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The Synthesis of Carbohydrate α-Amino Acids Utilizing the Corey–Link Reaction

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Various carbohydrate ketones (uloses) have been treated with chloroform under strongly basic conditions to yield trichloromethyl *tertiary* alcohols. These alcohols, when subjected to the conditions of the modified Corey–Link reaction (sodium azide and 1,8-diazabicyclo[5.4.0]undec-7-ene in methanol), generally gave the expected azido ester with complete stereocontrol. Subsequent transformations on these azido esters provided amino esters, azido acids, and, in one case, the amino acid. A similar sequence applied to a protected D-glucono-1,5-lactone was only partly successful.

Single-crystal X-ray structures are reported for 1,2:5,6-di-*O*-isopropylidene-3-*C*-trichloromethyl-α-D-allose, (3*S*)-3-*C*-azido-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, 1,2:5,6-di-*O*-cyclohexylidene-3-*C*-trichloromethyl-α-D-gulose, (3*S*)-3-*C*-amino-1,2:5,6-di-*O*-cyclohexylidene-3-deoxy-3-*C*-methoxycarbonyl-α-D-*xylo*-hexose, methyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*C*-trichloromethyl-α-D-alloside, methyl (2*S*)-2-*C*-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-*C*-methoxycarbonyl-α-D-*arabino*-hexoside, methyl 2,3-di-*O*-benzyl-6-deoxy-4-*C*-trichloromethyl-β-D-galactoside, 3,4,5,7-tetra-*O*-benzyl-1,1,1-trichloro-1-deoxy-α-D-*gluco*-hept-2-ulose, and 5-*O*-benzyl-1,2-*O*-isopropylidene-3-*C*-trichloromethyl-α-D-ribose.

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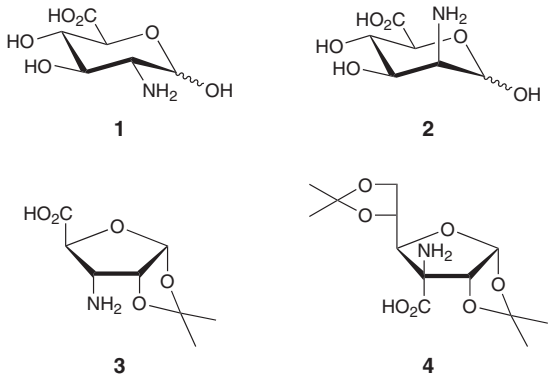
Introduction

Proteins, nucleic acids, and polysaccharides are the three classes of biopolymer that together are responsible for the well being of most life forms. The monomers from which these biopolymers are constituted are the amino acids, the nucleotides, and the monosaccharides. It is obvious that a change in the structure of each of these monomers could lead to new sorts of polymers. We envisaged that a carbohydrate α-amino acid, a monomer with the dual characteristics of an amino acid and a monosaccharide, could lead to interesting new polypeptides and polysaccharides. In addition, if the carbohydrate α-amino acid also incorporated a purine or pyrimidine base, there would be the chance to prepare interesting mimics of nucleic acids.

Carbohydrate (or sugar) amino acids are not novel—molecules such as **1**[1] and **2**[2] are components of polysaccharides and various reviews have appeared on structural variants thereof, for example, **3** (Scheme 1).[3–5] Not surprisingly, some of these variants have been converted into oligomers, generating both linear and cyclic oligopeptides of interesting structure.[6] We decided to focus our attention on carbohydrate α-amino acids, say of structure **4**, for two reasons: one, the amino acid is configurationally stable, having no α-hydrogen, and two, there seemed a ready synthetic route to such molecules.



Scheme 1.

One of the most reliable (and oldest) routes to α-amino acids involves the treatment of a ketone (here) with ammonium chloride and sodium cyanide, the so-called Strecker synthesis.[7] A variation of such a process has been applied to carbohydrate ketones (uloses), for example, the transformation of **5** into **6** (and thence potentially **7**), but the presence of a Lewis acid (titanium(IV) isopropoxide) was essential to form the intermediate imine, and hence the amino nitrile **6** (Scheme 2).[8] The related Bucherer–Bergs reaction provides hydantoins that are direct precursors of α-amino acids (Scheme 3).[8,9]

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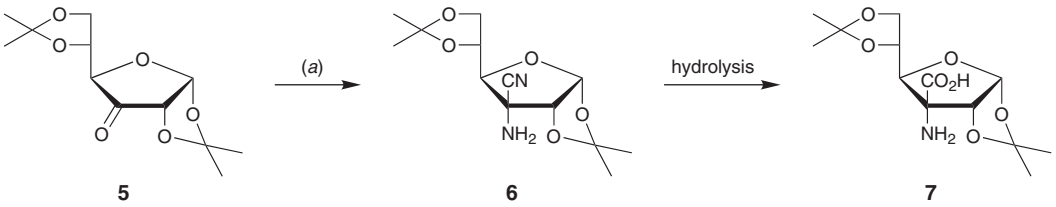
Corey and Link have reported a novel method for the synthesis of α-amino acids, involving the treatment of a trichloromethyl alcohol with sodium azide in aqueous base (Scheme 4A); a subsequent reduction step then provides the amino acid.[10] The whole process was improved somewhat by Domínguez and coworkers who used sodium azide and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in methanol to provide the azido ester, a direct precursor of the α-amino acid (Scheme 4B).[11]

We were attracted to this Corey–Link approach for two reasons: one, the required trichloromethyl alcohols, such as **8** (Scheme 5), would be readily available from the corresponding ketones,[11,12] and two, the stereochemical outcome of the process (**9** and **4**) would be the opposite of that for the Strecker and related reactions.

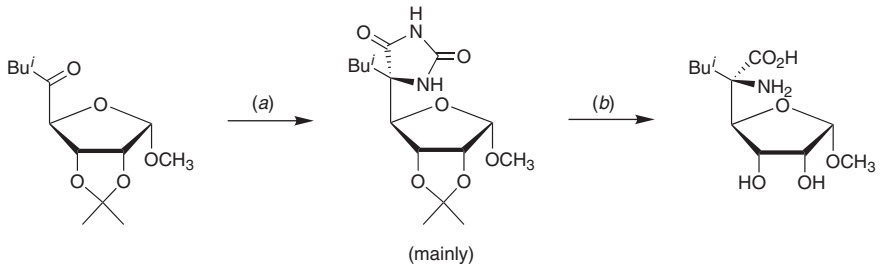
This paper describes our efforts towards the synthesis of carbohydrate α-amino acids and their precursors, using the modified Corey–Link reaction,[11,12] and is a full report on our earlier communication.[13]

Results and Discussion

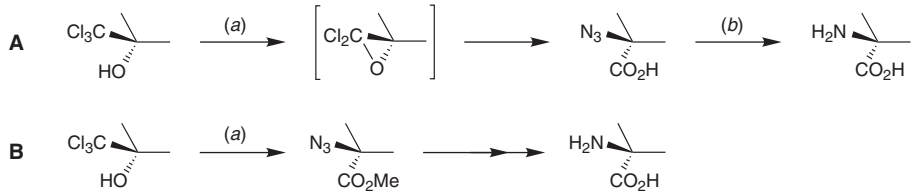
As a logical starting point, the ketone **5**[14] (Scheme 5) was converted into the (3*R*)-configured alcohol **8** [the ideal base was lithium bis(trimethylsilyl)amide[11]];[13] a single-crystal X-ray structure determination confirmed both the absolute



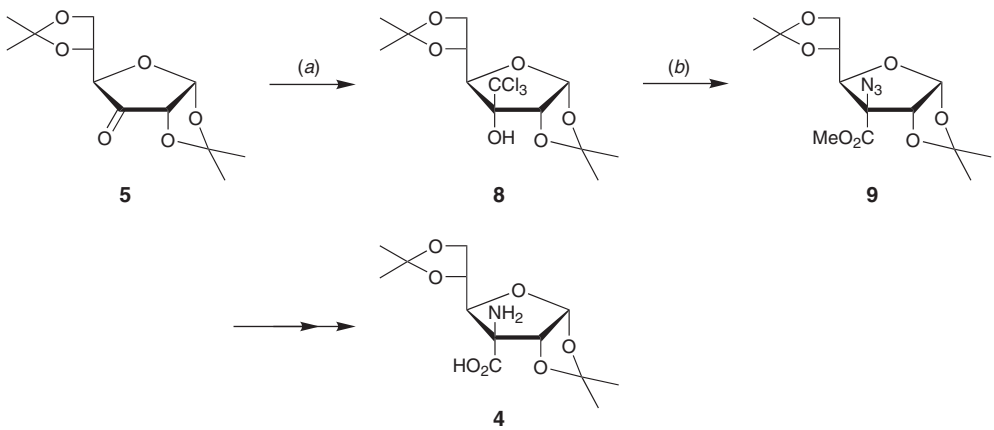
Scheme 2. (*a*) $Ti(OPr^i)_4$, NH_3, MeOH, followed by Me_3SiCN.



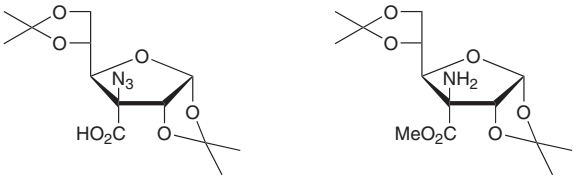
Scheme 3. (*a*) NaCN, $(NH_4)_2CO_3$, EtOH, H_2O; (*b*) CH_3COOH, H_2O, followed by $Ba(OH)_2 \cdot 8H_2O$, H_2O.



Scheme 4. **A**, (*a*) NaN_3, NaOH, H_2O, 1,2-dimethoxyethane; (*b*) H_2, Pd. **B**, (*a*) NaN_3, DBU, [18]crown-6, MeOH.

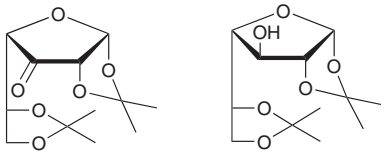


Scheme 5. (*a*) $CHCl_3$, base; (*b*) Corey–Link.



