# The synthesis of novel 3′,5′-homocyclic nucleotides as potential anti-HIV agents

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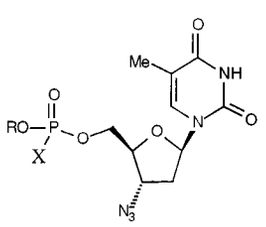
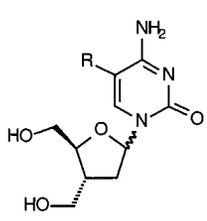
(5*S*)-(5-*tert*-Butyldimethylsiloxymethyl)furan-2(5*H*)-one has been converted into cytosine 2′,3′-dideoxy-3′,5′-homocyclic monophosphate (and its 5-fluoro congener) together with an adenosine homocyclic monophosphate. These were designed as inhibitors of HIV reverse transcriptase although they did not possess such activity.

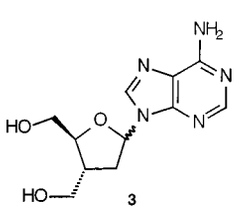
There is little doubt that of all approaches taken in the search for new drugs to treat HIV infection, inhibition of the enzyme reverse transcriptase has been the most successful strategy. Recent discoveries include biologically potent L-series nucleotides[1] and variously protected phosphates like **1** which are pro-



**1** R = subst. Aryl
X= $RCOSCH_2CH_2$ or $MeO_2CCH(R)NH$



**2a** R=H
**2b** R=F



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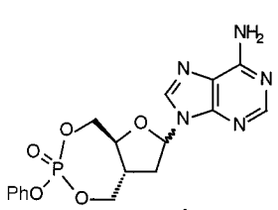
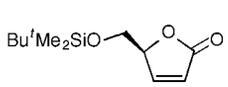


**4**



**5**

drugs of 3′-azido-3′-deoxythymidine (AZT) monophosphate.[2] We have already described the synthesis of the novel nucleoside analogues 2′,3′-dideoxy-3′-(hydroxymethyl)cytidine **2a** and the 5-fluorocytidine **2b** which possess potent anti-viral activity[3] at the micromolar level against herpes simplex 1 and 2 and against HIV-1. It is known that cellular kinases activate compounds of this type to produce their triphosphate forms and there is significant evidence that initial mono-phosphorylation is the rate limiting step.[4] While other anti-viral agents such as acyclovir are activated by virus-specific thymidine kinases (*e.g.* herpes simplex), 2′,3′-dideoxynucleosides have an absolute requirement for cellular kinases, for which they usually have poor affinity. This is often the reason for limited potency. With this in mind, we attempted to synthesise the novel monophosphate and cyclic phosphate forms of compounds **2a,b**. In an effort to complement this work, the novel 3′-hydroxymethyl-purine nucleoside **3** and its respective cyclic phosphate **4** were also prepared. These compounds, it was hoped, would be cleaved *in vivo* by host-specific phosphodiesterases to furnish the pro-active drug. In this paper we describe the successful synthesis of such compounds and their biological activity.

## Results and discussion

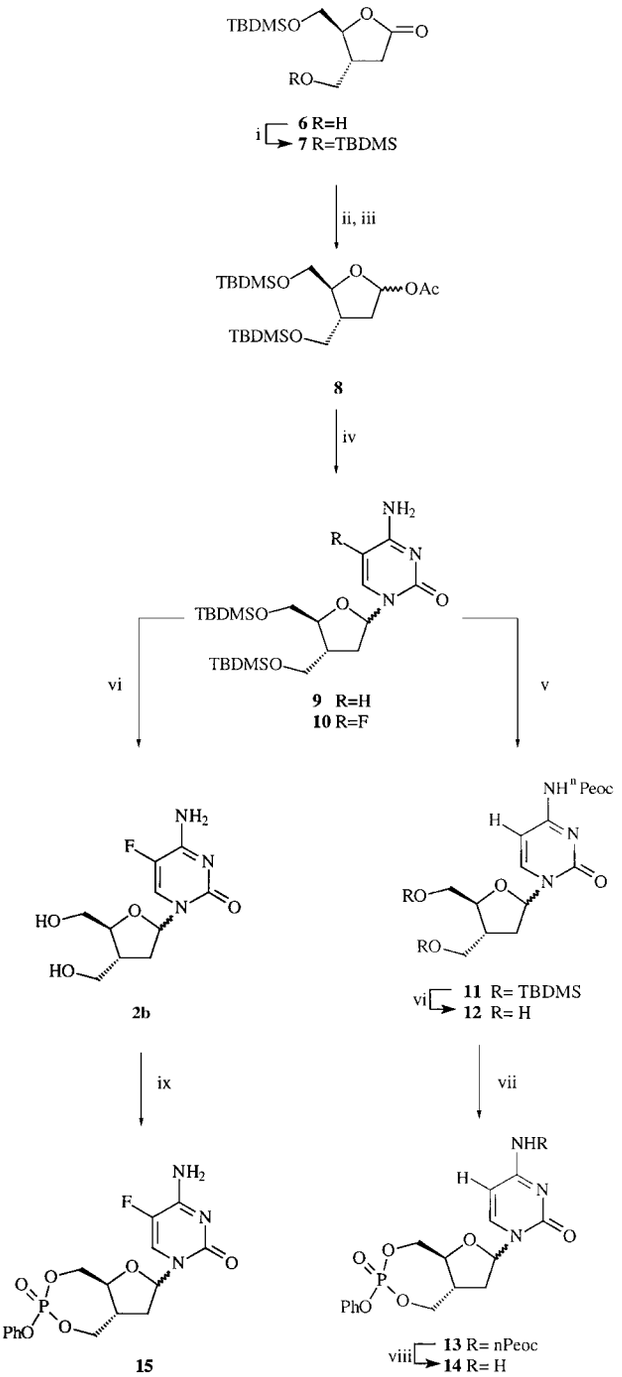
Photoinduced addition of methanol to (5*S*)-(5-*tert*-butyldimethylsiloxymethyl)furan-2(5*H*)-one **5** provided adduct **6** as previously described,[5] and this was converted into the bis-silylated adduct **7** which was reduced (DIBAL-H). The hemiacetal product was acetylated to generate the anomeric acetates **8** (Scheme 1). Since our previous studies had demonstrated the interesting biological properties of **2a** and **2b**, and the marked potency of **2b** relative to **2a**, it was of interest to prepare their cyclic phosphate analogues. These pyrimidines were attached using Vorbruggen-type condensation (TMSI),[6] to furnish the two nucleosides **9** and **10** as a mixture of anomers.

Protection of the free amino group of nucleoside **9** as its 2-(*p*-nitrophenyl)ethyl carbamate[7] (Peoc) yielded the fully protected nucleoside anomers **11**, which to our delight were now separable by flash chromatography. Indeed this technique has now been used to separate many substituted cytidines. All attempts to protect the free amino group of the corresponding 5-fluorocytidine derivatives **10** proved unsuccessful and this was attributed to the strong electron withdrawing properties of the α-fluorine atom.

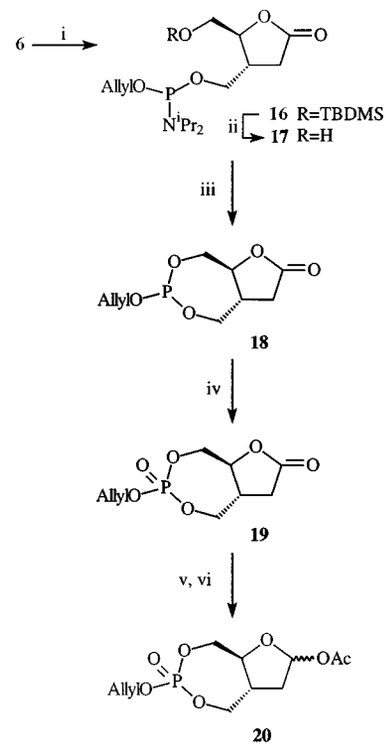
The silyl ether groups of the separated anomers **11α** and **11β**, and of the unprotected fluorocytidine **10**, were removed (*p*TSA in MeOH), and the resultant diols **12α**, **12β** and **2b** were subjected to phosphorylation. Treatment of **12α** and **12β** with bis(benzotriazolyl) phenyl phosphate (from 2 equiv. of 1-hydroxybenzotriazole and phenyl phosphorodichloridate in the presence of triethylamine) in pyridine,[8] afforded the desired cyclic phosphates **13α** and **13β** (35% α and 31% β after chromatography). An X-ray crystallographic study of **13**α was fully consistent with this structure (Fig. 1).† Subsequent carbamate hydrolysis ($MeOH–Et_3N–H_2O$) of the β-anomer was then achieved in moderate yield (42%), to generate the required 3′,5′-homocyclic-nucleotide analogue **14β**.

All attempts to phosphorylate fluoride **2b** under conditions similar to those previously employed failed to generate the required product. Only when treated directly with phenyl phosphorodichloridate in neat pyridine was the requisite phosphate **15** obtained, albeit in extremely poor yield (7%). Despite showing poor reactivity towards protection, it now seemed evident that the free amino group was sufficiently reactive

† This preliminary work has previously been communicated (ref. 9).




**Scheme 1** *Reagents and conditions:* i, TBDMSCl, imidazole, DCM, 0 °C→rt, 1 h (99%); ii, DIBAL-H, DCM, −78 °C, 3 h; iii, $Ac_2O$, Py, DMAP, 0 °C, 18 h (60%); iv, Bis(TMS)cytosine [bis(TMS)-5-fluorocytosine], TMSI, DCM, 25 °C, 2 h (98%); v, 2-(*p*-nitrophenyl)ethyl chloroformate, Py, DMAP, 18 h (83%); vi, TsOH, MeOH, 25 °C, 2 h (70%); vii, $PhOP(O)Cl_2$, HOBT, $Et_3N$, THF, Py, 4 h (35% and 31%); viii, $Et_3N$–MeOH–water 1 : 5 : 1, $CHCl_3$, 50 °C, 8 h (42%); ix, $PhOP(O)Cl_2$, Py, 25 °C, 18 h (10%).




**Scheme 2** *Reagents and conditions:* i, AllylOP($NPr^i_2$)$_2$, tetrazole, $Pr^i_2NH$, DCM, 25 °C, 20 min; ii, TBAF, THF, 25 °C, 1 h; iii, tetrazole, DCM, 25 °C, 18 h; iv, *t*-BuOOH, $Et_3N$, MeCN, 3 h, 25 °C; v, DIBAL-H, DCM, −78 °C, 2 h; vi, $Ac_2O$, Py, DMAP, 25 °C, 18 h.

to participate in unwanted phosphorylation side-reactions. Clearly the decision to phosphorylate in the presence of unprotected cytosine was an unwise one. While giving access to small quantities of cyclicphosphate necessary for biological screening, this reaction offered limited utility for accessing larger quantities needed for further investigations.

An alternative strategy could involve the installation of the cyclic phosphate unit prior to addition of the pyrimidine base. This approach would require the formation of the 5,7-fused ring phospholactone **19** (Scheme 2). This route benefits not only from the elimination of laborious protection/deprotection steps, but also allows greater flexibility in analogue formation as the choice of base need only be made at the very end of the synthesis. Treatment of the photoadduct **6** with the $P^{III}$ reagent allyl tetraisopropylphosphorodiamidite[10] resulted in formation of the phosphoramidite ester **16** in 85% yield. Deprotection of the primary hydroxy group (TBAF–THF) then afforded the cyclisation precursor **17**. Treatment of **17** with tetrazole, as a dilute solution in DCM, furnished the cyclic phosphite, **18** which was then readily oxidised (*tert*-butyl hydroperoxide), in high yield (98%), to the phosphate **19**. Purification was problematic due to the acid sensitivity of the intermediate phosphite and phosphoramidites: the use of silica and silica–$Et_3N$ chromatography systems resulted in considerable decomposition. Use of alumina and Florisil showed little improvement. With the exception therefore of the deprotected adduct, all intermediates were used without purification. As expected, $^1$H-NMR spectra of phosphate **19** showed a partial doubling of signals due to the presence of the phosphorus atom. Confirmation of our structural assignment and the stereochemical integrity of **19** was achieved by X-ray analysis and the ORTEP plot is shown in Fig. 2. Reduction of the lactone with DIBAL-H under standard conditions provided the lactol, which was acetylated ($Ac_2O$–pyridine) to afford the desired glycosidation precursor **20** (65% overall yield).

Formation of the protected nucleotide **21** was now achieved in good yield (Scheme 3), using the bis(TMS) derivative of 5-fluorocytosine in the presence of $SnCl_4$. Unfortunately, the resultant anomeric ratio showed no preference for the β-anomer. All that remained was for $Pd^0$-catalysed removal of the allyl group to afford the fully deprotected nucleotide analogue **22**.

