (hexane/AcOEt 7:1) gave 678 mg (49%) of **2b** and 231 mg (37%) of recovered unreacted 1,3-di(thiophen-2-yl)benzo[*c*]thiophene. **2b**: ^{1}H-NMR: 8.01–7.85 (*m*, 6 arom. H); 7.41–7.06 (11*m*, 13 arom. H); 5.68–5.64 (*m*, H–C(1), H–C(3)); 4.77, 4.62 (2*m*, H–C(4), 2 H–C(5)); 3.02 (*m*, H–C(2)); 2.45 (*s*, *Me*C$_6$H$_4$); 2.57 (*m*, H–C(2)); 2.44 (*s*, *Me*C$_6$H$_4$); 2.38 (*s*, *Me*C$_6$H$_4$). ^{13}C-NMR: 166.4, 166.1 (2 C=O); 143.9, 143.8, 141.6, 140.6, 140.1, 139.7 (6*s*, arom. C); 129.7, 129.6, 129.1, 129.0, 128.8, 127.5, 127.4, 127.1, 127.0 (10*d*, 19 arom. CH); 126.8 (*s*, arom. C); 126.1 (*d*, 2 arom. CH); 82.2, 80.0, 76.4 (3*d*, CH(1), CH(3), CH(4)); 64.6, 40.3 (2*t*, CH_2(5), CH_2(2)); 21.67, 21.63 (2*q*, 2 *C*H$_3$C$_6$H$_4$). HR-MS: 651.1358 ($C_{37}H_{31}O_5S_3^+$, $[M+H]^+$; calc. 651.1334).

*(1*S*)-1,4-Anhydro-1,2-dideoxy-1-{5-[3-(thiophen-2-yl)benzo[*c*]thiophen-1-yl]thiophen-2-yl}-D-*erythro-*pentitol* (**3b**). According to *G.P. B*, in the absence of light (flasks wrapped in Al-foil), with **2b** (548 mg, 0.842 mmol) and 0.5M NaOMe in MeOH (850 µl, 0.425 mmol) in MeOH/CH_2Cl_2 1:1 (5 ml): 243 mg (70%) of **3b**. Dark yellow solid. ^{1}H-NMR ((D$_8$)THF): 7.97–7.91 (*m*, 2 arom. H); 7.48 (*d*, *J* = 4.9, 1 arom. H); 7.38 (*d*, *J* = 3.2, 1 arom. H); 7.24–7.21, 7.15–7.10, 7.02–7.00 (3*m*, 5 arom. H); 5.28 (*t*, *J* = 7.4, H–C(1)); 4.41, 4.29, 3.90 (3*m*, H–C(3), H–C(4), 2 OH); 3.67–3.55 (*m*, 2 H–C(5)); 2.66, 2.08 (*m*, 2 H–C(2)). ^{13}C-NMR ((D$_8$)THF): 146.8, 133.4, 133.3, 133.1, 132.3 (5*s*, 5 arom. C); 125.9 (*d*, 1 arom. CH); 124.9, 124.0 (2*s*, 2 arom. C); 123.7, 123.5, 123.0, 122.8, 122.7, 122.4, 119.5, 119.3 (8*d*, 8 arom. CH); 84.5, 73.7, 70.1 (3*d*, CH(1), CH(3), CH(4)); 60.3, 42.1 (2*t*, CH_2(5), CH_2(2)).