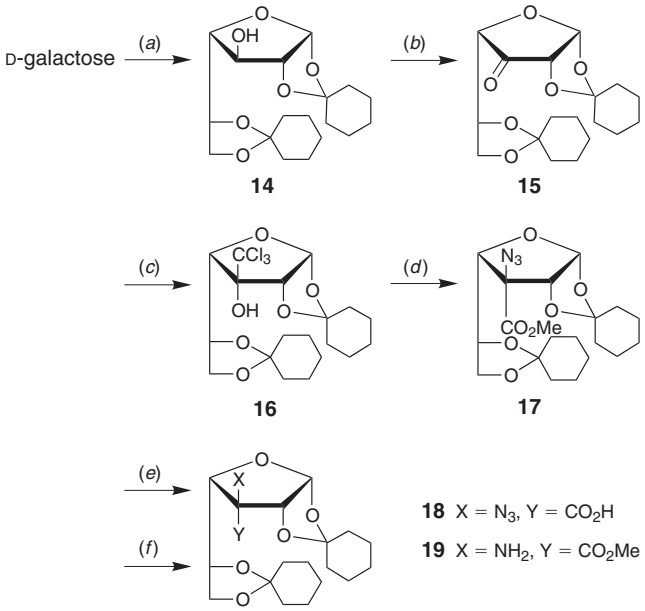
10 **11**

Scheme 6.



12 **13**

Scheme 7.



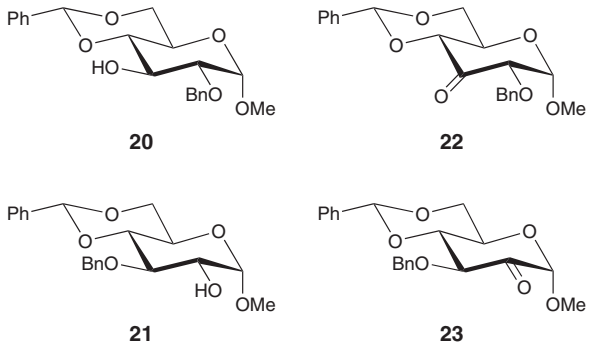
14 **15** **16** **17**

Scheme 8. (*a*) Cyclohexanone dimethyl acetal, pyridinium *p*-toluenesulfonate, dimethylformamide, PhMe; (*b*) pyridinium dichromate, Ac_2O, CH_2Cl_2; (*c*) $CHCl_3$, lithium bis(trimethylsilyl)amide, tetrahydrofuran; (*d*) NaN_3, DBU, [18]crown-6, MeOH; (*e*) KOH, MeOH; (*f*) H_2, Pd/C, MeOH.

and relative stereochemistries of **8**. Along with the other determinations presented in this paper, ring conformational descriptors are presented in Tables 1, 2, and 3 and molecular projections are given in Fig. 1.

The subsequent modified Corey–Link reaction gave an azido ester, presumably of structure **9**, and this was converted into an azido acid **10** (saponification; Scheme 6), amino ester **11** (hydrogenolysis), and amino acid **4** (saponification and hydrogenolysis; Scheme 5).[13] A single-crystal X-ray structure determination of **10** (Fig. 2) confirmed all of the assigned stereochemistries and indicated that the Corey–Link reaction had indeed proceeded with inversion of configuration (at C3).

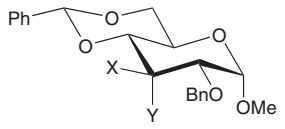
Although we next wanted to repeat the above sequence on the ketone **12** (Scheme 7), the synthetic routes to the prerequisite alcohol **13** are either long or unreliable. Therefore,



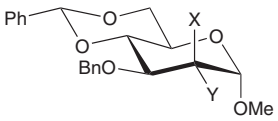
20 **22**

21 **23**

Scheme 9.



24 X = CCl_3, Y = OH
26 X = N_3, Y = CO_2Me
27 X = N_3, Y = CO_2H
28 X = NH_2, Y = CO_2Me



25 X = CCl_3, Y = OH
29 X = N_3, Y = CO_2Me
30 X = N_3, Y = CO_2H
31 X = NH_2, Y = CO_2Me

Scheme 10.

we prepared the related acetal **14** (Scheme 8) in a slightly improved manner[15] and oxidation gave the ketone **15**, the precursor of the alcohol **16**. A modified Corey–Link reaction on **16** gave the azido ester **17**, and subsequent transformations gave the azido acid **18** and the amino ester **19**. The configuration of the newly formed stereocentres in **16** and **19** were again confirmed by single-crystal X-ray structure determinations (Figs 3 and 4); in **16** alone, among the present structure determinations, *two* (rather than one) independent molecule(s) devoid of crystallographic symmetry comprise the asymmetric unit of the structure. Here, the two differ only trivially in geometrical descriptors.

With these successes in furanose examples we turned our attention to pyranoses—our improved synthesis of the alcohol **20**[16] still provided amounts of the isomeric **21** (Scheme 9). Oxidation of both alcohols gave the ketones **22** and **23** and the normal addition of chloroform gave the alcohols **24** and **25**, respectively (Scheme 10). Only the alcohol **24** was amenable to a single-crystal X-ray structure determination (Fig. 5).

The submission of the alcohols **24** and **25** to the modified Corey–Link reaction, followed by the usual transformations as outlined in Scheme 8, gave the suites of compounds **26**–**28** and **29**–**31**, respectively (Scheme 10). The structure of **29** was confirmed from a single-crystal X-ray structure determination (Fig. 6).

It seemed logical next to try the sequence on the alcohol **32**[17] (Scheme 11). Oxidation of **32** gave the ketone **33** and the normal addition of chloroform certainly gave an alcohol, of *suggested* structure **34**. However, all attempts to perform

the modified Corey–Link reaction on **34** failed to produce an azido ester—the only isolated product was benzyl alcohol! Also unsuccessful was the sequence starting with the methyl β-D-glucoside **35** (Scheme 12)—although the ketone **36** and

Table 1. Ring torsion angles [°] for five-membered mono-oxo rings

Bond	Compound/molecule				
	8	**10**	**16**/1,2	**19**	**46**
O(4)–C(1)	−32.1(1)	−24.2(4)	−39.7(6)	40.2(4)	−32.3(8)
C(1)–C(2)	11.4(1)	0.0(4)	21.5(6)	−22.3(5)	12.0(9)
C(2)–C(3)	11.2(1)	22.0(4)	−5.6(6)	−2.3(5)	10.8(8)
C(3)–C(4)	−29.8(1)	−36.8(4)	−11.3(6)	26.4(5)	−30.0(9)
C(4)–O(4)	39.4(1)	39.2(4)	26.2(6)	−42.1(4)	37.2(9)

Table 2. Ring torsion angles [°] for six-membered mono-oxo rings

Bond	Compound			
	24[A]	**29**	**39**	**42**
O(5)–C(1)	−57.6(2)	−56.8(2)	38.0(3)	−54.2(5)
C(1)–C(2)	40.2(2)	54.4(2)	26.0(3)	54.2(5)
C(2)–C(3)	−35.4(2)	−54.8(2)	−61.0(3)	−56.1(6)
C(3)–C(4)	47.1(2)	59.2(2)	33.5(4)	57.5(6)
C(4)–O(4)	−65.7(2)	−62.0(2)	24.8(3)	−54.4(5)
C(5)–O(5)	71.3(2)	60.3(2)	−65.7(5)	55.3(5)

[A] In the dioxo ring of **24**, torsions in the bonds O(4)–C(4), C(4)–C(5) and so forth are: −59.3(2), 55.1(3), −55.0(2), 59.2(2), −65.5(3), 65.5(2); those in **29** are: −60.7(2), 58.0(2), −55.3(2), 57.6(2), −61.6(2), 62.6(2)°. In the carbocyclic rings of **19**, torsions in C(*n*1)–C(*n*2), C(*n*2)–C(*n*3) and so forth are: 50.0(6), −52.1(6), 55.7(6), −57.5(6), 55.7(5), −51.9(6) ($n = 1$); 52.0(6), −54.7(7), 58.4(7), −57.2(7), 53.4(7), −51.6(6)° ($n = 5$).

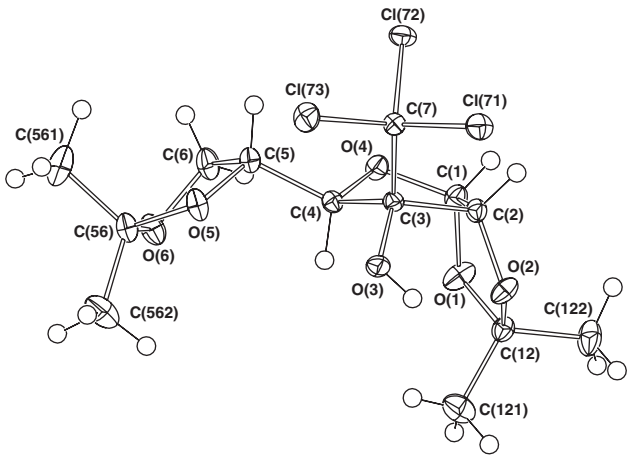


Fig. 1. Molecular projection of **8**.

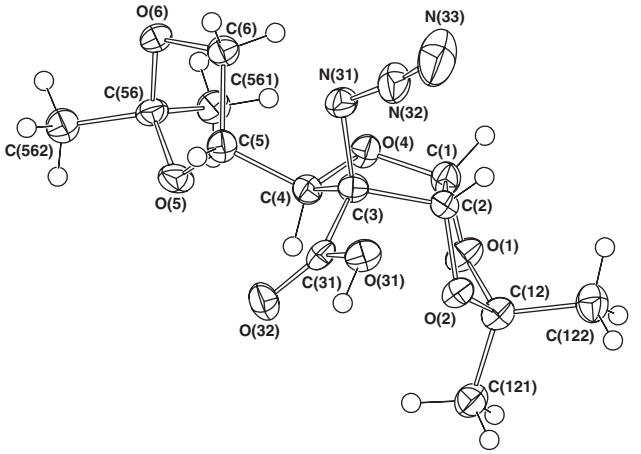


Fig. 2. Molecular projection of **10**.