Despite our success in the pyrimidine series and the relative ease of preparation of the key bicyclic phosphate unit **19**, it was disappointing to find that this approach could not be extended into the purine series for the synthesis of homocyclic adenosine analogues. A range of conditions were employed to effect

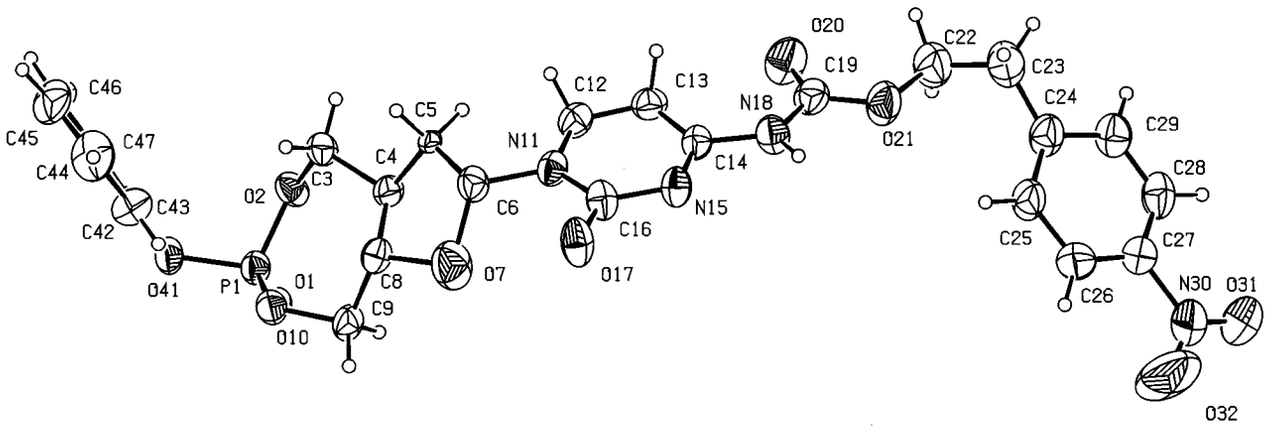



**Fig. 1** The structure of **13α** with the atomic numbering scheme. Ellipsoids shown at 30% occupancy.

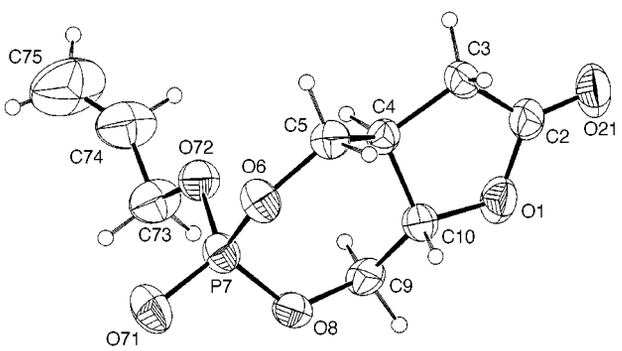
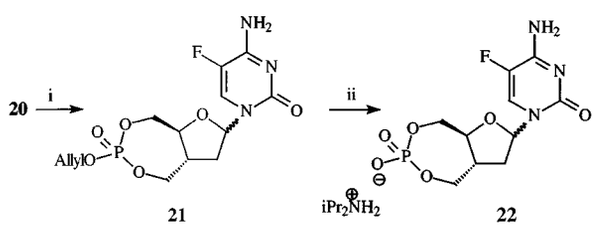
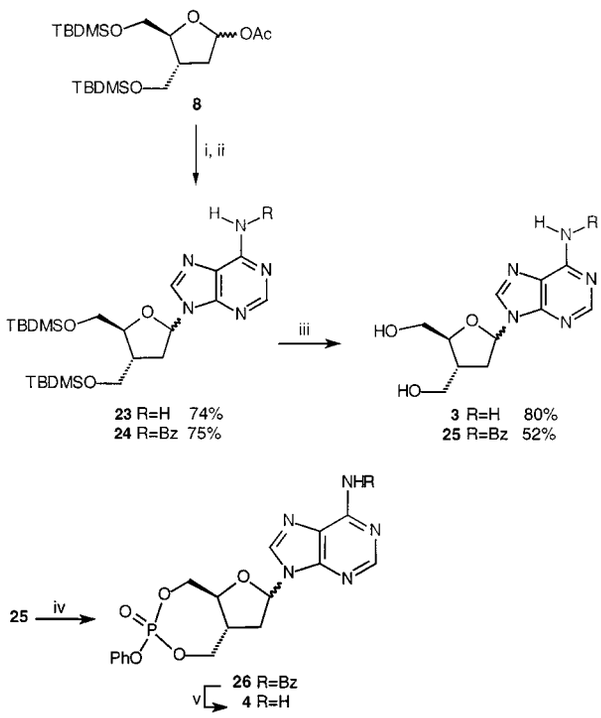



**Fig. 2** The structure of **19** with the atomic numbering scheme. Ellipsoids shown at 30% occupancy. One molecule (of three in the asymmetric unit) is shown.




**Scheme 3** *Reagents and conditions:* i, Bis(TMS)cytosine, $SnCl_4$, MeCN, 0 °C, 2 h; ii, $Pd(PPh_3)_4$, $Pr^i_2NH$, MeCN, 25 °C, 5 h.




**Scheme 4** *Reagents and conditions:* i, bis(TMS)adenine or bis(TMS)-6-*N*-benzoyladenine; ii, TESOTf, MeCN, 60 °C, 18 h; iii, TBAF, THF, 25 °C, 2 h; iv, $PhOP(O)Cl_2$, Py, 25 °C, 18 h (38%); v, $ZnBr_2$, MeOH, $CHCl_3$, 25 °C, 72 h (68%).

sugar/base coupling, including $SnCl_4$ and silyl triflates as Lewis acids, although these all proved unsatisfactory. $SnCl_4$ merely induced acetate destruction while triethylsilyl triflate caused de-allylation.

By returning to our original methodology of sugar/base coupling prior to phosphorylation, we were able to circumvent these problems. Formation of bis(trimethylsilyl)adenine using hexamethyldisilazane (HMDS), LiI and TMSCl, followed by triethylsilyl triflate catalysed adenylation of **8** afforded the requisite protected anomeric nucleoside **23** in 74% yield. The 6-*N*-benzoyladenosine derivative **24** was also shown to be equally accessible (Scheme 4). Double desilylation of **23** and **24** using TBAF–THF afforded the requisite unprotected nucleoside **3** and the phosphorylation precursor **25**. The 6-*N*-benzoyl-3′-hydroxymethyladenosine **25** was treated, as a dilute solution in dry pyridine, with phenyl phosphorodichloridate to generate the cyclic phosphate **26** in 38% yield. This was subsequently deprotected using $ZnBr_2$–MeOH–$CHCl_3$ (ref. 11) to afford the requisite 3′,5′-homocyclic nucleoside analogue **27**.

Extensive biological evaluation was carried out on compounds **3**, **14**, **15**, **22**, **26** and **4**. The compounds were screened for anti-viral activity against HIV-1, HIV-2, Herpes simplex 1 and 2 (HSV-1,2), Varicella zoster (VZV) and cytomegalovirus (CMV), but none of then exhibited any significant activity (compound **3** showed slight activity against VZV: $IC_{50} = 43$ μM). Compounds **3**, **25**, **26** and **4** were also screened as agonists of the various adenosine receptors, but none showed any activity. The lack of activity probably indicates that the compounds are not gaining access to the viral cells or are not substrates for endogenous phosphodiesterases.

## Experimental

General experimental details are given in ref. 3.

### (4*R*,5*S*)-5-(*tert*-Butyldimethylsiloxymethyl)-4-(hydroxymethyl)-tetrahydrofuran-2-one (6)

The protected butenolide (**5**)[3] (10 g, 43.8 mmol) and benzophenone (8 g, 43.9 mmol) were added to a Pyrex photochemical reactor containing AR methanol (350 ml). After degassing for 1 hour with a constant stream of argon, the reagents were irradiated for 6 hours with a 500 W medium pressure Hg discharge lamp. The now yellow solution was evaporated to dryness

*in vacuo* to afford a deep yellow solid. Purification by flash-column chromatography (gradient elution, 50:50 to 75:25 ether–light petroleum as eluant) afforded the title compound (**6**) as a light yellow oil (5.1 g, 19.6 mmol, 45%). $[\alpha]_D^{25}$ +4.0 (*c* 0.9 in $CHCl_3$); $\nu_{max}$ (film)/cm$^{-1}$ 3430s (OH), 3000–2800s (CH), 1760s (CO), 1473m (C–O); $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$) 0.08 (3H, s, Me), 0.09 (3H, s, Me), 0.90 [9H, s, $C(CH_3)_3$], 2.32 (1H, dd, $J_{gem}$ 16.9, $J_{3a,4}$ 4.8, 3a-H), 2.62–2.69 (2H, m, 4-H and OH), 2.73 (1H, dd, $J_{gem}$ 16.9, $J_{3b,4}$ 9.3, 3b-H), 3.65 (1H, dd, $J_{gem}$ 10.6, $J_{7a,4}$ 7.0, 7a-H), 3.71 (1H, dd, $J_{gem}$ 10.6, $J_{7b,4}$ 5.1, 7b-H), 3.77 (1H, dd, $J_{gem}$ 11.2, $J_{6a,5}$ 3.1, 6a-H), 3.86 (1H, dd, $J_{gem}$ 11.2, $J_{6b,5}$ 3.9, 6b-H), 4.42 (1H, m, 5-H); $\delta_C$(100 MHz; $CDCl_3$; $Me_4Si$) −5.8 (Me), −5.7 (Me), 18.2 [$C(CH_3)_3$], 25.6 [$C(CH_3)_3$], 31.7 (C-3), 39.2 (C-4), 63.4 (C-7), 64.5 (C-6), 82.6 (C-5), 176.9 (C-2); *m*/*z* (CI) [Found: $MNH_4^+$, 278.1788. $C_{12}H_{24}O_4Si$ requires $MNH_4^+$, 278.1788].

### (4*R*,5*S*)-4,5-Bis(*tert*-butyldimethylsiloxymethyl)tetrahydrofuran-2-one (7)

To a solution of photoadduct (**6**) (4.4 g, 17 mmol) and imidazole (1.29 g, 18.7 mmol) at 0 °C in DCM (40 ml) was added dropwise, a DCM solution of *tert*-butyldimethylsilyl chloride (2.72 g, 17.7 mmol). After stirring the mixture at 0 °C for 15 minutes and for a further 30 minutes at room temperature, water (50 ml) was added and the mixture extracted with DCM (3 × 30 ml). The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated to dryness *in vacuo*. Purification by flash-column chromatography (1.5:8.5 ether–light petroleum as eluant) afforded the title compound (**7**) as a light yellow oil (6.31 g, 16.8 mmol, 99%). $[\alpha]_D^{25}$ +5.1 (*c* 1.4 in $CHCl_3$); $\nu_{max}$ (film)/cm$^{-1}$ 3000–2800s (CH), 1763s (CO), 1471m (C–O), 1389m; $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$) 0.01 (6H, s, 2 × Me), 0.02 (3H, s, Me), 0.03 (3H, s, Me), 0.84 [9H, s, $C(CH_3)_3$], 0.85 [9H, s, $C(CH_3)_3$], 2.26 (1H, dd, $J_{gem}$ 16.5, $J_{3a,4}$ 3.7, 3a-H), 2.53–2.59 (1H, m, 4-H), 2.63 (1H, dd, $J_{gem}$ 16.5, $J_{3b,4}$ 9.5, 3b-H), 3.54 (1H, dd, $J_{gem}$ 9.9, $J_{7a,4}$ 6.2, 7a-H), 3.59 (1H, dd, $J_{gem}$ 9.9, $J_{7b,4}$ 4.6, 7b-H), 3.64 (1H, dd, $J_{gem}$ 11.4, $J_{6a,5}$ 2.9, 6a-H), 3.84 (1H, dd, $J_{gem}$ 11.4, $J_{6b,5}$ 2.9, 6b-H), 4.35 (1H, dt, $J_{5,4}$ 6.2, $J_{5,6}$ 2.9, 5-H); $\delta_C$(100 MHz; $CDCl_3$; $Me_4Si$) −5.6 ($Me_2Si$), 18.1 [$C(CH_3)_3$], 25.7 [$C(CH_3)_3$], 31.6 (C-3), 38.8 (C-4), 63.8 (C-7), 64.6 (C-6), 82.4 (C-5), 176.9 (C-2); *m*/*z* (CI) [Found: $MH^+$, 375.2374. $C_{18}H_{38}O_4Si_2$ requires $MH^+$, 375.2387].

### 1-*O*-Acetyl-3-*C*-(*tert*-butyldimethylsiloxymethyl)-5-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D- and -β-D-*erythro*-pentofuranose (8)

To a solution of lactone (**7**) (6.31 g, 16.8 mmol) in DCM (60 ml) at −78 °C ($CO_2$–acetone) was added dropwise DIBAL-H (19 ml, 1 M solution in toluene, 19 mmol). After 1 hour, MeOH (3 ml) was added and the solution stirred for a further 1 hour. The mixture was then treated with EtOAc (15 ml) and saturated aqueous $NaHCO_3$ (3 ml) and allowed to warm to room temperature over 2 hours. The solution was dried over $MgSO_4$, filtered through Celite and evaporated to afford the crude lactol as a light yellow oil. Without purification, the lactol was dissolved in DCM (20 ml) and pyridine (5 ml), and the solution cooled to 0 °C and treated with acetic anhydride (3 ml). After warming to room temperature and stirring for 3 days, water (30 ml) was added and the solution extracted with DCM (2 × 20 ml). The combined organic phases were washed with brine, dried ($MgSO_4$) and evaporated *in vacuo* to afford a light red oil. Purification by flash-column chromatography (9:1 light petroleum–ether as eluant) afforded the title compound (**8**) as a colourless oil (4.1 g, 9.8 mmol, 58%); $\nu_{max}$ (film)/cm$^{-1}$ 3000–2800s (CH), 1751s (CO), 1473m (C–O), 1362m, 1256w; $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$) α-anomer: 0.04 (6H, s, 2 × Me), 0.05 (6H, s, 2 × Me), 0.89 [18H, s, 2 × $C(CH_3)_3$], 1.98 (1H, dd, $J_{gem}$ 13.2, $J_{2a,3}$ 2.6, 2a-H), 2.03 (3H, s, CO*Me*), 2.29 (1H, dd, $J_{gem}$ 13.2, $J_{2b,3}$ 4.8, 2b-H), 2.36–2.46 (1H, m, 3-H), 3.61–3.77 (4H, m, 5-H and 6-H), 4.07 (1H, dd, $J_{4,3}$ 8.8, $J_{4,5}$ 4.0, 4-H), 6.29 (1H, d, $J_{1,2}$ 4.4, 1-H); β-anomer: 0.06 (6H, s, 2 × Me), 0.07 (6H, s, 2 × Me), 0.90 [18H, s, 2 × $C(CH_3)_3$], 1.85 (1H, dd, $J_{gem}$ 13.9, $J_{2a,3}$ 3.7, 2a-H), 2.04 (3H, s, COMe), 2.30 (1H, dd, $J_{gem}$ 13.9, $J_{2b,3}$ 5.5, 2b-H), 2.36–2.46 (1H, m, 3-H), 3.61–3.77 (4H, m, 5-H and 6-H), 3.93 (1H, dt, $J_{4,3}$ 7.7, $J_{4,5}$ 5.5, 4-H), 6.24 (1H, d, $J_{1,2}$ 4.8, 1-H); $\delta_C$(100 MHz; $CDCl_3$; $Me_4Si$) α-anomer: −5.4 (MeSi), −5.3 (MeSi), 18.4 [$C(CH_3)_3$], 21.4 (COMe), 25.9 [$C(CH_3)_3$], 35.0 (C-2), 41.5 (C-3), 64.8 (C-6), 64.9 (C-5), 83.6 (C-4), 99.5 (C-1), 170.4 (C=O); β-anomer: −5.5 (MeSi), −5.3 (MeSi), 18.3 [$C(CH_3)_3$], 21.5 (COMe), 25.8 [$C(CH_3)_3$], 35.9 (C-2), 41.6 (C-3), 63.7 (C-6), 66.2 (C-5), 83.7 (C-4), 99.0 (C-1) and 170.4 (C=O). *m*/*z* (CI) [Found: $(M - OAc)^+$, 359.2438. $C_{20}H_{42}O_5Si_2$ requires $(M - OAc)^+$, 359.2438].

