Synthesis of Imidazo-fused Bridgehead-nitrogen 2'-Deoxyribo-*C*-nucleosides: Coupling–Elimination Reactions of 2,5-Anhydro-3,4,6-tri-*O*-benzoyl-D-allonic Acid

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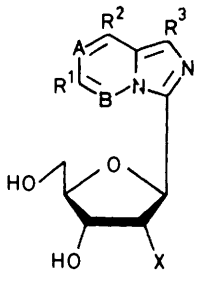
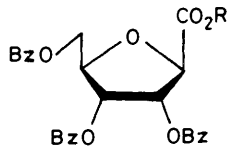
A short synthesis of imidazo-fused bridgehead-nitrogen 2'-deoxyribo-*C*-nucleosides has been developed.This is based on a coupling–elimination reaction of 2,5-anhydro-3,4,6-tri-*O*-benzoyl-D-allonic acid with a series of aminoalkyl-substituted heterocycles and alcohols. The intermediate α,β-unsaturated carboxamides and esters thus formed are converted into novel imidazo[1,5-*a*]pyridine, imidazo[1,5-*b*]pyridazine, and imidazo[5,1-*f*][1,2,4]triazine 2'-deoxyribo-*C*-nucleosides, including analogues of 2'-deoxyguanosine and 2'-deoxyadenosine. Assignment of the anomeric configuration of the nucleosides is made on the basis of proton n.O.e. experiments.

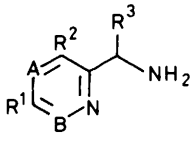
2'-Deoxyribo-*C*-nucleosides are of considerable interest as potential antiviral and antitumour agents. For example, 2'-deoxy-1-methylpseudouridine and 2'-deoxypseudoisocytidine both show inhibitory activity against mouse mastcytoma P815 cells in tissue culture.[1] However, in comparison with ribo-*C*-nucleosides only a relatively narrow range of 2'-deoxyribo-*C*-nucleosides have been reported. These include 2'-deoxypseudouridines and -isocytidines,[1-3] 2- and 8-(2'-deoxyribosyl)purines,[4] 5-(2'-deoxyribosyl)pyrazolo[4,3-*d*]pyrimidines,[5] and 6-(2'-deoxyribosyl)pyrazolo[3,4-*d*]pyrimidines.[6] Syntheses of 2'-deoxyshowdomycin[7,8] and the 2'-deoxy analogue of the antitumour agent 2-(β-D-ribofuranosyl)thiazole-4-carboxamide[9] have also been described. Notably, there are only three reports of 2'-deoxyribo-*C*-nucleosides *isosterically* related to natural purine 2'-deoxyribonucleosides.[10] We now describe a short, flexible route to a new class of imidazo-fused bridgehead-nitrogen 2'-deoxyribo-*C*-nucleosides of general structure (**1**), including a novel isostere of 2'-deoxyguanosine. The basis of this synthesis, starting from a *ribosyl* precursor, is a novel 'coupling-elimination' reaction[11] of 2,5-anhydro-3,4,6-tri-*O*-benzoyl-D-allonic acid (**3a**) with aminoalkyl-substituted heterocycles (**4**).



(1) X = H
(2) X = OH
A,B = CH,N

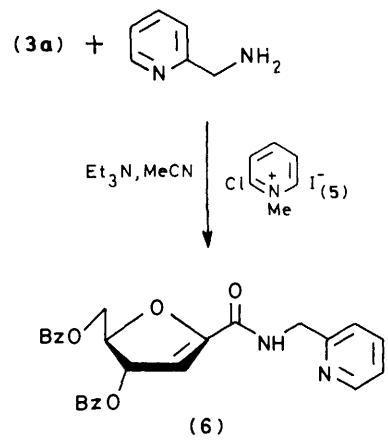


(3) a; R = H
b; R = CH_2Ph



(4)

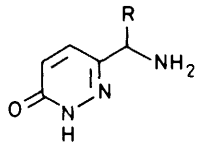
We have recently reported the synthesis of novel bridgehead-nitrogen ribo-*C*-nucleosides (**2**) *via* dehydrative coupling of (**3a**) and (**4**) using dicyclohexylcarbodi-imide (DCC).[12] However, in efforts to seek alternative coupling agents to DCC, the use of 2-chloro-*N*-methylpyridinium iodide[13] (**5**) was evaluated. Unexpectedly, when the acid (**3a**) was treated with compound (**5**) (2 equiv.) in the presence of triethylamine (4 equiv.) and 2-aminomethylpyridine (1.5 equiv.), in acetonitrile at room temperature, the α,β-unsaturated carboxamide (**6**) was obtained in 73% yield (Scheme 1). Similarly, with the heterocyclic amines (**7a** and **b**) (**8a** and **b**) the corresponding amides (**9a** and **b**) and (**10a** and **b**) were obtained in 45—61% yield. There was no evidence for the formation of the expected 2,5-anhydro-3,4,6-tri-*O*-benzoyl-D-allonic acid amides.[12]



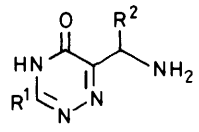
Scheme 1.

This 'coupling–elimination' process is also applicable to alcohols. Under the above conditions, but using benzyl alcohol in place of the aminoalkyl-substituted heterocycles, the novel α,β-unsaturated ester (**11a**) was obtained in high yield.[14] As with the reaction involving heterocyclic amines, the formation of benzyl 2,5-anhydro-3,4,6-tri-*O*-benzoyl-D-allonate (**3b**) was not observed. However, (**3b**) was the major product when only one equivalent of each of triethylamine, benzyl alcohol, and

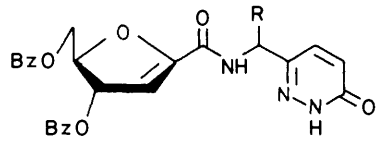
coupling agent (**5**) were used.* The 2-trimethylsilylethyl ester (**11b**) was prepared in a similar manner to (**11a**).



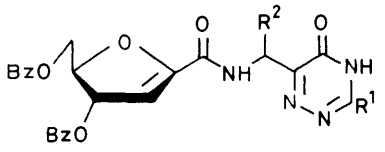
(7) a; R = H
b; R = Me



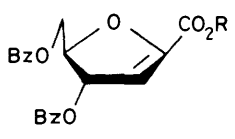
(8) a; R^1 = Me, R^2 = H
b; R^1 = R^2 = Me
c; R^1 = NH_2, R^2 = H
d; R^1 = NH_2, R^2 = Me



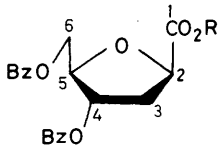
(9) a; R = H
b; R = Me



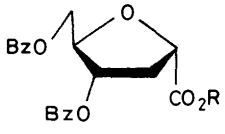
(10) a; R^1 = Me, R^2 = H
b; R^1 = R^2 = Me



(11) a; R = CH_2Ph
b; R = $CH_2CH_2SiMe_3$



(12) a; R = H
b; R = $CH_2CH_2SiMe_3$



(13) a; R = H
b; R = $CH_2CH_2SiMe_3$

Catalytic hydrogenation of (**11a**) (palladium–charcoal) afforded an anomeric mixture of the acids (**12a**) and (**13a**) in excellent yield. Similar hydrogenation of (**11b**) gave the esters (**12b**) and (**13b**) which were separated by chromatography and each anomer was deprotected using tetra-n-butylammonium fluoride to provide pure 2,5-anhydro-4,6-di-*O*-benzoyl-3-deoxy-D-*ribo*-hexonic acid (**12a**) and the D-*arabino*-hexonic acid (**13a**). Assignment of their anomeric configuration was based upon ^1H n.m.r. spectral data: low coupling constants (≤ 1 Hz) for $J_{2,3_b}$, $J_{3_b,4}$, and $J_{4,5}$ are unequivocally interpreted in terms of the D-*arabino*-hexonic acid (**13a**) (Table 1). The anomeric protons (2-H) in both (**12a**) and (**13a**) resonated as doublets of doublets with $J_{2,3_a} + J_{2,3_b}$ values of 16.5 Hz (**12a**) and 10 Hz (**13a**). These data are in close agreement with those recently reported for the corresponding methyl esters of 2,5-anhydro-3-deoxy-4,6-di-*O*-toluoyl-D-*ribo*-and -D-*arabino*-hexonic acids.[15] A seven-step synthesis of (**12a**) from D-mannitol has recently been carried out as a prelude to a synthesis of 2′-deoxyshowdomycin.[7]

Table 1. Coupling constants (Hz) of 2,5-anhydro-4,6-di-*O*-benzoyl-3-deoxy-D-*ribo*- and D-*arabino*-hexonic acids

	$J_{2,3_a}$	$J_{2,3_b}$	$J_{3_a,4}$	$J_{3_b,4}$	$J_{4,5}$
(**12a**)	10	6.5	6	2	2
(**13a**)	9	1	6	<1	<1

The hexonic acids (**12a**) and (**13a**) and the α,β-unsaturated carboxamides (**6**), (**9a** and **b**), and (**10a** and **b**) can clearly serve as precursors for the synthesis of 2′-deoxyribo-*C*-nucleosides. Thus, coupling of the anomeric mixture of (**12a**)/(**13a**) [obtained from catalytic hydrogenation of (**11a**)] with 3-amino-6-aminomethyl-4,5-dihydro-1,2,4-triazin-5-one (**8c**),[16] in the presence of 2-ethoxy-*N*-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ),† afforded the amides (**14a**). Cyclization of these intermediates, using phosphoryl trichloride in 1,2-dichloroethane at reflux,[12] gave the imidazo[5,1-*f*]triazinones (**15a**) and (**16a**) which were subsequently deblocked *via* ammonolysis. Separation of the anomeric mixture of (**17a**) and (**18a**) by fractional crystallization provided pure (**17a**), a novel *C*-nucleoside isostere of 2′-deoxyguanosine. A similar sequence, employing 3-amino-6-(1-aminoethyl)-4,5-dihydro-1,2,4-triazin-5-one (**8d**), and proceeding *via* (**14b**) and (**15b**)/(**16b**) has led to the corresponding 5-methyl analogues (**17b**) and (**18b**).

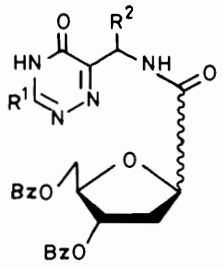
To exemplify the synthetic application of the α,β-unsaturated carboxamides, compounds (**6**), (**9a**), and (**10a**) have been converted into novel imidazo[1,5-*a*]pyridine, imidazo[1,5-*b*]-pyridazine, and imidazo[5,1-*f*]triazine 2′-deoxyribonucleosides. Catalytic hydrogenation of (**6**), to give the amides (**19**), followed by cyclization (phosphoryl trichloride–pyridine–1,2-dichloroethane) gave an anomeric mixture of the 3′,5′-di-*O*-benzoates (**20a**) and (**21a**) [47% from (**6**)] which were readily separated by a single crystallization. Debenzoylation of each anomer with methanolic ammonia afforded 3-(2′-deoxy-β-D-*erythro*-pentofuranosyl)imidazo[1,5-*a*]pyridine (**20b**) and the α-anomer (**21b**).‡ A similar reaction sequence, starting from the pyridazin-3(2*H*)-one (**9a**) and proceeding *via* (**22**) and the di-*O*-benzoates (**23a**) and (**24a**), provided the novel 2-chloro-7-(2′-deoxy-β- and -α-D-*erythro*-pentofuranosyl)imidazo[1,5-*b*]pyridazines (**23b**) and (**24b**) in 34% overall yield. Compounds (**23b**) and (**24b**) were conveniently separated by column chromatography on silica gel. As a third example, the triazin-5(4*H*)-one (**10a**) was converted, *via* (**14c**) and (**15c**)/(**16c**), into the 2′-deoxyinosine analogue (**17c**) and its α-anomer (**18c**).