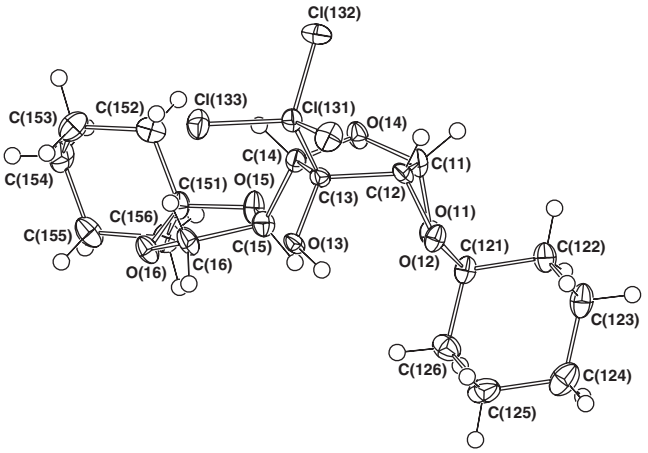


Fig. 3. Molecular projection of **16**.

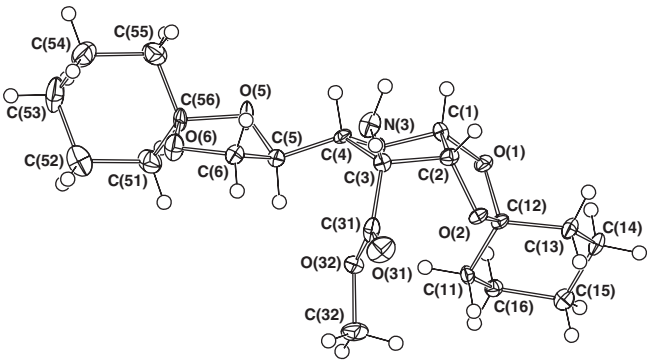


Fig. 4. Molecular projection of **19**.

Table 3. Ring torsion angles [°] for five-membered 1,3-dioxo rings[A]

Bond	Compound (rings)				
	8 (1,5)	**10** (1,5)	**16** (1,5 (molecules 1; 2))	**19** (1,5)	**46** (1)
C–C′	−21.6(5); 36.1(5)	−2.7(4); 18.1(3)	23.1(5), 13.7(6); 19.1(6), 25.4(5)	−21.6(5); 36.1(5)	10.0(10)
C–O	22.3(5); −34.4(5)	−17.5(4); 1.6(4)	−34.6(6), 6.7(6); −32.0(6), −7.4(6)	−22.3(5); −34.4(5)	−20.0(10)
C′–O′	13.0(5); −25.2(5)	21.9(4); −31.5(4)	−3.8(6), −29.1(6); 0.6(6), −34.6(5)	13.0(5); −25.2(5)	3.3(11)
O–C″	−14.3(5); 19.7(5)	31.4(4); −20.9(4)	33.0(6), −24.5(6); 33.1(6), −13.5(6)	−14.3(5); 19.7(5)	22.0(11)
O′–C″	−0.1(5); 4.5(5)	−32.8(4); 32.9(4)	−17.3(6), 33.5(6); −20.3(6), 30.4(6)	−0.1(5); 4.5(5)	−15.3(12)

[A] In rings 1, C,C′,C″ are C(1,2,12), O,O′ are O(1,2); in rings 5, counterparts are C(5,6,56), O(5,6).

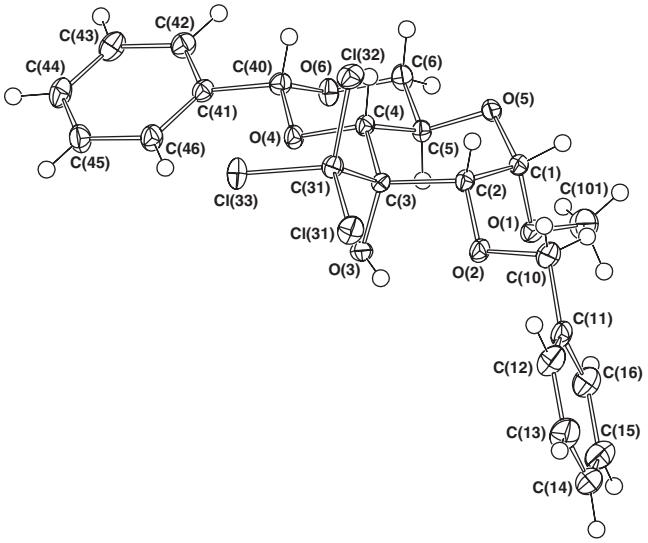


Fig. 5. Molecular projection of **24**.

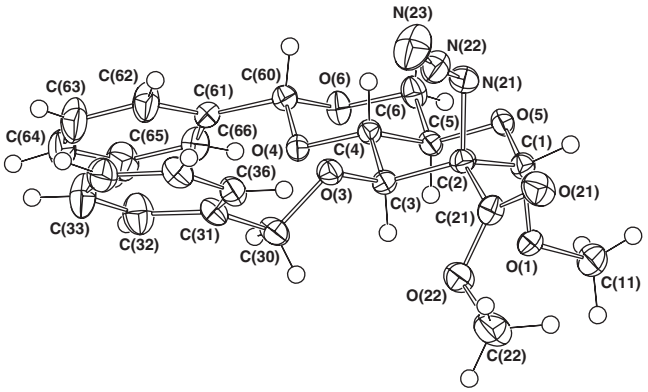


Fig. 6. Molecular projection of **29**.

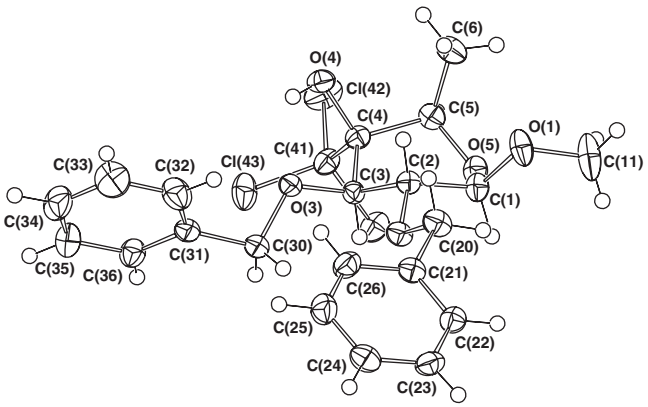
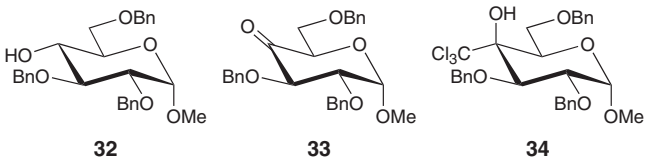


Fig. 7. Molecular projection of **39**.

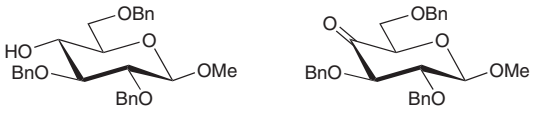
the probable alcohol **37** could be easily produced, benzyl alcohol was again the only product isolated from the treatment of **37** under modified Corey–Link conditions.

We suspected (for no real reason) that the culprit involved in the formation of benzyl alcohol from **34** and **37** was the 6-*O*-benzyl ether. Therefore, the 6-deoxy alcohol **38**[18] (Scheme 13) was oxidized and converted into the

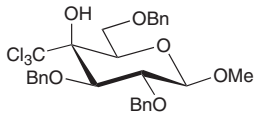


32 **33** **34**

Scheme 11.

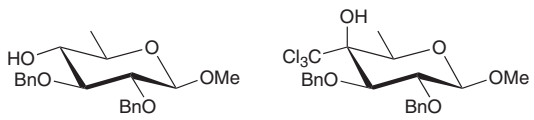


35 **36**



37

Scheme 12.



38 **39**

Scheme 13.

trichloromethyl alcohol **39** [which was, incidentally, crystalline and the subject of a single-crystal X-ray structure determination (Fig. 7)]. Somewhat to our dismay, benzyl alcohol was still formed when **39** was subjected to the modified Corey–Link procedure. Our last effort was to record the ^{1}H NMR spectrum of **34** in [D_4]ethanol immediately after the addition of a few drops of DBU (Fig. 8*b*)—the result is, at best, perplexing.

Although it is annoying and frustrating to yield to a chemical problem, we decided that the preparation of a 'mixed' ether such as **40** (Scheme 14), which would surely cast light on the untoward processes at hand, was not worth the effort.

Our final effort in the pyranose series was to treat the lactone **41**[19] (Scheme 15) with chloroform and lithium bis(trimethylsilyl)amide—although the desired ulose **42** was the major product [with the structure being confirmed by a single-crystal X-ray structure determination (Fig. 9)], the unsaturated lactone **43** was a significant by-product. Unfortunately, the treatment of **42** under modified Corey–Link conditions (again) gave only benzyl alcohol.

Our efforts so far had produced a variety of derivatives of carbohydrate α-amino acids that would be suitable building blocks for the construction of novel oligopeptides and oligosaccharides—what was still needed, for oligonucleotide synthesis, was a nucleoside α-amino acid.

