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The Synthesis of Some Oligopeptides Derived from Novel Carbohydrate α-Amino Acids

Adrian Scaffidi,[A] *Brian W. Skelton*,[A] *Robert V. Stick*,[A,B] *and Allan H. White*[A]

[A] Chemistry, School of Biomedical and Chemical Sciences M313, University of Western Australia, Crawley WA 6009, Australia.

[B] Author to whom correspondence should be addressed (e-mail: rvs@chem.uwa.edu.au).

The attempted coupling of a carbohydrate α-azido acid with a carbohydrate α-amino ester in the presence of a diimide, hopefully to produce a dipeptide, yielded only the carboxylic anhydride. However, the combination of 4-toluenesulfonyl chloride in pyridine was successful, and four carbohydrate dipeptides were separately produced. One of these dipeptides was further transformed into a tripeptide, and another into a hexapeptide.

A single-crystal X-ray structure is reported for (3*S*)-3-azido-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, amide with (3*S*)-3-amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*ribo*-hexose.

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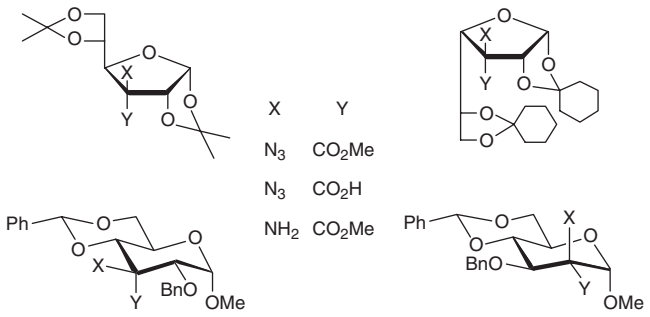
Introduction

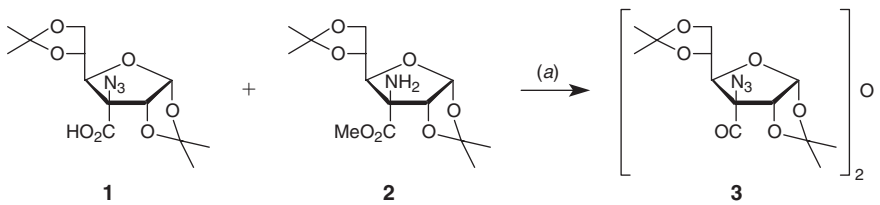
In the preceding paper we described the synthesis of four suites of precursors to novel carbohydrate α-amino acids (Scheme 1).[1] It was our next intent to couple some of these precursors together to form dipeptides and perhaps even higher oligopeptides. This paper, then, describes our efforts towards four new dipeptides and the extension of one of them up to a hexapeptide. Along the way we encountered some interesting aspects of peptide coupling.



Scheme 1.

In our initial investigations we decided to couple the azido acid **1** with the amino ester **2** (Scheme 2); the logical reagent was dicyclohexylcarbodiimide (DCC), in combination with 4-dimethylaminopyridine (DMAP).[2,3] To our surprise, the reaction did not appear (thin-layer chromatography, TLC) to give a product with the polarity expected of a dipeptide. The reaction was repeated with a different diimide, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC) hydrochloride, again in the presence of a base (ethyldiisopropylamine).[4] The outcome (TLC) appeared to be the same, even in the presence of 3-hydroxybenzotriazole. Eventually we isolated the anhydride **3** from both reaction mixtures, an observation made by others in related systems.[3] It appears that the anhydride **3**, once formed, is too hindered to acylate the amine **2**.

At this stage it was brought to our attention that 4-toluenesulfonyl (tosyl) chloride in pyridine was an effective combination for promoting the esterification of (hindered) alcohols;[5] the method can be modified for the synthesis of anhydrides and amides. It was somewhat curious to us that, for the synthesis of amides, the method involved the addition of just half a mole equivalent of tosyl chloride to



1 **2** **3**

Scheme 2. (*a*) DCC, DMAP, CH_2Cl_2 or EDC.HCl, $EtPr^i_2N$, CH_2Cl_2.

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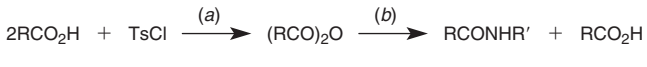
the carboxylic acid, thereby ensuring the formation of the intermediate carboxylic anhydride, able to acylate the added amine but wasteful of half of the acid (Scheme 3). A far better approach seemed to be to add (at least) a full equivalent of tosyl chloride, so forming a mixed anhydride, capable of acylating the added amine to form the amide (Scheme 4). In the event, the addition of about two mole equivalents of tosyl chloride to a mixture of the acid **1** and the amine **2** in pyridine gave a good yield of the amide **4** (Scheme 5). Apparently, the conversion of the amine **2** into the 4-toluenesulfonamide is a slow process in pyridine, and this was indeed found to be the case when a separate test experiment was conducted (TLC).

The dipeptide **4**, fortunately, was crystalline, allowing for a single-crystal X-ray structure determination (Fig. 1), one molecule, devoid of crystallographic symmetry, comprising the asymmetric unit of the structure. The most notable feature is the transoid nature of the newly formed amide moiety that provides the only hydrogen atom displaying significant interaction with any neighbouring group(s), the nearest such contact being intramolecular [N,H(3)···O(5′) 2.907(2), 2.15(3) Å]. In the azide group, the C–N–N angle is 114.1(1)°, while N(32′)–N(31′,33′) are 1.241(2), 1.120(3) Å, respectively. The conformations of the two C_4O rings are similar, albeit rather widely divergent, suggestive of some lack of rigidity; within the C_3O_2 rings, three of the four are diversely similar, with the conformation of the fourth the inverse (Table 1).

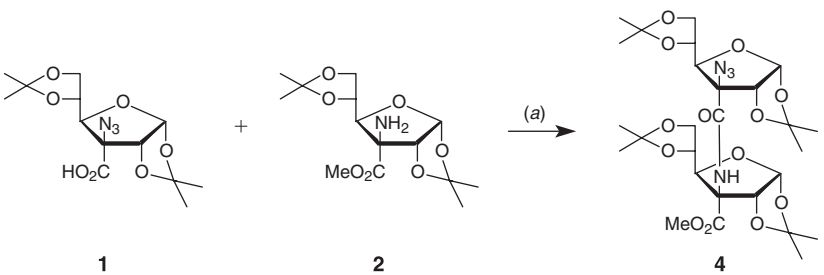
The tosyl chloride/pyridine method was then applied to mixtures of the three other azido acids and corresponding amino esters, to produce the dipeptides **5**, **6**, and **7** (Scheme 6).

Our next effort was to attempt the preparation of a higher oligopeptide by coupling the azido acid dipeptide **8** with the amino ester dipeptide **9** [both derived from **4**], again using tosyl chloride in pyridine (Scheme 7). Unfortunately, and surprisingly, the only product isolated was the anhydride **10**.