We were now faced with assigning the anomeric configuration of these 2′-deoxy-*C*-nucleosides. Deviations from the 'triplet–quartet peak-width' rule[17] have prompted Srivastava *et al.*[9] to offer an alternative criterion for the determination of anomeric configuration of 2′-deoxy-*N*-and -*C*-ribonucleosides. These workers show that methylene protons 2′-H_a and 2′-H_b adjacent to the anomeric centre in α-2′-deoxy-D-ribonucleosides display

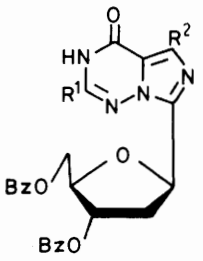
*We have similarly shown that when one equivalent of each of (**3a**), triethylamine, 2-aminomethylpyridine, and coupling agent (**5**) are used the major product is 2,5-anhydro-3,4,6-tri-*O*-benzoyl-*N*-(2-pyridylmethyl)-D-allonamide (59%).

† EEDQ was used as the coupling agent because it can function in aqueous ethanol, which was the preferred solvent system for the very polar aminoalkyltriazinones (**8c** and **d**).

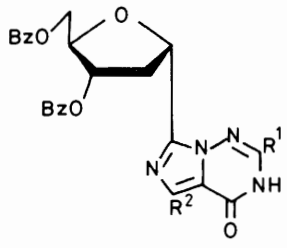
‡ In this case some anomerization was evident during the deprotection stage, but pure samples of (**20b**) and (**21b**) were obtained by column chromatography (see Experimental section).



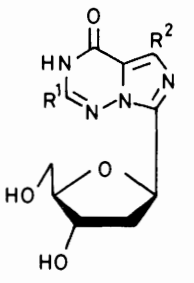
(14) a; $R^1 = NH_2$, $R^2 = H$
b; $R^1 = NH_2$, $R^2 = Me$
c; $R^1 = Me$, $R^2 = H$



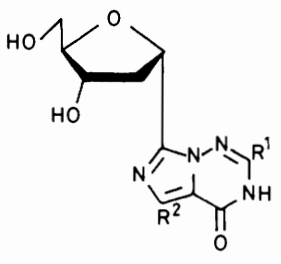
(15) a; $R^1 = NH_2$, $R^2 = H$
b; $R^1 = NH_2$, $R^2 = Me$
c; $R^1 = Me$, $R^2 = H$



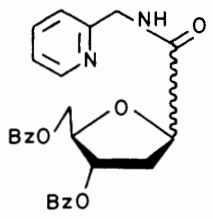
(16) a; $R^1 = NH_2$, $R^2 = H$
b; $R^1 = NH_2$, $R^2 = Me$
c; $R^1 = Me$, $R^2 = H$



(17) a; $R^1 = NH_2$, $R^2 = H$
b; $R^1 = NH_2$, $R^2 = Me$
c; $R^1 = Me$, $R^2 = H$



(18) a; $R^1 = NH_2$, $R^2 = H$
b; $R^1 = NH_2$, $R^2 = Me$
c; $R^1 = Me$, $R^2 = H$



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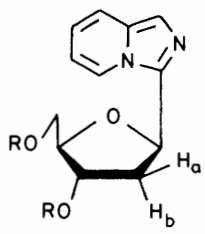
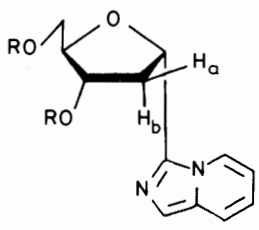
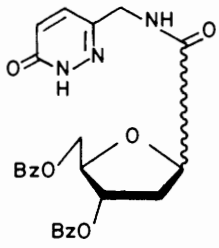


(20) a; R = Bz
b; R = H



(21) a; R = Bz
b; R = H



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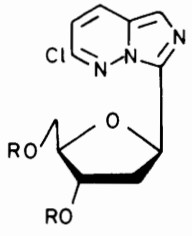
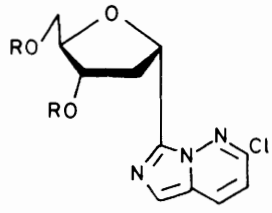


(23) a; R = Bz
b; R = H



(24) a; R = Bz
b; R = H

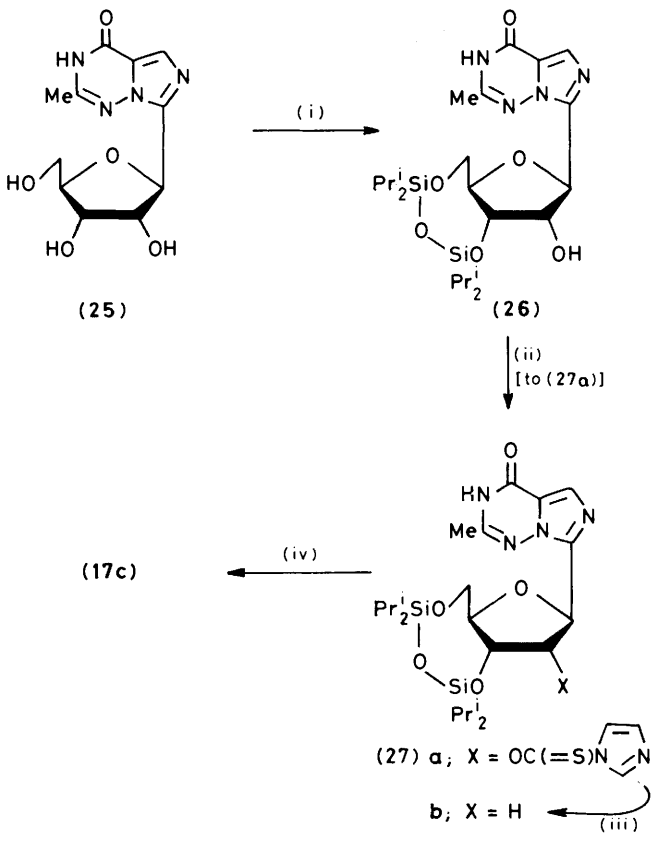
more chemical shift non-equivalence than those of the corresponding β-anomer, and they present data for five anomeric pairs to support this proposal.

The background of ambiguities surrounding the assignment of configuration to 2′-deoxyribonucleosides, coupled with our

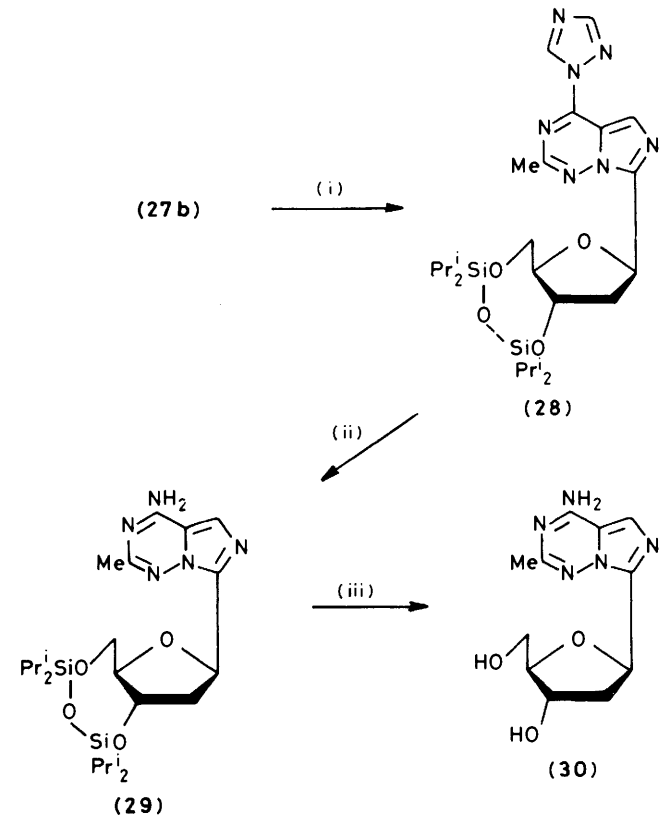
Table 2. ^{1}H N.m.r. chemical shifts (δ) [$(CD_3)_2SO$] of 2′-deoxyribo-*C*-nucleosides

Compound	1′-H	2′-H_a	2′-H_b	3′-H	4′-H	5′-H_2	Other
(17a)	5.44 (dd)	2.57 (m)	2.03 (m)	4.30 (m)	3.78 (m)	3.3—3.6 (m)	6.24 (br s, NH_2), 7.62 (s, 5-H)
(18a)[a]	*b*	2.42(m)		4.15 (m)	3.78 (m)	3.3—3.6 (m)	6.24 (br s, NH_2), 7.66 (s, 5-H)
(17b)	5.38 (dd)	2.45 (m)	2.00 (m)	4.28 (m)	3.76 (m)	3.3—3.6 (m)	6.17 (br s, NH_2), 2.41 (s, 5-Me)
(18b)	5.37 (dd)	2.36(m)		4.15 (m)	3.77 (dd)	3.3—3.6 (m)	6.18 (br s, NH_2), 2.43 (s, 5-Me)
(17c)	5.50 (dd)	2.60 (m)	2.07 (m)	4.33 (m)	3.84 (m)	3.3—3.5 (m)	2.28 (s, 2-Me), 7.71 (s, 5-H)
(18c)	5.51 (t)	2.50(m)		4.19 (q)	3.80 (q)	3.45 (dd), 3.55 (dd)	2.27 (s, 2-Me), 7.72 (s, 5-H)
(20b)	5.55 (dd)	2.73 (m)	2.12 (m)	4.35 (m)	3.88 (m)	3.3—3.5 (m)	6.70 (t, 6-H), 6.84 (dd, 7-H), 7.35 (s, 1-H), 7.58 (dd, 8-H), 8.42 (dd, 5-H)
(21b)	5.52 (t)	2.55(m)		4.27 (m)	3.72 (m)	3.4—3.6 (m)	6.72 (t, 6-H), 6.84 (dd, 7-H), 7.36 (s, 1-H), 7.59 (dd, 8-H), 8.40 (dd, 5-H)
(23b)	5.62 (dd)	2.72 (m)	2.12 (m)	4.34 (m)	3.85 (dt)	3.3—3.5 (m)	6.95 (d, 3-H), 7.62 (s, 5-H), 8.28 (d, 4-H)
(24b)	5.60 (t)	2.55(m)		4.19 (m)	3.75 (m)	3.35—3.6 (m)	6.95 (d, 3-H), 7.65 (s, 5-H), 8.28 (d, 4-H)
(30)	5.57 (dd)	2.65 (m)	2.06 (m)	4.35 (m)	3.85 (m)	3.3—3.5 (m)	2.28 (s, 2-Me), 7.70 (s, 5-H)

[a] Data obtained from spectrum of β/α-anomeric mixture. [b] Signal obscured by 1′-H of β-anomer.