### 1-[3′-*C*-(*tert*-Butyldimethylsiloxymethyl)-5′-*O*-(*tert*-butyldimethylsilyl)-2′,3′-dideoxy-α-D- and -β-D-*erythro*-pentofuranosyl]cytosine (9)

To a solution of iodine (0.76 g, 2.54 mmol) in $CH_2Cl_2$ (6.2 cm$^3$) was added hexamethyldisilane (0.68 cm$^3$, 2.8 mmol). The mixture was heated at reflux at 70 °C for 1 h, after which time the purple colour had disappeared leaving a near colourless solution. The solution of trimethylsilyl iodide (1 mol dm$^{-3}$) obtained was allowed to cool and was then used immediately.

To a solution of the acetate (**8**) (1.85 g, 4.42 mmol) in dry $CH_2Cl_2$ (35 cm$^3$) under an atmosphere of nitrogen was added 2-*O*,4-*N*-bis(trimethylsilyl)cytosine (5.0 mmol), followed by trimethylsilyl iodide (4.7 cm$^3$, 4.74 mmol), dropwise. The reaction mixture was stirred at room temperature for 2 h, and then quenched by the addition of water (10 cm$^3$). The organic layer was washed with saturated aqueous sodium thiosulfate solution (2 × 100 cm$^3$), dried ($MgSO_4$) and the solvent removed *in vacuo*. The residue was purified by flash chromatography (10% MeOH:90% $CH_2Cl_2$) to give the nucleoside (**9**) as a white amorphous solid (1.76 g, 85%) in a ratio of α:β = 1:1.3 by $^1$H NMR, $R_f$ 0.40 (10% MeOH:90% $CH_2Cl_2$); mp 98–99 °C ("softening"); $\nu_{max}$ ($CHCl_3$)/cm$^{-1}$ 3315 (br, $NH_2$), 3191 (br, $NH_2$), 2955, 2929, 2858, 1720, 1648 (C=O), 1485, 1472, 1255 and 1127; $\delta_H$(400 MHz, $CD_3OD$) α-anomer: 0.06 (6 H, s, 2 × Me), 0.10 (3 H, s, Me), 0.11 (3 H, s, Me), 0.89 (9 H, s, $^t$Bu), 0.93 (9 H, s, $^t$Bu), 1.88 (1 H, ddd, $J_{gem}$ 13.2, $J_{2',3'}$ 8.4, $J_{2',1'}$ 6.2, 2′-H), 2.47–2.52 (1 H, m, 3′-H), 2.63 (1 H, ddd, $J_{gem}$ 13.2, $J_{2',3'}$ 8.8, $J_{2',1'}$ 6.2, 2′-H), 3.64–3.75 (3 H, m, 5′-H, 2 × 6′-H), 3.87 (1 H, dd, $J_{gem}$ 11.0, $J_{5',4'}$ 3.2, 5′-H), 4.21–4.25 (1 H, m, 4′-H), 6.00 (1 H, d, $J_{5,6}$ 7.7, 5-H), 6.04–6.07 (1 H, m, 1′-H) and 7.84 (1 H, d, $J_{6,5}$ 7.7, 6-H), β-anomer: 0.08 (3 H, s, Me), 0.09 (3 H, s, Me), 0.13 (3 H, s, Me), 0.14 (3 H, s, Me), 0.92 (9 H, s, $^t$Bu), 0.95 (9 H, s, $^t$Bu), 2.11 (1 H, ddd, $J_{gem}$ 13.6, $J_{2',3'}$ 8.1, $J_{2',1'}$ 3.3, 2′-H), 2.36 (1 H, ddd, $J_{gem}$ 13.6, $J_{2',3'}$ 8.8, $J_{2',1'}$ 7.0, 2′-H), 2.47–2.52 (1 H, m, 3′-H), 3.64–3.75 (2 H, m, 5′-H, 6′-H), 3.84 (1 H, dd, $J_{gem}$ 11.7, $J_{6',3'}$ 2.6, 6′-H), 4.01 (1 H, dt, $J_{4',5'}$ 7.7, $J_{4',3'}$ 5.1, $J_{4',5'}$ 2.6, 4′-H), 4.07 (1 H, dd, $J_{gem}$ 11.4, $J_{5',4'}$ 2.6, 5′-H), 5.93 (1 H, d, $J_{5,6}$ 7.7, 5-H), 6.04–6.07 (1 H, m, 1′-H) and 8.29 (1 H, d, $J_{6,5}$ 7.7, 6-H); $\delta_C$(100.4 MHz, $CD_3OD$) α-anomer: −5.2 (2 × $Me_2Si$), 19.2 ($CMe_3$), 26.5 ($CMe_3$), 37.1 (C-2′), 43.4 (C-3′), 64.6 (C-6′), 66.3 (C-5′), 85.2 (C-4′), 89.1 (C-1′), 95.8 (C-5), 142.9 (C-6), 155.7 (C-4) and 165.9 (C=O): β-anomer: −5.3 (2 × $Me_2Si$), 19.3 ($CMe_3$), 26.4 ($CMe_3$), 37.7 (C-2′), 40.6 (C-3′), 64.6 (C-6′), 66.3 (C-5′), 85.8 (C-4′), 87.9 (C-1′), 95.2 (C-5), 143.7 (C-6), 156.0 (C-4) and 165.6 (C=O) [Found: $(M + H)^+$, 470.2888. $C_{22}H_{44}N_3O_4Si_2$ requires $MH^+$, 470.2870].

### 1-[3′-*C*-(*tert*-Butyldimethylsiloxymethyl)-5′-*O*-(*tert*-butyldimethylsilyl)-2′,3′-dideoxy-α-D- and -β-D-*erythro*-pentofuranosyl]-5-fluorocytosine (10)

A 1 M solution of TMSI was freshly prepared by refluxing hexamethyldisilane (0.3 g, 2.05 mmol) and iodine (0.44 g, 1.73 mmol) in DCM (3.5 ml) until a clear solution was obtained.

A suspension of 5-fluorocytosine (0.50 g, 3.9 mmol) and *N*,*O*-bis(trimethylsilyl)acetamide (5 ml, excess) was refluxed for 1 hour. Excess reagents were removed *in vacuo* and the residue co-evaporated with toluene (3 × 15 ml) until crystallisation occurred. The bis(trimethylsilyl)-5-fluorocytosine thus obtained, was re-dissolved in dry DCM (5 ml) and transferred to an oven-dried vessel under argon, containing acetate (**8**) (1.47 g, 3.5 mmol) and dry DCM (20 ml). TMSI solution (3.5 ml, 1 M solution prepared above, 3.5 mmol) was added and the solution stirred for 2 hours. Water (4 ml) was added and the mixture washed with $NaS_2O_3$ (25 ml) and extracted with DCM (3 × 30 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated to afford a gummy foam. Purification by flash-column chromatography (15:85 MeOH–DCM as eluant) afforded the title compound (**10**) as a white microcrystalline solid (1.602 g, 3.3 mmol, 94%); $\nu_{max}$ (film)/cm$^{-1}$ 3319s ($NH_2$), 3080s ($NH_2$), 3000–2800s (CH), 1690s (C=O), 1684s, 1620m (C=C), 1512m; $\delta_H$(250 MHz; $CDCl_3$; $Me_4Si$) α-anomer: 0.02 (3H, s, Me), 0.03 (3H, s, Me), 0.12 (3H, s, Me), 0.13 (3H, s, Me), 0.91 [9H, s, $C(CH_3)_3$], 0.93 (9H, s, $C(CH_3)_3$], 1.75–1.82 (2H, m, 2′a-H, 3′-H), 2.11 (1H, ddd, $J_{gem}$ 13.9, $J_{2'b,3'}$ 8.1, $J_{2'b,1'}$ 5.9, 2′b-H), 3.53–3.65 (2H, m, 6′-H), 3.68 (1H, dd, $J_{gem}$ 11.0, $J_{5'a,4'}$ 4.4, 5′a-H), 3.8 (1H, dd, $J_{gem}$ 11.0, $J_{5'b,4'}$ 3.7, 5′-H), 4.18 (1H, dt, $J_{4',5'}$ 4.4, $J_{4',3'}$ 2.2, 4′-H), 6.03 (1H, t, $J_{1',2'}$ 5.9, 1′-H), 7.59 (1H, d, $J_{H,F}$ 6.2, 6-H) β-anomer: 0.04 (3H, s, Me), 0.05 (3H, s, Me), 0.07 (3H, s, Me), 0.08 (3H, s, Me), 0.87 [9H, s, $C(CH_3)_3$], 0.88 [9H, s, $C(CH_3)_3$], 2.34–2.44 (2H, m, 2′a-H, 3′-H), 2.72 (1H, ddd, $J_{gem}$ 13.6, $J_{2'b,\ 3'}$ 8.4, $J_{2',1'}$ 6.6, 2′b-H), 3.53–3.65 (2H, m, 6′-H), 3.76 (1H, dd, $J_{gem}$ 11.7, $J_{5'a,4'}$ 2.2, 5′a-H), 3.98–4.0 (1H, m, 4′-H), 4.10 (1H, dd, $J_{gem}$ 11.7, $J_{5'b,4'}$ 2.2, 5′b-H), 6.02 (1H, t, $J_{1',2'}$ 5.9, 1′-H), 8.32 (1H, d, $J_{H,F}$ 6.2, 6-H); *m*/*z* (CI) [Found: $MH^+$, 488.2780. $C_{22}H_{42}N_3Si_2O_4F$ requires $MH^+$, 488.2776].

### 1-[3′-*C*-(*tert*-Butyldimethylsiloxymethyl)-5′-*O*-(*tert*-butyldimethylsilyl)-2′,3′-dideoxy-α-D- and -β-D-*erythro*-pentofuranosyl]-4-*N*-(*p*-nitrophenylethoxycarbonyl)cytosine (11)

To a solution of the nucleoside (**9**) (1.01 g, 2.15 mmol) in dry pyridine (14 cm$^3$) under an atmosphere of argon was added dimethylaminopyridine (68 mg), followed by 2-(*p*-nitrophenyl)-ethyl chloroformate (0.64 g, 2.8 mmol), and the reaction mixture was stirred at room temperature overnight. The reaction was quenched by the addition of water (30 cm$^3$), and the aqueous layer extracted with $CH_2Cl_2$ (3 × 30 cm$^3$). The combined organic extracts were washed with aqueous HCl (2 mol dm$^{-3}$, 3 × 60 cm$^3$), saturated aqueous $NaHCO_3$ solution (3 × 60 cm$^3$) and brine (2 × 60 cm$^3$). The organic layer was dried ($MgSO_4$), and the solvent removed under reduced pressure. The residue was purified by flash chromatography (45% EtOAc–40% petroleum ether–15% MeCN) to give the fully protected nucleoside (**11**) as two separable anomers (1.18 g, 83% overall).