Towards this end, an improved synthesis of the alcohol **44** (Scheme 16) led to the ketone **45** and the alcohol **46**, the structure of which was confirmed from a single-crystal

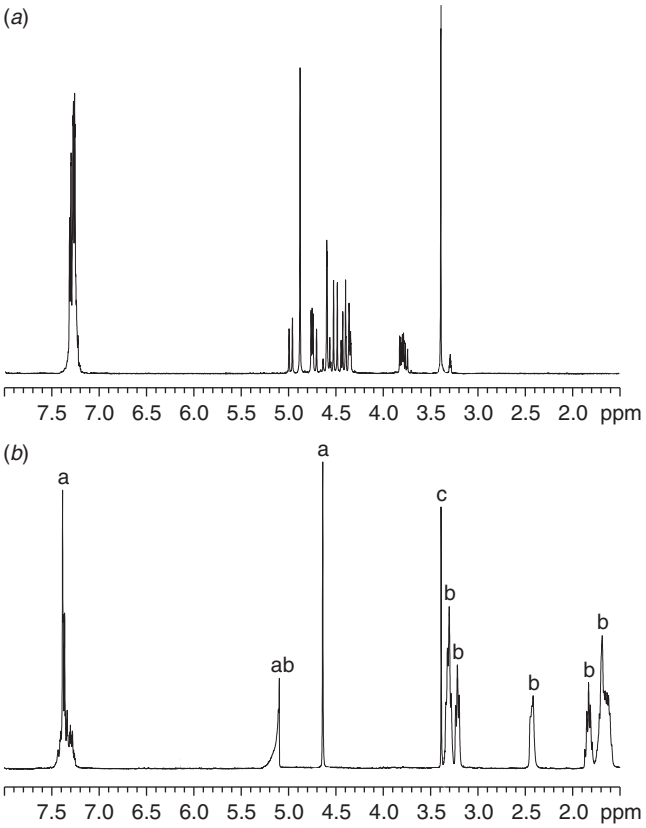
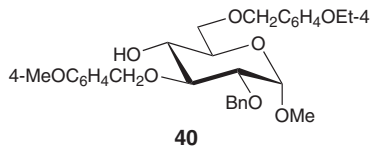
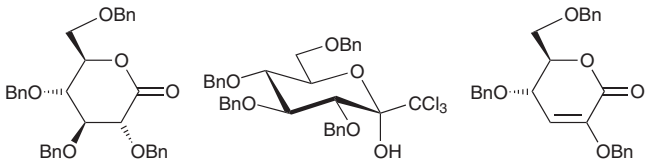


Fig. 8. (*a*) ^{1}H NMR (300 MHz, CD_3OD) spectrum of the alcohol **34**. (*b*) ^{1}H NMR (300 MHz, CD_3OD) spectrum of the same sample of the alcohol **34** immediately after the addition of a few drops of DBU (the labels a, b, and c indicate signals for benzyl alcohol, residual DBU, and an unidentified product, respectively).



40

Scheme 14.



Scheme 15.

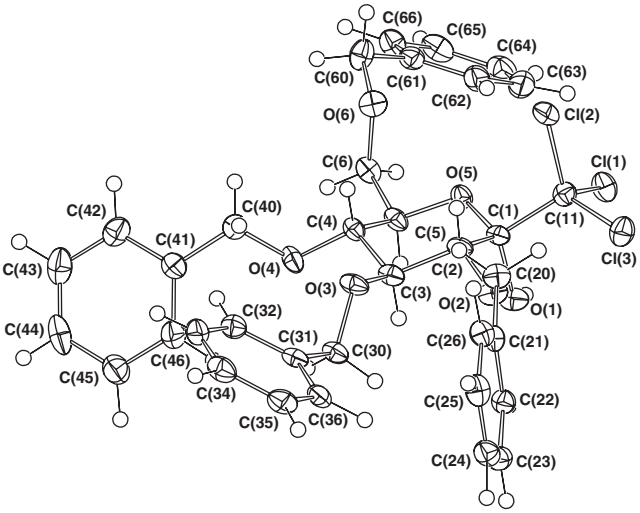
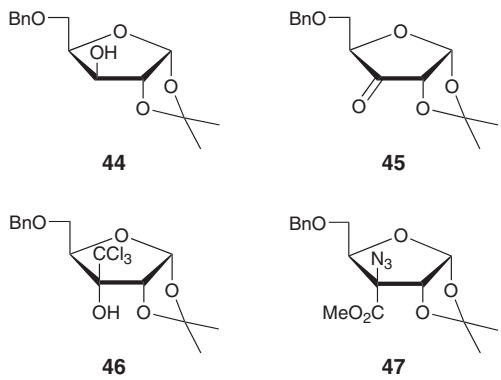


Fig. 9. Molecular projection of **42**.



Scheme 16.

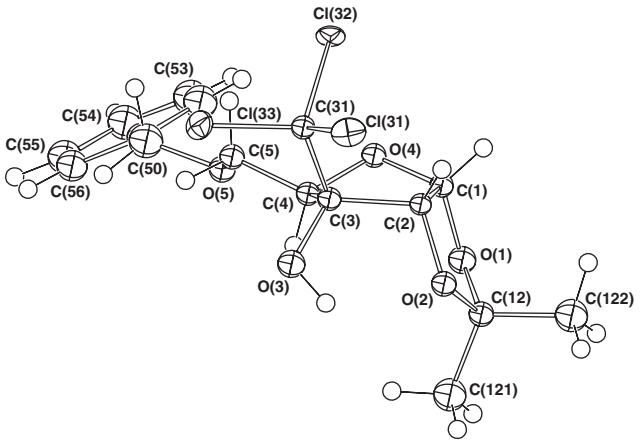
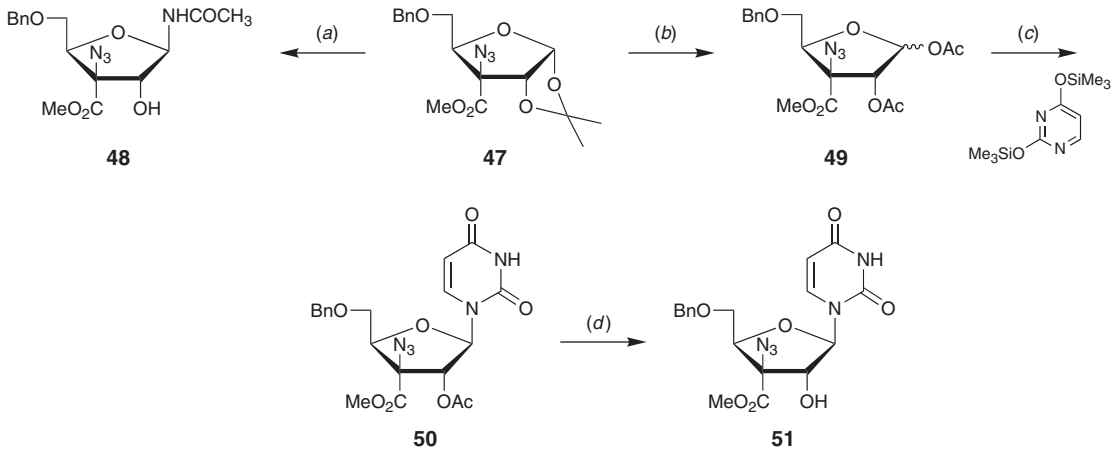


Fig. 10. Molecular projection of **46**.

X-ray structure determination (Fig. 10). A modified Corey–Link reaction on **46** gave the azido ester, presumably of structure **47**.

For the introduction of a pyrimidine base at C1 of **47**, we first tried the procedure recommended by Vorbrüggen and coworkers[20] (Scheme 17), which naturally first involved the removal of the isopropylidene group, but this procedure produced just the amide **48**, the product of an obvious Ritter reaction.[21] However, the required nucleoside α-amino acid precursor **50** was obtained when the diacetate **49** was treated with the pre-silylated pyrimidine base (uracil);[22] deacetylation then gave the alcohol **51**.

We had now completed our synthesis of the necessary monomeric carbohydrate α-amino acid precursors and the accompanying paper[26] describes our initial efforts into their combination to form oligopeptides.



Scheme 17. (*a*) 90% TFA/H_2O, followed by uracil, bis(trimethylsilyl)amine, $SnCl_4$, Me_3SiCl, MeCN; (*b*) 90% TFA/H_2O, followed by Ac_2O, pyridine; (*c*) Me_3SiOTf, $ClCH_2CH_2Cl$; (*d*) Na, MeOH.

Experimental

*Structure Determinations of **8**, **10**, **16**, **19**, **24**, **29**, **39**, **42**, and **46***

Full spheres of 'low'-temperature CCD area-detector diffractometer data were measured (Bruker AXS instrument, ω-scans; monochromatic $Mo_{K\alpha}$ radiation, λ 0.7107$_3$ Å; $T \approx 153$ K) yielding $N_{(total)}$ reflections, merging to N unique (R_{int} cited) after 'empirical'/multiscan absorption correction, N_o with $F > 4\sigma(F)$ considered 'observed' and used in the full matrix least-squares refinements, refining anisotropic displacement parameter forms for C, N, O, also (x, y, z, U_{iso})$_H$ unless otherwise stated, in which case the latter were constrained at estimated values. Conventional residuals R, R_w on $|F|$ are cited at convergence (weights: $(\sigma^2(F) + 0.000 n_w F^2)^{-1}$). Neutral atom complex scattering factors were employed within the context of the *Xtal 3.7* program system;[23] where $\Delta f''$ was significant, 'Friedel' data were retained distinct and x_{abs} refined unless otherwise stated. Pertinent results are given below and in Tables 1, 2, and 3 and Figs 1, 2, 3, 4, 5, 6, 7, 9, and 10, the figures showing 50% probability amplitude displacement ellipsoids for the non-hydrogen atoms, hydrogen atoms having arbitrary radii of 0.1 Å. Individual variations in procedure are cited as 'variata'. CCDC nos 226185–226193.

Crystal/Refinement Data

Compound **8**, $C_{13}H_{19}Cl_3O_6$, M 377.7. Monoclinic, space group $P2_1$ (C_2^2, no. 4), a 5.8235(4), b 9.8871(6), c 14.1337(9) Å, β 90.439(1)°, V 813.$_8$ Å^3. D_c(Z 2) 1.54$_1$ g cm^{-3}. μ_{Mo} 0.59 mm^{-1}; specimen: 0.5 × 0.4 × 0.35 mm^3; 'T'$_{min/max}$ 0.91. 2θ_{max} 75°; N_t 15888, N 4286 (R_{int} 0.014), N_o 4164; R 0.021, R_w 0.026. $|\Delta\rho_{max}|$ 0.36(3) e Å^{-3}. x_{abs} 0.01(2).

Compound **10**, $C_{13}H_{19}N_3O_7$, M 329.3. Monoclinic, space group $P2_1$, a 6.374(3), b 8.855(3), c 13.932(5) Å, β 97.024(6)°, V 780.$_4$ Å^3. D_c (Z 2) 1.40$_1$ g cm^{-3}. μ_{Mo} 0.12 mm^{-1}; specimen: 0.22 × 0.18 × 0.08 mm^3; 'T'$_{min/max}$ 0.79. 2θ_{max} 52.5°; N_t 6959, N 1566 (R_{int} 0.053), N_o 1427; R 0.045, R_w 0.051. $|\Delta\rho_{max}|$ 0.20(4) e Å^{-3}. (x, y, z, U_{iso})$_H$, x_{abs} not refined.