Scheme 3. (*a*) pyridine; (*b*) $R'NH_2$.

Scheme 4. (*a*) pyridine; (*b*) $R'NH_2$.



1 **2** **4**

Scheme 5. (*a*) TsCl, pyridine.

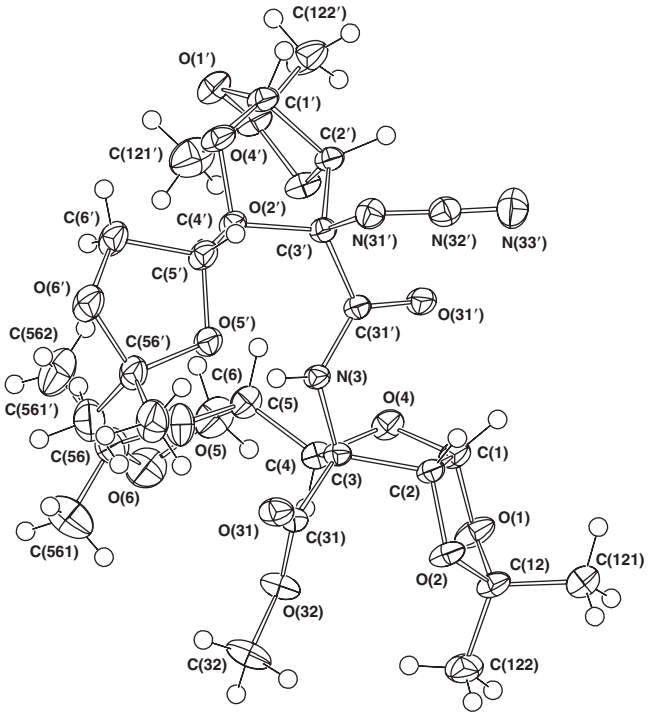


Fig. 1. Projection of a single molecule of **4**, showing 50% probability amplitude displacement envelopes for C, N, and O, with hydrogen atoms having arbitrary radii of 0.1 Å.

Table 1. Ring conformational descriptors

Torsion angles (degrees) are given for each of the rings for the bonds designated, the two values in each entry being for unprimed, primed atoms, respectively

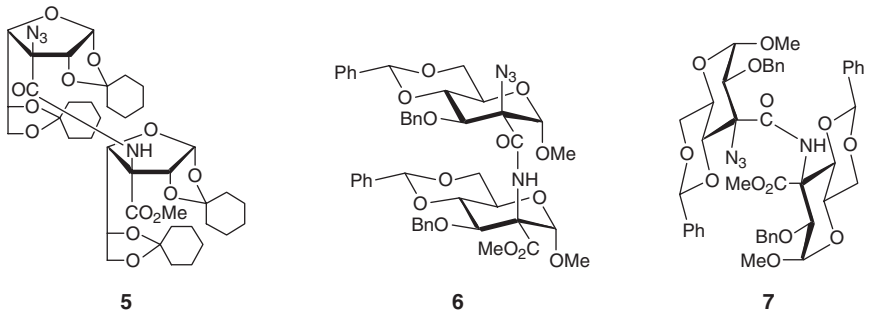
Atoms	Angles
C_4O rings	
C(1)–C(2)	5.6(2), −6.8(2)
C(2)–C(3)	15.9(2), 27.4(2)
C(3)–C(4)	−32.3(2), −39.2(2)
C(4)–O(4)	38.1(2), 37.6(2)
O(4)–C(1)	−27.5(2), −19.1(2)
C_3O_2 rings	
C(1)–C(2)	5.9(2), −9.7(2)
C(1)–O(1)	−21.4(2), −11.5(2)
C(2)–O(2)	11.4(2), 27.1(2)
O(1)–C(12)	28.8(2), 28.4(2)
O(2)–C(12)	−24.5(2), −34.8(2)
C(5)–C(6)	−16.7(3), 32.0(2)
C(5)–O(5)	−4.3(3), −16.1(2)
C(6)–O(6)	31.8(3), −36.7(2)
O(5)–C(56)	23.7(3), −5.8(2)
O(6)–C(56)	−35.0(3), 27.2(2)

The addition of 4-dimethylaminopyridine to the reaction mixture still did not cause any formation of the desired tetrapeptide. The same problem was encountered when we tried to couple the azido acid tripeptide **11** with the amino ester tripeptide **12** (Scheme 8 and below)—only the anhydride **13** was isolated, with no evidence for formation of the desired hexapeptide.

Although a slight molar excess of acid (**8** and **11**) over amine (**9** and **12**) was employed in both of the above reactions, it is difficult to comprehend why the carboxylate ion (leading to the observed anhydrides **10** and **13**) should be more reactive than the amine (leading to the desired tetra- and hexa-peptide) towards the purported mixed anhydride intermediate. With this frustrating result in hand, we decided to 'creep up' on our target oligopeptides by adding just one amino acid unit at a time.

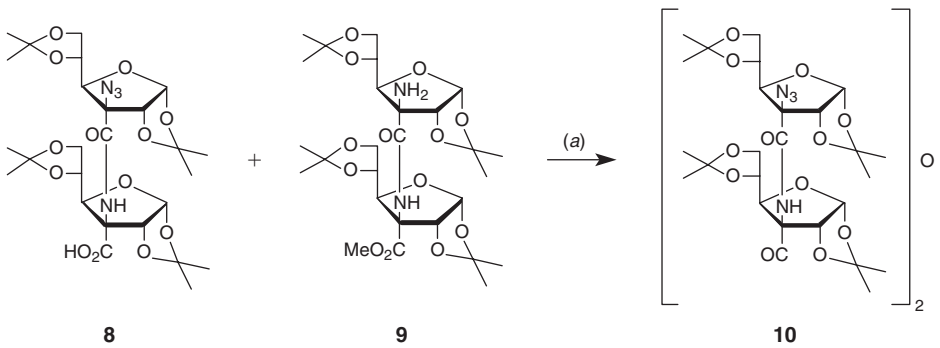
So, the amino ester **14** [derived from **6**] and the azido acid **15** were treated with tosyl chloride in pyridine to yield the azido ester tripeptide **16** in moderate yield (Scheme 9). Similarly successful was a synthesis of the tripeptide **17** from the amino ester **9** and the azido acid **1** (Scheme 10). In fact, we had considerable amounts of the tripeptide **17** and were able, through an iterative process involving azide reduction (to the amine) and coupling with the azido acid **1**, to access the azido ester tetra- **18**, penta- **19**, and hexa-peptides **20** from the corresponding amino ester tri- **21**, tetra- **22**, and penta-peptides **23** (Scheme 11).