α-Anomer: white powder (0.61 g, 43%), $R_f$ 0.63 (45% EtOAc–40% light petroleum–15% MeCN); mp 172–174 °C; $[\alpha]_D^{23}$ −44.8 (*c* 1.1, $CHCl_3$); $\nu_{max}$ ($CDCl_3$)/cm$^{-1}$ 2954, 2931, 2856, 1748 (C=O, nPeoc), 1736, 1664, 1655, 1625, 1520 (C–$NO_2$), 1346 (C–$NO_2$) and 1231; $\delta_H$(400 MHz, $CDCl_3$) 0.01 (6 H, s, 2 × Me), 0.02 (3 H, s, Me), 0.08 (3 H, s, Me), 0.85 (9 H, s, $^t$Bu), 0.91 (9 H, s, $^t$Bu), 1.77–1.84 (1 H, m, 2′-H), 2.46–2.49 (1 H, m, 2′-H), 2.97–3.0 (1 H, m, 3′-H), 3.12 (2 H, t, *J* 6.8, $CH_2$-nPeoc), 3.50–3.54 (1 H, m, 6′-H), 3.61 (1 H, dd, $J_{gem}$ 10.3, $J_{6',3'}$ 4.8, 6′-H), 3.70 (1 H, dd, $J_{gem}$ 11.0, $J_{5',4'}$ 4.4, 5′-H), 3.83 (1 H, dd, $J_{gem}$ 11.0, $J_{5',4'}$ 3.3, 5′-H), 4.21–4.24 (1 H, m, 4′-H), 4.44 (2 H, t, *J* 6.8, $CH_2$-nPeoc), 6.05 (1 H, t, $J_{1',2'}$ 6.0, 1′-H), 7.16 (1 H, d, $J_{5,6}$ 7.5, 5-H), 7.40 (2 H, d, *J* 8.6, *p*-$NO_2$Ph), 7.78 (1 H, br s, NH), 7.93 (1 H, d, $J_{6,5}$ 7.5, 6-H) and 8.18 (2 H, d, *J* 8.6, *p*-$NO_2$Ph); $\delta_C$(100.4 MHz, $CDCl_3$) −5.5 (2 × Me), −5.4 (Me), −5.3 (Me), 18.2 (*C*$Me_3$), 18.3 (*C*$Me_3$), 25.8 (C*Me*$_3$), 25.9 (C*Me*$_3$), 34.9 ($CH_2$-nPeoc), 36.6 (C-2′), 42.2 (C-3′), 63.1 (C-6′), 65.0 (C-5′), 65.5 ($CH_2$-nPeoc), 84.0 (C-4′), 88.6 (C-1′), 94.2 (C-5), 123.9 (Ar), 129.8 (Ar), 143.4 (C-6), 145.0 (C–$NO_2$), 147.0 (C-quart, Ar), 152.1 (C-4), 154.9 (C=O, nPeoc) and 162.0 (C-2).

β-Anomer: white amorphous solid (0.58 g, 40%), $R_f$ 0.60 (45% EtOAc–40% light petroleum–15% MeCN); $[\alpha]_D^{21}$ +39.1 (*c* 0.5, $CHCl_3$); $\nu_{max}$ ($CDCl_3$)/cm$^{-1}$ 2952, 2928, 2857, 1747 (C=O, nPeoc), 1735, 1668, 1662, 1623, 1519 (C–$NO_2$), 1501, 1345 (C–$NO_2$), 1227 and 1197; $\delta_H$(400 MHz, $CDCl_3$) 0.04 (3 H, s, Me), 0.05 (3 H, s, Me), 0.11 (3 H, s, Me), 0.13 (3 H, s, Me), 0.88 (9 H, s, $^t$Bu), 0.93 (9 H, s, $^t$Bu), 2.08–2.16 (1 H, m, 2′-H), 2.40–2.48 (2 H, m, 2′-H, 3′-H), 3.11 (2 H, t, *J* 6.6, $CH_2$-nPeoc), 3.61 (1 H, dd, $J_{gem}$ 10.3, $J_{6',3'}$ 5.3, 6′-H), 3.65 (1 H, dd, $J_{gem}$ 10.3, $J_{6',3'}$ 4.4, 6′-H), 3.77 (1 H, dd, $J_{gem}$ 11.7, $J_{5',4'}$ 2.0, 5′-H), 4.03–4.12 (2 H, m, 4′-H, 5′-H), 4.44 (2 H, t, *J* 6.6, $CH_2$-nPeoc), 6.05–6.07 (1 H, m, 1′-H), 7.09 (1 H, d, $J_{5,6}$ 7.0, 5-H), 7.40 (2 H, d, *J* 8.6, *p*-$NO_2$Ph), 7.50 (1 H, br s, NH), 8.19 (2 H, d, *J* 8.6, *p*-$NO_2$Ph) and 8.60 (1 H, d, $J_{6,5}$ 7.0, 6-H); $\delta_C$(100.4 MHz, $CDCl_3$) −5.5 (2 × Me), −5.4 (2 × Me), 18.3 (*C*$Me_3$), 18.5 (*C*$Me_3$), 25.9 (C*Me*$_3$), 26.0 (C*Me*$_3$), 35.0 ($CH_2$-nPeoc), 36.7 (C-2′), 38.3 (C-3′), 62.4 (C-6′), 62.8 (C-5′), 65.4 ($CH_2$-nPeoc), 84.6 (C-4′), 87.1 (C-1′), 93.7 (C-5), 123.9 (Ar), 129.8 (Ar), 145.0 (C–$NO_2$), 145.3 (C-6), 147.0 (C-quart, Ar), 152.1 (C-4), 155.0 (C=O, nPeoc) and 161.9 (C-2).

### 1-[2′,3′-Dideoxy-3′-*C*-(hydroxymethyl)-α-D-*erythro*-pentofuranosyl]-4-*N*-(*p*-nitrophenylethoxycarbonyl)cytosine (12α)

To a solution of the α-anomer of the fully protected nucleoside (**11**) (0.43 g, 0.78 mmol) in dry THF (11 cm$^3$) under an atmosphere of argon was added tetrabutylammonium fluoride (1.0 mol dm$^{-3}$ in THF, 1.2 cm$^3$), and the reaction mixture stirred at room temperature for 2 h. The solvent was removed *in vacuo*, and the residue purified by flash chromatography (10–20% MeOH–$OH_2Cl_2$) to give the diol (**12α**) (0.23 g, 67%) as a white amorphous solid, $R_f$ 0.36 (10% MeOH–90% $CH_2Cl_2$); mp 82–84 °C ("softening"); $[\alpha]_D^{25}$ −47.1 (*c* 0.5, MeOH); $\nu_{max}$ ($CHCl_3$)/cm$^{-1}$ 3387 (br, OH), 2934, 1748 (C=O, nPeoc), 1736, 1649 (C=O, cytosine), 1619, 1560, 1501 and 1348 ($NO_2$); $\delta_H$(400 MHz, $d_6$–DMSO) 1.71–1.78 (1 H, m, 2′-H), 2.26–2.31 (1 H, m, 3′-H), 2.52–2.58 (1 H, m, 2′-H), 3.08 (2 H, t, *J* 6.6, $CH_2$-nPeoc), 3.37–3.40 (2 H, m, 2 × 6′-H), 3.41–3.47 (1 H, m, 5′-H), 3.55–3.60 (1 H, m, 5′-H), 4.12–4.16 (1 H, m, 4′-H), 4.36 (2 H, t, *J* 6.6, $CH_2$-nPeoc), 5.94 (1 H, $J_{1',2'}$ 6.0, 1′-H), 7.01 (1 H, d, $J_{5,6}$ 7.5, 5-H), 7.61 (2 H, d, *J* 8.8, *p*-$NO_2$Ph), 8.08 (1 H, d, $J_{6,5}$ 7.5, 6-H), 8.17 (2 H, d, *J* 8.8, *p*-$NO_2$Ph) and 10.7 (1 H, br s, NH); $\delta_C$(100.4 MHz, $d_6$-DMSO) 34.2 ($CH_2$-nPeoc), 36.1 (C-2′), 42.0 (C-3′), 61.6 (C-6′), 63.0 (C-5′), 64.9 ($CH_2$-nPeoc), 84.1 (C-4′), 87.3 (C-1′), 94.0 (C-5), 123.3 (Ar), 130.4 (Ar), 144.3 (C-6), 146.3 (C–$NO_2$), 146.4 (C-quart, Ar), 154.8 (C=O, nPeoc) and 162.7 (C-2) [Found: $(M + H)^+$, 435.1536. $C_{19}H_{23}N_4O_8$ requires $MH^+$, 435.1516].

### 1-[2′,3′-Dideoxy-3′-*C*-(hydroxymethyl)-β-D-*erythro*-pentofuranosyl]-4-*N*-(*p*-nitrophenylethoxycarbonyl)cytosine (12β)

To a solution of the β-anomer of the fully protected nucleoside (**11**) (0.24 g, 0.43 mmol) in MeOH (AnalaR, 4.0 cm$^3$) and $H_2O$ (0.9 cm$^3$) was added toluene-*p*-sulfonic acid monohydrate (89 mg, 0.47 mmol), and the reaction mixture stirred at room temperature for 2 h. After neutralisation with basic resins (IRA 93, 3.2 cm$^3$), the mixture was stirred for a further 4 h and then filtered. The solvent was removed *in vacuo*, and the residue purified by flash chromatography (10-20% MeOH–$CH_2Cl_2$) to give the diol (**12β**) (0.11 g, 59%) as a white amorphous solid, $R_f$ 0.41 (10% MeOH–90% $CH_2Cl_2$); mp 82–84 °C ('softening'); $[\alpha]_D^{23}$ +27.5 (*c* 0.2, MeOH); $\nu_{max}$ ($CHCl_3$)/cm$^{-1}$ 3247 (br, OH), 2950, 2933, 1738(C=O, nPeoc), 1733, 1641, 1564, 1517 ($NO_2$), 1506, 1346 ($NO_2$), 1257 and 1109; $\delta_H$ (400 MHz, $d_6$-DMSO) 1.97–2.05 (1 H, m, 2′-H), 2.21–2.30 (2 H, m, 2′-H, 3′-H), 3.08 (2 H, t, *J* 6.4, $CH_2$-nPeoc), 3.42–3.47 (2 H, m, 2 × 6′-H), 3.60 (1 H, dd, $J_{gem}$ 12.1, $J_{5',4'}$ 3.7, 5′-H), 3.76 (1 H, dd, $J_{gem}$ 12.1, $J_{5',4'}$

2.8, 5′-H), 3.85–3.87 (1 H, m, 4′-H), 4.36 (2 H, t, *J* 6.4, $CH_2$-nPeoc), 5.90–5.91 (1 H, m, 1′-H), 6.96 (1 H, d, $J_{5,6}$ 7.5, 5-H), 7.61 (2 H, d, *J* 8.4, *p*-$NO_2$Ph), 8.17 (2 H, d, *J* 8.4, *p*-$NO_2$Ph), 8.48 (1 H, d, $J_{6,5}$ 7.5, 6-H), and 10.7 (1 H, br s, NH); $\delta_C$(100.4 MHz, $d_6$-DMSO) 34.2 ($CH_2$-nPeoc), 36.2 (C-2′), 38.9 (C-3′), 60.9 (C-6′), 61.2 (C-5′), 64.9 ($CH_2$-nPeoc), 84.4 (C-4′), 86.2 (C-1′), 93.5 (C-5), 123.4 (Ar), 130.5 (Ar), 144.6 (C-6), 146.4 (C–$NO_2$), 154.2 (C=O, nPeoc) and 162.3 (C-2).

### 1-[2′,3′-Dideoxy-3′-*C*-(hydroxymethyl)-α-D-*erythro*-pentofuranosyl]-4-*N*-(*p*-nitrophenylethoxycarbonyl)cytosine phenyl 5′,6′-cyclic phosphate (13α)

To a solution of 1-hydroxybenzotriazole (98 mg, 0.72 mmol) in dry THF (2 $cm^3$) under an atmosphere of argon, was added $Et_3N$ (0.10 $cm^3$, 0.72 mmol) followed by phenyl phosphorodichloridate (0.05 $cm^3$, 0.36 mmol) dropwise. A white precipitate formed immediately on addition of the phosphorylating agent, and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture containing bis-benzotriazolyl phenyl phosphate was filtered through a Whatman 1.0 μm syringe filter and added directly to a solution of the diol (**12α**) (0.13 g, 0.30 mmol) in dry pyridine (5 $cm^3$), dropwise over a period of 2 h. The reaction mixture was stirred at room temperature under an atmosphere of argon overnight. $Et_3N$ (0.22 $cm^3$, 1.5 mmol) was added and the reaction mixture stirred at room temperature for a further 24 h. The reaction was quenched by the addition of MeOH (2.0 $cm^3$), the solvent removed *in vacuo* and the residue purified by flash chromatography with gradient elution (0–10% MeOH–$OH_2Cl_2$) to give the cyclic phosphate ester (**13α**) (60 mg, 35%) as an off-white solid, $R_f$ 0.34 (0.5% MeOH–95% $CH_2Cl_2$); $\delta_H$ (400 MHz, $CDCl_3$ and $CD_3OD$), integration values for the discrete diastereoisomers have not been given but were in the approximate ratio of 2:1 with respect to the signals for the discrete diastereomers, 1.75–1.84 (m, 2 × 2′-H), 2.45–2.51 (m, 2′-H), 2.80–2.87 (m, 2 × 3′-H), 2.93–2.99 (m, 2′-H), 3.14 (t, *J* 6.6, $CH_2$-nPeoc), 3.51 (dd, $J_{gem}$ 11.0, $J_{6',3'}$ 6.6, 6′-H), 3.59 (dd, $J_{gem}$ 11.0, $J_{6',3'}$ 5.1, 6′-H), 3.76 (dd, $J_{gem}$ 11.0, $J_{6',3'}$ 4.4, 6′-H), 3.82 (dd, $J_{gem}$ 11.0, $J_{6',3'}$ 4.0, 6′-H), 4.12–4.25 (m, 5′-H, 2 × 4′-H), 4.40 (ddd, $J_{5',P}$ 24.9, $J_{gem}$ 11.7, $J_{5',3'}$ 3.7, 5′-H), 4.47 (t, *J* 6.6, 2 × $CH_2$-nPeoc), 4.50–4.55 (m, 5′-H), 4.59 (ddd, $J_{5',P}$ 19.2, $J_{gem}$ 10.3, $J_{5',4'}$ 4.2, 5′-H), 6.02 (t, $J_{1',2'}$ 5.9, 1′-H), 6.09 (t, $J_{1',2'}$ 6.6, 1′-H), 7.20–7.27 (m, 2 × 5-H, 4 × ArH), 7.38 (t, *J* 7.7, 6 × ArH), 7.46 (d, *J* 8.8, 4 × Ar nPeoc), 7.95 (d, $J_{6,5}$ 7.7, 6-H), 7.99 (d, $J_{6,5}$ 7.3, 6-H) and 8.19 (d, *J* 8.8, 4 × Ar nPeoc); $\delta_C$ (100.4 MHz, $CDCl_3$ and $CD_3OD$) 34.8 ($CH_2$-nPeoc), 35.7 (C-2′), 36.6 (C-2′), 42.7 (C-3′), 42.8 (C-3′), 62.4 (C-6′), 65.0 (C-6′), 65.4 ($CH_2$-nPeoc), 67.2 (C-5′), 68.4 (C-5′), 81.5 (C-4′), 84.4 (C-4′), 88.3 (C-1′), 88.7 (C-1′), 119.7 (2 × C-5), 123.6 (Ar), 123.8 (Ar), 125.7 (Ar), 129.8 (Ar), 142.8 (Ar), 142.9 (Ar), 143.3 (C-6), 143.4 (C-6), 145.2 (C–$NO_2$), 146.9 (C-quart), 150.0 (C-quart), 152.8 (2 × C-4), 155.6 (2 × C=O, nPeoc) and 163.2 (2 × C-2).