Compound **16**, $C_{19}H_{27}Cl_3O_6$, M 457.8. Monoclinic, space group $P2_1$, a 9.625(1), b 12.164(2), c 17.454(2) Å, β 92.401(2)°, V 2042 Å^3. D_c (Z 4) 1.48$_9$ g cm^{-3}. μ_{Mo} 0.48 mm^{-1}; specimen: 0.45 × 0.40 × 0.32 mm; 'T'$_{min/max}$ 0.92. 2θ_{max} 58°; N_t 18911, N 5035 (R_{int} 0.039), N_o 4082; R 0.050, R_w 0.060. $|\Delta\rho_{max}|$ 0.41(8) e Å^{-3}. (x, y, z, U_{iso})$_H$ not refined; x_{abs} 0.06(8).

Compound **19**, $C_{20}H_{31}NO_7$, M 397.5. Orthorhombic, space group $P2_12_12_1$ (D_2^4, no. 19), a 6.615(3), b 11.422(5), c 26.335(12) Å, V 1990 Å^3. D_c (Z 4) 1.32$_7$ g cm^{-3}. μ_{Mo} 0.10 mm^{-1}; specimen: 0.88 × 0.05 × 0.03 mm^3; 'T'$_{min/max}$ 0.84. 2θ_{max} 55°; N_t 14952, N 2623 (R_{int} 0.10), N_o 1823; R 0.064, R_w 0.071. $|\Delta\rho_{max}|$ 0.41(7) e Å^{-3}. (x, y, z, U_{iso})$_H$, x_{abs} not refined.

Compound **24**, $C_{22}H_{23}Cl_3O_6$, M 489.8. Monoclinic, space group $P2_1$, a 11.7701(8), b 6.3566(4), c 14.873(1) Å, β 100.590(2)°, V 1094 Å^3. D_c (Z 2) 1.48$_2$ g cm^{-3}. μ_{Mo} 0.46 mm^{-1}; specimen: 0.25 × 0.15 × 0.10 mm^3; 'T'$_{min/max}$ 0.93. 2θ_{max} 75°; N_t 22368, N 6160 (R_{int} 0.035), N_o 5314; R 0.042, R_w 0.043. $|\Delta\rho_{max}|$ 0.53(5) e Å^{-3}. x_{abs} not refined.

Compound **29**, $C_{23}H_{25}N_3O_7$, M 455.5. Orthorhombic, space group $P2_12_12_1$, a 9.1062(6), b 11.1661(7), c 22.368(2) Å, V 2274 Å^3. D_c (Z 4) 1.33$_0$ g cm^{-3}. μ_{Mo} 0.10 mm^{-1}; specimen: 0.38 × 0.20 × 0.08 mm^3; 'T'$_{min/max}$ 0.86. 2θ_{max} 60°; N_t 19670, N 3677 (R_{int} 0.055), N_o 3173; R 0.040, R_w 0.043. $|\Delta\rho_{max}|$ 0.34(3) e Å^{-3}. x_{abs} not refined.

Compound **39**, $C_{22}H_{25}Cl_3O_5$, M 475.8. Orthorhombic, space group $P2_12_12_1$, a 9.792(3), b 10.507(3), c 21.995(6) Å, V 2263 Å^3. D_c (Z 4) 1.39$_6$ g cm^{-3}. μ_{Mo} 0.44 mm^{-1}; specimen: 0.35 × 0.22 × 0.15 mm^3; 'T'$_{min/max}$ 0.89. 2θ_{max} 59°; N_t 20548, N 3150 (R_{int} 0.020), N_o 2897; R 0.031, R_w 0.037. $|\Delta\rho_{max}|$ 0.31(2) e Å^{-3}. (x, y, z, U_{iso})$_H$ not refined; x_{abs} 0.03(6).

Compound **42**, $C_{35}H_{35}Cl_3O_6$, M 658.0. Monoclinic, space group $P2_1$, a 11.436(2), b 5.7208(8), c 24.457(2) Å, β 99.552(2)°, V 1578 Å^3. D_c (Z 2) 1.38$_5$ g cm^{-3}. μ_{Mo} 0.34 mm^{-1}; specimen: 0.13 × 0.05 × 0.04 mm^3; 'T'$_{min/max}$ 0.95. 2θ_{max} 58°; N_t 15422, N 4240 (R_{int} 0.033), N_o 3395; R 0.045, R_w 0.056. $|\Delta\rho_{max}|$ 0.37(6) e Å^{-3}. (x, y, z, U_{iso})$_H$ not refined; x_{abs} 0.06(9).

Compound **46**, $C_{16}H_{19}Cl_3O_5$, M 397.7. Monoclinic, space group $P2_1$, a 5.795(2), b 9.808(4), c 15.354(7) Å, β 92.982(3)°, V 872 Å^3. D_c (Z 2) 1.51$_5$ g cm^{-3}. μ_{Mo} 0.55 mm^{-1}; specimen: 0.22 × 0.07 × 0.04 mm^3; 'T'$_{min/max}$ 0.66. 2θ_{max} 53°; N_t 7349, N 1887 (R_{int} 0.082), N_o 1343; R 0.069, R_w 0.073. $|\Delta\rho_{max}|$ 0.5(1) e Å^{-3}. (x, y, z, U_{iso})$_H$, x_{abs} not refined.

Within the structures, bond lengths and angles are essentially as expected and not commented on further, beyond noting that in **10** and **29**, the C–N–N angles at the pendant azides are 114.5(4) and 114.5(2)°. Lattice interactions of interest are primarily concerned with hydrogen-bonding interactions arising from any hydroxyl, carboxylic acid, or amine groups present, as follows:

Compound **8**, intramolecular: O,H(3)···O(2) 2.605(2), 2.09(3) Å (intermolecular: O,H(3)···O(4) (x−1, y, z) are 2.878(1) and 2.24(3) Å).

Compound **10**, intermolecular: O,H(31)···O(6) (x, 1+y, z) 2.709(5), 1.8 Å (est.).

Compound **16**, intermolecular: O,H(13)···O(16) (1−x, ½+y, 1−z) 2.748(6), 1.9 Å (est.). O,H(23)···O(26) (2−x, ½+y, z) 2.757(6), 2.0 Å (est.).

Compound **19**, 'intramolecular': N(3),H(3b)···O(31) 2.736(6), 2.3 Å (est.).

Compound **24**, intramolecular: O,H(3)···O(2) 2.577(2), 2.13(3) Å.

Compound **39**, intramolecular: O,H(4)···O(3) 2.535(3), 2.00(3) Å.

Compound **42**, intermolecular: O,H(1)···O(6) (x, y−1, z) 2.795(5), 2.06(7) Å.

General

General experimental procedures have been given previously.[24] As well, detailed procedures were given in our communication[13] for the preparation of the various trichloromethyl alcohols, azido esters, azido acids, and amino esters—only specific compound details are given here. Notation such as A (AB) is used to describe the A part of an AB pattern.

*General Procedure for the Swern Oxidation[25] of the Alcohols **20**, **21**, **32**, **35**, and **44***

Dimethyl sulfoxide (3.0 equiv.) in CH_2Cl_2 was added dropwise to oxalyl chloride (2.0 equiv.) in CH_2Cl_2 at −55°C and the solution stirred (0.5 h). The alcohol (1.0 equiv.) in CH_2Cl_2 was then added dropwise to the solution and the resulting solution stirred at −55°C (1.5 h). The solution was then warmed to −30°C, followed by the dropwise addition of Et_3N (3.0 equiv., 0.25 h). The solution was then warmed to room temperature and a standard workup (CH_2Cl_2) yielded the ketone that was used in the next step without any further purification.

*1,2:5,6-Di-*O*-cyclohexylidene-3-*C*-trichloromethyl-α-D-gulose **16***

The ketone **15**[13] afforded (flash chromatography, EtOAc/petrol 1 : 4) the *alcohol* **16** as plates (75%), mp 126–128°C (Et_2O), $[\alpha]_D$ −13.1° (Found: C 49.5, H 5.8%. $C_{19}H_{27}Cl_3O_6$ requires C 49.8, H 5.9%). δ_H (300 MHz) 1.70–2.00 (20H, m, CH_2), 3.98 (dd, $J_{6,6}$ 9.1, $J_{5,6}$ 6.4, H6), 4.13 (dd, $J_{5,6}$ 6.2, H6), 4.16 (s, OH), 4.36–4.45 (m, H5), 4.50 (d, $J_{4,5}$ 8.8, H4), 4.77 (d, $J_{1,2}$ 4.4, H2), 6.05 (d, H1). δ_C (75.5 MHz) 23.28, 23.62, 23.77, 23.96, 24.63, 25.09, 34.76, 35.95, 36.00, 36.22 (10C, CH_2), 65.91 (C6), 76.46, 80.59, 86.97 (C2, C4, C5), 87.15 (C3), 103.44 (CCl_3), 105.67 (C1), 109.60, 114.27 (2C, OCO). *m/z* (FAB) 455.0796; [M − H ($^{12}C_{19}H_{26}{}^{35}Cl_3O_6$)]$^+$ requires 455.0795.

*(3*S*)-3-Azido-1,2:5,6-di-*O*-cyclohexylidene-3-deoxy-3-*C*-methoxycarbonyl-α-D-*xylo*-hexose **17***

The alcohol **16** afforded (flash chromatography, EtOAc/petrol 1 : 4) the *azido ester* **17** as needles (93%), mp 88–90°C (EtOAc/petrol), $[\alpha]_D$ +49.2° (Found: C 56.7, H 7.1, N 9.8. $C_{20}H_{29}N_3O_7$ requires C 56.7, H 6.9, N 9.9%). ν_{max}/cm^{-1} (KBr) 2125 (N_3), 1760 (OC=O). δ_H (300 MHz) 1.51–2.00 (20H, m, CH_2), 3.65 (dd, $J_{6,6}$ 8.6, $J_{5,6}$ 6.6, H6), 3.74 (d, $J_{4,5}$ 8.7, H4), 3.84 (s, CO_2CH_3), 3.90 (dd, $J_{5,6}$ 6.4, H6), 4.67–4.77 (m, H5), 4.68 (d, $J_{1,2}$ 3.6, H2), 5.87 (d, H1). δ_C (75.5 MHz) 23.57, 23.67, 23.76, 23.89, 24.69, 25.04, 34.62, 36.19, 36.45, 36.55 (10C, CH_2), 52.86 (CO_2CH_3), 65.30 (C6), 73.71 (C3), 74.49, 86.09, 86.47 (C2, C4, C5), 103.94 (C1), 110.21, 117.10 (2C, OCO), 166.87 (CO_2CH_3). *m/z* (FAB) 424.2072; [M + H]$^+$ requires 424.2084.