*(1*S*)-1,4-Anhydro-1,2-dideoxy-5-*O*-(4,4′-dimethoxytrityl)-1-{5-[3-(thiophen-2-yl)benzo[*c*]thiophen-1-yl]thiophen-2-yl}-D-*erythro-*pentitol* (**4b**). According to *G.P. C*, in the absence of light (flasks wrapped in Al-foil), with (MeO)$_2$Tr-Cl (210 mg, 0.620 mmol), ^{i}PrEtN (180 µl, 1.051 mmol), a spatula tip of DMAP, **3b** (104 mg, 0.251 mmol), and pyridine/CH_2Cl_2 1:1 (5 ml), 3 days. Purification gave 94 mg (52%) of **4b**. Dark yellow foam. ^{1}H-NMR: 7.99–7.95 (*m*, 2 arom. H); 7.49–7.15 (*m*, 15 arom. H); 7.06 (*d*, *J* = 3.6, 1 arom. H); 6.87 (*d*, *J* = 8.8, 4 arom. H); 5.42 (*t*, *J* = 7.1, H–C(1)); 4.47, 4.21 (2*m*, H–C(3), H–C(4)); 3.82 (*s*, 2 MeO); 3.46 (*dd*, *J* = 9.5, 4.4, H–C(5)); 4.21 (*dd*, *J* = 9.5, 6.0, H–C(5)); 2.81 (*m*, 1 H–C(2)); 2.31–2.24 (*m*, 1 H–C(2), 1 OH); 2.03 (*d*, *J* = 5.0, 1 OH). ^{13}C-NMR: 158.5, 146.8, 144.7, 135.9, 135.6, 135.3, 135.2, 135.1 (8*s*, 10 arom. C); 130.0, 128.1, 127.9, 126.5 (4*d*, 9 arom. CH); 126.6, 126.4 (2*s*, 2 arom. C); 125.6, 125.5, 125.2, 125.1, 124.8, 121.6, 121.5, 113.2 (8*d*, 13 arom. CH); 86.4 (*s*, 1 C); 84.3, 75.9, 74.9 (3*d*, CH(1), CH(3). CH(4)); 64.5 (*t*, CH_2(5)); 55.2 (*q*, 2 MeO); 42.9 (*t*, CH_2(2)).

*(1*S*)-1,4-Anhydro-1,2-dideoxy-5-*O*-(4,4′-dimethoxytrityl)-1-{5-[3-(thiophen-2-yl)benzo[*c*]thiophen-1-yl]thiophen-2-yl}-D-*erythro-*pentitol 3-(2-cyanoethyl Diisopropylphosphoramidite)* (**5b**). According to *G.P. D*, in the absence of light (flasks wrapped in Al-foil), with 2-cyanoethyl diisopropylphosphoramidochloridite (166 mg,

0.701 mmol), $^{i}Pr_2EtN$ (300 µl, 1.75 mmol), **4b** (318 mg, 0.444 mmol), and CH_2Cl_2 (10 ml). Purification gave 302 mg (74%) of **5b**. Dark yellow foam. ^{1}H-NMR (mixture of 2 diastereoisomers): 7.73–7.67, 7.59–7.25, 6.91–6.87 (3*m*, 26 arom. H); 5.33, 4.65, 4.43 (3*m,* H–C(1), H–C(3), H–C(4)); 3.84, 3.83 (2*s*, 2 MeO); 3.66–3.35, 3.26–3.23 (2*m*, 2 Me_2CHN, OCH_2CH_2CN, 2 H–C(5)); 2.81 (*m*, 1 H–C(2)); 2.50–2.18 (*m*, OCH_2CH_2CN, 1 H–C(2)); 1.20–1.06 (*m*, 2 Me_2CHN). ^{13}C-NMR: 158.4, 144.9, 142.5, 142.2, 140.7, 140.0, 139.9, 139.7, 139.5, 136.1 (10*s*, 10 arom. C); 130.1, 128.8, 128.3, 127.8, 127.5, 127.40, 127.36, 127.31, 127.0, 126.9, 126.7, 126.5, 126.4, (14*d*, 22 arom. CH); 117.6, 117.5 (2*s*, CN); 113.1 (*d*, 4 arom. CH); 86.1 (*s*, 1 C); 84.8, 79.9 (2*d*, CH(1), CH(4)); 75.7, 75.2 (2*d*, CH(3)); 64.3, 64.0 (2*t*, CH_2(5)); 58.3, 58.1 (2*t*, OCH_2CH_2CN); 55.2 (*q*, 2 MeO); 43.2, 43.1 (2*d*, 2 Me_2CHN); 42.5 (*t*, CH_2(2)); 24.5, 24.4, 24.3 (3*q*, 2 Me_2CHN); 20.2, 20.1 (2*t*, OCH_2CH_2CN). HR-MS: 916.2831 ($C_{53}H_{57}N_2NaO_6P^+$, $[M+Na]^+$; calc. 916.2803).