Scheme 2. *Reagents:* (i) $(Pr_2^iSiCl)_2O$–pyridine; (ii) (imidazol-1-yl)$_2$ C=S–DMF; (iii) Bu^n_3SnH–AIBN–toluene; (iv) $Bu^n_4N^+F^-$–THF



Scheme 3. *Reagents:* (i) $POCl_3$–Et_3N–1,2,4-triazole; (ii) NH_3–THF; (iii) $Bu^n_4N^+F^-$–THF

belief that generalizations can only reliably be made within a given series of 2′-deoxyribonucleosides, directed us to develop a self-consistent determination for the present group of compounds. Two approaches have been adopted: (a) proton n.O.e. difference experiments and (b) unambiguous chemical synthesis.

It is clear from the proton chemical shift data for 2′-H_a and 2′-H_b of the nucleoside analogues (Table 2), that the α- and β-anomers fall into two distinct categories. Since the differences in chemical shifts and vicinal coupling constants of the 2′-deoxyriboxyl protons are not interpretable with certainty, assignment of configuration was made on the basis of proton n.O.e. data. Thus, the data summarized in Table 3 confirm that for (**20b**) and (**23b**) 1′-H and 4′-H are located on the same face of the 2′-deoxyribosyl ring; conversely, for (**21b**) and (**24b**) 1′-H and 3′-H are on the same face of the sugar ring. To our knowledge, this represents the first use of this technique to assign unequivocally the anomeric configurations of 2′-deoxyribonucleosides. From the patterns of chemical shift data the configuration assignments of the remaining nucleosides are as denoted in Table 2.

Further structural confirmation was provided by synthesis. Robins *et al.*[18] have recently reported a four-step regiospecific and stereoselective conversion of ribonucleosides into 2′-deoxyribonucleosides. Concurrently, in their synthesis of 2′-deoxypseudouridines, Watanabe and co-workers[3] described a variant of this procedure by utilizing deoxygenation of 2′-*O*-(imidazol-1-yl)thiocarbonyl derivatives. Application of the latter approach to the previously synthesized[12] β-D-ribo-*C*-nucleoside (**25**) provided the 2′-deoxy derivative (**17c**) (Scheme 2), identical with the β-anomer prepared *via* the 'coupling-elimination' route and assigned on the basis of n.O.e. experiments. No epimerization at C-1′ was observed during the interconversions (**25**) ⟶ (**26**) ⟶ (**27a** and **b**) ⟶ (**17c**).

In the present work the signals for the anomeric protons clearly deviate from the triplet–quartet peak-width rule: the β-anomers exhibit a doublet of doublets for 1′-H (multiplet width 15.5 ± 0.5 Hz) while the α-anomers [except (**18b**)] show a 'pseudo-triplet' (multiplet width 14.5 ± 0.5 Hz). Furthermore, Δδ for the 2′-H_a and 2′-H_b multiplets are at variance with the data given by Srivastava *et al.*,[9] the α-anomers having a *smaller* 'band-width' than the corresponding β-anomers.* These apparent discrepancies presumably reflect different shielding effects of the *C*-linked bicyclic bridgehead-nitrogen heterocyclic system† and/or conformational changes of the carbohydrate moiety.

Compound (**27b**) has now been converted into the novel 2′-deoxyadenosine analogue (**30**). From their studies on oligonucleotide synthesis Divakar and Reese[19] have developed an efficient process for the preparation of cytidine derivatives from uridines *via* the intermediacy of 4-(1,2,4-triazol-1-yl) and 4-(3-nitro-1,2,4-triazol-1-yl) derivatives. We have found this methodology to be extremely effective for analogous modification of imidazo[5,1-*f*]triazinone nucleosides. Thus, treatment of the 3′,5′-tetraisopropyldisiloxane-1,3-diyl-protected nucleoside (**27b**) (Scheme 3) with tri-(1*H*-1,2,4-triazol-1-yl)phosphine oxide (prepared[20] *in situ*) afforded the 4-(1,2,4-triazol-1-yl)imidazo[5,1-*f*]triazine (**28**). When compound (**28**) was allowed to react with ammonia under strictly anhydrous conditions the 4-amino derivative (**29**) was obtained. De-silylation under standard conditions provided the deprotected nucleoside (**30**) in 79% overall yield from (**27b**).

* Significantly, when the ^{1}H n.m.r. spectra of (**17b**) and (**18b**) were recorded in CD_3OD, Δδ for the 2′-H_a and 2′-H_b multiplets were 0.20 p.p.m. and 0.22 p.p.m., respectively (see Experimental section).

† *Cf.* ref. 10(b).

Table 3. N.O.e. data[a] for irradiation of 1′-H (values given are percentage enhancements)

	(21b)	(20b)	(24b)	(23b)
2′-H_a	6.6[b]	—	7.3[b]	—
2′-H_b		5[b]		6.5
3′-H	3.3	—	2.5	—
4′-H	—	4	—	3.5

[a] Using the n.O.e. difference method (Bruker WM 250 spectrometer). FIDs were acquired in the sequence 32 scans on-resonance, 32 scans off-resonance during a 4-h period with a decoupling power, γH_2 12 Hz (DP 20L). The FID off-resonance was then subtracted from the FID on-resonance to give the n.O.e. difference spectrum. The percentage enhancements were obtained from integration of the positive n.O.e. signals compared with the (negative) integration of the signal being saturated. [b] These multiplets appeared as a combination of positive and negative peaks due to selective population transfer which occurs because 1′-H is scalar-coupled to 2′-H_a and 2′-H_b.

The methodology described in this paper can provide access to a range of imidazo-fused 2′-deoxyribo-*C*-nucleosides of general structure (**1**). Further investigation of the hydrogenation stage may allow modification of the β:α anomeric ratio. However, since (a) the mixtures of β- and α-anomers are separable by the usual methods and (b) α-anomers of nucleosides can exhibit interesting biological activity,[21] the formation of both anomers is not considered detrimental to the synthetic sequence.

Experimental

For general experimental details see ref. 12.

Benzyl 2,5-*Anhydro*-3,4,6-*tri*-O-*benzoyl*-D-*allonate* (**3b**).—*Method A.* 2,5-Anhydro-3,4,6-tri-*O*-benzoyl-D-allonic acid (**3a**) (2.00 g, 4.08 mmol) was dissolved in 1,1,1-trichloroethane and dicyclohexylcarbodi-imide (0.84 g, 4.08 mmol) was added followed by 4-dimethylaminopyridine (50 mg, 0.45 mmol) and benzyl alcohol (0.44 g, 4.08 mmol). The reaction mixture was stirred for 14 h at room temperature and filtered (to remove dicyclohexylurea). The filtrate was evaporated to dryness and the resultant gum was purified by flash chromatography on silica gel. Elution initially with cyclohexane and later with cyclohexane–ethyl acetate (4:1) provided the *title compound* (**3b**) (2.01 g, 85%) as a gum, $\nu_{max.}(CHBr_3)$ 1 730 cm^{-1}; $\delta(CDCl_3)$ 4.55—4.80 (3 H, m, 5-H and 6-H_2), 4.85 (1 H, d, *J* 4 Hz, 2-H), 5.18 and 5.22 (2 H, ABq, *J* 12 Hz, CH_2Ph), 5.78 (1 H, t, 4-H), 5.95 (1 H, t, 3-H), 7.20—7.60 (14 H, m, ArH), and 7.85—8.10 (6 H, m, ArH) (Found: $[M + H]^+$, 581.1828. $C_{34}H_{29}O_9$ requires 581.1812).

Method B. 2,5-Anhydro-3,4,6-tri-*O*-benzoyl-D-allonic acid (**3a**) (1.00 g, 2.04 mmol) was dissolved in acetonitrile (100 ml) and 2-chloro-*N*-methylpyridinium iodide (**5**) (521 mg, 2.04 mmol) was added to the stirred solution. Triethylamine (207 mg, 2.04 mmol) was added to this solution and the mixture was stirred for 1 h. Benzyl alcohol (221 mg, 2.04 mmol) was added and the reaction mixture was kept at room temperature for 16 h. The solvent was removed under reduced pressure and the residue was partitioned between ethyl acetate (100 ml) and 0.02M hydrochloric acid (100 ml). The organic layer was separated, dried ($MgSO_4$), and evaporated to give a gum which was purified by flash chromatography on silica gel. Elution with cyclohexane–ethyl acetate (4:1) gave the ester (**3b**) (494 mg, 42%), identical with that prepared by Method A.

Benzyl (4S,trans)-4-*Benzoyloxy*-5-*benzoyloxymethyl*-4,5-*dihydrofuran*-2-*carboxylate* (**11a**).—2,5-Anhydro-3,4,6-tri-*O*-benzoyl -D-allonic acid (**3a**) (15.0 g, 30.6 mmol) was dissolved in acetonitrile (600 ml) and 2-chloro-*N*-methylpyridinium iodide (**5**) (15.5 g, 60.6 mmol) was added to the stirred solution. Triethylamine (10.8 g, 107.1 mmol) was added to this solution and the mixture was stirred for 1.5 h before benzyl alcohol (5.0 g, 46 mmol) was added. After being kept overnight at room temperature, the solution was evaporated to afford a gum which was taken up in ethyl acetate (400 ml) and the solution was washed with 0.02M hydrochloric acid (300 ml). The organic layer was separated, dried ($MgSO_4$), and evaporated to give a gum which was purified by flash chromatography on silica gel. Elution with benzene provided the *title compound* (**11a**) (11.7 g, 84%) which solidified after a time. Recrystallization from cyclohexane gave the ester (**11a**) as crystals, m.p. 112—114 °C (Found: C, 70.3; H, 4.85. $C_{27}H_{22}O_7$ requires C, 70.7; H, 4.85%); $[\alpha]_D^{22}$ +196° (*c* 2.03 in chloroform); $\nu_{max.}$(Nujol) 1 720 and 1 635 cm^{-1}; $\delta(CDCl_3)$ 4.64 (2 H, d, 6-H_2), 5.07 (1 H, dt, 5-H), 5.25 and 5.32 (2 H, ABq, *J* 12 Hz, CH_2Ph), 6.12 (1 H, t, 4-H), 6.20 (1 H, d, *J* 3 Hz, 3-H), 7.30—7.65 (11 H, m, ArH), and 8.04 (4 H, m, ArH).

2-(*Trimethylsilyl*)*ethyl* (4S,trans)-4-*Benzoyloxy*-5-*benzoyloxymethyl*-4,5-*dihydrofuran*-2-*carboxylate* (**11b**).—This *compound* (73%) was prepared from the allonic acid (**3a**) and 2-(trimethylsilyl)ethanol, as described for the preparation of (**11a**), and was obtained as a gum (Found: C, 63.8; H, 6.1. $C_{25}H_{28}O_7Si$ requires: 64.1; H, 6.0%); $[\alpha]_D^{21}$ +179° (*c* 2.27 in chloroform); $\nu_{max.}(CHBr_3)$ 1 718 cm^{-1}; $\delta(CDCl_3)$ 0.05 (9 H, s, 3 CH_3), 1.09 (2 H, m, CH_2Si), 4.35 (2 H, m, CO_2CH_2), 4.64 (2 H, d, 6-H_2), 5.07 (1 H, m, 5-H), 6.1—6.18 (2 H, d + t, 3- and 4-H), 7.40—7.65 (6 H, m, ArH), and 8.03 (4 H, m, ArH).