All of the peptides described in this paper were fully characterized by elemental analysis (where appropriate), accurate mass determination, NMR spectroscopy, and IR spectroscopy. Of particular relevance in the NMR spectra was the presence of the various α-carbon atoms, certainly



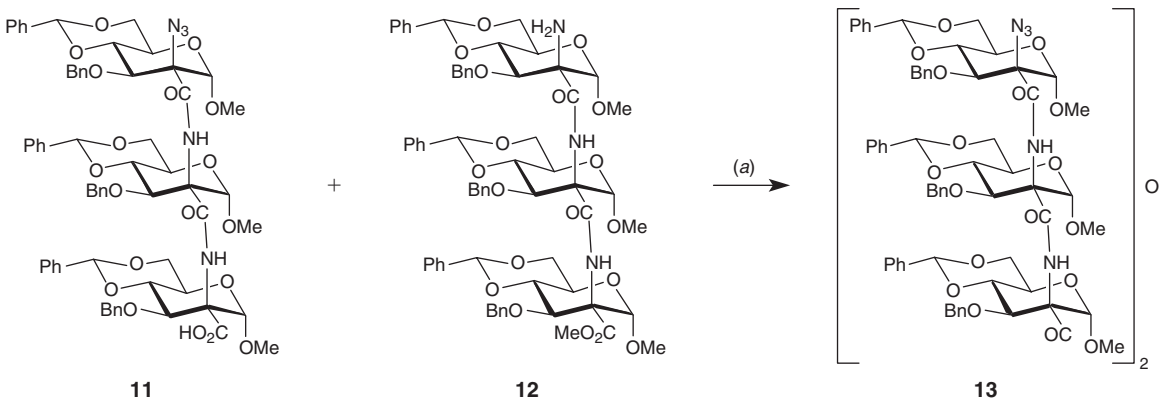
5 **6** **7**

Scheme 6.



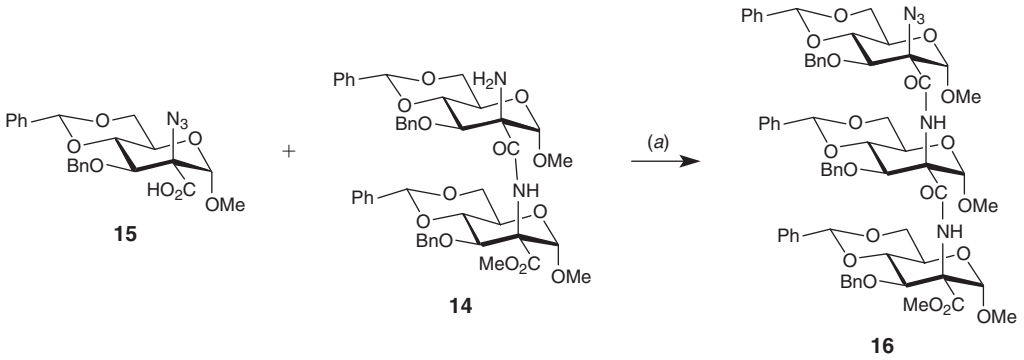
8 **9** **10**

Scheme 7. (*a*) TsCl, pyridine.

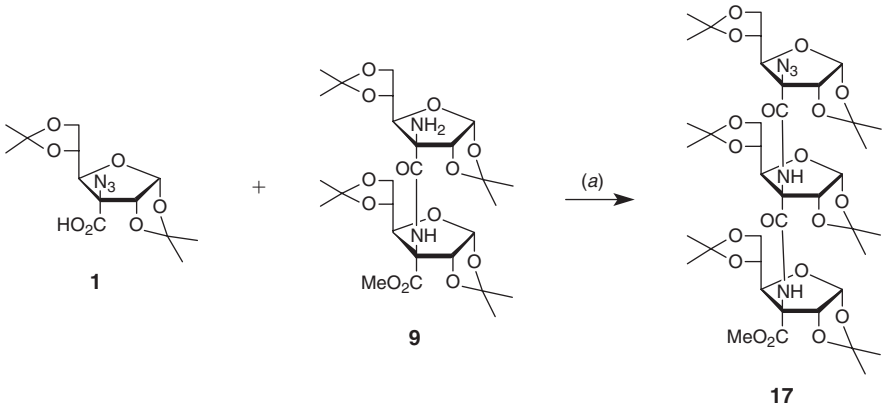


11 **12** **13**

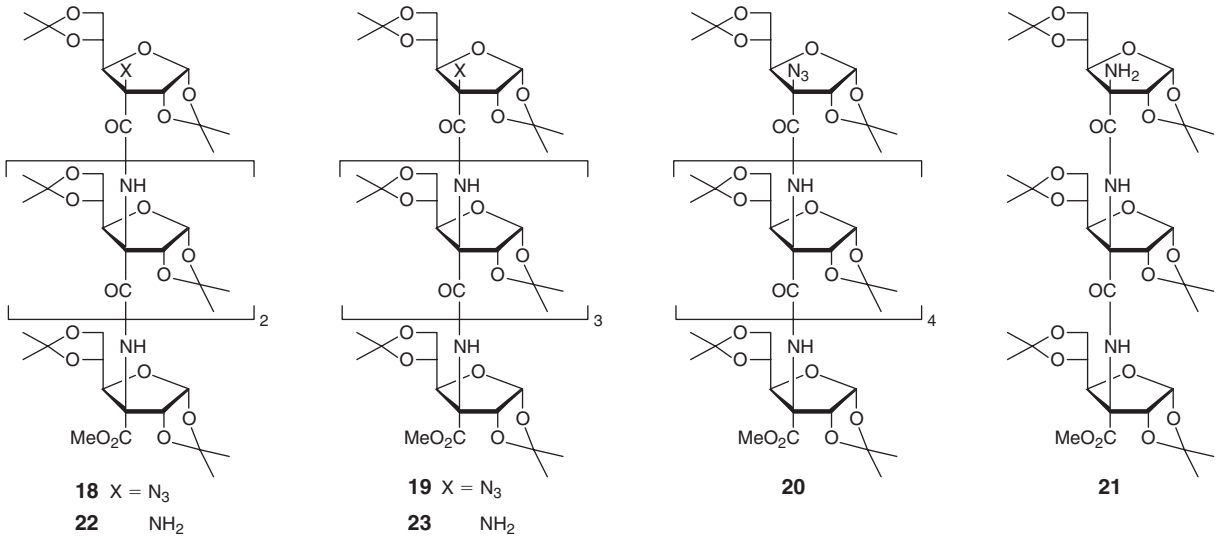
Scheme 8. (*a*) TsCl, pyridine.



Scheme 9. (*a*) TsCl, pyridine.



Scheme 10. (*a*) TsCl, pyridine.



Scheme 11.

simplifying the ^{1}H spectra and giving a reliable marker in the ^{13}C spectra. As well, the infrared spectra of the higher oligopeptides consistently showed one amide carbonyl absorption at around 1740 cm^{-1}, with the rest at approximately 1690 cm^{-1}.