3. *Terphenyl Nucleoside. (1*S*)-1,4-Anhydro-1,2-dideoxy-1-([1,1′:4′,1″-terphenyl]-4-yl)-3,5-di*-O-(p-*toluoyl)*-D-erythro-*pentitol* (**2c**). A soln. of 1,2-dibromoethane (2.3 ml, 26.7 mmol) in THF (50 ml) was slowly added to a mixture of Mg turnings (1.131 g, 46.54 mmol) in THF (100 ml) at r.t. After addition of *ca.* 5 ml of the dibromoethane soln., the *Grignard* reaction started. Then 4-bromo-1,1′:4′,1″-terphenyl (**1c**, 5.433 g, 17.57 mmol) was added to the suspension, and the rest of the dibromoethane solution was added slowly during 40 min at 50°. After stirring for 3 h, $CdCl_2$ (2.213 g, 12.07 mmol) was added and the mixture was stirred for 2 h under reflux. After cooling to r.t., a soln. of the chlorosugar (6.832 g, 17.57 mmol) in THF (50 ml) was added, and the mixture was stirred for 16 h at r.t. Then CH_2Cl_2 (200 ml) was added and the mixture washed twice with 10% NH_4Cl soln. The aq. layers were extracted with CH_2Cl_2/THF 1:1 and the org. layers dried ($MgSO_4$) and evaporated. Purification by FC (hexane/AcOEt 7:1) gave 2.339 g (23%) of **2c**. White powder. ^{1}H-NMR: 8.02 (*d*, *J* = 8.0, 2 arom. H); 7.73–7.66, 7.57–7.48, 7.42–7.39 (3*m*, 13 arom. H); 7.28, 7.17 (2*d*, *J* = 8.9, 4 arom. H); 5.66, 5.48 (2*m*, H–C(1), H–C(3)); 4.77, 4.64 (2*m*, H–C(4), 2 H–C(5)); 3.01 (*m*, H–C(2)); 2.45 (*s*, *Me*C_6H_4); 2.43 (*m*, H–C(2)); 2.40 (*s*, *Me*C_6H_4). ^{13}C-NMR: 166.4, 166.1 (2 C=O); 143.9, 143.8, 141.6, 140.6, 140.1, 139.7 (6*s*, arom. C); 129.7, 129.6, 129.1, 129.0, 128.8, 127.5, 127.4, 127.1, 127.0 (10*d*, 19 arom. CH); 126.8 (*s*, arom. C); 126.1 (*d*, 2 arom. CH); 82.2, 80.0, 76.4 (3*d*, CH(1), CH(3), CH(4)); 64.6, 40.3 (2*t*, CH_2(5), CH_2(2)); 21.67, 21.63 (2*q*, 2 *C*$H_3C_6H_4$). HR-MS: 582.2427 ($C_{39}H_{34}O_5^+$, M^+; calc. 582.2406).

*(1*S*)-1,4-Anhydro-1,2-dideoxy-1-([1,1′:4′,1″-terphenyl]-4-yl)*-D-erythro-*pentitol* (**3c**). According to *G.P. B*, with **2c** (427 mg, 0.732 mmol) and 0.5M NaOMe in MeOH (730 µl, 0.365 mmol) in MeOH/CH_2Cl_2 1:1 (5 ml): 201 mg (79%) of **3c**. White powder. ^{1}H-NMR ((D$_8$)THF): 7.70–7.61, 7.48–7.39, 7.33–7.28 (3*m*, 13 arom. H); 5.05 (*m*, H–C(1)); 4.37, 4.16, 3.90, 3.82, 3.65, 3.60 (6*m*, H–C(3), H–C(4), 2 H–C(5), 2 OH)); 2.61, 1.86 (2*m*, 2 H–C(2)). ^{13}C-NMR ((D$_5$)pyridine): 144.1, 140.9, 140.2, 139.6 (4*s*, arom. C); 129.4, 127.9, 127.8, 127.3, 127.2, 127.1 (6*d*, arom. CH); 88.0, 79.8, 73.1 (3*d*, H–C(1), H–C(3), H–C(4)); 63.3, 45.1 (2*t*, CH_2(5), CH_2(2)). HR-MS: 346.1553 ($C_{23}H_{22}O_3^+$, M^+; calc. 346.1569).