2,5-*Anhydro*-4,6-*di*-O-*benzoyl*-3-*deoxy*-D-ribo- *and* -D-arabino-*hexonic Acids* (**12a**) *and* (**13a**).—Benzyl (4*S*,*trans*)-4-benzoyloxy-5-benzoyloxymethyl-4,5-dihydrofuran-2-carboxylate (**11a**) (8.08 g, 17.6 mmol) in tetrahydrofuran (THF) (250 ml)–ethanol (250 ml) was hydrogenated over 10% palladium–carbon at 1 atm for 48 h. The catalyst was removed by filtration and the filtrate was evaporated to afford a gum which was dissolved in diethyl ether (400 ml) and extracted into saturated aqueous sodium hydrogen carbonate (3 × 150 ml). The combined aqueous extracts were acidified to pH *ca.* 3 with 5M hydrochloric acid, and extracted with ethyl acetate (3 × 200 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated to afford a mixture of the title compounds (**12a**) and (**13a**) (*ca.* 2:1) as a gum (5.76 g, 88%).

2-(*Trimethylsilyl*)*ethyl* 2,5-*Anhydro*-4,6-*di*-O-*benzoyl*-3-*deoxy*-D-ribo- *and* -D-arabino-*hexonate* (**12b**) *and* (**13b**).—2-(Trimethylsilyl)ethyl (4*S*,*trans*)-4-benzoyloxy-5-benzoyloxymethyl-4,5-dihydrofuran-2-carboxylate (**11b**) (2.50 g, 5.34 mmol) in ethanol (100 ml) was hydrogenated over 10% palladium–carbon at 1 atm for 48 h. The catalyst was removed by filtration and the filtrate was evaporated to afford a gum. Column chromatography of this material on silica gel (Art 7729), with initial elution with benzene and later with benzene–diethyl ether (19:1), afforded starting material (**11b**) (100 mg, 4% recovery); pure ribo-*hexonate* (**12b**) (533 mg, 22%) as a gum (Found: C, 63.95; H, 6.45. $C_{25}H_{30}O_7Si$ requires C, 63.8; H, 6.45%); $[\alpha]_D^{21}$ + 12.6° (*c* 4.98 in chloroform); $\delta(CDCl_3)$ 0.02 (9 H, s, Me_3), 2.55 (2 H, m, 3-H_2), 0.95 (2 H, m, CH_2Si), 4.22 (2 H, m, CO_2CH_2), 4.58 (3 H, m, 5-H and 6-H_2), 4.74 (1 H, t, *J* 8 Hz, 2-H), 5.57 (1 H, m, 4-H), 7.35—7.60 (6 H, m, ArH), and 8.04 (4 H, m, ArH); a mixture of (**12b**) and (**13b**) (400 mg, 17%); and finally pure arabino-*hexonate* (**13b**) (810 mg, 34%) as a gum which crystallized with time, m.p. 58—62 °C (Found: C, 64.2; H, 6.5. $C_{25}H_{30}SiO_7$ requires C, 63.8; H, 6.45%); $[\alpha]_D^{21}$ + 38.5° (*c* 5.06 in chloroform); $\delta(CDCl_3)$ 0.00 (9 H, s, Me_3), 2.55—2.82 (2 H, m, 3-

H_2), 0.95 (2 H, m, CH_2Si), 4.24 (2 H, m, CO_2CH_2), 4.60 (2 H, m, 6-H_2), 4.78 (1 H, m, 5-H), 4.84 (1 H, dd, *J* 9 and 2.5 Hz, 2-H), 5.55 (1 H, m, 4-H), 7.40—7.65 (6 H, m, ArH), and 7.98—8.12 (4 H, m, ArH).

2,5-*Anhydro*-4,6-*di*-O-*benzoyl*-3-*deoxy*-D-ribo-*hexonic Acid* (**12a**).—2-(Trimethylsilyl)ethyl 2,5-anhydro-4,6-di-*O*-benzoyl-3-deoxy-D-*ribo*-hexonate (**12b**) (460 mg, 0.98 mmol) was dissolved in dry THF (50 ml) and tetra-n-butylammonium fluoride (1.2 ml, 1.2 mmol; 1M in THF) was added. The solution was kept at room temperature for 22 h. The solvent was removed and the resultant gum was dissolved in ether (50 ml) and extracted into saturated aqueous sodium hydrogen carbonate (3 × 50ml). The basic extracts were combined, acidified to pH *ca.* 3 with 2M hydrochloric acid, and extracted with ethyl acetate (3 × 50 ml). The combined organic extracts were dried ($MgSO_4$) and the solvent was evaporated off to give the *title compound* (**12a**) (342 mg, 94%) as a gum which crystallized after a time, m.p. 104—107 °C (Found: C, 64.75; H, 4.9. $C_{20}H_{18}O_7$ requires C, 64.85, H, 4.9%); $[\alpha]_D^{21}$ +29.6° (*c* 1.15 in chloroform); $\nu_{max.}$($CHBr_3$) 1 765 and 1 720 cm^{-1}; $\lambda_{max.}$(EtOH) 229 (ε 24 300), 274 (1 800), and 281 nm (1 500); δ($CDCl_3$) 2.50 (1 H, ddd, 3-H_a), 2.68 (1 H, ddd, 3-H_b), 4.50—4.80 (3 H, m, 5-H and 6-H_2), 4.85 (1 H, dd, 2-H), 5.57 (1 H, br dt, 4-H), 7.40—7.65 (6 H, m, ArH), and 8.05 (4 H, d, ArH).

2,5-*Anhydro*-4,6-*di*-O-*benzoyl*-3-*deoxy*-D-arabino-*hexonic Acid* (**13a**).—This compound (98%) was prepared from the ester (**13b**), as described for the preparation of the corresponding isomer (**12a**), and was obtained as a gum (Found: C, 64.45; H, 5.05. $C_{20}H_{18}O_7$ requires C, 64.85; H, 4.9%); $[\alpha]_D^{21}$ +39.9° (*c* 1.33 in chloroform); $\nu_{max.}$($CHBr_3$) 1 770 and 1 720 cm^{-1}; $\lambda_{max.}$(EtOH) 229 (ε 23 300), 274 (1 700), and 281 nm (1 400); δ($CDCl_3$) 2.62 (1 H, br d, 3-H_b), 2.79 (1 H, ddd, 3-H_a), 4.54 (2 H, d, 6-H_2), 4.76 (1 H, t, 5-H), 4.88 (1 H, dd, 2-H), 5.58 (1 H, br d, 4-H), 7.35—7.65 (6 H, m, ArH), and 7.90—8.10 (4 H, m, ArH).

(4S,trans)-4-*Benzoyloxy*-5-*benzoyloxymethyl*-4,5-*dihydro*-N-(2-*pyridylmethyl*)*furan*-2-*carboxamide* (**6**).—2,5-Anhydro-3,4,6-tri-*O*-benzoyl-D-allonic acid (**3a**) (12.0 g, 24.5 mmol) was dissolved in acetonitrile (400 ml) and 2-chloro-*N*-methylpyridinium iodide (**5**) (12.8 g, 50.0 mmol) was added. The mixture was stirred at room temperature for 15 min and then triethylamine (10.5 g, 104.0 mmol) was added. After 2 h 2-aminomethylpyridine (4.0 g, 37.0 mmol) was added and the reaction mixture was stirred at room temperature for a further 16 h. The reaction mixture was evaporated to dryness and the residue was partitioned between ethyl acetate (300 ml) and water (200 ml). The ethyl acetate layer was separated and the aqueous layer was further extracted with ethyl acetate (2 × 100 ml). The combined organic extracts were dried ($MgSO_4$), evaporated, and the residue was purified by flash chromatography on silica gel. Elution with benzene provided the *title compound* (**6**) (8.2 g, 73%) as a gum which solidified after a time, m.p. 95.5—97.5 °C (from ethyl acetate–cyclohexane) (Found: C, 67.9; H, 4.8; N, 5.95. $C_{26}H_{22}N_2O_6$ requires C, 68.1; H, 4.85; N, 6.1%); $[\alpha]_D^{21}$ +197° (*c* 1.03 in chloroform); $\nu_{max.}$($CHBr_3$) 3 420, 1 720, and 1 680 cm^{-1}; δ($CDCl_3$) 4.68 (2 H, d, *J* 6 Hz, NHCH_2), 4.55—4.78 (2 H, m, 6-H_2), 5.08 (1 H, m, 5-H), 6.11 (1 H, t, 4-H), 6.16 (1 H, d, *J* 2.5 Hz, 3-H), 7.20 (1 H, dd, pyr 5-H), 7.26 (1 H, d, pyr 3-H), 7.40—7.70 (8 H, m, ArH, NH, and pyr 4-H), 8.03 (4 H, m, ArH), and 8.52 (1 H, br d, pyr 6-H).

(4S,trans)-4-*Benzoyloxy*-5-*benzoyloxymethyl*-N-[(1,6-*dihydro*-6-*oxopyridazin*-3-*yl*)*methyl*]-4,5-*dihydrofuran*-2-*carboxamide* (**9a**).—2,5-Anhydro-3,4,6-tri-*O*-benzoyl-D-allonic acid (**3a**) (5.80 g, 11.8 mmol) was dissolved in acetonitrile (400 ml) and 2-chloro-*N*-methylpyridinium iodide (**5**) (6.19 g, 24.2 mmol) was added. The mixture was stirred at room temperature for 15 min, and then triethylamine (3.63 g, 35.9 mmol) was added. After 1.5 h, a solution of α-(1,6-dihydro-6-oxopyridazin-3-yl)methylamine (**7a**) [from its hydrochloride salt[12] (2.87 g, 17.8 mmol)] in acetonitrile (70 ml) was added and the reaction mixture was stirred at room temperature for a further 16 h. The reaction mixture was filtered and the white solid collected was thoroughly washed with water, dried, and recrystallized from ethanol to give the *title compound* (**9a**) (2.51 g, 45%), m.p. 143—144 °C (Found: C, 62.85; H, 4.4; N, 8.65. $C_{25}H_{21}N_3O_7$ requires C, 63.15; H, 4.45; N, 8.85%); $[\alpha]_D^{25}$ +181° (*c* 1.56 in chloroform); $\nu_{max.}$ 3 420, 3 380, 1 720, and 1 680 cm^{-1}; δ[$CDCl_3$–$(CD_3)_2SO$] 4.35 (2 H, br d, NHCH_2), 4.65 (2 H, m, 6-H_2), 5.05 (1 H, m, 5-H), 6.05 (2 H, m, 4- and 3-H), 6.78 (1 H, d, *J* 10 Hz, pyr 5-H), 7.28 (1 H, d, *J* 10 Hz, pyr 4-H), 7.3—7.8 (7 H, m, ArH and NH), 7.9—8.25 (4 H, m, ArH), and 12.72 (1 H, br, NH). The filtrate was evaporated to dryness and the residue was partitioned between water (30 ml) and ethyl acetate (2 × 150 ml). The combined organic phases were dried (Na_2SO_4), and the solvent was evaporated off. The residue was purified by flash chromatography on silica gel, with ethyl acetate as eluant, to afford a further crop of the product (**9a**) (0.40 g, 7%).