*(3*S*)-3-Azido-3-*C*-carboxy-1,2:5,6-di-*O*-cyclohexylidene-3-deoxy-α-D-*xylo*-hexose **18***

The azido ester **17** furnished the azido acid **18** as an oil, $[\alpha]_D$ +17.8°. δ_H (300 MHz) 1.35–1.94 (20H, m, CH_2), 3.72 (dd, $J_{6,6}$ 8.6, $J_{5,6}$ 6.9, H6), 3.88 (d, $J_{4,5}$ 8.5, H4), 4.01 (dd, $J_{5,6}$ 6.3, H6), 4.58–4.67 (m, H5), 4.65 (d, $J_{1,2}$ 3.6, H2), 5.41 (br s, OH), 5.93 (d, H1). δ_C (75.5 MHz) 23.45–36.21 (CH_2), 65.70 (C6), 73.50 (C3), 74.28, 85.65, 86.22 (C2, C4, C5), 104.25 (C1), 110.39, 116.98 (2C, OCO), 168.89 (CO_2H). *m/z* (FAB) 410.1933; [M + H]$^+$ requires 410.1927.

*(3*S*)-3-Amino-1,2:5,6-di-*O*-cyclohexylidene-3-deoxy-3-*C*-methoxycarbonyl-α-D-*xylo*-hexose **19***

The azido ester **17** afforded (flash chromatography, Et_3N/EtOAc/petrol 1 : 8 : 12) the *amino ester* **19** as prisms (97%), mp 163–165°C (EtOAc/pentane), $[\alpha]_D$ +11.9° (Found: C 60.7, H 8.1, N 3.3. $C_{20}H_{31}NO_7$ requires C 60.4, H 7.9, N 3.5%). ν_{max}/cm^{-1} (KBr) 1750 (OC=O). δ_H (300 MHz) 1.22–1.85 (20H, m, CH_2), 3.68 (dd, $J_{6,6}$ 8.7, $J_{5,6}$ 6.2, H6), 3.75 (d, $J_{4,5}$ 10.1, H4), 3.78 (s, CO_2CH_3), 3.95 (dd, $J_{5,6}$ 6.4, H6), 4.38 (d, $J_{1,2}$ 3.6, H2), 4.76 (ddd, H5), 5.90 (d, H1). δ_C (75.5 MHz) 23.64, 23.74, 23.83, 24.00, 24.85, 25.15, 34.49, 36.29, 36.42, 36.49 (10C, CH_2), 52.34 (CO_2CH_3), 65.98 (C6), 68.11 (C3), 75.12, 88.88, 90.25 (C2, C4, C5), 104.23 (C1), 109.84, 115.81 (2C, OCO), 174.23 (CO_2CH_3). *m/z* (FAB) 398.2193; [M + H]$^+$ requires 398.2179.

*Methyl 2-*O*-Benzyl-4,6-*O*-benzylidene-3-*C*-trichloromethyl-α-D-alloside **24***

The ketone **22** furnished (flash chromatography, EtOAc/petrol 1 : 4) the *alcohol* **24** as needles (71%), mp 125–127°C (Et_2O), $[\alpha]_D$ +3.8° (Found: C 53.7, H 4.7. $C_{22}H_{23}Cl_3O_6$ requires C 53.9, H 4.7%). δ_H (300 MHz) 3.36 (s, OCH_3), 3.70–3.80 (m, H5), 4.18, 4.50 (AB, $J_{1,2}$ 4.0, H1, H2), 4.20–4.24 (2H, m, H4, H6), 4.25 (s, OH), 4.32–4.37 (m, H6), 4.62, 4.84 (AB, *J* 11.7, CH_2Ph), 5.60 (s, C*H*Ph), 7.25–7.32 (10H, m, Ph). δ_C (75.5 MHz) 56.04 (OCH_3), 59.74, 75.32, 77.93 (C2, C4, C5), 69.24 (C6), 74.15 (*C*H_2Ph), 81.78 (C3), 98.23 (C1), 101.45 (*C*HPh), 103.54 (CCl_3), 126.14–137.10 (Ph). *m/z* (FAB) 489.0605; [M + H]$^+$ requires 489.0638.

*Methyl 3-*O*-Benzyl-4,6-*O*-benzylidene-2-*C*-trichloromethyl-α-D-glucoside **25***

The ketone **23** yielded (flash chromatography, EtOAc/petrol 1 : 4) the alcohol **25** as a yellow oil (85%), $[\alpha]_D$ −6.4°. δ_H (300 MHz) 3.53 (s, OCH_3), 3.83 (dd, $J_{6,6} \approx J_{5,6}$ 10.1, H6), 3.94–4.02 (m, H5), 4.02 (s, OH), 4.21 (d, $J_{3,4}$ 8.7, H3), 4.33 (dd, $J_{5,6}$ 4.5, H6), 4.43 (dd, $J_{4,5}$ 9.3, H4), 4.85, 4.97 (AB, *J* 11.9, CH_2Ph), 5.35 (s, H1), 5.60 (s, C*H*Ph), 7.23–7.55 (10H, m, Ph). δ_C (75.5 MHz) 55.90 (OCH_3), 63.32, 79.57, 83.21 (C3, C4, C5), 69.06 (C6), 75.12 (*C*H_2Ph), 82.54 (C2), 100.08 (C1), 101.62 (*C*HPh), 102.02 (CCl_3), 126.11–137.72 (Ph). *m/z* (FAB) 489.0613; [M + H]$^+$ requires 489.0638.

*Methyl (3*S*)-3-Azido-2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-3-*C*-methoxycarbonyl-α-D-*ribo*-hexoside **26***

The alcohol **24** furnished (flash chromatography, EtOAc/petrol 1 : 4) the azido ester **26** as an oil (86%), $[\alpha]_D$ −38.3°. ν_{max}/cm^{-1} (film) 2120 (N_3), 1750 (OC=O). δ_H (300 MHz) 3.38 (s, OCH_3), 3.62 (dd, $J_{6,6} \approx J_{5,6}$ 10.3, H6), 3.63 (d, $J_{1,2}$ 4.4, H2), 3.68 (d, $J_{4,5}$ 9.8, H4), 3.88 (s, CO_2CH_3), 4.33 (dd, $J_{5,6}$ 5.2, H6), 4.53 (d, H1), 4.62–4.70 (m, H5), 4.75, 4.85 (AB, *J* 12.2, CH_2Ph), 5.51 (s, C*H*Ph), 7.30–7.45 (10H, m, Ph). δ_C (75.5 MHz) 52.96 (CO_2CH_3), 55.68 (OCH_3), 59.81, 79.20, 82.56 (C2, C4, C5), 69.48 (C6), 70.56 (C3), 73.37 (*C*H_2Ph), 98.12 (C1), 101.97 (*C*HPh), 126.13–136.98 (Ph), 166.32 (CO_2CH_3). *m/z* (FAB) 456.1777; [M + H]$^+$ requires 456.1771.

*Methyl (3*S*)-3-Azido-2-*O*-benzyl-4,6-*O*-benzylidene-3-*C*-carboxy-3-deoxy-α-D-*ribo*-hexoside **27***

The azido ester **26** afforded the azido acid **27** as a gum, $[\alpha]_D$ +86.9°. δ_H (300 MHz) 3.45 (s, OCH_3), 3.67 (dd, $J_{6,6} \approx J_{5,6}$ 10.2, H6), 3.73 (d, $J_{1,2}$ 4.3, H2), 3.78 (d, $J_{4,5}$ 10.0, H4), 4.14 (ddd, $J_{5,6}$ 5.1, H5), 4.34 (dd, H6), 4.61 (d, H1), 4.68, 4.87 (AB, *J* 12.0, CH_2Ph), 5.56 (s, C*H*Ph), 7.30–7.48 (10H, m, Ph). δ_C (75.5 MHz) 55.87 (OCH_3), 60.14, 78.35, 81.44 (C2, C4, C5), 68.93 (C6), 74.02 (*C*H_2Ph), 71.11 (C3), 97.20 (C1), 101.90 (*C*HPh), 126.09–136.41 (Ph), 164.94 (CO_2H). *m/z* (FAB) 442.1613; [M + H]$^+$ requires 442.1614.

*Methyl (3*S*)-3-Amino-2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-3-*C*-methoxycarbonyl-α-D-*ribo*-hexoside **28***

The azido ester **26** yielded (flash chromatography, Et_3N/EtOAc/petrol 1 : 8 : 12) the amino ester **28** as an oil (96%), $[\alpha]_D$ +50.1°. ν_{max}/cm^{-1} (film) 1750 (OC=O). δ_H (300 MHz) 2.25 (br s, NH_2), 3.38 (s, OCH_3), 3.55–3.64 (3H, m, H4, H5, H6), 3.79 (s, CO_2CH_3), 4.32 (dd, $J_{6,6}$ 10.3, $J_{5,6}$ 5.2, H6), 4.62–4.79 (4H, m, H1, H2, CH_2Ph), 5.45 (s, C*H*Ph), 7.30–7.47 (10H, m, Ph). δ_C (75.5 MHz) 52.22 (CO_2CH_3), 55.35 (OCH_3), 59.98, 82.20, 82.70 (C2, C4, C5), 61.58 (C3), 69.64 (C6), 73.25 (*C*H_2Ph), 97.37 (C1), 102.25 (*C*HPh), 126.30–137.46 (Ph), 171.44 (CO_2CH_3). *m/z* (FAB) 430.1861; [M + H]$^+$ requires 430.1866.

*Methyl (2*S*)-2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-*C*-methoxycarbonyl-α-D-*arabino*-hexoside **29***

The alcohol **25** afforded (flash chromatography, EtOAc/petrol 1 : 4) the *azido ester* **29** as prisms (89%), mp 123–125°C (EtOAc/pentane), $[\alpha]_D$ +23.5° (Found: C 60.7, H 5.6, N 9.1. $C_{23}H_{25}N_3O_7$ requires C 60.7, H 5.5, N 9.2%). ν_{max}/cm^{-1} (KBr) 2120 (N_3), 1760 (OC=O).