*(1*S*)-1,4-Anhydro-1,2-dideoxy-5-*O*-(4,4′-dimethoxytrityl)-1-([1,1′:4′,1″-terphenyl]-4-yl)*-D-erythro-*pentitol* (**4c**). According to *G.P. C* $(MeO)_2$Tr-Cl (135 mg, 0.398 mmol), $^{i}Pr_2EtN$ (70 µl, 0.409 mmol), a spatula tip of DMAP, **3c** (94 mg, 0.271 mmol), and pyridine/CH_2Cl_2 1:1 (4 ml), for 5 h. Purification gave 144 mg (82%) of **4c**. White foam. ^{1}H-NMR: 7.72–7.66, 7.55–7.25 (2*m*, 22 arom. H); 6.89 (*d*, *J* = 8.9, 4 arom. H); 5.23 (*t*, *J* = 7.4, H–C(1)); 4.50, 4.26 (2*m*, H–C(3), H–C(4)); 3.83 (*s*, 2 MeO); 3.45 (*dd*, *J* = 9.5, 4.6, H–C(5)); 3.30 (*dd*, *J* = 9.5, 6.0, H–C(5)); 2.77, 2.12 (2*m*, 2 H–C(2)). ^{13}C-NMR: 158.5, 144.8, 142.1, 140.7, 140.1, 139.8, 139.7, 135.9 (8*s*, 10 arom. C); 130.0, 128.8, 128.1, 127.9, 127.5, 127.4, 127.3, 127.1, 127.0, 126.8, 126.3, 113.2 (12*d*, 26 arom. CH); 86.4 (*s*, 1 C); 84.5, 79.5, 75.2 (3*d*, CH(1), CH(3), CH(4)); 64.7 (*t*, CH_2(5)); 55.2 (*q*, 2 MeO); 43.1 (*t*, CH_2(2)). HR-MS: 671.2786 ($C_{44}H_{40}NaO_5^+$, $[M+Na]^+$; calc. 671.2773).

*(1*S*)-1,4-Anhydro-1,2-dideoxy-5-*O*-(4,4′-dimethoxytrityl)-1-([1,1′:4′,1″-terphenyl]-4-yl)*-D-erythro-*pentitol 3-(2-Cyanoethyl Diisopropylphosphoramidite)* (**5c**). According to *G.P. D*, with 2-cyanoethyl diisopropylphosphoramidochloridite (276 mg, 1.166 mmol) and $^{i}Pr_2EtN$ (500 µl, 2.92 mmol) were reacted with **4c** (494 mg, 0.761 mmol) in CH_2Cl_2 (10 ml). Purification gave 554 mg (86%) of **5c**. White foam. ^{1}H-NMR (mixture of 2 diastereoisomers): 7.73–7.67, 7.59–7.25, 6.91–6.87 (3*m*, 26 arom. H); 5.33, 4.65, 4.43 (3*m*, H–C(1), H–C(3), H–C(4)); 3.84, 3.83 (2*s*, 2 MeO); 3.66–3.35, 3.26–3.23 (2*m*, 2 Me_2CHN, OCH_2CH_2CN, 2 H–C(5)); 2.81 (*m*, 1 H–C(2)); 2.50–2.18 (*m*, OCH_2CH_2CN, 1 H–C(2)); 1.20–1.06 (*m*, 2 Me_2CHN). ^{13}C-NMR: 158.4, 144.9, 142.5, 142.2, 140.7, 140.0, 139.9, 139.7, 139.5, 136.1 (10*s*, 10 arom. C); 130.1, 128.8, 128.3, 127.8, 127.5, 127.40, 127.36, 127.31, 127.0, 126.9, 126.7, 126.5, 126.4 (14*d*, 22 arom. CH); 117.6, 117.5 (2*s*, CN); 113.1 (*d*, 4 arom. CH); 86.1 (*s*, 1 C); 84.8, 79.9 (2*d*, CH(1), CH(4)); 75.7, 75.2 (2*d*, CH(3)); 64.3, 64.0 (2*t*, CH_2(5)); 58.3, 58.1 (2*t*, OCH_2CH_2CN); 55.2 (*q*, 2 MeO); 43.2, 43.1 (2*d*, 2 Me_2CHN); 42.5 (*t*, CH_2(2)); 24.5, 24.4, 24.3 (3*q*, 2 Me_2CHN); 20.2, 20.1 (2*t*, OCH_2CH_2CN). HR-MS: 871.3846 ($C_{53}H_{57}N_2NaO_6P^+$, $[M+Na]^+$; calc. 871.3852).