(4S,trans)-4-*Benzoyloxy*-5-*benzoyloxymethyl*-N-[1-(1,6-*dihydro*-6-*oxopyridazin*-3-*yl*)*ethyl*]-4,5-*dihydrofuran*-2-*carboxamide* (**9b**).—Coupling of 1-(1,6-dihydro-6-oxopyridazin-3-yl)ethylamine (**7b**) [from its hydrochloride salt[12]] with the 2,5-anhydro-D-allonic acid (**3a**) was carried out as described for the preparation of (**6**). The *amide* (**9b**) (53%) was obtained as white crystals, after purification by column chromatography on silica gel [ethyl acetate as eluant], m.p. 144—145 °C (from ethyl acetate) (Found: C, 63.7; H, 4.8; N, 8.4. $C_{26}H_{23}N_3O_7$ requires C, 63.8; H, 4.75; N, 8.6%); $\nu_{max.}$($CHBr_3$) 3 400, 3 370, 1 715, and 1 675 cm^{-1}; δ($CDCl_3$) 1.48 and 1.50 (3 H, 2 d, CHCH_3*), 4.60—4.80 (2 H, m, 6-H_2), 5.00—5.15 (2 H, m, 5-H and C*H*CH_3), 6.10 (1 H, t, 4-H), 6.14 (1 H, d, *J* 3 Hz, 3-H), 6.86 and 6.95 (1 H, 2 d, pyr 5-H*). 7.01 (1 H, d, NH), 7.22—7.31 (1 H, 2 d, pyr 4-H*), 7.40—7.75 (6 H, m, ArH), 8.02 (4 H, m, ArH), and 11.64 (1 H, br, NH).

(4S,trans)-4-*Benzoyloxy*-5-*benzoyloxymethyl*-N-[(4,5-*dihydro*-3-*methyl*-5-*oxo*-1,2,4-*triazin*-6-*yl*)*methyl*]-4,5-*dihydrofuran*-2-*carboxamide* (**10a**).—Coupling of 6-aminomethyl-4,5-dihydro-3-methyl-1,2,4-triazin-5-one (**8a**) with the 2,5-anhydro-D-allonic acid (**3a**) was carried out as described for the preparation of (**9a**). The *amide* (**10a**) (45%) was obtained a white solid, m.p. 127—129 °C (Found: C, 58.25; H, 4.45; N, 10.75. $C_{25}H_{22}N_4O_7 \cdot 1.5\,H_2O$ requires C, 58.0; H, 4.8; N, 10.8%); $[\alpha]_D^{23}$ +166° (*c* 0.05 in chloroform); $\nu_{max.}$($CHBr_3$) 3 380, 1 720, 1 682, 1 655, and 1 535 cm^{-1}; δ[$(CD_3)_2SO$] 2.30 (3 H, s, CH_3), 4.24 and 4.37 (2 H, 2 dd, 6-H_2), 4.64 (2 H, m, NCH_2), 5.28 (1 H, q, 5-H), 6.05 (1 H, d, *J* 3 Hz, 3-H), 6.14 (1 H, t, 4-H), 7.50—7.75 (6 H, m, ArH), 8.02 (4 H, m, ArH), and 8.58 (1 H, t, N*H*CH_2).

(4S,trans)-4-*Benzoyloxy*-5-*benzoyloxymethyl*-N-[1-(4,5-*dihydro*-3-*methyl*-5-*oxo*-1,2,4-*triazin*-6-*yl*)*ethyl*]-4,5-*dihydrofuran*-2-*carboxamide* (**10b**).—Coupling of 6-(1-aminoethyl)-4,5-dihydro-3-methyl-1,2,4-triazin-5-one (**8b**) (from its hydrochloride salt[12]) with the 2,5-anhydro-D-allonic acid (**3a**) was carried out as described for the preparation of (**6**). The amide (**10b**) (51%) was obtained as a gum, after purification by column chromatography on silica gel [ethyl acetate–ethanol (19:1) as eluant]; $\nu_{max.}$($CHBr_3$) 3 450, 3 240, 1 720, and 1 650 cm^{-1}; δ($CDCl_3$) 1.58 (3 H, d, *J* 7 Hz, CHCH_3), 2.50 (3 H, s, 3-Me), 4.62 (2 H, m, 6-H_2), 4.90—5.50 (2 H, m, C*H*CH_3 and 5-H), 6.15 (2 H, m, 3- and 4-H), and 7.3—8.2 (10 H, m, ArH).

* Mixture of diastereoisomers.

N-[(3-*Amino*-4,5-*dihydro*-5-*oxo*-1,2,4-*triazin*-6-*yl*)*methyl*]-2,5-*anhydro*-4,6-*di*-O-*benzoyl*-3-*deoxy*-D-arabino- *and* -D-ribo-*hexonamide* (**14a**).—3-Amino-6-aminomethyl-4,5-dihydro-1,2,4-triazin-5-one hydrochloride (**8c**)·HCl (4.46 g, 25.1 mmol) in water (100 ml) was treated with 2M sodium hydroxide (12.6 ml, 25.2 mmol). A solution of 2,5-anhydro-4,6-di-*O*-benzoyl-3-deoxy-D-*arabino*- and -D-ribo-hexonic acids (**12a**) and (**13a**) (9.50 g, 25.7 mmol) in ethanol (300 ml) was added, followed by *N*-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ) (7.00 g, 28.3 mmol). The reaction mixture was heated at 70 °C for 3 h, cooled, and evaporated to dryness. The residue was partitioned between ethyl acetate (180 ml) and water (100 ml). The organic phase was separated and the aqueous layer was further extracted with ethyl acetate (2 × 100 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated to give a foam. This material was purified by flash chromatography on silica gel, with ethyl acetate–ethanol (9:1) as eluant, to provide the amides (**14a**) (6.25 g, 50%), m.p. 174—179 °C (from ethanol); $\nu_{max.}$(Nujol) 3 400—3 100, 1 720, and 1 660 cm^{-1}; δ[$CDCl_3$–$(CD_3)_2SO$] 2.45 and 2.65 (2 H, 2 m, 3-H_2), 2.75* (2 H, m, 3-H_2), 4.28 (2 H, d, CH_2NH), 4.65 (3 H, m, 5-H and 6-H_2), 4.78 (1 H, m, 2-H), 5.52* (1 H, t, 4-H), and 5.58 (1 H, d, 4-H).

N-[1-(3-*Amino*-4,5-*dihydro*-5-*oxo*-1,2,4-*triazin*-6-*yl*)*ethyl*]-2,5-*anhydro*-4,6-*di*-O-*benzoyl*-3-*deoxy*-D-arabino-*and* -D-ribo-*hexonamide* (**14b**).—Coupling of 3-amino-6-(1-aminoethyl)-1,2,4-triazin-5-one (**8d**) with the *ribo*-hexonic acids (**12a**) and (**13a**) was carried out essentially as described for the preparation of (**14a**). The *amides* (**14b**) (41%) were obtained as a white foam, after purification by flash chromatography on silica gel [dichloromethane–ethanol (9:1) as eluant] (Found: C, 58.9; H, 5.1; N, 12.65. $C_{25}H_{25}N_5O_7$·0.5 $CH_3CO_2CH_2CH_3$ requires C, 58.8; H, 5.3; N, 12.7%); $\nu_{max.}$(CHBr$_3$) 3 400—3 100, 1 720, and 1 660 cm^{-1}; δ($CDCl_3$) 1.32 and 1.50 (3 H, 2 d, $CHCH_3$†), 2.40—2.90 (2 H, m, 3-H_2), 4.5—5.0 (3 H, overlapping multiplets, 5-H and 6-H_2), 5.0—5.7 (2 H, overlapping multiplets, 2- and 4-H), and 7.30—8.30 (10 H, m, ArH).

2,5-*Anhydro*-4,6-*di*-O-*benzoyl*-3-*deoxy*-N-[(4,5-*dihydro*-3-*methyl*-5-*oxo*-1,2,4-*triazin*-6-yl)*methyl*]-D-arabino- *and* -D-ribo-*hexonamide* (**14c**).—These *compounds* (77%) were prepared by hydrogenation of the amide (**10a**), as described for the preparation of (**19**), and were obtained as a foam after purification by flash chromatography on silica gel [ethyl acetate–ethanol (9:1) as eluant]; δ($CDCl_3$) 2.32 and 2.40 (3 H, 2 s, triazine 3-Me), 2.40—2.55 and 2.60—2.75 (2 H, m, 3-H_2), 5.47 and 5.58 (1 H, 2 m, 4-H), 7.30—8.10 (11 H, m, ArH and NH) (Found: M^+ − $PhCO_2H$, 370.1299. $C_{18}H_{18}N_4O_5$ requires *m*/*z*, 370.1277) (NH_3 chemical ionization).

2-*Amino*-7-(3′,5′-*di*-O-*benzoyl*-2′-*deoxy*-β- *and* -α-D-erythro-*pentofuranosyl*)-3,4-*dihydroimidazo*[5,1-f][1,2,4]*triazin*-4-*one* (**15a**) *and* (**16a**).‡—*N*-[(3-Amino-4,5-dihydro-5-oxo-1,2,4-triazin-6-yl)methyl]-2,5-anhydro-4,6-di-*O*-benzoyl-3-deoxy-D-*arabino*- and -D-*ribo*-hexonamide (**14a**) (5.50 g, 11.2 mmol) and phosphoryl trichloride (5.2 ml, 55.7 mmol) in dry 1,2-dichloroethane (500 ml) were heated at reflux for 4 h. The solvent and excess of phosphoryl trichloride were removed under reduced pressure and the residue was thoroughly shaken with saturated aqueous sodium hydrogen carbonate (200 ml) and ethyl acetate (200 ml). The ethyl acetate phase was separated and the aqueous layer was further extracted with ethyl acetate (200 ml). The combined ethyl acetate extracts were dried ($MgSO_4$), the solvent was evaporated off, and the residue was purified by flash chromatography on silica gel [ethyl acetate as eluant] to give the *title compounds* (**15a**) and (**16a**) (3.55 g, 67%) (7:3, β:α ratio) as a foam (Found: C, 58.8; H, 4.65; N, 13.8. $C_{24}H_{21}N_5O_6$·H_2O requires C, 58.4; H, 4.7; N, 14.2%); $\nu_{max.}$(CHBr$_3$) 3 480—3 380, 1 720, and 1 650 cm^{-1}; δ($CDCl_3$) 2.50—2.65 (2 H, m, 2′-H_2), 4.55—4.75 (3 H, m, 4′-H and 5′-H_2), 5.55—5.75 (2 H, m, 1′-and 3′-H), and 7.25—8.15 (11 H, m, ArH and 5-H).