### 1-[2′,3′-Dideoxy-3′-*C*-(hydroxymethyl)-β-D-*erythro*-pentofuranosyl]-4-*N*-(*p*-nitrophenylethoxycarbonyl)cytosine phenyl 5′,6′-cyclic phosphate (13β)

To a solution of 1-hydroxybenzotriazole (83 mg, 0.62 mmol) in dry THF (1.7 $cm^3$) under an atmosphere of argon, cooled to 0 °C, was added $Et_3N$ (0.09 $cm^3$, 0.62 mmol) followed by phenyl phosphorodichloridate (0.04 $cm^3$, 0.31 mmol), dropwise. A white precipitate formed immediately on addition of the phosphorylating agent. The reaction mixture was allowed to warm to room temperature and stirred at this temperature for 1 h. The reaction mixture containing bis-benzotriazolyl phenyl phosphate was filtered through a Whatman 1.0 μm syringe filter and added directly to a solution of the diol (**12β**) (0.11 g, 0.25 mmol) in dry pyridine (4.5 $cm^3$), dropwise over a period of 1 h. The reaction mixture was stirred at room temperature under an atmosphere of argon for 4 h. $Et_3N$ (0.18 $cm^3$, 1.25 mmol) was added and the reaction mixture stirred at room temperature overnight. The reaction was quenched by the addition of MeOH (1.5 $cm^3$), the solvent removed *in vacuo* by azeotroping with toluene (2 × 3 $cm^3$), and the residue was purified by flash chromatography with gradient elution (0–5% MeOH–EtOAc) to give the cyclic phosphate ester (**13β**) (45 mg, 31%) as an off-white solid, $R_f$ 0.42 and 0.38 (5% MeOH–95% $CH_2Cl_2$); $\delta_H$(400 MHz, $CDCl_3$), integration values for the discrete diastereomers have not been given but were in the approximate ratio of 5:1 with respect to the signals for the discrete diastereomers: 2.29–2.43 (m, 4 × 2-H′), 2.56–2.64 (m, 2 × 3′-H), 3.11 (t, *J* 6.6, 2 × $CH_2$-nPeoc), 4.09 (dd, $J_{gem}$ 12.8, $J_{6',3'}$ 10.3, 6′-H), 4.14–4.24 (m, 3 × 6′-H), 4.32 (dd, $J_{gem}$ 11.7, $J_{5',4'}$ 3.7, 5′-H), 4.34–4.42 (m, 2 × 4′-H, 5′-H), 4.45 (t, *J* 6.6, 2 × $CH_2$-nPeoc), 4.49–4.58 (m, 5′-H), 4.67 (ddd, $J_{5',P}$ 18.3, $J_{gem}$ 10.6, $J_{5',4'}$ 4.4, 5′-H), 6.05 (dd, $J_{1',2'}$ 6.8, $J_{1',2'}$ 1.6, 1′-H), 6.12 (d, $J_{1',2'}$ 7.0, 1′-H), 7.22 (d, *J* 7.7, 4 × Ar), 7.32–7.38 (m, 2 × 5-H, 6 × Ar), 7.41 (d, *J* 8.4, 4 × Ar-nPeoc), 7.76 (d, $J_{6,5}$ 7.3, 6-H), 7.89 (d, $J_{6,5}$ 6.6, 6-H) and 8.17 (d, *J* 8.4, 4 × Ar nPeoc); $\delta_P$(81 MHz, $CDCl_3$) −5.2 and −5.7 (Found: $M^+$, 572.1294. $C_{25}H_{25}N_4O_{10}P$ requires $M^+$, 572.1308).

### 1-[2′,3′-Dideoxy-3′-*C*-(hydroxymethyl)-β-D-*erythro*-pentofuranosyl]cytosine phenyl 5′,6′-cyclic phosphate (14β)

To a solution of the protected nucleotide (**13β**) (36 mg, 0.06 mmol) in $CHCl_3$ (1.0 $cm^3$) was added a solution of $Et_3N$–MeOH–$H_2O$, 1:5:1 (1.0 $cm^3$). The reaction mixture was stirred at room temperature for 3 days, and then heated at 50 °C for a further 8 h. The solvent was removed under reduced pressure and the residue purified by flash chromatography with gradient elution (10–30% EtOH–$CH_2Cl_2$) to give the *title compound* (**14β**) (10 mg, 42%) as a white amorphous solid, $R_f$ 0.28 (20% EtOH–80% $CH_2Cl_2$ and 8 drops AcOH); $\delta_H$(400 MHz, $CD_3OD$), integration values for the discrete diastereomers have not been given but were in the approximate ratio of 2:1 with respect to the signals for the discrete diastereomers, 2.16–2.21 (m, 4 × 2-H′), 2.71–2.78 (m, 2 × 3′-H), 4.0 (dd, $J_{5',P}$ 20.9, $J_{gem}$ 11.0, 5′-H), 4.05–4.17 (m, 2 × 4′-H, 2 × 5′-H), 4.23 (ddd, $J_{6',P}$ 22.3, $J_{gem}$ 10.3, $J_{6',3'}$ 8.2, 6′-H), 4.32–4.44 (m, 3 × 6′-H), 4.49 (ddd, $J_{5',P}$ 20.0, $J_{gem}$ 10.3, $J_{5',4'}$ 3.9, 5′-H), 5.81 (d, $J_{5,6}$ 7.7, 5-H), 5.83 (d, $J_{5,6}$ 7.7, 5-H), 5.99 (dd, $J_{1',2'}$ 6.6, $J_{1',2'}$ 3.7, 1′-H), 6.03 (dd, $J_{1',2'}$ 6.9, $J_{1',2'}$ 2.9, 1′-H), 7.15 (t, *J* 7.9, 6 × Ar), 7.30 (t, *J* 7.9, 4 × Ar), 7.57 (d, *J* 7.7, 6-H) and 7.59 (d, *J* 7.7, 6-H) [Found: $(M + H)^+$, 380.1011. $C_{16}H_{19}N_3O_6P$ requires $MH^+$, 380.1011].

### 1-[2′,3′-Dideoxy-3′-*C*-(hydroxymethyl)-α-D- and -β-D-*erythro*-pentofuranosyl]-5-fluorocytosine (2b)

To a 10% aqueous methanolic solution (60 ml) of bis-silyl nucleoside (**10**) (2.4 g, 4.92 mmol) was added toluene-*p*-sulfonic acid (1.87 g, 9.84 mmol). After 2 hours IRA-93 ion exchange resin (100 ml) was added and the mixture stirred for a further 2 hours until pH 7 was achieved. The mixture was filtered and the filtrate evaporated to dryness. Purification of the residue by flash column chromatography (20:80 MeOH–DCM as eluant) afforded the title compound **2b** as a white amorphous powder (0.88 g, 3.4 mmol, 70%); mp 81–87 °C; $\nu_{max}$ (film)/$cm^{-1}$ 3330s (OH), 2925s ($NH_2$), 1680s (C=O), 1611s (C=C), 1511m, 1462m, 1378m; $\delta_H$(250 MHz; $CDCl_3$; $Me_4Si$) α-anomer: 1.67 (1H, ddd, $J_{gem}$ 13.6, $J_{2'a,3'}$ 9.2, $J_{2'a,1'}$ 6.6, 2′a-H), 2.09–2.38 (1H, m, 3′-H), 2.49 (1H, ddd, $J_{gem}$ 13.6, $J_{2'b,3'}$ 8.1, $J_{2'b,1'}$ 6.2, 2′b-H), 3.44 (1H, dd, $J_{gem}$ 12.5, $J_{5'a,4'}$ 5.5, 5′a-H), 3.48–3.59 (2H, m, 6′-H), 3.61 (1H, dd, $J_{gem}$ 12.5, $J_{5'b,4'}$ 2.6, 5′b-H), 4.05 (1H, ddd, $J_{4',3'}$ 8.1, $J_{4',5'a}$ 5.5, $J_{4',5'b}$ 2.6, 4′-H), 5.83 (1H, dt, $J_{1',2'}$ 6.2, $J_{1',3'}$ 1.5, 1′-H), 7.70 (1H, d, $J_{H,F}$ 6.6, 6-H) β-anomer: 1.93–2.03 (1H, m, 2′a-H), 2.09–2.38 (2H, m, 2′b-H, 3′-H), 3.48–3.59 (3H, m, 5′a-H, 6′-H), 3.73 (1H, dd, $J_{gem}$ 12.8, $J_{5'b,4'}$ 2.9, 5′b-H), 3.79 (1H, ddd, $J_{4',3'}$ 8.1, $J_{4',5'a}$ 4.8, $J_{4',5'b}$ 2.9, 4′-H), 5.81–5.82 (1H, m, 1′-H), 7.9 (1H, d, $J_{H,F}$ 6.6, 6-H); *m/z* (CI) [Found: $MH^+$, 260.1039. $C_{10}H_{14}N_3O_4F$ requires $MH^+$, 260.1046].

**1-[2′,3′-Dideoxy-3′-*C*-(hydroxymethyl)-β-D- and -α-D-*erythro*-pentofuranosyl]-5-fluorocytosine phenyl 5′,6′-cyclic phosphate (15)**

To a stirred solution of diol (**2b**) (100 mg, 0.38 mmol) in freshly distilled pyridine (5 ml) under an atmosphere of argon was added dropwise, in pyridine (1 ml), phenyl phosphorodichloridate (100 mg, 0.46 mmol). After 18 hours, DCM (15 ml) was added and the mixture washed with saturated aqueous $NaHCO_3$ (3 ml). The organic phase was washed with brine, dried ($MgSO_4$) and evaporated. Purification of the residue by flash-column chromatography (gradient elution, 90:10 to 85:15 DCM–MeOH as eluant) afforded the title compound (**15**) as an amorphous white solid (12 mg, 0.030 mmol, 7%). mp 103–108 °C; due to the complexity of this NMR spectrum, it was not usually possible to differentiate α/β signals (1:4 ratio); $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$) 1.7–1.85, 2.81–2.9 (1H, m, 2′a-H), 2.18–2.2 (1H, m, 2′b-H), 2.55–2.63, 2.7–2.8, 2.9–3.0 (1H, m, 3′-H), 3.85–4.02 (1H, m, 6′a-H), 4.03–4.25, 4.25–4.7 (4H, m, 6′b-H, 4′-H, 5′-H), 5.6–5.9 (1H, br s, NH), 5.95 [0.2H, t, $J_{1',2'}$ 6.6, 1′-H (α-anomer)], 5.99–6.05 [0.8H, 2 × d, $J_{1',2'}$ 7.0, 1′-H (β-anomer)], 7.15–7.38 (5H, m, Ph), 7.39–7.45 [0.8H, 2 × d, $J_{6,F}$ 6.23, 6-H (β-anomer)], 7.45–7.55 [0.2H, 2 × d, $J_{6,F}$ 7.0, 6-H (α-anomer)], 7.6–7.8 (1H, br s, NH); $\delta_C$(100 MHz; $CDCl_3$; $Me_4Si$) 35.0, 35.7, 35.8, 36.0 (2′-C), 43.6, 44.6, 46.2, 47.3 (3′-C), 65.5, 70.1, 72.3, 72.4 (5′-C and 6′-C), 81.0, 82.2, 82.3, 82.6 (4′-C), 86.3, 86.7, 88.0, 88.3 (1′-C), 119.8, 119.9, 120.0, 125.5, 125.6, 129.7, 129.9, 136.0, 138.1 (OPh), 124.0, 124.3, 124.4 (6-C), 150.0 (5-C), 153.2 (4-C), 158.0 (2-C); *m*/*z* (CI) [Found: $MH^+$, 398.0936. $C_{16}H_{17}N_3PO_6F$ requires $MH^+$, 398.0917].