4. *Stilbene Nucleoside. (1*S*)-1,4-Anhydro-1,2-dideoxy-1-[4-(2-phenylethenyl)phenyl]-3,5-di*-O-(p-*toluoyl)*-D-erythro-*pentitol* (**2e**). A soln. of *p*-bromostilbene (= 1-bromo-4-(2-phenylethenyl)benzene; 1.444 g,

5.572 mmol) in THF (25 ml) was slowly added to Mg turnings (234 mg, 9.63 mmol). After the addition of 2 ml of the *p*-bromostilbene soln., I_2 crystals, and 2 drops of dibromoethane were added to start the reaction. The rest of the *p*-bromostilbene was added slowly, then the soln. was heated under reflux for 2 h. Subsequently, $CdCl_2$ (1.22 g, 6.67 mmol) was added and the mixture heated for another 2 h under reflux. After cooling to r.t., a soln. of chlorosugar (2.731 g, 6.686 mmol) was added slowly *via* a dropping funnel and stirred for 16 h. The soln. was dried *in vacuo* to remove the THF, the residue dissolved in CH_2Cl_2, and the soln. washed twice with aq. sat. NH_4Cl soln., dried ($MgSO_4$), and evaporated. Purification by FC (hexanes/AcOEt 7:1) gave 2.279 g (77%) of **2e**. White powder. ^{1}H-NMR: 8.00 (*d*, *J* = 5.1, 4 H); 7.70 (*d*, *J* = 5.1, 2 H); 7.54 (*m*, 3 H); 7.42 (*m*, 3 H); 7.28 (*m*, 5 H); 7.27 (*m*, 2 H); 5.42 (*m*, 1 H); 5.40 (*t*, *J* = 4.2, 1 H); 4.68 (*m*, 1 H); 4.60 (*d*, *J* = 4.2, 2 H); 2.94 (*q*, *J* = 4.2, 1 H); 2.44 (*s*, 3 H); 2.42 (*s*, 3 H); 1.62 (*s*, 1 H); 1.28 (*t*, *J* = 4.5, 1 H). ^{13}C-NMR: 144.7; 138.6; 137.1; 129.3 (2*s*); 128.9; 128.1; 127.2; 127.1; 126.8; 87.6; 80.1; 73.2; 45.3; 25.7; 25.5; 25.3; 25.1; 24.9. HR-MS: 532.3067 ($C_{35}H_{32}O_5^+$, M^+; calc. 532.2250).

(1S)-1,4-Anhydro-1,2-dideoxy-1-[4-(2-phenylethenyl)phenyl]-D-erythro-*pentitol* (**3e**). According to *G.P. B*, with **2e** (203 mg, 0.381 mmol) and 0.5M NaOMe in MeOH (0.76 ml, 0.38 mmol) in MeOH/CH_2Cl_2 2.5:1 (5 ml): 610 mg (75%) of **3e**. ^{1}H-NMR: 7.42 (*m*, 4 H); 7.24 (*dm*, 4 H); 7.08 (*m*, 2 H); 4.86 (*q*, *J* = 4.1, 1 H); 4.22 (*q*, *J* = 4.0, 1 H); 3.70 (*q*, *J* = 2.7), 3.68 (*q*, *J* = 2.7), 3.45 (*s*, 6 H); 2.46 (*q*, *J* = 4.1, 1 H); 1.72 (*m*, 2 H); 1.17 (*s*, 1 H). ^{13}C-NMR: 166.4; 166.1; 143.9; 143.8; 141.8; 137.3; 136.5; 129.7; 129.6; 129.1; 129.0; 128.7; 128.6; 128.3; 127.6; 127.0; 126.8; 126.5; 126.4; 126.2; 126.0; 82.1; 81.9; 80.0; 76.3; 75.4, 65.1; 64.6; 55.2; 40.3; 39.2; 21.6. HR-MS: 296.1409 ($C_{19}H_{20}O_3^+$, M^+; calc. 296.1412).