2-*Amino*-7-(3′,5′-*di*-O-*benzoyl*-2′-*deoxy*-β- *and* -α-D-erythro-*pentofuranosyl*)-3,4-*dihydro*-5-*methylimidazo*[5,1-f][1,2,4]*triazin*-4-*one* (**15b**) *and* (**16b**).—The amides (**14b**) were cyclized as described for the preparation of (**15a**) and (**16a**). The crude product was purified by flash chromatography on silica gel, with ethyl acetate–dichloromethane (1:1) as eluant, to give β-*anomer* (**15b**) (38%) as a solid, m.p. 147—152 °C (Found: C, 59.95; H, 4.75; N, 14.05. $C_{25}H_{23}N_5O_6$·0.5H_2O requires C, 60.24; H, 4.85; N, 14.05%); $[\alpha]_D^{20}$ +61.7° (*c* 0.35 in chloroform); δ($CDCl_3$) 2.45—2.65 (4 H, m, 5-Me and 2′-H_b), 3.10—3.26 (1 H, m, 2′-H_a), 4.50—4.80 (3 H, m, 4′- and 5′-H_2), 4.85 (2 H, br s, NH_2), 5.68 (1 H, dd, 1′-H), 5.74 (1 H, m, 3′-H), 7.35—8.20 (10 H, m, ArH), and 10.22 (1 H, br s, NH), a mixture of β- and α-anomer (5%), and pure α-*anomer* (**16b**) (24%) as an off-white foam (Found: C, 59.35; H, 4.7; N, 13.5. $C_{25}H_{23}N_5O_6$·H_2O requires C, 59.15; H, 4.6; N, 13.8%); $[\alpha]_D^{20}$ −13.8° (*c* 0.53 in chloroform); δ($CDCl_3$) 2.58 (3 H, s, 5-Me), 2.75—2.95 (1 H, dt, 2′-H_b), 3.05—3.20 (1 H, dt, 2′-H_a), 4.50—4.90 (3 H, m, 4′-H and 5′-H_2), 5.54 (1 H, dd, 1′-H), 5.63 (1 H, dt, 3′-H), 5.83 (2 H, br s, NH_2), 7.40—8.15 (10 H, m, ArH), and 10.32 (1 H, br s, NH).

7-(3′,5′-*Di*-O-*benzoyl*-2′-*deoxy*-β- *and* -α-D-erythro-*pentofuranosyl*)-3,4-*dihydro*-2-*methylimidazo*[5,1-f][1,2,4]*triazin*-4-*one* (**15c**) *and* (**16c**).—The amides (**14c**) were cyclized as described for the preparation of (**23a**)/(**24a**). The crude product was purified by flash chromatography on silica gel, with ethyl acetate–dichloromethane (1:1) as eluant, to give pure β-*anomer* (**15c**) (22%) as a solid, m.p. 182—187 °C (Found: C, 62.45; H, 4.75; N, 11.35. $C_{25}H_{22}N_4O_6$·0.5H_2O requires C, 62.1; H, 4.8; N, 11.6%); $[\alpha]_D^{23}$ −31° (*c* 0.02 in chloroform); $\nu_{max.}$(Nujol) 1 725, 1 710, and 1 692 cm^{-1}; δ[$CDCl_3$–$(CD_3)_2SO$] 2.32 (3 H, s, 2-CH_3), 2.55 (1 H, m, 2′-H_b), 3.30 (1 H, ddd, 2′-H_a), 4.48—4.70 (3 H, m, 4′-H and 5′-H_2), 5.78 (1 H, d, 3′-H), 5.82 (1 H, dd, 1′-H), 7.80 (1 H, s, 5-H), and 7.40—8.20 (10 H, m, ArH); a mixture of β- and α-*anomer* (*ca.* 2:1) (37%), and pure α-*anomer* (**16c**) (2%) as a foam (Found: $[M + H]^+$, 475.1614. $C_{25}H_{23}N_4O_6$ requires *m*/*z* 475.1617); δ($CDCl_3$) 2.40 (3 H, s, 2-CH_3), 2.88—3.13 (2 H, m, 2′-H_2), 4.66 (1 H, br d, 5′-H_2), 4.81 (1 H, q, 4′-H), 5.67 (1 H, dd, 1′-H), 5.85 (1 H, t, 3′-H), 7.90 (1 H, s, 5-H), and 7.35—8.15 (10 H, m, ArH).

2-*Amino*-7-(2′-*deoxy*-β- *and* -α-D-erythro-*pentofuranosyl*)-3,4-*dihydroimidazo*[5,1-f][1,2,4]*triazin*-4-*one* (**17a**) *and* (**18a**).—The 3′,5′-dibenzoates [(**15a**):(**16a**), 7:3] (3.53 g, 7.43 mmol) were kept in saturated methanolic ammonia (250 ml) at room temperature for 4 d. The solvent was removed under reduced pressure and the residue was triturated with diethyl ether (3 × 35 ml). The solid was collected by filtration and recrystallized from water to afford the *title compounds* (**17a**) and (**18a**) (927 mg, 47%) as a (1:1) mixture of anomers. The mother liquours were concentrated to afford 2-*amino*-7-(2′-*deoxy*-β-D-erythro-*pentofuranosyl*)-3,4-*dihydroimidazo*[5,1-f][1,2,4]-*triazin*-4-*one* (**17a**) (300 mg, 15%) as a solid, m.p. 259—260 °C (Found: C, 43.1; H, 4.8; N, 25.05. $C_{10}H_{13}N_5O_4$·0.5H_2O requires C, 43.45; H, 5.1; N, 25.35%); $\nu_{max.}$(Nujol) 3 660—3 050 and 1 720 cm^{-1}; $\lambda_{max.}$(EtOH) 263 nm (ε 4 900).

* D-*arabino*-Hexonamide.

† Mixture of diastereoisomers.

‡ For the nucleoside analogues (**15**)—(**18**), (**20**), (**21**), and (**23**)—(**30**), primed locants are used to denote the carbohydrate atoms.

2-*Amino*-7-(2′-*deoxy*-β-D-erythro-*pentofuranosyl*)-3,4-*dihydro*-5-*methylimidazo*[5,1-f][1,2,4]*triazin*-4-*one* (**17b**).—The 3′,5′-dibenzoate (**15b**) (1.22 g, 2.49 mmol) was kept in saturated methanolic ammonia (200 ml) at room temperature for 24 h. The solvent was removed under reduced pressure and the *residue was* triturated with diethyl ether (3 × 200 ml). The solid was collected by filtration (750 mg) and recrystallized from ethanol–ethyl acetate to provide the *title compound* (**17b**) (190 mg, 27%) as crystals, m.p. 155—159 °C; δ(CD_3OD) 2.18 (1 H, ddd, *J* 13.5, 5.5, and 2 Hz, 2′-H_b), 2.38 (1 H, ddd, *J* 13.5, 10, and 5.5 Hz, 2′-H_a), 2.52 (3 H, s, 5-Me), 3.64 (1 H, dd, *J* 12.5 and 4.5 Hz, 5′-H_a), 3.75 (1 H, dd, *J* 12.5 and 3.5 Hz, 5′-H_b), 3.95 (1 H, ddd, *J* 4.5, 4.5, and 2.5 Hz, 4′-H), 4.44 (1 H, ddd, *J* 6, 2, and 2 Hz, 3′-H), and 5.55 (1 H, dd, *J* 10 and 6 Hz, 1′-H) (Found: C, 43.95; H, 5.45; N, 22.55. $C_{11}H_{15}N_5O_4 \cdot 1.25H_2O$ requires C, 43.5; H, 5.8; N, 23.05%) (Found: $M^{+\bullet}$ [$(Me_3Si)_4$ derivative], 569.2742. $C_{23}H_{47}N_5O_4Si_4$ requires *m/z*, 569.2705).

2-*Amino*-7-(2′-*deoxy*-α-D-erythro-*pentofuranosyl*)-3,4-*dihydro*-5-*methylimidazo*[5,1-f][1,2,4]*triazin*-4-*one* (**18b**).—The 3′,5′-dibenzoate (**16b**) was deblocked as described for the preparation of (**17b**). The crude product was purified by flash chromatography on silica gel, with dichloromethane–ethanol (4:1) as eluant, to give the *title compound* (**18b**) (75%), m.p. 258—262 °C (decomp.) (from ethanol–ethyl acetate); δ(CD_3OD) 2.36 (1 H, ddd, *J* 13, 7, and 7 Hz, 2′-H_b), 2.58 (1 H, ddd, *J* 13, 7, and 7 Hz, 2′-H_a), 2.50 (3 H, s, 5-Me), 3.31 (1 H, dd, *J* 12.5 and 5 Hz, 5′-H_a), 3.39 (1 H, dd, *J* 12.5 and 4 Hz, 5′-H_b), 4.05 (1 H, q, *J* 4.5 Hz, 4′-H), 4.32 (1 H, ddd, *J* 7, 5, and 5 Hz, 3′-H), and 5.53 (1 H, dd, *J* 8, and 6 Hz, 1′-H) (Found: $M^{+\bullet}$ [$(Me_3Si)_4$ derivative], 569.2705. $C_{23}H_{47}N_5O_4Si_4$ requires *m/z*, 569.2705); $\nu_{max.}$(KBr) 3 460 and 1 690 cm^{-1}; $\lambda_{max.}$(EtOH) 229 (ε 29 900) and 266 nm (5 900).

7-(2′-*Deoxy*-β-D-erythro-*pentofuranosyl*)-3,4-*dihydro*-2-*methylimidazo*[5,1-f][1,2,4]*triazin*-4-*one* (**17c**).—*Method A*. A solution of 7-[2′-deoxy-3′,5′-*O*-(tetraisopropyldisiloxane-1,3-diyl)-β-D-*erythro*-pentofuranosyl]-3,4-dihydro-2-methylimidazo-[5,1-*f*][1,2,4]triazin-4-one (**27b**) (*vide infra*) (220 mg, 0.43 mmol) in THF (15 ml) was treated with tetra-n-butylammonium fluoride (1 ml; 1M in THF). The solution was kept at room temperature for 2 h, and then evaporated to dryness. The residue was purified by flash chromatography on silica gel, with dichloromethane–ethanol (9:1) as eluant, to provide the *title compound* (**17c**) (110 mg, 96%) as a solid, m.p. 214—216 °C (from ethanol–ethyl acetate) (Found: C, 49.8; H, 5.25; N, 20.85. $C_{11}H_{14}N_4O_4$ requires C, 49.6; H, 5.3; N, 21.05%); $\nu_{max.}$(Nujol) 3 420—3 200 and 1 730 cm^{-1}; $\lambda_{max.}$(EtOH) 250nm (ε 8 600).

Method B. The 3′,5′-dibenzoate (**15c**) (100 mg, 0.22 mmol) was disolved in 33% methylamine–ethanol (25 ml) and the mixture was kept at room temperature for 18 h. The solvent was evaporated off and the residue was purified by flash chromatography on silica gel. Elution with dichloromethane–ethanol (9:1) provided the *title compound* (**17c**) (52 mg, 88%), identical with that prepared by Method A.

7-(2′-*Deoxy*-α-D-erythro-*pentofuranosyl*)-3,4-*dihydro*-2-*methylimidazo*[5,1-f][1,2,4]*triazin*-4-*one* (**18c**).—The 3′,5′-dibenzoate (**16c**) was deblocked as described for the preparation of (**17c**) (Method B). The crude product was purified by column chromatography on silica gel, with dichloromethane–ethanol (9:1) as eluant, to give the *title compound* (**18c**) (83%) as a white solid, m.p. 185—188 °C [Found: $(M + H)^+$, 267.1090. $C_{11}H_{15}N_4O_4$ requires *m/z*, 267.1092].