**(4*R*,5*S*)-[Allyloxy(diisopropylamino)phosphinoxymethyl]-5-(*tert*-butyldimethylsiloxymethyl)tetrahydrofuran-2-one (16)**

To a stirred solution of tetrazole (70 mg, 1.0 mmol) in dry DCM at 25 °C under an atmosphere of argon was added diisopropylamine (100 mg, 1.0 mmol). After 1 hour and the formation of a thick suspension, the photoadduct (**6**) (0.5 g, 1.92 mmol) was added. This mixture was again stirred for 1 hour and then treated with allyl tetraisopropyl phosphorodiamidite (0.63 ml, 2.0 mmol). After 2 hours the mixture was washed with aq. $NaHCO_3$ (5 ml) and extracted with DCM (3 × 10 ml). The combined organic extracts were dried over $MgSO_4$ and evaporated. Purification of the residue by *rapid* flash-column chromatography (15:85 ether–light petroleum as eluant) afforded the title compound (**16**) as a light yellow oil (0.73 g, 1.60 mmol, 85%); $\nu_{max}$ (film)/$cm^{-1}$ 3000–2800s (CH), 1783s (CO), 1463m (C–O), 1364m, 1256m, 1184s, 1125, 1026s, 976s; $\delta_H$(250 MHz; $CDCl_3$; $Me_4Si$) 0.06 (3H, s, SiMe), 0.07 (3H, s, SiMe), 0.88 [9H, s, $C(CH_3)_3$], 1.16 (6H, d, $J_{Me,CH}$ 1.58, 2 × isopropyl-Me), 1.18 (6H, d, $J_{Me,CH}$ 1.58, 2 × isopropyl-Me), 2.36 (1H, dd, $J_{gem}$ 12.6, $J_{3a,4}$ 9.2, 3a-H), 2.65–2.84 (2H, m, 4-H and 3b-H), 3.52–3.75 (5H, m, 6a-H and 7-H and 2 × isopropyl-CH), 3.88 (1H, dd, $J_{gem}$ 11.3, $J_{6b,5}$ 2.9, 6b-H), 4.03–4.2 (2H, m, $OCH_2C$=C), 4.44 (1H, ddd, $J_{5,4}$ 8.9, $J_{5,6a}$ 2.8, $J_{5,6b}$ 2.8, 5-H), 5.11–5.16 (1H, m, $J_{cis}$ 10.3, CH=C$H_{2\ cis}$), 5.28 (1H, ddd, $J_{trans}$ 17.2, $J_{gem}$ 3.5, $J_{H,P}$ 1.7, CH=C$H_{2\ trans}$), 5.83–6.05 (1H, m, C*H*=$CH_2$); $\delta_C$(66 MHz; $CDCl_3$; $Me_4Si$) −5.5 (2 × MeSi), 18.2 [*C*$(CH_3)_3$], 24.4, 24.5, 24.6, 24.7 (4 × isopropyl $CH_3$), 25.8 [C(*C*$H_3)_3$], 31.9 (3-C), 37.8 (4-C), 42.9, 43.1 (2 × isopropyl CH), 64.2, 64.3, 64.4, 64.5 (2 × $CH_2$-O-P), 82.4 (5-C), 115.7 (C=*C*$H_2$), 135.4, 135.5 (C=*C*H-O), 176.8 (C=O); *m*/*z* (CI) [Found: $MH^+$, 447.2560. $C_{21}H_{42}NPO_5Si$ requires $MH^+$, 447.2569].

**(4*R*,5*S*)-[Allyloxy(diisopropylamino)phosphinoxymethyl]-5-(hydroxmethyl)tetrahydrofuran-2-one (17)**

To a THF (20 ml) solution of silyl-phosphoramidite ester (**16**) (1.5 g, 2.92 mmol) at 25 °C was added TBAF (2.9 ml, 1 M solution in THF, 2.9 mmol). After one hour the black solution was evaporated *in vacuo* to afford a thick black oil. Purification by *rapid short path* flash chromatography (2:8 EtOAc–ether as eluant) afforded the title compound (**17**) as a light yellow oil (0.81 g, 2.4 mmol, 83%); *m*/*z* (CI) [Found: $MH^+$, 334.1793. $C_{15}H_{28}NPO_5$ requires $MH^+$, 334.1783]. Due to the presence of tetrabutylammonium fluoride residues and the instability of this compound, further characterisation or purification was not possible.

**(1*R*,7*S*)-4-(Prop-2′-enyloxy)-3,5,8-trioxa-4-phosphabicyclo-[5.3.0]decan-9-one (18)**

To a stirred solution of phosphoramidite (**17**) (130 mg, 0.34 mmol) in dry DCM (10 ml) at 0 °C (ice–water) under argon was added tetrazole (30 mg, 0.37 mmol). The solution was stirred at 0 °C for 2 hours and then gradually allowed to warm to room temperature over 18 hours. Evaporation of the solvent *in vacuo* followed by *rapid* flash-column chromatography of the residue (100% ether as eluant) afforded the title compound (**18**) as a colourless oil (40 mg, 0.17 mmol, 51%); $\nu_{max}$ (film)/$cm^{-1}$ 3000–2800s (CH), 1790s (CO), 1468m (C–O), 1190s, 876w; $\delta_H$(250 MHz; $CDCl_3$; $Me_4Si$) (all multiplicities and coupling constants are assigned using P-decoupled spectra). Conformer No. 1: 2.25 (1H, dd, $J_{gem}$ 17.0, $J_{10a,1}$ 2.5, 10-H$^a$), 2.67 (1H, dd, $J_{gem}$ 17.0, $J_{10b,1}$ 8.1, 10-H$^b$), 3.15–3.35 (1H, m, 1-H), 3.75 (1H, dd, $J_{gem}$ 11.7, $J_{2a,1}$ 8.5, 2-H$^a$), 4.2 (1H, dd, $J_{gem}$ 10.3, $J_{6a,7}$ 6.23, 6-H$^a$), 4.2–4.35 (3H, m, 6-H$^b$, 2-H$^b$ and 7-H), 4.36–4.45 (2H, m, 1′-H), 5.24 (1H, dd, $J_{cis}$ 10.3, $J_{gem}$ 1.5, 3′-H), 5.34 (1H, dd, $J_{trans}$ 17.2, $J_{gem}$ 1.5, 3′-H), 5.87–6.04 (1H, m, 2′-H). Conformer No. 2: 2.31 (1H, dd, $J_{gem}$ 17.0, $J_{10,1}$ 2.5, 10-H$^a$), 2.62 (1H, dd, $J_{gem}$ 17.0, $J_{10b,1}$ 8.0, 10-H$^b$), 2.72–2.91 (1H, m, 1-H), 3.85 (1H, dd, $J_{gem}$ 11.0, $J_{6a,7}$ 9.5, 6-H$^a$), 3.96–4.03 (2H, m, 2-H), 4.2–4.4 (2H, m, 1′-H), 4.51 (1H, dd, $J_{gem}$ 11.0, $J_{6b,7}$ 5.8, 6-H$^b$), 4.73–4.85 (1H, m, 7-H), 5.22 (1H, dd, $J_{cis}$ 10.3, $J_{gem}$ 1.5, 3′-H), 5.32 (1H, dd, $J_{trans}$ 17.2, $J_{gem}$ 1.6, 3′-H), 5.87–6.04 (1H, m, 2′-H); $\delta_C$(66 MHz; $CDCl_3$; $Me_4Si$) Conformer No. 1: 33.7 (10-C), 44.5 (1-C), 64.7 (6-C), 64.8 (1′-C), 66.7 (2-C), 81.5 (7-C), 117.4 (3′-C), 134.0 (2′-C), 174.3 (2-C). Conformer No. 2: 33.2 (10-C), 44.5 (1-C), 63.0 (6-C), 64.9 (1′-C), 67.9 (2-C), 81.5 (7-C), 117.4 (3′-C), 134.2 (2′-C), 174.4 (9-C); *m*/*z* (CI) [Found: $(M + NH_4)^+$, 251.0922. $C_9H_{13}PO_5$ requires $MNH_4^+$, 251.0922].

**(1*R*,7*S*)-4-(Prop-2′-enyloxy)-3,5,8-trioxa-4λ$^5$-phosphabicyclo-[5.3.0]decane-4,9-dione (19)**

To a stirred solution of cyclic phosphite (**18**) (230 mg, 0.99 mmol), distilled $Et_3N$ (0.25 ml) and dry MeCN (20 ml) at room temperature under argon was added *tert*-butyl hydroperoxide (0.18 ml, 5.6 M solution in decane, excess). After 1 hour isopropanol (5 ml) was added. The solution was stirred for a further 2 hours and then evaporated *in vacuo* to afford a gummy oil. Flash-column chromatography of the residue (100% EtOAc as eluant) afforded the title compound (**19**) as a white crystalline solid (240 mg, 0.97 mmol, 98%); $\nu_{max}$ (film)/$cm^{-1}$ 3000–2800s (CH), 1791s (CO), 1471w (C–O), 1423w, 1276s (P=O), 1203s, 1118s, 1027s (P–O–Alkyl), 834m; $\delta_H$(250 MHz; $CDCl_3$; $Me_4Si$) (all multiplicities and coupling constants are assigned using P-decoupled spectra). Conformer No. 1: 2.35 (1H, dd, $J_{gem}$ 17.0, $J_{10a,1}$ 6.8, 10-H$^a$), 2.57 (1H, dd, $J_{gem}$ 17.0, $J_{10b,1}$ 7.9, 10-H$^b$), 2.83–3.03 (1H, m, 1-H), 3.92 (1H, m, 6-H$^a$), 4.14 (1H, dd, $J_{gem}$ 11.5, $J_{2a,1}$ 5.8, 2-H$^a$), 4.28 (1H, dd, $J_{gem}$ 11.5, $J_{2b,1}$ 3.9, 2-H$^b$), 4.56–4.65 (3H, m, 1′-H and 6-H$^b$), 4.83 (1H, dt, $J_{6,7}$ 9.9, $J_{1,7}$ 5.2, 7-H), 5.3 (1H, dd, $J_{cis}$ 10.4, $J_{gem}$ 1.6, 3′-H$^a$), 5.39 (1H, dd, $J_{trans}$ 18.6, $J_{gem}$ 1.6, 3′-H$^b$), 5.87–6.04 (1H, m, 2′-H). Conformer No. 2: 2.41 (1H, dd, $J_{gem}$ 16.9, $J_{10a,1}$ 7.1, 10-H$^a$), 2.7 (1H, dd, $J_{gem}$ 16.9, $J_{10b,1}$ 8.2, 10-H$^b$), 3.28–3.47 (1H, m, 1-H), 3.87–3.95 (1H, m, 2-H$^a$), 4.07–4.19 (1H, m, 6-H$^a$), 4.4–4.51 (3H, m, 7-H, 2-H$^b$ and 6-H$^b$), 4.57–4.65 (2H, m, 1′-H), 5.3 (1H, dd, $J_{cis}$ 10.4, $J_{gem}$ 1.6, 3′-H$^a$), 5.4 (1H, dd, $J_{trans}$ 18.5, $J_{gem}$ 1.6, 3′-H$^b$), 5.87–6.04 (1H, m, 2′-H); $\delta_C$(62.5 MHz; $CDCl_3$; $Me_4Si$) Conformer No. 1: 31.7 (10-C), 43.9 (1-C), 66.4 (2-C), 67.6 (6-C), 69.6 (1′-C),

80.1 (7-C), 119.6 (3′-C), 132.0 (2′-C), 173.1 (9-C). Conformer No. 2: 32.4 (10-C), 43.3 (1-C), 66.7 (6-C), 67.5 (2-C), 69.7 (1′-C), 80.3 (7-C), 119.5 (3′-C), 132.1 (9′-C), 173.1 (2-C); *m*/*z* (CI) [Found: $MH^+$, 249.0528. $C_9H_{13}PO_6$ requires $MH^+$, 249.0528].

### (1*R*,7*S*)-4-Oxo-4-(prop-2′-enyloxy)-3,5,8-trioxa-4-phosphabicyclo[5.3.0]decan-9-yl acetate (20)

To a solution of lactone (**19**) (0.25 g, 1.0 mmol) in DCM (20 ml) at −78 °C ($CO_2$–acetone) under argon was added dropwise DIBAL-H (1.3 ml, 1 M solution in toluene, 1.3 mmol). After 2 hours, MeOH (0.5 ml) was added and the solution stirred for a further 1 hour. The mixture was treated with EtOAc (2 ml) and saturated aqueous $NaHCO_3$ (1 ml) and then allowed to warm to room temperature over 2 hours. The solution was then dried over $MgSO_4$, filtered through Celite and evaporated to afford the crude lactol as a colourless oil. Without purification this was dissolved in DCM (20 ml) and pyridine (0.24 ml, 3.0 mmol), cooled to 0 °C and treated with acetic anhydride (3 ml) and DMAP (5 mg, cat.). After warming to room temperature and stirring for 1 hour, water (5 ml) was added and the solution extracted with DCM (2 × 10 ml). The combined organic phases were washed with brine, dried ($MgSO_4$) and evaporated *in vacuo* to afford a colourless oil. Purification by flash-column chromatography (100% EtOAc as eluant) afforded the title compound (**20**) as a colourless oil (0.19 g, 0.65 mmol, 65%); $\nu_{max}$ (film)/$cm^{-1}$ 3000–2800s (CH), 1739s (CO), 1378w (C–O), 1236s (P=O), 1020s (P–O–Alkyl), 931w, 834m; $\delta_H$(250 MHz; $CDCl_3$; $Me_4Si$) 1.6–2.0 (2H, m, 10-H), 2.05 (3H, 2 × s, Me), 2.51–2.7 (1H, m, 1-H), 3.7–4.5 (5H, m, 2-H, 6-H and 7-H), 4.51–4.66 (2H, m, 1′-H), 5.26 (1H, dd, $J_{cis}$ 10.2, $J_{gem}$ 1.5, 3′-H[a]), 5.38 (1H, dd, $J_{trans}$ 17.0, $J_{gem}$ 1.5, 3′-H[b]), 5.85–6.05 (1H, m, 2′-H), 6.30 (1H, dd, $J_{9,10a}$ 6.0, $J_{9,10b}$ 3.8, 9-H); $\delta_C$(62.5 MHz; $CDCl_3$; $Me_4Si$) 21.1, 21.2, 21.3 (CO*Me*), 34.2, 34.9, 35.0, 35.8 (10-C), 43.3, 43.9, 45.3, 46.2 (1-C), 66.9, 67.0 (2-C), 68.7, 68.8 (6-C), 68.9, 69.0 (1′-C), 80.1, 80.8, 81.9, 82.5 (7-C), 97.3, 97.4, 97.5, 97.9 (9-C), 118.7, 118.9 (3′-C), 131.9, 132.0, 132.1 (2′-C), 170.0, 170.1, 170.2, 170.3 (CO); *m*/*z* (CI) [Found: $MH^+$, 293.0777. $C_{11}H_{17}PO_7$ requires $MH^+$, 293.0790].