(1S)-1,4-Anhydro-1,2-dideoxy-5-O-*(4,4′-dimethoxytrityl)-1-[4-(2-phenylethenyl)phenyl]*-D-erythro-*pentitol* (**4e**). According to *G.P. C*, with $(MeO)_2$Tr-Cl (841 mg, 2.46 mmol), ^{i}Pr$_2$EtN (0.54 ml, 3.09 mmol), a spatula tip of DMAP, **3e** (610 mg, 2.058 mmol), and dry pyridine (10 ml), for 4 h. Purification by FC (silica gel preequilibrated with 5% Et_3N in hexanes; hexanes/AcOEt 6:1 → 1:2): 1.037 mg (84%) of **4e**. Light yellow foam. ^{1}H-NMR: 7.54 (*m*, 6 H); 7.45 (*m*, 13 H); 6.88 (*s*, 2 H); 6.86 (*s*, 2 H); 5.16 (*t*, *J* = 4.6, 1 H); 4.46 (*q*, *J* = 2.9, 1 H); 4.22 (*q*, *J* = 3.6, 1 H); 3.82 (*s*, 6 H); 3.43 (*q*, *J* = 2.9, 1 H); 3.27 (*dd*, *J* = 3.8, 2.1, 1 H); 2.72 (*q*, *J* = 3.9, 1 H); 1.97 (*d*, *J* = 2.8, 1 H); 1.61 (*s*, 1 H). ^{13}C-NMR: 158.5; 144.8; 142.3; 137.3; 135.9; 130.0; 128.6; 128.5; 128.3; 128.1; 127.9; 127.6; 126.8; 126.6; 126.4; 126.1; 113.1; 86.3; 84.4; 79.5; 75.2; 64.7; 55.2; 43.0.

(1S)-1,4-Anhydro-1,2-dideoxy-5-O-*(4,4′-dimethoxytrityl)-1-[4-(2-phenylethenyl)phenyl]*-D-erythro-*pentitol 3-(2-Cyanoethyl Diisopropylphosphoramidite)* (**5e**). According to *G.P. D*, with 2-cyanoethyl diisopropylphosphoramidochloridite (0.578 ml, 2.59 mmol), ^{i}Pr$_2$EtN (1.2 ml, 6.9 mmol), **4e** (1.034 mg, 1.727 mmol) and CH_2Cl_2 (20 ml), for 4 h. Purification by FC (hexanes/AcOEt 3:1) gave 966 mg (70%) of **5e**. White foam. ^{1}H-NMR: 7.54 (*m*, 3 H); 7.41 (*m*, 7 H); 7.13 (*s*, 1 H); 6.86 (*dd*, *J* = 1.9, 3.7, 2 H); 5.16 (*t*, *J* = 4.6, 1 H); 4.60 (*dm*, 1 H); 4.39 (*q*, *J* = 2.6, 1 H); 3.81 (*s*, 6 H); 3.52 (*m*, 2 H); 3.29 (*m*, 4 H); 2.85 (*m*, 1 H); 2.20 (*m*, 1 H); 1.59 (*s*, 2 H); 1.15 (*m*, 6 H); 1.11 (*d*, *J* = 4.2); 1.05 (*d*, *J* = 4.2). ^{13}C-NMR: 158.3; 144.8; 142.3; 137.3; 135.9; 130.1; 128.6; 128.5; 128.3; 128.1; 127.9; 127.6; 126.8; 126.6; 126.4; 126.1; 113.0; 86.3; 84.4; 80.0; 75.2; 64.7; 55.1; 42.7; 24.6.

5. *Cyclohexene Nucleoside. (1S)-1,4-Anhydro-1-(cyclohex-1-en-1-yl)-1,2-dideoxy-3,5-di*-O-(p-*toluoyl)*-D-erythro-*pentitol* (**2f**). A soln. of 1-*di*-O-(p-*tol*-bromocyclohexene (**1f**; 2.090 g, 12.98 mmol) and 1,2-dibromoethane (900 µl, 10.44 mmol) in THF (40 ml) was slowly added to Mg turnings (647 mg, 26.62 mmol) in THF (10 ml). To start the *Grignard* reaction, the mixture was slightly heated. After complete addition of the bromo compound, the mixture was stirred for 2 h at 50°. $ZnCl_2$ (901 mg, 6.61 mmol) was added and the mixture stirred for 2 h under reflux. Then, the mixture was cooled to r.t. and a soln. of *Hoffer*'s chlorosugar (5.076 g, 13.05 mmol) in THF (25 ml) added. After stirring for 16 h at r.t., the solvent was evaporated, the residue suspended in CH_2Cl_2 and washed twice with 10% NH_4Cl soln. The aq. layers were extracted with CH_2Cl_2 and the org. layers dried ($MgSO_4$) and evaporated. Purification by FC (hexanes/AcOEt 6:1) gave 2.313 g (41%) of **2f**. Colorless oil which contained *ca.* 13% of a double-bond isomer as an impurity. ^{1}H-NMR: 7.92 (*m*, 4 arom. H); 7.22 (*m*, 4 arom. H); 5.80 (*m*, 1 H); 5.50 (*m*, H–C(1)); 4.61, 4.53–4.44 (2*m*, H–C(3), H–C(4), 2 H–C(5)); 2.62 (*m*, 1 H–C(2)); 2.41, 2.39 (2*s*, 2 *Me*C$_6$H$_4$); 2.15–2.01, 1.67–1.54 (2*m*, 1 H–C(2), 8 H of chx). ^{13}C-NMR: 166.3, 166.1 (2 C=O); 143.9, 143.7 (2*s*, 2 arom. C); 136.7 (*s*, 1 C of chx); 129.7, 129.6, 129.1, 129.0 (4*d*, 8 arom. CH); 127.1, 127.0 (2*s*, 2 arom. C); 123.6 (1*d*, 1 CH of chx); 82.5, 81.2, 76.3 (3*d*, CH(1), CH(3), CH(4)); 64.7, 36.4 (2*t*, CH_2(5), CH_2(2)); 24.9, 23.7, 22.5 (3*t*, 4 CH_2 of chx); 21.6 (*q*, $CH_3C_6H_4$). HR-MS: 435.2185 ($C_{27}H_{31}O_5^+$, $[M+H]^+$; calc. 435.2171).