2,5-*Anhydro*-4,6-*di*-O-*benzoyl*-3-*deoxy*-N-(2-*pyridylmethyl*)-D-arabino- *and* -D-ribo-*hexonamide* (**19**).—(4*S*,*trans*)-4-Benzoyloxy-5-benzoyloxymethyl-4,5-dihydro-*N*-(2-pyridylmethyl)-furan-2-carboxamide (**6**) (5.40 g, 11.8 mmol) in ethyl acetate (200 ml) was hydrogenated over 10% palladium—carbon at 1 atm for 4 d. The catalyst was removed by filtration and the filtrate was evaporated to dryness. The residue was purified by column chromatography on silica gel, with ethyl acetate–ethanol (9:1) as eluant, to give the *title compounds* (**19**) (2.96 g, 55%) as a gum (Found: C, 67.4; H, 5.3; N, 5.7. $C_{26}H_{24}N_2O_6$ requires C, 67.8; H, 5.25; N, 6.1%); $\nu_{max.}$($CHBr_3$) 3 410, 1 720, and 1 670 cm^{-1}; $\lambda_{max.}$(EtOH) 230 (ε 26 700), 255 (4 300), 261 (4 600), 267.5 (4 000), and 281 nm (1 600). Partial separation of the individual anomers was achieved during the chromatography; the α-anomer* had $[\alpha]_D^{21}$ +12.1° (*c* 1.03 in chloroform); δ($CDCl_3$) 2.34—2.50 (1 H, m, 3-H_b), 2.68—2.80 (1 H, m, 3-H_a), 4.40—4.80 (5 H, m, NHCH_2, 5-H, and 6-H_2), 4.84 (1 H, dd, *J* 8 Hz, 2-H), 5.55 (1 H, d, *J* 6 Hz, 4-H), 7.08—7.65 (9 H, m, ArH, pyr 3- and 5-H, and NH), 7.85—8.15 (5 H, m, ArH and pyr 4-H), and 8.41 (1 H, m, pyr 6-H); the β-anomer* had $[\alpha]_D^{21}$ +67.0° (*c* 0.67 in chloroform); δ($CDCl_3$) 2.70—2.82 (2 H, m, 3-H_2), 4.40—4.70 (4 H, m, NHCH_2 and 6-H_2), 4.75 (1 H, dt, *J* 4.5 and 2 Hz, 5-H), 4.82 (1 H, t, *J* 6 Hz, 2-H), 5.53 (1 H, m, 4-H), 7.05—7.65 (9 H, m, ArH, pyr 3- and 5-H, and NH), 7.87 (2 H, d, ArH), 7.95 (1 H, m, pyr 4-H), 8.06 (2 H, d, ArH), and 8.56 (1 H, m, pyr 6-H).

3-(3′,5′-*Di*-O-*benzoyl*-2′-*deoxy*-β- and -α-D-erythro-*pentofuranosyl*)*imidazo*[1,5-a]*pyridine* (**20a**) *and* (**21a**).—2,5-Anhydro-4,6-di-*O*-benzoyl-3-deoxy-N-(2-pyridylmethyl-D-*arabino*- and -D-*ribo*-hexonamide (**19**) (4.20 g, 9.12 mmol) and phosphoryl trichloride (8.23 g, 53.7 mmol) in dry 1,2-dichloroethane (350 ml) were heated at reflux for 1.5 h. Dry pyridine (18 ml) was added and the reaction mixture was heated at reflux for a further 2 h. The solvents and excess of phosphoryl trichloride were removed under reduced pressure and the residue was partitioned between ethyl acetate (300 ml) and saturated aqueous sodium hydrogen carbonate (350 ml). The organic layer was separated and the aqueous phase was further extracted with ethyl acetate (3 × 100 ml). The combined ethyl acetate extracts were dried ($MgSO_4$) and the solvent was evaporated off. The residue was purified by flash chromatography on silica gel, with ethyl acetate–cyclohexane (1:1) as eluant, to afford the *title compounds* as a solid. Crystallization from ethyl acetate–cyclohexane gave the α-*anomer* (**21a**) (1.24 g, 31%) as crystals, m.p. 153—157 °C (Found: C, 70.75; H, 5.0; N, 6.2. $C_{26}H_{22}N_2O_5$ requires C, 70.6; H, 5.0; N, 6.35%); $[\alpha]_D^{21}$ +131.7° (*c* 2.61 in chloroform); $\nu_{max.}$($CHBr_3$) 1 715 cm^{-1}; $\lambda_{max.}$(EtOH) 279 (ε 9 100), 290 (6 400), and 334 nm (2 100); δ($CDCl_3$) 2.98—3.12 (1 H, dt, *J* 14, 7.5, and 7.5 Hz, 2′-H_b), 3.30—3.45 (1 H, ddd, *J* 14, 7.5, and 4.5 Hz, 2′-H_a), 4.50—4.80 (3 H, m, 4′-H, and 5′-H_2), 5.68 (1 H, ddd, *J* 7.5, 4.5, and 4 Hz, 3′-H), 5.74 (1 H, t, *J* 7.5 Hz, 1′-H), 6.56 (1 H, t, 6-H), 6.74 (1 H, dd, 7-H), 7.45—8.15 (12 H, m, ArH and 1- and 8-H), and 8.24 (1 H, br d, 5-H). The mother liquors from the above crystallization were evaporated to provide the β-*anomer* (**20a**) (2.25 g, 55%) as a fawn gum (Found: C, 70.2; H, 5.0; N, 5.95. $C_{26}H_{22}N_2O_5$ requires C, 70.6; H, 5.0; N, 6.35%); $[\alpha]_D^{21}$ −86.9° (*c* 2.50 in chloroform); $\nu_{max.}$($CHBr_3$) 1 720 cm^{-1}; $\lambda_{max.}$(EtOH) 268 (ε 7 500), 278 (9 600), 290 (6 900), and 332 nm (2 200); δ($CDCl_3$) 2.65—2.75 (1 H, ddd, *J* 14, 5.5, and 1.5 Hz, 2′-H_b), 3.26—3.40 (1 H, ddd, *J* 14, 10, and 6.5 Hz, 2′-$H)_a$), 4.48—4.65 (3 H, m, 4′-H and 5′-H_2), 5.71 (1 H, dd, *J* 10 and 5.5 Hz, 1′-H), 5.76 (1 H, dt, *J* 6.5, 1.5, and 1.5 Hz, 3′-H), 6.42 (1 H, dt, *J* 7 and 1.5 Hz, 6-H), 6.71 (1 H, dd, *J* 8 and 7 Hz, 7-H), 7.45—8.18 (12 H, m, ArH and 1- and 8-H), and 8.24 (1 H, dd, 5-H).

3-(2′-*Deoxy*-β- *and* -α-D-erythro-*pentofuranosyl*)*imidazo*[1,5-a]*pyridine* (**20b**) *and* (**21b**).—The 3′,5′-dibenzoate (**20a**) (2.00 g, 4.52 mmol) was kept in saturated methanolic ammonia (400 ml) at room temperature for 36 h. The solvent was removed under reduced pressure and the residue was subjected to flash

* Tentative assignments.

chromatography on silica gel. Elution with ethyl acetate–ethanol (9:1) afforded the *title compounds* (760 mg, 66%) as a mixture of anomers. Re-chromatography over silica gel (Merck 60, Art 7734), with dichloromethane–ethanol (19:1) as eluant, gave the α-*anomer* (**21b**) (150 mg, 13%) as a solid, m.p. 133—136 °C (Found: $M^{+\bullet}$, 234.0994. $C_{12}H_{14}N_2O_3$ requires *M*, 234.1005); $\lambda_{max.}$(EtOH) 269sh (ε 5 600), 279 (7 600), 290 (6 350), and 333 nm (2 000). Further elution with dichloromethane–ethanol (4:1) provided the β-anomer (**20b**) 380 mg, 33%) as a foam (Found: C, 59.4; H, 6.1; N, 11.15. $C_{12}H_{14}N_2O_3{\cdot}0.5H_2O$ requires C, 59.25; H, 6.2; N, 11 5%) (Found: $M^{+\bullet}$, 234.0996. $C_{12}H_{14}N_2O_3$ requires *M*, 234.1005).

2,5-*Anhydro*-4,6-*di*-O-*benzoyl*-3-*deoxy*-N-[(1,6-*dihydro*-6-*oxopyridazin*-3-*yl*)*methyl*]-D-arabino- *and* -D-ribo-*hexonamide* (**22**).—These *compounds* (73%) were prepared by hydrogenation of the amide (**9a**), as described for the preparation of (**19**), and were obtained as a foam after purification by column chromatography on silica gel (ethyl acetate as eluant) (Found: C, 62.5; H, 4.65; N, 8.6. $C_{25}H_{23}N_3O_7$ requires C, 62.9; H, 4.85; N, 8.8%); $\nu_{max.}$($CHBr_3$) 3 410, 3 370, 1 720, and 1 680 cm^{-1}; δ($CDCl_3$) 2.30—2.43 and 2.66—2.82 (2 H, m, 3-H_2), 4.25—4.46 (2 H, 2 d, NHCH_2), 4.50—4.85 (4 H, m, 2-and 5-H and 6-H_2), 5.50 and 5.58 (1 H, m, 4-H), 6.72 and 6.81 (1 H, 2 d, pyr 5-H), 7.13 and 7.17 (1 H, 2 d, pyr 4-H), 7.30—8.10 (11 H, m, ArH and NH), and 11.5 (1 H, br s, NH).

2-*Chloro*-7-(3′,5′-*di*-O-*benzoyl*-2′-*deoxy*-β- *and* -α-D-erythro-*pentofuranosyl*)*imidazo*[1,5-b]*pyridazine* (**23a**) *and* (**24a**).—2,5-Anhydro-4,6-di-*O*-benzoyl-3-deoxy-*N*-[(1,6-dihydro-6-oxopyridazin-3-yl)methyl]-D-*arabino*- and -D-*ribo*-hexonamide (**22**) (0.90 g, 1.89 mmol) and phosphoryl trichloride (1.65 g, 10.73 mmol) in dry 1,2-dichloroethane (35 ml) were heated at reflux for 1.25 h. The solvent and excess of phosphoryl trichloride were removed under reduced pressure and the residue was thoroughly shaken with saturated aqueous sodium hydrogen carbonate (50 ml) and ethyl acetate (50 ml). The ethyl acetate phase was separated and the aqueous layer was further extracted with ethyl acetate (2 × 50 ml). The combined ethyl acetate extracts were dried (Na_2SO_4) and the solvent was evaporated off to give a brown foam. This material was purified by flash chromatography on silica gel, with diethyl ether as eluant, to provide the *title compounds* (**23a**) and (**24a**) (0.55 g, 61%) as a yellow foam (2:1 mixture of β- and α-anomer) (Found: C, 63.2; H, 4.1; N, 8.8. $C_{25}H_{20}ClN_3O_5$ requires C, 62.85; H, 4.2; N, 8.8%); $\nu_{max.}$($CHBr_3$) 1 730 cm^{-1}; $\lambda_{max.}$(EtOH) 232 (ε 54 800) and 262 nm (5 100); δ($CDCl_3$) (*inter alia*) 5.68 (1 H, q, 1′-H, α-anomer) and 5.80 (1 H, d, 1′-H, β-anomer).

2-*Chloro*-7-(2′-*deoxy*-β- *and* -α-D-erythro-*pentofuranosyl*)-*imidazo*[1,5-b]*pyridazine* (**23b**) and (**24b**).—The 3′,5′-dibenzoates (**23a**) and (**24a**) (230 mg, 0.48 mmol) were kept in saturated methanolic ammonia (50 ml) at room temperature for 24 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel. Elution with dichloromethane–ethanol (9:1) gave the α-*anomer* (**24b**) (46 mg, 35%) as a pale yellow solid, m.p. 137—139 °C (Found: $[M + H]^+$, 270.0648. $C_{11}H_{13}{}^{35}ClN_3O_3$ requires *m/z* 270.0645), a mixture of α- and β-anomer (10 mg, 8%), followed by the β-*anomer* (**23b**) (35 mg, 27%) as a pale yellow solid, m.p. 106.5—110.5 °C (Found: $[M + H]^+$, 270.0649. $C_{11}H_{13}{}^{35}ClN_3O_3$ requires *m/z* 270.0645); $\lambda_{max.}$(EtOH) 232 (ε 11 000), 260sh (1 100), and 370 nm (600).