We have much work left to do in this area. We still do not fully understand the chemistry involved in the peptide coupling reactions used here; perhaps other approaches, for example, a Staudinger reaction between an azide and a carboxylic acid, could generate an amide directly.[6] As well, we seek to make cyclic oligopeptides, for example, by cyclization of the reduced (azide to amine) form of the hexapeptide **20**. There are then the exciting possibilities for these oligomers that are, on the one hand, oligopeptides and, on the other, molecules that still seem oligosaccharide-like.

Experimental

General experimental procedures have been given previously.[7] For the ^{1}H NMR spectra it was not possible to unambiguously assign any of the ring hydrogen atoms for the peptides.

*[(3*S*)-3-Azido-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose **1**, Anhydride with (3*S*)-3-Azido-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene- α-D-*ribo*-hexose **1**] **3***

1,3-Dicyclohexylcarbodiimide (75 mg, 0.36 mmol) was added to the acid **1**[8] (100 mg, 0.30 mmol), the amine **2**[8] (80 mg, 0.25 mmol), and DMAP (5 mg, 0.04 mmol) in CH_2Cl_2 (10 mL) and the mixture left for 1 h. The standard workup (CH_2Cl_2) followed by flash chromatography (EtOAc/petrol, 1 : 5) afforded the anhydride **3** as an oil (72 mg, 74%). ν_{max} (film)/cm^{-1} 1750, 1780 (C=O), 2120 (N_3). δ_H (300 MHz) 1.32, 1.43, 1.55 (12H, 3 s, CH_3), 4.01 (dd, $J_{6,6}$ 8.6, $J_{5,6}$ 4.8, H6), 4.15 (dd, $J_{5,6}$ 6.3, H6), 4.20–4.26 (m, H5), 4.68 (d, $J_{4,5}$ 7.5, H4), 4.71 (d, $J_{1,2}$ 3.7, H2), 5.96 (d, H1). δ_C (75.5 MHz) 25.00, 25.90, 26.42, 26.57 (4C, CH_3), 67.08 (C6), 72.91, 81.67, 84.77 (C2, C4, C5), 75.12 (C3), 105.14 (C1), 110.03, 114.01 (2C, OCO), 159.25 (C=O). *m/z* (FAB) 641.2426, $[M + H]^+$ requires 641.2419.

*[(3*S*)-3-Azido-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose **1**, Amide with (3*S*)-3-Amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*ribo*-hexose **2**] **4***

The azido acid **1** and the amino ester **2** yielded[8] the *azido ester dipeptide* **4** (Found: C 51.6, H 6.4, N 8.8. $C_{27}H_{40}N_4O_{13}$ requires C 51.6, H 6.4, N 8.9%).

*[(3*S*)-3-Azido-3-*C*-carboxy-1,2:5,6-di-*O*-cyclohexylidene-3-deoxy-α-D-*xylo*-hexose, Amide with (3*S*)-3-Amino-1,2:5,6-di-*O*-cyclohexylidene-3-deoxy-3-*C*-methoxycarbonyl-α-D-*xylo*-hexose] **5***

(3*S*)-3-Azido-3-*C*-carboxy-1,2 : 5,6-di-*O*-cyclohexylidene-3-deoxy-α-D-*xylo*-hexose,[1] (3*S*)-3-amino-1,2:5,6-di-*O*-cyclohexylidene-3-deoxy-3-*C*-methoxycarbonyl-α-D-*xylo*-hexose,[1] and tosyl chloride in pyridine afforded[8] (flash chromatography, EtOAc/petrol, 1 : 2) the azido ester dipeptide **5** as a glass (75%), $[\alpha]_D$ +34.9°. ν_{max} (film)/cm^{-1} 3300 (NH), 2110 (N_3), 1740 (OC=O), 1675 (NHC=O). δ_H (300 MHz) 1.30–1.94 (40H, m, CH_2), 3.55 (dd, $J_{6,6}$ 8.4, $J_{5,6}$ 6.8, H6), 3.64 (dd, $J_{6',6'}$ 8.4, $J_{5',6'}$ 6.7, H6′), 3.78 (s, CO_2CH_3), 3.80 (dd, $J_{5,6}$ 6.2, H6), 3.91 (dd, $J_{5',6'}$ 6.4, H6′), 4.32 (d, $J_{1,2}$ 3.4, H2), 4.34 (d, $J_{4,5}$ 9.2, H4), 4.45–4.65 (m, H4′, H5, H5′), 4.96 (d, $J_{1',2'}$ 3.6, H2′), 5.90 (d, H1), 6.03 (d, H1′), 8.36 (br s, NH). δ_C (75.5 MHz) 23.43–36.60 (CH_2), 52.79 (CO_2CH_3), 64.63, 66.16 (C6, C6′), 69.08, 72.83 (C3, C3′), 73.43, 75.12, 83.44, 83.65, 86.19, 86.27 (C2, C2′, C4, C4′, C5, C5′), 104.20, 105.18 (C1, C1′), 110.18, 110.33, 116.44, 116.99 (4C, OCO), 165.68, 167.46 (CO_2CH_3, NCO). *m/z* (FAB) 789.3876, $[M + H]^+$ requires 789.3922.

*[Methyl (2*S*)-2-Azido-3-O-benzyl-4,6-O-benzylidene-2-C-carboxy-2-deoxy-α-D-arabino-hexoside **15**, Amide with Methyl (2*S*)-2-Amino-3-O-benzyl-4,6-O-benzylidene-2-deoxy-2-C-methoxycarbonyl-α-D-arabino-hexoside] **6***

The azido acid **15**,[1] methyl (2*S*)-2-amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-*C*-methoxycarbonyl-α-D-*arabino*-hexoside,[1] and tosyl chloride in pyridine furnished[8] (flash chromatography, EtOAc/petrol, 2 : 3) the azido ester dipeptide **6** as a glass (62%), $[\alpha]_D$ −1.1°. ν_{max} (film)/cm^{-1} 3285 (NH), 2125 (N_3), 1750 (OC=O), 1705 (NHC=O). δ_H (300 MHz) 3.35, 3.42 (6H, 2 s, OCH_3), 3.50–3.58, 3.75–3.98, 4.08–4.33, 4.56–4.65, 4.73–4.96 (14H, 5 m, H3, H3′, H4, H4′, H5, H5′, H6, H6′, CH_2Ph), 3.73 (s, CO_2CH_3), 4.59, 5.40, 5.62, 5.83 (4H, 4 s, H1, H1′, C*H*Ph), 7.05 (br s, NH), 7.20–7.76 (20H, m, Ph). δ_C (75.5 MHz) 52.71 (CO_2CH_3), 55.88, 55.92 (2C, OCH_3), 62.49, 63.49, 75.47, 76.87, 80.41, 80.51 (C3, C3′, C4, C4′, C5, C5′), 67.15, 72.58 (C2, C2′), 68.62, 68.68 (C6, C6′), 74.93, 75.30 (2C, *C*H_2Ph), 99.00, 101.00 (C1, C1′), 101.62, 101.66 (2C, *C*HPh), 125.94–138.43 (Ph), 165.41, 168.35 (CO_2CH_3, NCO). *m/z* (FAB) 853.3302, $[M + H]^+$ requires 853.3296.