(1S)-1,4-Anhydro-1-(cyclohex-1-en-1-yl)-1,2-dideoxy-D-erythro-*pentitol* (**3f**). According to *G.P. B*, with **2f** (276 mg, 0.635 mmol) and 0.5M NaOMe in MeOH (630 µl, 0.315 mmol) in MeOH/CH_2Cl_2 1:1 (5 ml): 101 mg (80%) of **3f**. Colorless oil. ^{1}H-NMR: 5.75 (br. *s*, 1 H of chx); 4.38, 4.29 (2*m*, H–C(1), H–C(3)); 3.83, 3.73, 3.65 (3*m*, H–C(4), 2 H–C(5)); 2.92, 2.68 (br. *s*, 2 OH); 2.29 (1*m*, 1 H–C(2)); 1.96–1.87, 1.67–1.54 (2*m*, 1 H–C(2),

8 CH of chx). ^{13}C-NMR: 137.6 (1*s*, 1 C); 123.5 (1*d*, 1 CH); 84.7, 81.7, 72.6 (3*d*, CH(1), CH(3′), CH(4′)); 62.3, 38.9 (2*t*, CH_2(5′), CH_2(2′)); 24.9, 23.5, 22.4 (3*t*, 4 CH_2 of chx). HR-MS: 198.1252 ($C_{11}H_{18}O_3^+$; calc. 198.1256).

*(1S)-1,4-Anhydro-1-(cyclohex-1-en-1-yl)-1,2-dideoxy-5-*O*-(4,4′-dimethoxytrityl)-*D*-erythro-pentitol* (**4f**). According to *G.P. C*, with $(MeO)_2$Tr-Cl (179 mg, 0.528 mmol), ^{i}Pr$_2$EtN (150 µl, 0.876 mmol), a spatula tip of DMAP, **3f** (85 mg, 0.428 mmol), and pyridine/CH_2Cl_2 1:1 (5 ml), for 3 days. Purification gave 182 mg (85%) of **4f**. Colorless oil. ^{1}H-NMR: 7.35 (*m*, 2 arom. H); 7.25–7.09 (*m*, 7 arom. H); 6.74 (*m*, 4 arom. H); 5.67 (*m*, 1 H of chx); 4.32 (*t*, *J* = 7.4, H–C(1)); 4.18, 3.91 (2*m*, H–C(3), H–C(4)); 3.69 (*s*, 2 MeO); 3.23 (*dd*, *J* = 9.4, 4.6, 1 H–C(5)); 3.03 (*dd*, *J* = 9.4, 6.4, 1 H–C(5)); 2.21 (*m*, 1 H–C(2)); 2.11–1.93 (*m*, 4 CH of chx); 1.81 (*m*, 1 H–C(2)); 1.64–1.44 (*m*, 4 CH of chx). ^{13}C-NMR: 158.4, 144.8, 138.1, 136.0 (4*s*, 5 arom. C, 1 C of chx); 130.0, 128.1, 127.8, 126.7, 122.9, 113.1 (6*d*, 13 arom. CH, 1 CH of chx); 86.2 (*s*, 1 C); 83.9, 81.8, 75.1 (3*d*, CH(1), CH(3′), CH(4′)); 64.9 (*t*, CH_2(5)); 55.2 (*q*, 2 MeO); 40.7 (*t*, CH_2(2)); 24.9, 23.9, 22.5 (3*t*, 4 CH_2 of chx). HR-MS: 523.2480 ($C_{32}H_{36}NaO_5^+$, $[M+Na]^+$; calc. 523.2460).