3,4-*Dihydro*-2-*methyl*-7-[3′,5′-O-(*tetraisopropyldisiloxane*-1,3-*diyl*)-β-D-*ribofuranosyl*]*imidazo*[5,1-f][1,2,4]*triazin*-4-*one* (**26**).—A solution of 3,4-dihydro-2-methyl-7-(β-D-ribofuranosyl)imidazo[5,1-*f*][1,2,4]triazin-4-one (**25**) (665 mg, 2.35 mmol) and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (857 mg, 2.81 mmol) in pyridine (18 ml) was kept at room temperature for 18 h. The pyridine was evaporated off under reduced pressure and the residue was partitioned between water (100 ml) and ethyl acetate (100 ml). The ethyl acetate phase was separated and the aqueous layer was further extracted with ethyl acetate (2 × 100 ml). The combined ethyl acetate extracts were dried (Na_2SO_4) and the solvent was evaporated to give a gum. This material was purified by flash chromatography on silica gel, with ethyl acetate–cyclohexane (1:1) as eluant, to provide the *title compound* (**26**) (870 mg, 71%) as a foam (Found: M^+, 524.2491. $C_{23}H_{40}N_4O_6Si_2$ requires *M*, 524.2493); $[\alpha]_D{}^{23}$ −83° (*c* 0.38 in chloroform); $\nu_{max.}$(Nujol) 3 600—3 100 and 1 710 cm^{-1}; δ($CDCl_3$) 0.90—1.30 [28 H, m, 4 $CH(CH_3)_2$], 2.40 (3 H, s, 2-Me), 3.90—4.15 (3 H, m, 4′-H and 5′-H_2), 4.65—4.80 (2 H, m, 2′- and 3′-H), 5.40 (1 H, d, *J* 2.5 Hz, 1′-H), 7.86 (1 H, s, 5-H), and 10.83 (1 H, br s, NH).

3,4-*Dihydro*-7-{2′-O-[(*imidazol*-1-*yl*)*thiocarbonyl*]-3′,5′-O-(*tetraisopropyldisiloxane*-1,3-*diyl*)-β-D-*ribofuranosyl*}-2-*methyl*-*imidazo*[5,1-f][1,2,4]*triazin*-4-*one* (**27a**).—A solution of the protected imidazotriazinone (**26**) (1.13 g, 2.14 mmol) in dimethylformamide (10 ml) was treated with thiocarbonyldiimidazole (1.01 g, 5.66 mmol) and the mixture was kept at room temperature for 18 h. The solvent was evaporated off under reduced pressure and the residue was partitioned between ethyl acetate (50 ml) and water (50 ml). The ethyl acetate phase was separated and the aqueous layer was further extracted with ethyl acetate (2 × 50 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated to give a foam. This material was purified by flash chromatography on silica gel, with ethyl acetate–dichloromethane (1:1) as eluant, to afford the *title compound* (**27a**) (1.20 g, 88%) as a foam [Found: $(M + H)^+$, 635.2450. $C_{27}H_{43}N_6O_6SSi_2$ requires *m/z*, 635.2499]; $[\alpha]_D{}^{24}$ −69.3° (*c* 0.27 in chloroform); $\nu_{max.}$($CHBr_3$) 1 720 cm^{-1}; δ($CDCl_3$) 0.90—1.30 [28 H, m, 4 $CH(CH_3)_2$], 2.41 (3 H, s, 2-Me), 4.00—4.20 (3 H, m, 4′-H and 5′-H_2), 5.12 (1 H, dd, 3′-H), 5.70 (1 H, d, *J* 1 Hz, 1′-H), 6.44 (1 H, m, 2′-H), 7.08 (1 H, br s, imidazole 4-H), 7.68 (1 H, br s, imidazole 5-H), 7.88 (1 H, s, 5-H), 8.42 (1 H, br s, imidazole 2-H), and 10.82 (1 H, br s, NH).

7-[2′-*Deoxy*-3′,5′-O-(*tetraisopropyldisiloxane*-1,3-*diyl*)-β-D-erythro-*pentofuranosyl*]-3,4-*dihydro*-2-*methylimidazo*[5,1-f]-[1,2,4]*triazin*-4-*one* (**27b**).—A solution of compound (**27a**) (1.17 g, 1.83 mmol) in dry toluene (10 ml) was heated to reflux under nitrogen. A solution of azobisisobutyronitrile (AIBN) (0.31 g, 1.89 mmol) and tri-n-butyltin hydride (2.25 g, 7.73 mmol) in toluene (40 ml) was added dropwise during 20 min and the mixture was refluxed for 1.5 h. The reaction mixture was concentrated to *ca.* 10 ml and applied to a column of silica gel. Flash chromatography, initially with ethyl acetate–cyclohexane (3:7), and then (7:3), as eluant, provided the *title compound* (**27b**) (0.85 g, 91%) as a foam (Found: C, 54.15; H, 7.9; N, 10.65. $C_{23}H_{40}N_4O_5Si_2$ requires C, 54.3; H, 7.9; N, 11.0%); $[\alpha]_D{}^{24}$ −104° (*c* 0.05 in chloroform); $\nu_{max.}$ ($CHBr_3$) 1 710 cm^{-1}; $\lambda_{max.}$(EtOH) 250nm (ε 8 300); δ($CDCl_3$) 0.90—1.20 [28 H, m, 4 $CH(CH_3)_2$], 2.39 (1 H, m, 2′-H_b), 2.42 (3 H, s, 2-CH_3), 2.90 (1 H, m, 2′-H_a), 3.95 (1 H, m, 4′-H), 3.85 and 4.05 (2 H, 2 dd, 5′-H_2), 4.80 (1 H, dt, 3′-H), 5.62 (1 H, t, 1′-H), 7.86 (1 H, s, 5-H), and 10.65 (1 H, br s, NH).

7-[2′-*Deoxy*-3′,5′-O-(*tetraisopropyldisiloxane*-1,3-*diyl*)-β-D-erythro-*pentofuranosyl*]-2-*methyl*-4-(1,2,4-*triazol*-1-*yl*)*imidazo*-[5,1-f][1,2,4]*triazine* (**28**).—Phosphoryl trichloride (0.64 g, 4.16 mmol) and 1,2,4-triazole (1.34 g, 19.4 mmol) were added to acetonitrile (25 ml) and the solution was cooled to 0 °C. Triethylamine (1.89 g, 18.7 mmol) was added dropwise to the stirred mixture, followed by a solution of 7-[2′-deoxy-3′,5′-*O*-(tetra-

isopropyldisiloxane-1,3-diyl)-β-D-*erythro*-pentofuranosyl]-3,4-dihydro-2-methylimidazo[5,1-*f*][1,2,4]triazin-4-one (**27b**) (0.75 g, 1.46 mmol) in acetonitrile–toluene (2:1; 25 ml). The reaction mixture was kept at room temperature for 16 h. Triethylamine (2.5 ml) and water (1 ml) were added and the solution was evaporated to dryness. The residue was treated with saturated aqueous sodium hydrogen carbonate (100 ml) and the resultant suspension was extracted with ethyl acetate (3 × 50 ml). The combined extracts were dried ($MgSO_4$) and evaporated to give a gum. This material was purified by flash chromatography on silica gel, with ethyl acetate–cyclohexane (3:7) as eluant, to provide the *title compound* (**28**) 0.75 g, 91%) as a light yellow solid, m.p. 150—154 °C (Found: C, 54.0; H, 7.4; N, 17.0. $C_{25}H_{41}N_7O_4Si_2$ requires C, 53.65; H, 7.4; N, 17.5%); $[\alpha]_D^{24}$ − 84° (*c* 0.52 in chloroform); $\lambda_{max.}$(EtOH) 247 (ε 28 000), 274 (8 200), and 356 nm (1 800); δ($CDCl_3$) 0.80—1.20 [28 H, m, 4 $CH(CH_3)_2$], 2.47 (1 H, m, 2′-H_b), 2.64 (3 H, s, 2-CH_3), 2.96 (1 H, m, 2′-H_a), 3.98 (1 H, m, 4′-H), 3.86 and 4.07 (2 H, 2 dd, 5′-H_2), 4.88 (1 H, dt, 3′-H), 5.83 (1 H, t, 1′-H), 8.27, 8.43, and 9.36 (3 H, 3 s, 5-H and triazole 3- and 5-H).

4-*Amino*-7-[2′-*deoxy*-3′,5′-O-(*tetraisopropyldisiloxane*-1,3-*diyl*)-β-D-erythro-*pentofuranosyl*]-2-*methylimidazo*[5,1-f][1,2,4]-*triazine* (**29**).—The imidazotriazinone (**28**) (750 mg, 1.34 mmol) was dissolved in anhydrous THF saturated with ammonia and the solution was kept at room temperature for 30 min. The solvent was removed under reduced pressure and the resultant foam was purified by flash chromatography [ethyl acetate as eluant] to afford the *title compound* (**29**) (640 mg, 94%) as a solid, m.p. 164—166 °C (Found: C, 54.8; H, 8.1; N, 13.4. $C_{23}H_{41}N_5O_4Si_2$ requires C, 54.4; H, 8.15; N, 13.8%); $[\alpha]_D^{24}$ − 78° (*c* 0.50 in chloroform); $\nu_{max.}$($CHBr_3$) 3 520 and 3 400 cm^{-1}; $\lambda_{max.}$(EtOH) 236 (ε 29 800) and 296 nm (3 150); δ($CDCl_3$) 0.80—1.20 [28 H, m, 4 $CH(CH_3)_2$], 2.40 (1 H, m, 2′-H_b), 2.41 (3 H, s, 2-CH_3), 2.92 (1 H, m, 2′-H_a), 3.97 (1 H, m, 4′-H), 3.85 and 4.08 (2 H, 2 dd, 5′-H_2), 4.80 (1 H, dt, 3′-H), 5.73 (1 H, t, 1′-H), 6.00 (2 H, br s, NH_2), and 7.56 (1 H, s, 5-H).

4-*Amino*-7-[2′-*deoxy*-β-D-erythro-*pentofuranosyl*]-2-*methylimidazo*[5,1-f][1,2,4]*triazine* (**30**).—A solution of the imidazotriazine (**29**) (600 mg, 1.18 mmol) in dry THF (100 ml) was treated with a solution of tetra-n-butylammonium fluoride (1M in THF; 2.75 ml) and the mixture was stirred at room temperature for 45 min. The solvent was evaporated off to give a gum. This was purified by flash chromatography on silica gel, with dichloromethane–ethanol (4:1) as eluant, to give the *title compound* (**30**) (290 mg, 92%) as a solid, m.p. 133—135 °C (from ethyl acetate–ethanol) (Found: $[M + H]^+$, 266.1248. $C_{11}H_{16}N_5O_3$ requires *m/z*, 266.1253. Found: *M* − 89, 176.0936 (base peak). $C_8H_{10}N_5$ requires *m/z*, 176.0936); $\nu_{max.}$(Nujol) 3 500 and 3 000 cm^{-1}; $\lambda_{max.}$(EtOH) 238 (ε 26 500) and 298 nm (2 800).

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