*[Methyl (3*S*)-3-Azido-2-O-benzyl-4,6-O-benzylidene-3-C-carboxy-3-deoxy-α-D-ribo-hexoside, Amide with Methyl (3*S*)-3-Amino-2-O-benzyl-4,6-O-benzylidene-3-deoxy-3-C-methoxycarbonyl-α-D-ribo-hexoside] **7***

Methyl (3*S*)-3-azido-2-*O*-benzyl-4,6-*O*-benzylidene-3-*C*-carboxy-3-deoxy-α-D-*ribo*-hexoside,[1] methyl (3*S*)-3-amino-2-*O*-benzyl-4,6-*O*-benzylidene-3-deoxy-3-*C*-methoxycarbonyl-α-D-*ribo*-hexoside,[1] and tosyl chloride in pyridine yielded[8] (flash chromatography, EtOAc/petrol, 2 : 3) the azido ester dipeptide **7** as a glass (65%), $[\alpha]_D$ −48.4°. ν_{max} (film)/cm^{-1} 3250 (NH), 2110 (N_3), 1735 (OC=O), 1685 (NHC=O). δ_H (300 MHz) 3.27, 3.35 (6H, 2 s, OCH_3), 3.57 (d, $J_{1,2}$ 4.3, H2), 3.60–3.70, 3.85–3.90, 4.22–4.31, 4.38–4.68, 4.70–4.85 (13H, 5 m, H1, H4, H4′, H5, H5′, H6, H6′, CH_2Ph), 3.82 (s, CO_2CH_3), 4.35 (d, $J_{1',2'}$ 5.3, H2′), 5.03 (d, H1′), 5.20, 5.52 (2 H, 2 × s, C*H*Ph), 7.12–7.30 (20H, m, Ph), 8.81 (br s, NH). δ_C (75.5 MHz) 53.04 (CO_2CH_3), 55.49, 55.75 (2C, OCH_3), 59.76, 60.20, 74.36, 75.73, 79.07, 83.37 (C2, C2′, C4, C4′, C5, C5′), 67.92, 71.09 (C3, C3′), 69.42, 69.44 (C6, C6′), 73.88, 74.25 (2C, *C*H_2Ph), 97.84, 98.98 (C1, C1′), 101.40, 101.64 (2C, *C*HPh), 125.92–138.32 (Ph), 164.86, 168.73 (CO_2CH_3, NCO). *m/z* (FAB) 853.3285, $[M + H]^+$ requires 853.3296.

*[(3*S*)-3-Azido-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-ribo-hexose **1**, Amide with (3*S*)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-ribo-hexose] **8***

Potassium hydroxide (15 mL, 1.2 M in MeOH) was added to the azido ester dipeptide **4** (100 mg, 0.16 mmol) and the solution stirred at 50°C (1 h). Water was added, followed by evaporation of the MeOH and addition of 1 M HCl until the mixture reached pH 4. A standard workup (EtOAc) afforded the azido acid dipeptide **8** as an oil (87 mg), $[\alpha]_D$ +73.1°. δ_H (300 MHz) 1.25, 1.27, 1.31, 1.33, 1.34, 1.35, 1.47, 1.52 (24H, 8 s, CH_3), 3.92–4.35 (7H, m, H4, H5, H5′, H6, H6′), 4.70 (d, $J_{1,2}$ 3.5, H2), 4.75 (d, $J_{4',5'}$ 7.5, H4′), 5.20 (d, $J_{1',2'}$ 3.9, H2′), 5.83 (d, H1), 6.12 (d, H1′), 8.11 (br s, OH), 8.20 (br s, NH). δ_C (75.5 MHz) 25.10, 25.28, 26.00, 26.05, 26.15, 26.43, 26.50, 26.66 (8C, CH_3), 66.81, 67.65 (C6, C6′), 71.74, 73.91, 81.09, 81.77, 84.96, 85.11 (C2, C2′, C4, C4′, C5, C5′), 72.06, 75.09 (C3, C3′), 103.79, 106.00 (C1, C1′), 109.54, 110.62, 112.42, 113.58 (4C, OCO), 165.38, 169.72 (CO_2H, NCO). *m/z* (FAB) 615.2494, $[M + H]^+$ requires 615.2514.

*[(3*S*)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-ribo-hexose, Amide with (3*S*)-3-Amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-ribo-hexose **2**] **9***

Palladium on activated charcoal (20 mg, 10% w/w) was added to the azido ester dipeptide **4** (200 mg) in MeOH (10 mL) and the mixture stirred under an atmosphere of hydrogen at room temperature (16 h). Removal of the solvent gave a black residue that was subjected to flash chromatography ($MeOH/CHCl_3$, 1 : 19) to afford the amino ester dipeptide **9** as a powder (188 mg, 98%), mp >230°C (EtOAc/pentane), $[\alpha]_D$ +62.3°. δ_H (300 MHz) 1.20, 1.24, 1.27, 1.29, 1.31, 1.32, 1.48, 1.53 (24H, 8 s, CH_3), 1.76 (br s, NH_2), 3.75 (s, CO_2CH_3), 3.90–4.17, 4.37–4.40 (7H, 2 m, H4, H5, H5′, H6, H6′), 4.30 (d, $J_{1,2}$ 3.5, H2), 4.75 (d, $J_{4',5'}$ 8.0, H4′), 5.20 (d, $J_{1',2'}$ 4.0, H2′), 5.85 (d, H1), 6.18 (d, H1′), 7.88 (br s, NH). δ_C (75.5 MHz) 25.11–26.67 (CH_3), 52.64 (CO_2CH_3), 67.10, 67.93 (C6, C6′), 67.74, 71.58 (C3, C3′), 72.27, 73.65, 82.36, 83.35, 85.56, 87.41 (C2, C2′, C4, C4′, C5, C5′), 104.68, 106.94 (C1, C1′), 109.10, 110.12, 111.89, 113.06 (4C, OCO), 168.26, 168.77 (CO_2CH_3, NCO). *m/z* (FAB) 603.2794, $[M + H]^+$ requires 603.2765.