δ_H (300 MHz) 3.37 (s, OCH_3), 3.84 (s, CO_2CH_3), 3.80–3.94, 4.07–4.15, 4.25–4.32 (4H, 3 m, H4, H5, H6), 4.56 (d, $J_{3,4}$ 9.6, H3), 4.70 (s, H1), 4.83, 4.95 (AB, *J* 11.0, C*H*$_2$Ph), 5.64 (s, C*H*Ph), 7.25–7.50 (10H, m, Ph). δ_C (75.5 MHz) 53.12 (CO_2CH_3), 55.61 (OCH_3), 63.42, 76.58, 80.30 (C3, C4, C5), 68.54 (C6), 72.55 (C2), 75.67 (*C*H$_2$Ph), 100.71 (C1), 101.59 (*C*HPh), 125.94–138.18 (Ph), 167.57 (CO_2CH_3). *m/z* (FAB) 456.1765; $[M + H]^+$ requires 456.1771.

*Methyl (2*S*)-2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside **30***

The azido ester **29** yielded the azido acid **30** as a foam, $[\alpha]_D$ +12.5°. δ_H (300 MHz) 3.40 (s, OCH_3), 3.86–4.00, 4.12–4.20, 4.32–4.37 (4H, 3m, H4, H5, H6), 4.58 (d, $J_{3,4}$ 9.6, H3), 4.78 (s, H1), 4.84, 4.98 (AB, *J* 10.9, C*H*$_2$Ph), 5.67 (s, C*H*Ph), 7.20–7.55 (10H, m, Ph). δ_C (75.5 MHz) 55.68 (OCH_3), 60.69 (C2), 63.49, 72.26, 80.26 (C3, C4, C5), 68.48 (C6), 75.72 (*C*H$_2$Ph), 100.57 (C1), 101.66 (*C*HPh), 125.94–137.96 (Ph), 171.41 (CO_2H). *m/z* (FAB) 442.1636; $[M + H]^+$ requires 442.1614.

*Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-*C*-methoxycarbonyl-α-D-*arabino*-hexoside **31***

The azido ester **29** furnished (flash chromatography, Et_3N/EtOAc/petrol 1 : 8 : 12) the *amino ester* **31** as needles (95%), mp 133–135°C (EtOAc/pentane), $[\alpha]_D$ +62.5° (Found: C 64.2, H 6.6, N 3.2. $C_{23}H_{27}NO_7$ requires C 64.3, H 6.3, N 3.3%). ν_{max}/cm^{-1} (KBr) 1745 (OC=O). δ_H (300 MHz) 3.36 (s, OCH_3), 3.75 (s, CO_2CH_3), 3.86–3.95, 4.25–4.35 (3H, 2 m, H4, H6), 4.10–4.20 (m, H5), 4.46 (d, $J_{3,4}$ 9.5, H3), 4.54 (s, H1), 4.80, 4.95 (AB, *J* 10.8, C*H*$_2$Ph), 5.65 (s, C*H*Ph), 7.25–7.53 (10H, m, Ph). δ_C (75.5 MHz) 52.53 (CO_2CH_3), 55.57 (OCH_3), 63.48, 75.71, 80.27 (C3, C4, C5), 65.42 (C2), 68.76 (C6), 75.40 (*C*H$_2$Ph), 101.49 (C1), 103.07 (*C*HPh), 125.97–138.56 (Ph), 173.64 (CO_2CH_3). *m/z* (FAB) 430.1865; $[M + H]^+$ requires 430.1866.

*Methyl 2,3,6-Tri-*O*-benzyl-4-*C*-trichloromethyl-α-D-galactoside **34***

The ketone **33** yielded (flash chromatography, EtOAc/petrol 1 : 4) the alcohol **34** as a yellow oil (80%), $[\alpha]_D$ +56.1°. δ_H (300 MHz) 3.45 (s, OCH_3), 3.85 (dd, $J_{2,3}$ 8.7, $J_{1,2}$ 3.3, H2), 3.90 (dd, $J_{6,6}$ 10.8, $J_{5,6}$ 5.6, H6), 4.30–4.37, 4.85–4.88 (2H, 2 m, H5, H6), 4.50 (d, H3), 4.51, 4.63 (AB, *J* 11.9, C*H*$_2$Ph), 4.62, 4.74 (AB, *J* 11.9, C*H*$_2$Ph), 4.68 (d, H1), 4.82, 5.10 (AB, *J* 10.7, C*H*$_2$Ph), 7.25–7.37 (15H, m, Ph). δ_C (75.5 MHz) 55.59 (OCH_3), 70.72, 76.07, 79.62 (C2, C3, C5), 72.12 (C6), 73.35, 73.40, 74.98 (3C, *C*H$_2$Ph), 83.81 (C4), 96.44 (C1), 104.69 (CCl_3), 127.45–137.76 (Ph). *m/z* (FAB) 579.1111; $[M - H (^{12}C_{29}H_{27}{}^{35}Cl_3O_6)]^+$ requires 579.1108.

*Methyl 2,3,6-Tri-*O*-benzyl-4-*C*-trichloromethyl-β-D-galactoside **37***

The ketone **36** yielded (flash chromatography, EtOAc/petrol 1 : 4) the alcohol **37** as a yellow oil (74%), $[\alpha]_D$ +12.1°. δ_H (300 MHz) 3.55 (s, OCH_3), 3.85–3.98, 4.70–4.90 (8H, 2 m, H1, H2, H5, H6, C*H*$_2$Ph), 4.25 (d, $J_{2,3}$ 10.2, H3), 4.39 (br s, OH), 4.58, 4.66 (AB, *J* 11.8, C*H*$_2$Ph), 5.10 [A(AB), *J* 10.1, C*H*$_2$Ph], 7.18–7.43 (15H, m, Ph). δ_C (75.5 MHz) 55.55 (OCH_3), 70.41 (C6), 73.08, 74.26, 74.98 (3C, *C*H$_2$Ph), 75.82, 76.73, 80.47 (C2, C3, C5), 82.52 (C4), 104.50 (C1), 106.09 (CCl_3), 125.26–138.18 (Ph). *m/z* (FAB) 579.1137; $[M - H (^{12}C_{29}H_{27}{}^{35}Cl_3O_6)]^+$ requires 579.1108.

*Methyl 2,3-Di-*O*-benzyl-6-deoxy-4-*C*-trichloromethyl-β-D-galactoside **39***

Methyl 2,3-di-*O*-benzyl-6-deoxy-β-D-*xylo*-hexopyranos-4-uloside furnished (flash chromatography, EtOAc/petrol 1 : 4) the *alcohol* **39** as needles (78%), mp 66–68°C (EtOAc/pentane), $[\alpha]_D$ +7.7° (Found: C 55.6, H 5.4. $C_{22}H_{25}Cl_3O_5$ requires C 55.5, H 5.3%). δ_H (300 MHz) 1.52 (3H, d, $J_{5,6}$ 7.2, H6), 3.50 (s, OCH_3), 3.91 (dd, $J_{2,3}$ 10.1, $J_{1,2}$ 6.3, H2), 4.21 (d, H3), 4.47 (br s, OH), 4.62 (ddd, H5), 4.72, 4.85 (AB, *J* 11.2, C*H*$_2$Ph), 4.78, 5.11 (AB, *J* 10.2, C*H*$_2$Ph), 4.78 (d, H1), 7.23–7.38 (10H, m, Ph). δ_C (75.5 MHz) 19.23 (C6), 54.95 (OCH_3), 74.28, 74.95 (2C, *C*H$_2$Ph), 74.65, 76.05, 80.29 (C2, C3, C5), 82.48 (C4), 104.48 (C1), 106.63 (CCl_3), 127.66–138.03 (Ph). *m/z* (FAB) 473.0718; $[M - H (^{12}C_{22}H_{24}{}^{35}Cl_3O_5)]^+$ requires 473.0689.

*3,4,5,7-Tetra-*O*-benzyl-1,1,1-trichloro-1-deoxy-α-D-*gluco*-hept-2-ulose **42***

The lactone **41**[19] yielded (flash chromatography, EtOAc/petrol 1 : 4) the *hemiacetal* **42** as prisms (42%), mp 90–92°C (EtOAc/pentane), $[\alpha]_D$ +56.9° (Found: C 64.0, H 5.4. $C_{35}H_{35}Cl_3O_6$ requires C 63.9, H 5.4%). δ_H (300 MHz) 3.76–4.10 (5H, m, H4, H5, H6, H7), 4.34 (br s, OH), 4.37 (d, $J_{3,4}$ 8.5, H3), 4.66, 4.76 (AB, *J* 12.3, C*H*$_2$Ph), 4.76, 4.88 (AB, *J* 10.9, C*H*$_2$Ph), 4.89, 5.03 (AB, *J* 10.6, C*H*$_2$Ph), 4.93, 5.03 (AB, *J* 10.6, C*H*$_2$Ph), 7.25–7.45 (20H, m, Ph). δ_C (75.5 MHz) 67.64 (C7), 73.29, 73.90, 74.92, 75.02 (4C, *C*H$_2$Ph), 76.01, 77.16, 78.51, 85.00 (C3, C4, C5, C6), 100.02 (C2), 103.21 (C1), 127.42–138.39 (Ph). *m/z* (FAB) 657.1529; $[M + H]^+$ requires 657.1577.

*5-*O*-Benzyl-1,2-*O*-isopropylidene-3-*C*-trichloromethyl-α-D-ribose **46***

The ketone **45** furnished (flash chromatography, EtOAc/petrol 1 : 4) the *alcohol* **46** as plates (81%), mp 110–112°C (EtOAc/pentane), $[\alpha]_D$ +14.2° (Found: C 48.4, H 4.6. $C_{16}H_{19}Cl_3O_5$ requires C 48.5, H 4.6%). δ_H (300 MHz) 1.45, 1.64 (6H, 2 s, CH_3), 3.90 (dd, $J_{5,5}$ 10.5, $J_{4,5}$ 8.6, H5), 3.97 (br s, OH), 4.15 (dd, $J_{4,5}$ 3.3, H5), 4.42 (dd, H4), 4.56, 4.67 (AB, *J* 12.0, C*H*$_2$Ph), 4.79 (d, $J_{1,2}$ 4.5, H2), 6.02 (d, H1), 7.23–7.38 (m, Ph). δ_C (75.5 MHz) 26.34, 27.03 (2C, CH_3), 67.33 (C5), 73.45 (*C*H$_2$Ph), 81.67, 84.36 (C2, C4), 87.24 (C3), 100.72 (CCl_3), 104.31 (C1), 113.48 (OCO), 127.62–137.64 (Ph). *m/z* (FAB) 395.0214; $[M + H]^+$ requires 395.0220.