### Allyl 1-[2′,3′-dideoxy-3′-*C*-(hydroxymethyl)-β-D- and -α-D-*erythro*-pentofuranosyl]-5-fluorocytosine 5′,6′-cyclic phosphate (21)

A suspension of 5-fluorocytosine (37 mg, 0.29 mmol) and *N*,*O*-bis(trimethylsilyl)acetamide (1 ml, excess) was refluxed for 1 hour. Excess reagents were removed *in vacuo* and the residue co-evaporated with toluene (3 × 2 ml) until crystallisation occurred. The bis(trimethylsilyl)-5-fluorocytosine thus obtained was re-dissolved in dry MeCN (5 ml) and transferred to an oven-dried vessel under argon, containing acetate (**20**) (75 mg, 0.26 mmol). The flask was cooled to 0 °C, and the mixture treated with $SnCl_4$ (0.28 ml, 1 M solution in DCM, 0.28 mmol), and stirred for 4 hours. After warming to room temperature, aqueous sodium potassium tartrate (5 ml) was added, and the mixture was stirred for a further 1 hour and extracted with DCM (3 × 5 ml). The combined organic phases were dried over $MgSO_4$ and evaporated. Purification by flash-column chromatography (10:90 MeOH–DCM as eluant) afforded the title compound (**21**) as an impure clear oil (75 mg, 0.20 mmol, 80%, crude). Repeated purification failed to remove impurities. This compound was de-allylated without exhaustive characterisation or further purification.

### 1-[2′,3′-Dideoxy-3′-*C*-(hydroxymethyl)-β-D- and -α-D-*erythro*-pentofuranosyl]-5-fluorocytosine diisopropylammonium 5′,6′-cyclic phosphate (22)

To a stirred solution of allyl phosphate (**21**) (40 mg, 0.11 mmol), diisopropylamine (100 mg) and MeCN (5 ml) at 25 °C was added tetrakis(triphenylphosphine)palladium (2 mg, 1.7 μM). After 5 hours the formation of a white precipitate was observed. The solvent was evaporated *in vacuo* and the residue purified by flash-column chromatography (40:60 MeOH–DCM as eluant) to afford the title compound (**22**) as a white glassy solid (30 mg, 0.07 mmol, 65%); mp 135–138 °C; $\nu_{max}$ (film)/$cm^{-1}$ 3500–3200s ($NH_2$), 3000–2800s (CH), 1682s (C=O), 1614s (C=C), 1510m (C=N), 1397w, 1232s (P=O), 1077s (P–O–Alkyl); $\delta_H$(250 MHz; $CDCl_3$; $Me_4Si$) α-anomer: 1.35 (12H, d, $J_{CH,CH_3}$ 6.5, 4 × $CH_3$), 2.20 (1H, dd, $J_{2'a,2'b}$ 9.9, $J_{2'a,1'}$ 4.6, 2′a-H), 2.21 (1H, dd, $J_{2'b,2'a}$ 9.9, $J_{2'b,3'}$ 4.6, 2′b-H), 2.9–3.0 (1H, m, 3′-H), 3.51 (2H, septet, $J_{CH,CH3}$ 6.5, C*H*$CH_3$), 3.7–3.95 (1H, m, 5′a-H), 4.0–4.25 (3H, m, 5′b, 6′-H), 4.25–4.4 (1H, m, 4′-H), 6.07–6.14 (1H, m, 1′-H), 7.78 (1H, d, $J_{H,F}$ 6.5, 6-H); β-anomer: 1.35 (12H, d, $J_{CH,CH_3}$ 6.5, 4 × $CH_3$), 1.79 (1H, ddd, $J_{gem}$ 12.7, $J_{2'a,3'}$ 7.7, 2′a-H), 2.72 (1H, ddd, $J_{gem}$ 12.7, $J_{2'b,1'}$ 6.3, 2′b-H), 2.8–3.0 (1H, m, 3′-H), 3.51 (2H, septet, $J_{CH,CH_3}$ 6.5, $CHCH_3$), 3.7–3.95 (2H, m, 6′a-H, 5′a-H), 4.0–4.3 (2H, m, 6′b-H, 5′a-H), 4.5 (1H, dt, $J_{4',5'}$ 9.6, $J_{4',3'}$ 4.7, 4′-H), 6.12 (1H, dd unresolved, $J_{1',2'b}$ 6.3, 1′-H), 7.96 (1H, d, $J_{H,F}$ 6.5, 6-H); $\delta_C$(62.5 MHz; $CDCl_3$; $Me_4Si$). α-anomer: 19.7 (4 × $CH_3$), 37.4 (2′-C), 45.2 (3′-C), 49.2 (*C*$HCH_3$), 66.9 (6′-C), 67.7 (5′-C), 85.0 (4′-C), 88.0 (1′-C), 126.7 (d, 6-C), 138.1 (d, 5-C), 157.2 (4-C) 160.1 (2-C) β-anomer: 19.7 (4 × $CH_3$), 37.6 (2′-C), 47.9 (3′-C), 49.2 (*C*$HCH_3$), 67.0 (6′-C), 67.8 (5′-C), 84.1 (4′-C), 89.3 (1′-C), 126.5 (d, 6-C), 138.2 (d, 5-C), 157.2 (4-C) 160.1 (2-C) *m*/*z*; (CI) [Found: M − (5FC + $^i$Pr)$H^+$, 194. $C_{16}H_{28}N_4PO_6F$ requires $M$ − (5FC + $^i$Pr)$H^+$, 194; Found: (M = 5FC)$H^+$, 130.0410. $C_4H_4FN_3O$ requires ($M$ = 5FC)$H^+$, 130.0416.

### 9-[3′-*C*-(*tert*-Butyldimethylsiloxymethyl)-5′-*O*-(*tert*-butyldimethylsilyl)-2′,3′-dideoxy-α-D- and -β-D-*erythro*-pentofuranosyl]adenine (23)

To an oven-dried vessel containing bis(TBDMS)-acetate (**8**) (250 mg, 0.6 mmol), bis(trimethylsilyl)adenine (200 mg, 0.72 mmol) and HPLC grade MeCN (5 ml) was added triethylsilyl triflate (14 μL, 0.06 mmol). After 18 hours at 60 °C the solvent was evaporated and the residue purified by flash column chromatography (9:91 MeOH–DCM as eluant). This afforded the title compound (**23**) as a colourless oil in 1:1.25 α:β anomeric ratio. (220 mg, 0.50 mmol, 74%); $\nu_{max}$ (film)/$cm^{-1}$ 3322 and 3172br s ($NH_2$), 2954–2860s (CH), 1649m ($NH_2$ bending), 1590m, 1471m, 1254, 1092br, 837s, 777m; $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$) α-anomer: 0.03–0.07 (12H, 4 × s, 4 × MeSi), 0.84–0.88 [18H, 2 × s, C$(CH_3)_3$], 2.42–2.7 (3H, m, 2′-H, 3′-H), 3.67 (2H, d, $J_{6',3'}$ 4.4, 6′-H), 3.72 (1H, dd, $J_{gem}$ 11.0, $J_{5'a,4'}$ 4.0, 5′a-H), 3.82 (1H, dd, $J_{gem}$ 11.0, $J_{5'b,4'}$ 4.0, 5′b-H), 4.25 (1H, ddd, $J_{4',3'}$ 7.7, $J_{4',5'a}$ 4.0, $J_{4',5'b}$ 4.0, 4′-H), 5.8 (2H, br, $NH_2$), 6.28 (1H, m, 1′-H), 8.03 (1H, s, 8-H), 8.31 (1H, s, 2-H); β-anomer: 0.03–0.07 (12H, 4 × s, 4 × MeSi), 0.84–0.88 [18H, 2 × s, C$(CH_3)_3$], 2.42–2.7 (3H, m, 2′-H, 3′-H), 3.67 (2H, d, $J_{6',3'}$ 4.4, 6′-H), 3.77 (1H, dd, $J_{gem}$ 11.36, $J_{5'a,4'}$ 3.3, 5′a-H), 3.98 (1H, dd, $J_{gem}$ 11.36, $J_{5'b,4'}$ 3.3, 5′b-H), 4.03 (1H, ddd, $J_{4',3'}$ 6.6, $J_{4',5'a}$ 3.3, $J_{4',5'b}$ 3.3, 4′-H), 5.8 (2H, br, $NH_2$), 6.28 (1H, m, 1′-H), 8.28–8.3 (2H, 2 × s, 8-H, 2-H); $\delta_C$(62.5 MHz; $CDCl_3$; $Me_4Si$) α/β anomers: −5.5, −5.3 (MeSi), 18.3, 18.4 [*C*$(CH_3)_3$], 25.8, 25.8 [C$(CH_3)_3$], 35.6, 36.3 (2′-C), 40.2, 42.7 (3′-C), 62.8, 63.1 (6′-C), 63.9, 64.8 (5′-C), 82.8, 83.8 (4′-C), 84.7, 85.3 (1′-C), 138.5, 139.1 (8-C), 152.7, 152.8 (2-C), 120.5, 120.6, 148.5, 149.5, 155.3, 155.4 (4-C, 5-C, 6-C); *m*/*z* (CI) [Found: $MH^+$, 494.2990. $C_{23}H_{43}N_5O_3Si_2$ requires $MH^+$, 494.2983].

### 6-*N*-Benzoyl-9-[3′-*C*-(*tert*-butyldimethylsiloxymethyl)-5′-*O*-(*tert*-butyldimethylsilyl)-2′,3′-dideoxy-α-D- and -β-D-*erythro*-pentofuranosyl]adenine (24)

To an oven-dried flask under argon containing *N*-benzoyladenine (167 mg, 0.70 mmol), dry pyridine (0.5 ml), TMSCl (1 drop) and HPLC grade MeCN (5 ml) was added bis(trimethylsilyl)trifluoroacetamide (360 mg, 1.4 mmol). After 20

minutes, acetate (**8**) (0.28 g, 0.67 mmol) and triethylsilyl triflate (10 μL, 0.04 mmol) were added and the solution heated at 60 °C for 18 hours. The solvent was evaporated and the residue purified by flash column chromatography (4:96 MeOH–DCM as eluant). This afforded the title compound as a colourless oil in a 1:1.25 α/β anomeric ratio (296 mg, 0.50 mmol, 75%); $\nu_{max}$ (film)/cm$^{-1}$ 3260br s (NH), 3000–2800s (CH), 1702s (C=O), 1611 and 1580 (NH bending), 1514m, 1255m, 1093s, 837s, 778m; $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$) α-anomer: 0.03–0.07 (12H, 4 × s, 4 × MeSi), 0.83–0.9 [18H, 2 × s, $C(CH_3)_3$], 2.46–2.8 (3H, m, 2′-H, 3′-H), 3.68 (2H, d, $J_{6',3'}$ 5.12, 6′-H), 3.68–3.73 (1H, m, 5′a-H), 3.84 (1H, dd, $J_{gem}$ 11.0, $J_{5'b,4'}$ 3.66, 5′b-H), 4.29 (1H, m, 4′-H), 6.37 (1H, m, 1′-H), 7.45–7.6 (3H, m, Ph), 7.98 (2H, m, Ph), 8.21 (1H, s, 8-H), 8.75 (1H, s, 2-H), 9.0–9.2 (1H, br s, NH); β-anomer: 0.03–0.07 (12H, 4 × s, 4 × MeSi), 0.83–0.9 [18H, 2 × s, $C(CH_3)_3$], 2.46–2.8 (3H, m, 2′-H, 3′-H), 3.55–3.7 (2H, m, 6′-H), 3.77 (1H, dd, $J_{gem}$ 11.36, $J_{5'a,4'}$ 3.3, 5′a-H), 3.98 (1H, dd, $J_{gem}$ 11.36, $J_{5'b,4'}$ 2.9, 5′b-H), 4.07 (1H, m, 4′-H), 6.37 (1H, m, 1′-H), 7.45–7.6 (3H, m, Ph), 7.98 (2H, m, Ph), 8.46 (1H, s, 8-H), 8.74 (1H, s, 2-H), 9.0–9.2 (1H, br s, NH); $\delta_C$(62.5 MHz; $CDCl_3$; $Me_4Si$) α/β anomers: −5.5, −5.3 (MeSi), 18.3, 18.5 [*C*$(CH_3)_3$], 25.8, 25.9 [C(*C*$H_3)_3$], 35.6, 36.3 (2′-C), 40.2, 42.6 (3′-C), 62.7, 63.1 (6′-C), 63.9, 64.8 (5′-C), 83.0, 84.0 (4′-C), 85.1, 85.5 (1′-C), 127.8, 128.7, 132.6 (Ph), 141.0, 141.6 (8-C), 150.9, 152.4 (2-C), 123.2, 123.3, 132.8, 133.0, 149.3, 150.6 (4-C, 5-C, 6-C), 154.3 (C=O); *m*/*z* (CI) [Found: MH$^+$, 598.3246. $C_{30}H_{47}N_5O_4Si_2$ requires *M*H$^+$, 598.3245].