*{[(3*S*)-3-Azido-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-ribo-hexose **1**, Amide with (3*S*)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-ribo-hexose] **8**, Anhydride with [(3*S*)-3-Azido-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-ribo-hexose **1**, Amide with (3*S*)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-ribo-hexose] **8**} **10***

4-Toluenesulfonyl chloride (100 mg, 0.52 mmol) was added to the azido acid dipeptide **8** (150 mg, 0.25 mmol) and the amino ester dipeptide **9** (125 mg, 0.21 mmol) in pyridine (10 mL) at 0°C. The resulting solution

was stirred at 25°C (2 h) before being diluted with saturated $NaHCO_3$ solution. A standard workup (CH_2Cl_2) followed by flash chromatography (EtOAc/petrol, 1 : 4) furnished the anhydride **10** as an oil (110 mg, 75%). δ_H 1.20, 1.30, 1.34, 1.35, 1.54, 1.65 (24H, 6 s, CH_3), 3.94–4.15, 4.25–4.33 (6H, 2 m, H5, H5′, H6, H6′), 4.38 (d, $J_{4,5}$ 5.4, H4), 4.40 (d, $J_{1,2}$ 3.6, H2), 4.61 (d, $J_{4',5'}$ 7.1, H4′), 4.65 (d, $J_{1',2'}$ 3.6, H2′), 5.95 (d, H1′), 6.10 (d, H1). δ_C (75.5 MHz) 24.62, 25.03, 25.94, 26.17, 26.59, 26.67, 26.69, 26.81 (8C, CH_3), 66.82, 67.21 (C6, C6′), 71.13, 75.54 (C3, C3′), 73.00, 73.29, 80.75, 84.65, 85.20, 85.69 (C2, C2′, C4, C4′, C5, C5′), 105.11, 106.88 (C1, C1′), 109.62, 109.77, 113.76, 114.15 (4C, OCO), 161.41 (OC=O), 170.75 (NC=O). *m/z* (FAB) 597.2385, $[M - C_{26}H_{37}N_4O_{13}]^+$ requires 597.2408.

*[Methyl (2*S*)-2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside **15**, Amide with Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside, Amide with Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-O-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside] **11***

The azido ester tripeptide **16** (150 mg) was treated with KOH as for the ester **4** to afford the azido acid tripeptide **11** as a glass (130 mg), $[\alpha]_D$ +20.5°. δ_H (partial, 300 MHz) 3.20, 3.43, 3.45 (9H, 3 s, OCH_3), 4.97, 5.35, 5.60, 5.65, 5.66, 6.04 (6H, 6 s, H1, H1′, H1″, C*H*Ph), 7.15–7.55 (40H, Ph), 8.00 (br s, OH), 8.72 (br s, NH). δ_C (75.5 MHz) 55.79, 56.07, 56.08 (3C, OCH_3), 62.09, 62.63, 63.40, 74.87, 75.66, 76.18, 80.20, 80.22, 80.38 (C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 67.59, 68.74, 72.44 (C2, C2′, C2″), 68.42, 68.60, 68.65 (C6, C6′, C6″), 75.19, 75.28, 75.55 (3C, *C*H_2Ph), 96.38, 98.75, 100.86, 101.50, 101.68, 101.83 (6C, C1, C1′, C1″, *C*HPh), 125.82–138.67 (Ph), 169.13, 169.56, 169.81 (3C, CO_2H, NCO). *m/z* (FAB) 1236.4684, $[M + H]^+$ requires 1236.4665.

*[Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside, Amide with Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside, Amide with Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-O-benzylidene-2-deoxy-2-*C*-methoxycarbonyl-α-D-*arabino*-hexoside] **12***

The azido ester tripeptide **16** in MeOH was treated with hydrogen and palladium on activated charcoal as for the azide **4** to yield the amino ester **12** as a glass (96%), $[\alpha]_D$ +22.6°. δ_H (partial, 300 MHz) 3.13, 3.39, 3.46 (9H, 3 s, OCH_3), 3.67 (s, CO_2CH_3), 4.55 (d, $J_{3,4}$ 9.6, H3), 4.58, 4.85, 5.60, 5.64, 5.65, 6.05 (6H, 6 s, H1, H1′, H1″, C*H*Ph), 4.79 (dd, $J_{3,4}$ 9.6, $J_{4,5}$ 3.7, H4), 7.22–7.55 (40H, m, Ph), 8.47, 8.55 (2H, 2 br s, NH). δ_C (75.5 MHz) 52.16 (CO_2CH_3), 55.26, 55.43, 55.78 (3C, OCH_3), 61.99, 62.76, 63.26, 74.78, 75.26, 76.36, 80.36, 80.57, 81.30 (C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 65.53, 66.00, 68.55 (C2, C2′, C2″), 68.70, 68.87, 69.10 (C6, C6′, C6″), 74.78, 74.90, 75.17 (3C, *C*H_2Ph), 96.47, 101.64, 101.70, 101.75, 101.94, 102.42 (6C, C1, C1′, C1″, *C*HPh), 125.93–139.55 (Ph), 167.07, 168.54, 172.22 (3C, *C*O_2CH_3, NCO). *m/z* (FAB) 1224.4967, $C_{67}H_{74}N_3O_{19}$ $(M + H)^+$ requires 1224.4916.

*{[Methyl (2*S*)-2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside **15**, Amide with Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside, Amide with Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-O-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside] **11**, Anhydride with Methyl (2*S*)-2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside **15**, Amide with Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside, Amide with Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside **11**} **13***

The azido acid tripeptide **11** (100 mg, 0.08 mmol) and the amino ester tripeptide **12** (80 mg, 0.07 mmol) in pyridine (10 mL) were treated with tosyl chloride (30 mg, 0.16 mmol) as for the acid **8** and the amine **9** to furnish the anhydride **13** as an oil (72 mg, 73%). δ_H (partial) 3.12, 3.25, 3.45 (9H, 3 s, OCH_3), 5.48, 5.50, 5.62 (3 s, H1, H1′, H1″), 6.25 (br s, NH), 7.07–7.50 (30H, m, Ph). *m/z* (FAB) 1218.4631; $[M - C_{66}H_{68}N_5O_{19}]^+$ requires 1218.4559.

*[Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside, Amide with Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-*C*-methoxycarbonyl-α-D-*arabino*-hexoside] **14***

The azido ester dipeptide **6** in MeOH was treated with hydrogen and palladium on activated charcoal as for the azide **4** to yield the amino ester dipeptide **14** as a glass (96%), $[\alpha]_D$ +11.7°. δ_H (300 MHz) 2.10 (br s, NH_2), 3.18, 3.42 (6H, 2 s, OCH_3), 3.70–4.10, 4.25–4.37 (8H, 2 m, H4, H4′, H5, H5′, H6, H6′), 3.74 (s, CO_2CH_3), 4.51, 5.58, 5.60, 5.64 (4H, 4 s, H1, H1′, C*H*Ph), 4.61 (d, $J_{3,4}$ 9.5, H3), 4.74 (d, $J_{3',4'}$ 9.3, H3′), 4.81, 4.90 (AB, *J* 10.9, CH_2Ph), 4.98 (s, CH_2Ph), 7.23–7.56 (20H, m, Ph), 8.40 (br s, NH). δ_C (75.5 MHz) 52.09 (CO_2CH_3), 55.40, 55.50 (2C, OCH_3), 62.44, 62.66, 75.12, 75.75, 80.32, 80.99 (C3, C3′, C4, C4′, C5, C5′), 65.38, 65.88 (C2, C2′), 68.59, 68.61 (C6, C6′), 74.71, 74.73 (2C, *C*H_2Ph), 100.00, 101.44, 101.50, 102.22 (4C, C1, C1′, *C*HPh), 125.79–138.99 (Ph), 168.60, 168.92 (*C*O_2CH_3, NCO). *m/z* (FAB) 827.3376, $[M + H]^+$ requires 827.3391.