*(3*S*)-3-Azido-5-*O*-benzyl-3-deoxy-1,2-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*erythro*-pentose **47***

The alcohol **46** afforded (flash chromatography, EtOAc/petrol 1 : 4) the azido ester **47** as an oil (93%), $[\alpha]_D$ +79.8°. ν_{max}/cm^{-1} (film) 2120 (N_3), 1760 (OC=O). δ_H (300 MHz) 1.32, 1.53 (6H, 2 s, CH_3), 3.67–3.71 (2H, m, H5), 3.81 (s, CO_2CH_3), 4.52, 4.61 (AB, *J* 12.0, C*H*$_2$Ph), 4.68 (d, $J_{1,2}$ 4.7, H2), 4.85 (dd, $J_{4,5}$ 5.7, H4), 5.99 (d, H1), 7.25–7.38 (m, Ph). δ_C (75.5 MHz) 26.35, 26.66 (2C, CH_3), 52.97 (CO_2CH_3), 67.64 (C5), 73.30 (*C*H$_2$Ph), 74.27 (C3), 78.78, 84.29 (C2, C4), 104.73 (C1), 113.25 (OCO), 127.55–137.74 (Ph), 166.65 (CO_2CH_3). *m/z* (FAB) 364.1524; $[M + H]^+$ requires 364.1509.

N-*Acetyl-3-azido-5-*O*-benzyl-3-deoxy-3-*C*-methoxycarbonyl-β-D-*erythro*-pentofuranosylamine **48***

The azido ester **47** (500 mg, 1.4 mmol) in trifluoroacetic acid (TFA)/H_2O (10 mL, 9 : 1) was stirred at room temperature (3 h). Concentration of the mixture gave a yellow residue that was dissolved in CH_3CN (15 mL). $SnCl_4$ (180 μL, 1.5 mmol) and uracil (200 mg, 1.8 mmol) were added, followed by the dropwise addition of chlorotrimethylsilane (TMSCl) (150 μL, 1.6 mmol) and 1,1,1,3,3,3-hexamethyldisilazane (HMDS) (250 μL, 2.0 mmol), and the mixture stirred (2 h). Standard workup (CH_2Cl_2) followed by flash chromatography (EtOAc/petrol, 7 : 3) afforded the acetamide **48** as an oil (409 mg, 82%). δ_H (300 MHz) 2.05 (s, $COCH_3$), 3.70–3.80 (2H, m, H5), 3.78 (s, CO_2CH_3), 4.38 (dd, $J_{4,5}$ 6.1, H4), 4.50, 4.55 (AB, *J* 11.7, C*H*$_2$Ph), 4.77 (d, $J_{1,2}$ 5.5, H2), 6.15 (d, H1), 7.25–7.35 (m, Ph). δ_C (75.5 MHz) 13.65 ($COCH_3$), 53.11 (CO_2CH_3), 66.89 (*C*H$_2$Ph), 73.29 (C5), 74.11 (C3), 78.35, 84.74 (C2, C4) 100.87 (C1), 127.49–137.58 (Ph), 166.63, 168.29 ($COCH_3$, CO_2CH_3). *m/z* (FAB) 365.1466; $[M + H]^+$ requires 365.1461.

*(3*S*)-1,2-Di-*O*-acetyl-3-azido-5-*O*-benzyl-3-deoxy-3-*C*-methoxycarbonyl-D-*erythro*-pentose **49***

The azido ester **47** (1.0 g, 2.8 mmol) in TFA/H_2O (15 mL, 9 : 1) was stirred at room temperature (3 h). The solvent was removed, followed by the addition of Ac_2O (1.2 mL, 11 mmol) in pyridine (15 mL). The solution was stirred at room temperature (3 h) before being quenched with methanol. Standard workup (CH_2Cl_2) followed by flash chromotography (EtOAc/toluene, 1 : 4) yielded the β-anomer of **49** as a gum (540 mg, 54%), $[\alpha]_D$ +20.0°. δ_H (300 MHz) 2.08, 2.10 (6H, 2 s, $COCH_3$), 3.67–3.73 (2H, m, H5), 3.75 (s, CO_2CH_3), 4.50, 4.55 (AB, *J* 11.9, C*H*$_2$Ph), 4.85 (dd, $J_{4,5}$ 6.1, H4), 5.36 (s, H2), 6.16 (s, H1), 7.22–7.36 (m, Ph). δ_C (75.5 MHz) 20.25, 20.73 (2C, $COCH_3$), 53.18 (CO_2CH_3), 67.76

(C5), 71.48 (C3), 73.10 (*C*H$_2$Ph), 79.42, 82.21 (C2, C4), 98.60 (C1), 127.39–137.51 (Ph), 166.50, (*C*O$_2$CH$_3$), 168.8, 168.93 (2C, *C*OCH$_3$). *m/z* (FAB) 406.1263; $[M - H]^+$ requires 406.1250.

Next to elute was the α-anomer of **49** as a gum (380 mg, 38%), $[\alpha]_D$ +84.6°. δ_H (300 MHz) 2.07 (6H, s, COCH$_3$), 3.65–3.39 (2H, m, H5), 3.78 (s, CO$_2$CH$_3$), 4.54 (s, C*H*$_2$Ph), 4.93–4.98 (m, H4), 5.40 (d, $J_{1,2}$ 4.6, H2), 6.47 (d, H1), 7.25–7.38 (m, Ph). δ_C (75.5 MHz) 20.08, 20.61 (2C, CO*C*H$_3$), 53.10 (CO$_2$*C*H$_3$), 67.28 (C5), 73.28 (*C*H$_2$Ph), 73.42 (C3), 77.00, 80.67 (C2, C4), 94.16 (C1), 127.44–137.41 (Ph), 166.45 (*C*O$_2$CH$_3$), 168.60, 168.97 (2C, *C*OCH$_3$). *m/z* (FAB) 406.1260; $[M - H]^+$ requires 406.1250.

*(3′*S*)-2′*-O-*Acetyl-3′-azido-5′*-O-*benzyl-3′-deoxy-3′*-C-*(methoxycarbonyl)uridine* ***50***

Uracil (850 mg, 7.6 mmol) and $(NH_4)_2SO_4$ (100 mg, 0.8 mmol) were treated in HMDS (30 mL, 240 mmol) at reflux until a homogeneous solution resulted. Concentration of the mixture was followed by the addition of the diacetate **49** (1.0 g, 2.5 mmol) in ClCH$_2$CH$_2$Cl (20 mL), along with the dropwise addition of trimethylsilyl triflate (TMSOTf) (1.0 mL, 3.7 mmol). The mixture was refluxed (3 h) before being quenched with sat. NaHCO$_3$ solution. Standard workup (CH_2Cl_2) followed by flash chromatography (EtOAc/toluene, 2 : 3) afforded the nucleoside **50** as a gum (780 mg, 67%), $[\alpha]_D$ +34.1°. δ_H (300 MHz) 2.12 (s, COCH$_3$), 3.73–3.77 (2H, m, H5′), 3.75 (s, CO$_2$CH$_3$), 4.51, 4.57 (AB, *J* 11.4, C*H*$_2$Ph), 4.73 (dd, $J_{4',5'}$ 5.3, H4′), 5.42 (d, $J_{1',2'}$ 3.4, H2′), 5.67 (d, $J_{5,6}$ 8.2, H5), 6.12 (d, H1′), 7.20–7.38 (m, Ph), 7.69 (d, H6), 10.04 (br s, NH). δ_C (75.5 MHz) 20.22 (CO*C*H$_3$), 53.38 (CO$_2$*C*H$_3$), 66.94 (C5′), 72.09 (*C*H$_2$Ph), 73.37 (C3′), 79.91, 81.23 (C2′, C4′), 87.51 (C1′), 102.68 (C5), 127.65–136.86 (Ph), 139.24 (C6), 150.23 (C2), 166.34 (C4), 166.34 (*C*OCH$_3$), 169.02 (*C*O$_2$CH$_3$). *m/z* (FAB) 460.1435; $[M + H]^+$ requires 460.1468.

*(3′*S*)-3′-Azido-5′*-O-*benzyl-3′-deoxy-3′*-C-*(methoxycarbonyl)uridine* ***51***

A small piece of Na was added to the nucleoside **50** (200 mg, 0.40 mmol) in dry methanol (10 mL) and the mixture stirred at room temperature (3 h). The reaction was neutralized by the addition of resin (Dowex-50, H^+). Filtration, evaporation, and flash chromatography (EtOAc/toluene, 1 : 1) of the residue yielded the nucleoside **51** as an oil (175 mg, 96%), $[\alpha]_D$ +49.3°. δ_H (300 MHz) 3.43 (br s, OH), 3.76–3.85 (2H, m, H5′), 3.84 (s, CO$_2$CH$_3$), 4.53 (d, $J_{1',2'}$ 1.6, H2′), 4.60 (s, C*H*$_2$Ph), 4.92 (dd, $J_{4',5'}$ 5.6, 3.9, H4′), 5.62 (d, $J_{5,6}$ 8.2, H5), 5.85 (d, H1′), 7.28–7.36 (m, Ph), 7.75 (d, H6), 10.66 (br s, NH). δ_C (75.5 MHz) 53.21 (CO$_2$*C*H$_3$), 67.65 (C5′), 73.18 (*C*H$_2$Ph), 73.32 (C3′), 80.25, 81.29 (C2′, C4′), 91.50 (C1′), 101.83 (C5), 127.52–137.23 (Ph), 139.92 (C6), 150.93 (C2), 164.07 (C4), 167.00 (*C*O$_2$CH$_3$). *m/z* (FAB) 418.1372; $[M + H]^+$ requires 418.1363.

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