### 9-[2′,3′-Dideoxy-3′-*C*-(hydroxymethyl)-α-D- and -β-D-*erythro*-pentofuranosyl]adenine (3)

To a THF solution (10 ml) of bis-silyl nucleoside (**23**) (160 mg, 0.32 mmol) at room temperature was added TBAF (0.64 ml, 1 M solution in THF, 0.64 mmol). After 2 hours the solvent was removed *in vacuo* and the residue purified by flash column chromatography (10:90 MeOH–DCM as eluant). This afforded the title compound as a white amorphous solid (80 mg, 0.3 mmol, 80%); mp 151–153 °C (decomp.); (Found: C, 49.3; H, 5.8; N, 25.3; $C_{11}H_{15}N_5O_3$ requires C, 49.8; H, 5.7; N, 26.39%); $\nu_{max}$ (film)/cm$^{-1}$ 3600–3100br (OH, $NH_2$), 3000–2800m (CH), 1648 and 1603s, ($NH_2$ bending) 1477w, 1417w, 1246w, 1103w, 1044w; $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$) α-anomer: 2.4–2.8 (3H, m, 2′-H, 3′-H), 3.66–3.78 (3H, m, 6′-H, 5′b-H), 3.83 (1H, dd, $J_{5'a,5'b}$ 12.1, $J_{5'a,4'}$ 3.7, 5′a-H), 4.31 (1H, ddd, $J_{4',3'}$ 8.1, $J_{4',5'b}$ 4.4, $J_{4',5'a}$ 3.7, 4′-H), 6.30 (1H, dd, $J_{1',2'a}$ 5.9, $J_{1',2'b}$ 5.9, 1′-H), 8.23 (1H, s, 8-H), 8.4 (1H, s, 2-H); β-anomer: 2.4–2.8 (3H, m, 2′-H, 3′-H), 3.66–3.78 (3H, m, 6′-H, 5′b-H), 3.95 (1H, dd, $J_{5'a,5'b}$ 12.2, $J_{5'a,4'}$ 2.7, 5′a-H), 4.1 (1H, ddd, $J_{4',3'}$ 6.6, $J_{4',5'a}$ 2.7, $J_{4',5'b}$ 3.3, 4′-H), 6.34 (1H, dd, $J_{1',2'}$ 6.6, 1′-H), 8.28 (1H, s, 8-H), 8.3 (1H, s, 2-H); $\delta_C$(100 MHz; $CDCl_3$; $Me_4Si$) α-anomer: 35.4 (2′-C), 42.1 (3′-C), 61.3 (6′-C), 61.9 (5′-C), 82.9 (4′-C), 84.3 (1′-C), 119.0, 147.8, 155.2 (2-C, 4-C, 6-C), 138.5 (8-C), 151.7 (5-C); β-anomer: 34.5 (2′-C), 40.5 (3′-C), 62.5 (6′-C), 62.6 (5′-C), 84.1 (4′-C), 85.4 (1′-C), 119.3, 148.4, 155.2 (2-C, 4-C, 6-C), 139.1 (8-C), 151.9 (5-C); *m*/*z* (CI) [Found: MH$^+$, 266.1260. $C_{11}H_{15}N_5O_3$ requires *M*H$^+$, 266.1253].

### 6-*N*-Benzoyl-9-[2′,3′-dideoxy-3′-*C*-(hydroxymethyl)-α-D- and -β-D-*erythro*-pentofuranosyl]adenine (25)

To a THF solution (30 ml) of bis-silyl nucleoside (**24**) (630 mg, 1.05 mmol) at room temperature was added TBAF (2.1 ml, 1 M solution in THF, 2.10 mmol). After 2 hours the solvent was removed *in vacuo* and the residue purified by flash column chromatography (9:91 MeOH–DCM as eluant). This afforded the title compound as a white amorphous solid (200 mg, 0.54 mmol, 52%) (Found: C, 57.8; H, 5.8; N, 19.5; $C_{18}H_{19}N_5O_4$ requires C, 58.5; H, 5.2; N, 18.9%); mp 69–71 °C; $\nu_{max}$ (film)/cm$^{-1}$ 3600–3100br (OH, $NH_2$), 3000–2800m (CH), 1697s (C=O), 1613 and 1581s ($NH_2$ bending), 1457s, 1256w, 1094w; $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$) α-anomer: 2.51–2.64 (2H, m, 2′a-H, 3′-H), 2.77–2.81 (1H, m, 2′-b), 3.65–3.7 (4H, m, 6′-H, 5′-H), 4.33 (1H, m, 4′-H), 6.4 (1H, m, 1′-H), 7.3–7.6 (3H, m, Ph), 8.1 (2H, d, $J_{Ph}$ 7.7, Ph), 8.39 (1H, s, 8-H), 8.75 (1H, s, 2-H), 10.2–10.5 (1H, br, NH); β-anomer: 2.41 (1H, ddd, $J_{gem}$ 13.9, $J_{2'a,1'}$ 6.9, $J_{2'a,3'}$ 6.9, 2′a-H), 2.62–2.81 (2H, m, 2′b-H, 3′-H), 3.71–3.81 (3H, m, 6′-H, 5′a-H), 3.96 (1H, dd, $J_{gem}$ 12.1, $J_{5'b,4'}$ 3.3, 5′b-H), 4.11 (1H, ddd, $J_{4',3'}$ 6.6, $J_{4',5'a}$ 3.3, $J_{4',5'b}$ 3.3, 4′-H), 6.35 (1H, m, 1′-H), 7.3–7.6 (3H, m, Ph), 8.1 (2H, d, $J_{Ph}$ 7.7, Ph), 8.43 (1H, s, 8-H), 8.77 (1H, s, 2-H), 10.2–10.5 (1H, br, NH); $\delta_C$(100 MHz; $CDCl_3$; $Me_4Si$) α/β anomers: 35.1, 36.3 (2′-C), 41.3, 43.3 (3′-C), 62.0, 63.1 (6′-C), 63.4, 63.5 (5′-C), 83.9, 85.4 (4′-C), 85.2, 86.4 (1′-C), 123.4, 123.6, 149.9, 150.0, 151.0, 151.5 (4-C, 5-C, 6-C), 128.3, 128.8, 132.9, 133.7 (Ph), 141.7, 142.3 (8-C), 152.3, 152.5 (2-C), 165.8 (C=O); *m*/*z* (CI) [Found: MH$^+$, 370.1522 $C_{18}H_{19}N_5O_4$ requires *M*H$^+$, 370.1515].

### 6-*N*-Benzoyl-9-[2′,3′-dideoxy-3′-*C*-(hydroxymethyl)-β-D- and -α-D-*erythro*-pentofuranosyl]adenine phenyl 5′,6′-cyclic phosphate (26)

To a solution of diol (**25**) (200 mg, 0.54 mmol) in dry pyridine (10 ml) at 25 °C under argon was added dropwise phenyl phosphorodichloridate (150 μL, 0.75 mmol). After 18 hours of stirring, the solvent was evaporated and the residue purified by flash-column chromatography (10:90 MeOH–DCM). This afforded the title compound as a colourless oil (105 mg, 0.21 mmol, 38%); $\nu_{max}$ (film)/cm$^{-1}$ 3500–3000m (NH amide), 3000–2800w (CH), 1694s (C=O amide), 1613 and 1581s (NH bending), 1488s, 1455s, 1286s, 1260s (P=O), 1212s (P–O–Aryl), 1050s (P–O–Alkyl); $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$) α-anomer: 2.75–2.9 (2.5 H, m, 2′-H, 0.5 3′-H), 3.1–3.25 (0.5H, m, 3′-H), 3.96–4.6 (4H, m, 6′-H, 5′-H), 4.76–4.97 (1H, 2 × m, 4′-H), 6.3–6.35 (1H, m, 1′-H), 7.2–7.4 (5H, m, O-Ph), 7.5–7.66 (3H, m, Bz), 8.02 (2H, d, $J_{Ph}$ 7.7, Bz), 8.08 (1H, 2 × s, 8-H), 8.8 (1H, 2 × s, 2-H), 9.3 (1H, br, NH); β-anomer: 2.35–2.42 (1H, m, 2′a-H), 2.75–2.9 (1H, m, 2′b-H), 3.6 (1H, m, 3′-H), 3.96–4.6 (5H, m, 6′-H, 5′-H, 4′-H), 6.35–6.4 (1H, m, 1′-H), 7.2–7.4 (5H, m, O-Ph), 7.5–7.66 (3H, m, Bz), 8.02 (2H, d, $J_{Ph}$ 7.7, Bz), 8.05 (1H, 2 × s, 8-H), 8.75 (1H, 2 × s, 2-H), 9.3 (1H, br, NH); $\delta_C$(100 MHz; $CDCl_3$; $Me_4Si$) α/β anomers: 33.4, 33.5, 34.4, 35.3 (2′-C), 44.3, 44.8, 46.6, 47.3 (3′-C), 66.8, 66.9, 67.2, 67.4, 67.6, 68.0, 68.1, 68.3 (5′-C, 6′-C), 81.5, 81.8, 82.5, 82.8 (4′-C), 84.8, 85.2, 85.4, 85.8 (1′-C), 119.7, 119.9, 125.5, 127.8, 128.7, 129.1, 129.8, 132.8, 133.3 (Ph), 123.5, 123.8, 123.9, 124.0, 149.7, 150.1, 150.3, 151.3, 151.4 (4-C, 5-C, 6-C), 140.9, 141.6, 141.7, 142.3 (8-C), 152.5, 152.6, 152.7 (2-C), 164.7 (C=O); *m*/*z* (CI) [Found: MH$^+$, 508.1361. $C_{24}H_{22}N_5PO_6$ requires *M*H$^+$, 508.1386].

### 9-[2′,3′-Dideoxy-3′-*C*-(hydroxymethyl)-β-D- and -α-D-*erythro*-pentofuranosyl]adenine phenyl 5′,6′-cyclic phenylphosphate (4)

To a MeOH–$CHCl_3$ (4:1, 10 ml) solution of benzoyl adenine (**26**) (100 mg, 0.2 mmol) at room temperature was added zinc bromide (90 mg, 4 mmol, 20 equiv.). After stirring for 72 hours the solvent was evaporated and the residue purified by flash column chromatography (10:90 MeOH–DCM as eluant). This afforded the title compound as an amorphous white solid (55 mg, 0.136 mmol, 68%); $\nu_{max}$ (film)/cm$^{-1}$ 3600–3100s ($NH_2$), 1620s, 1500m, 1252m, 1150m, 1046s, 920s; $\delta_H$(400 MHz; $CD_3OD$; $Me_4Si$) 2.42–2.53 (0.5H, m, 2′-H), 2.61–2.84 (1.5H, m, 2′-H), 2.9 (0.5H, m, 3′-H), 3.6–3.7 (0.5H, m, 3′-H), 4.0–4.61 (4H, m, 5′-H, 6′-H), 4.75–4.9 (1H, m, 4′-H), 6.4 (1H, m, *1*′-H), 7.23–7.4 (5H, m, O-Ph), 8.2–8.3 (2H, 8 × s, 8-H, 2-H); $\delta_C$(100 MHz; $CD_3OD$; $Me_4Si$) α/β anomers: 34.6, 35.6, 35.8 (2′-C), 45.8, 45.9, 48.0 (3′-C), 69.2, 69.3, 69.4, 69.5, 69.6, 69.7, 69.9, 70.0, 70.1, 70.2 (5′-C, 6′-C), 82.5, 83.6 (4′-C), 86.1, 86.4, 86.6, 86.8 (1′-C), 120.6, 120.7, 120.8, 120.9, 121.0, 126.8, 131.1, 131.2 (Ph), 141.9, 142.2, 142.5, 142.6 (8-C), 149.7, 150.3, 150.4, 151.6, 151.7, 157.1 (4-C, 5-C, 6-C), 153.7 (2-C); *m*/*z* (CI) [Found: MH$^+$, 404.1123. $C_{17}H_{18}N_5PO_5$ requires *M*H$^+$, 404.1124].

**Crystal data ‡**

**Compound 13α.** $C_9H_{13}PO_6$, $M = 248.16$, monoclinic, space group $P2_1$, $a = 9.856(12)$, $b = 6.064(6)$, $c = 11.657(14)$ Å, $\beta = 126.02(1)°$, $V = 563.6$ Å$^3$, $Z = 2$, $D_c = 1.462$ Mg m$^{-3}$, $F(000)$ 260, $\mu = 0.254$ mm$^{-1}$. Reflections collected 1481, independent reflections 891 [$R$(int) = 0.0230], Final $R$ indices [$I > 2\sigma(I)$] $R1 = 0.0513$, w$R2 = 0.1463$.

**Compound 19.** $C_{25}H_{25}N_4O_{10}P$, $M = 572.5$, orthorhombic, space group $P2_12_12_1$, $a = 11.589(12)$, $b = 24.07(2)$, $c = 28.51(2)$ Å, $V = 7953(13)$ Å$^3$, $Z = 12$, $D_c = 1.434$ Mg m$^{-3}$, $F(000) = 3576$, $\mu = 0.168$ mm$^{-1}$. Reflections collected 14542, independent reflections 9591 [$R$(int) = 0.0311], Final $R$ indices [$I > 2\sigma(I)$], $R1 = 0.0701$, w$R2 = 0.1954$.

Data for both crystals were collected with Mo-Kα radiation using the MARresearch Image Plate System. The crystals were positioned 70 mm from the Image Plate. 95 Frames were measured at 2° intervals with a counting time of 2 min. Data analysis was carried out with the XDS program.[12] Both structures were solved using direct methods with the Shelxs86 program.[13] In compound **13α** there were three molecules in the asymmetric unit with similar conformations. In both structures the non-hydrogen atoms were refined with anisotropic thermal parameters. The hydrogen atoms were included in geometric positions and given thermal parameters equivalent to 1.2 times those of the atom to which they were bonded. Both structures were refined to convergence on $F^2$ using Shelxl.[14]

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‡ Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC web page http://www.rsc.org/authors. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/307.

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