*[Methyl (2*S*)-2-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside **15**, Amide with Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-*O*-benzylidene-2-*C*-carboxy-2-deoxy-α-D-*arabino*-hexoside, Amide with Methyl (2*S*)-2-Amino-3-*O*-benzyl-4,6-O-benzylidene-2-deoxy-2-*C*-methoxycarbonyl-α-D-*arabino*-hexoside] **16***

The azido acid **15**, the amino ester dipeptide **14**, and tosyl chloride in pyridine afforded[8] (flash chromatography, MeOH/$CHCl_3$, 1 : 49) the azido ester tripeptide **16** as a glass (64%), $[\alpha]_D$ +10.6°. δ_H (partial, 300 MHz) 3.20, 3.42, 3.50 (9H, 3 s, OCH_3), 3.74 (s, CO_2CH_3), 4.58 (d, $J_{3,4}$ 9.6, H3), 4.63, 5.65, 5.67, 5.68, 6.12 (6H, 5 s, H1, H1′, H1″, C*H*Ph), 7.20–7.58 (40H, Ph), 8.34 (br s, NH). δ_C (75.5 MHz) 52.08 (CO_2CH_3), 55.44, 55.57, 55.66 (3C, OCH_3), 61.98, 63.06, 63.16, 74.75, 76.26, 76.51, 80.07, 80.36, 80.43 (C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 65.58, 68.59, 72.97 (C2, C2′, C2″), 68.36, 68.52, 68.56 (C6, C6′, C6″), 74.75, 75.01, 75.27 (3C, *C*H_2Ph), 96.40, 100.83, 101.46, 101.55, 101.64, 101.66 (6C, C1, C1′, C1″, *C*HPh), 125.77–139.11 (Ph), 166.16, 168.11, 168.30 (3C, *C*O_2CH_3, NCO). *m/z* (FAB) 1250.4739, $[M + H]^+$ requires 1250.4822.

*[(3*S*)-3-Azido-3-*C*-carboxy-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-*hexose* **1**, Amide with (3*S*)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-*hexose*, Amide with (3*S*)-3-Amino-3-deoxy-1,2:5,6-di-O-isopropylidene-3-*C*-methoxycarbonyl-α-D-ribo-*hexose* **2**] **17***

The azido acid **1**, the amino ester dipeptide **9**, and tosyl chloride in pyridine afforded[8] (flash chromatography, MeOH/$CHCl_3$, 1 : 49) the azido ester tripeptide **17** as a glass (86%), $[\alpha]_D$ +84.7°. ν_{max} (film)/cm^{-1} 3250 (NH), 2120 (N_3), 1755 (OC=O), 1745 (NHC=O), 1685 (NHC=O). δ_H (partial, 300 MHz) 1.27, 1.29, 1.31, 1.32, 1.36, 1.37, 1.39, 1.46, 1.51, 1.54, 1.60 (36H, 11 s, CH_3), 3.75 (s, CO_2CH_3), 4.58 (d, $J_{4,5}$ 8.7, H4), 4.62 (d, $J_{1,2}$ 3.8, H2), 4.64 (d, $J_{4',5'}$ 5.2, H4′), 4.78 (d, $J_{4'',5''}$ 5.2, H4″), 4.80 (d, $J_{1',2'}$ 3.6, H2′), 5.20 (d, $J_{1'',2''}$ 3.7, H2″), 5.91 (d, $J_{1'',2''}$ 3.7, H1′), 6.00 (d, H1″), 6.04 (d, H1), 8.46, 8.75 (2H, 2 br s, NH). δ_C (75.5 MHz) 25.08–27.02 (CH_3), 52.61 (CO_2CH_3), 65.78, 66.56, 67.50 (C6, C6′, C6″), 70.52, 70.58, 74.77 (C3, C3′, C3″), 72.58, 73.52, 73.93, 80.36, 82.09, 82.35, 83.03, 85.68, 85.85 (C2, C2′, C2″, C4, C4′, C4″, C5, C5′, C5″), 104.92, 105.06, 105.22 (C1, C1′, C1″), 108.70, 109.76, 110.11, 112.60, 112.79, 113.81 (6C, OCO), 165.62, 166.32, 167.31 (3C, *C*O_2CH_3, NCO). *m/z* (FAB) 914.3817, $[M + H]^+$ requires 914.3883.

*[(3S)-3-Azido-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose **1**, Amide with (3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*ribo*-hexose **2**] **18***

The azido acid **1**, the amino ester tripeptide **21**, and tosyl chloride in pyridine afforded[8] (flash chromatography, EtOAc/petrol, 2 : 3) the azido ester tetrapeptide **18** as a glass (87%), $[\alpha]_D$ +71.0°. ν_{max} (film)/cm^{-1} 3280 (NH), 2120 (N_3), 1755 (OC=O), 1740 (NHC=O), 1695 (NHC=O), 1680 (NHC=O). δ_H (partial, 300 MHz) 1.21–1.60 (48H, m, CH_3), 3.79 (s, CO_2CH_3), 4.36 (d, $J_{4,5}$ 8.1, H4), 4.53 (d, $J_{4',5'}$ 8.6, H4′), 4.58 (d, $J_{4'',5''}$ 5.3, H4″), 4.62 (d, $J_{1,2}$ 3.7, H2), 4.80 (d, $J_{4''',5'''}$ 8.8, H4‴), 4.94 (d, $J_{1',2'}$ 3.6, H2′), 5.17 (d, $J_{1'',2''}$ 3.7, H2″), 5.28 (d, $J_{1''',2'''}$ 4.0, H2‴), 5.90 (d, H1″), 5.91 (d, H1), 6.02 (d, H1′), 6.14 (d, H1‴), 8.06, 8.43, 8.60 (3H, 3 br s, NH). δ_C (75.5 MHz) 25.24–26.87 (CH_3), 52.57 (CO_2CH_3), 66.51, 67.23, 67.46, 67.51 (C6, C6′, C6″, C6‴), 70.28, 70.44, 72.09, 74.65 (C3, C3′, C3″, C3‴), 71.99, 72.51, 73.63, 74.06, 80.97, 82.60, 83.10, 83.21, 83.48, 84.56, 85.37, 85.56 (C2, C2′, C2″, C2‴, C4, C4′, C4″, C4‴, C5, C5′, C5″, C5‴), 104.91, 105.12, 105.46, 107.13 (C1, C1′, C1″, C1‴), 109.08, 109.68, 110.04, 110.08, 111.70, 112.62, 112.75, 113.77 (8C, OCO), 164.74, 165.31, 165.77, 168.17 (4C, CO_2CH_3, NCO). *m/z* (FAB) 1199.5093, $[M+H]^+$ requires 1199.5095.