*(1S)-1,4-Anhydro-1-(cyclohex-1-en-1-yl)-1,2-dideoxy-5-*O*-(4,4′-dimethoxytrityl)-*D*-erythro-pentitol 3-(2-Cyanoethyl Diisopropylphosphoramidite)* (**5f**). According to *G.P. D*, with 2-cyanoethyl diisopropylphosphoramidochloridite (433 mg, 1.829 mmol), ^{i}Pr$_2$EtN (800 µl, 4 mmol), **4f** (586 mg, 1.170 mmol), and CH_2Cl_2 (10 ml). Purification gave 662 mg (81%) of **5f**. White foam. ^{1}H-NMR (mixture of 2 diastereoisomers): 7.53–7.50, 7.42–7.17, 7.09–7.01, 6.93–6.91, 6.86–6.82 (5*m*, 20 arom. H); 5.43 (*m*, H–C(1)); 4.57, 4.34 (2*m*, H–C(3), H–C(4)); 3.81, 3.80 (2*s*, 2 MeO); 3.72–3.48, 3.38–3.27, 3.17–3.13 (3*m*, 2 Me_2CHN, OCH_2CH_2CN, 2 H–C(5)); 2.75 (*m*, 1 H–C(2)); 2.56–2.51 (*m*, OCH_2CH_2CN); 2.37 (*m*, 1 H–C(2)); 1.17–1.03 (*m*, 2 Me_2CHN). ^{13}C-NMR: 158.4, 146.1, 144.9, 137.1, 136.4, 136.1, 136.0 (7*s*, 10 arom. C); 130.1, 128.2, 127.9, 127.8, 126.7, 124.9, 124.4, 124.3, 124.0, 123.6, 123.2 (11*d*, 16 arom. CH); 117.5 (*s*, CN); 113.1 (*d*, 4 arom. CH); 86.1 (*s*, 1 C); 84.7, 76.3 (2*d*, CH(1), CH(4)); 75.0, 74.8 (2*d*, CH(3′)); 63.8 (*t*, CH_2(5′)); 58.2, 58.1 (2*t*, OCH_2CH_2CN); 55.2 (*q*, 2 MeO); 43.2, 43.1 (2*d*, 2 Me_2CHN); 42.4 (*t*, CH_2(2)); 24.6, 24.5, 24.4, 24.3 (4*q*, 2 Me_2CHN); 20.1, 20.0 (2*t*, OCH_2CH_2CN). HR-MS: 723.3528 ($C_{41}H_{53}N_2NaO_6P^+$, $[M+Na]^+$; calc. 723.3539).

6. *Absorption Spectra*. Absorption spectra were measured for 10 µM solns. in MeOH at r.t. on a *Cary*-I-UV/VIS spectrometer.

7. *Emission Spectra and Quantum Yields*. Fluorescence spectra of 10 µM solns. in MeOH (except for terthiophene **7**, in CH_2Cl_2) were measured on a *SPEX-1680* double spectrometer at r.t. The solvents were deoxygenated by bubbling N_2 through the solvent for 2 h. The spectra were corrected for instrument response. All slits were set to 2 mm, resulting in a *ca*. 3.4-nm resolution. Fluorescence quantum yields (Φ_f) were calculated by the equation $\Phi_f = (FA_s\eta^2\Phi_s)/(AF_s\eta_0^2)$, where the subscript s refers to the standard and Φ is the quantum yield, *F* the corrected, integrated fluorescence, *A* the absorption at the excitation wavelength, η the refractive index of MeOH (or CH_2Cl_2), and η_0 the refractive index of H_2O [30]. Quantum-yield standards were quinine sulfate (*Aldrich*, 99+%, used without further purification), 10 µM in 1N H_2SO_4 ($\Phi_f = 0.55$ [31][32]), and fluorescein (*Aldrich*, recrystallized from 1N NaOH by adding 10% AcOH/H_2O), 10 µM in 0.1N NaOH ($\Phi_f = 0.90$ [31]).

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Received August 31, 1999