*[(3S)-3-Azido-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose **1**, Amide with (3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-deoxy-3-*C*-carboxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*ribo*-hexose **2**] **19***

The azido acid **1**, the amino ester tetrapeptide **22**, and tosyl chloride in pyridine afforded[8] (flash chromatography, EtOAc/petrol, 2 : 3) the azido ester pentapeptide **19** as a fluffy solid (73%), mp >230°C (EtOAc/pentane), $[\alpha]_D$ +26.0°. ν_{max} (KBr)/cm^{-1} 3380 (NH), 2120 (N_3), 1760 (OC=O), 1740 (NHC=O), 1700 (NHC=O), 1685 (NHC=O). δ_H (partial, 300 MHz) 1.20–1.65 (60H, m, CH_3), 3.85 (s, CO_2CH_3), 4.45 (d, $J_{4,5}$ 7.8, H4), 4.48 (d, $J_{4',5'}$ 8.6, H4′), 4.62 (d, $J_{1,2}$ 3.7, H2), 4.74 (d, $J_{4'',5''}$ 8.6, H4″), 4.99 (d, $J_{1',2'}$ 3.6, H2′), 5.05 (d, $J_{1'',2''}$ 3.6, H2″), 5.10 (d, $J_{1''',2'''}$ 4.0, H2‴), 5.12 (d, $J_{1'''',2''''}$ 3.5, H2⁗), 5.89 (d, H1″), 6.08 (d, H1‴), 6.11 (d, H1), 6.13 (d, H1′), 6.14 (d, H1⁗), 7.80, 8.10, 8.24, 8.29 (4H, 4 br s, NH). δ_C (75.5 MHz) 25.08–26.69 (CH_3), 52.63 (CO_2CH_3), 66.68, 66.75, 67.13, 67.40, 67.51 (C6, C6′, C6″, C6‴, C6⁗), 69.87, 69.91, 69.93, 71.88, 74.84 (C3, C3′, C3″, C3‴, C3⁗), 72.28, 72.47, 72.74, 73.41, 73.62, 82.61, 82.91, 83.05, 83.32, 83.45, 83.62, 83.64, 84.98, 85.18, 85.26 (C2, C2′, C2″, C2‴, C2⁗, C4, C4′, C4″, C4‴, C4⁗, C5, C5′, C5″, C5‴, C5⁗), 104.90, 106.08, 106.18, 106.75, 107.08 (C1, C1′, C1″, C1‴, C1⁗), 109.03, 109.32, 109.60, 109.78, 110.00, 111.83, 112.14, 112.60, 112.67, 113.73 (10C, OCO), 163.99, 164.84, 164.95, 165.18, 168.07 (5C, CO_2CH_3, NCO). *m/z* (FAB) 1484.6190, $[M+H]^+$ requires 1484.6307.

*[(3S)-3-Azido-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose **1**, Amide with (3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*ribo*-hexose **2**] **20***

The azido acid **1**, the amino ester pentapeptide **23**, and tosyl chloride in pyridine afforded[8] (flash chromatography, MeOH/$CHCl_3$, 1 : 49) the azido ester hexapeptide **20** as a fluffy solid (62%), mp >230°C (EtOAc/pentane), $[\alpha]_D$ +9.7°. ν_{max} (KBr)/cm^{-1} 3380 (NH), 2120 (N_3), 1730 (OC=O), 1705 (NHC=O), 1680 (NHC=O). δ_H (partial, 500 MHz) 1.22–1.70 (72H, m, CH_3), 3.76 (s, CO_2CH_3), 4.38 (d, $J_{4,5}$ 7.8, H4), 4.40 (d, $J_{4',5'}$ 8.0, H4′), 4.43 (d, $J_{4'',5''}$ 7.5, H4″), 4.48 (d, $J_{4''',5'''}$ 6.9, H4‴), 4.52 (d, $J_{4'''',5''''}$ 8.5, H4⁗), 4.64, 5.06, 5.07, 5.15, 5.90, 6.17, 6.18, 6.19 (8 d, H1, H1′, H1″, H1‴, H2, H2′, H2″, H2‴), 4.77 (d, $J_{4''''',5'''''}$ 8.9, H4⁗′), 5.03 (d, $J_{1'''',2''''}$ 3.6, H2⁗), 5.13 (d, $J_{1''''',2'''''}$ 3.9, H2⁗′), 6.10 (d, H1⁗′), 6.16 (d, H1⁗), 7.80, 8.05, 8.13, 8.25, 8.27 (5H, 5 br s, NH). δ_C (125.8 MHz) 25.05–26.72 (CH_3), 52.66 (CO_2CH_3), 66.78, 66.80, 67.00, 67.22, 67.42, 67.54 (C6, C6′, C6″, C6‴, C6⁗, C6⁗′), 69.87, 69.90, 69.96, 69.98, 71.99 (C3, C3′, C3″, C3‴, C3⁗, C3⁗′), 72.23, 72.48, 72.74, 72.81, 73.35, 73.67, 74.87, 82.93, 83.09, 83.23, 83.38, 83.41, 83.69, 83.94, 84.81, 84.94, 85.17, 85.54 (C2, C2′, C2″, C2‴, C2⁗, C2⁗′, C4, C4′, C4″, C4‴, C4⁗, C4⁗′, C5, C5′, C5″, C5‴, C5⁗, C5⁗′), 104.91, 106.29, 106.38, 106.83, 107.00, 107.22 (C1, C1′, C1″, C1‴, C1⁗, C1⁗′), 109.06, 109.23, 109.38, 109.57, 109.78, 110.04, 111.82, 112.08, 112.21, 112.48, 112.58, 113.76 (12C, OCO), 163.86, 164.63, 164.80, 164.84, 165.09, 168.13 (6C, CO_2CH_3, NCO). *m/z* (FAB) 1768.7469, $[M+H]^+$ requires 1768.7441.

*[(3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*ribo*-hexose **2**] **21***

The azido ester dipeptide **17** in MeOH was treated with hydrogen and palladium on activated charcoal as for the azide **4** to yield the amino ester tripeptide **21** as a glass (97%), $[\alpha]_D$ +122.8°. δ_H (partial, 300 MHz) 1.26–1.28 (15H, m, CH_3), 1.33, 1.37, 1.40, 1.48, 1.50, 1.52, 1.57 (21H, 7 s, CH_3), 3.73 (s, CO_2CH_3), 4.24 (d, $J_{1,2}$ 3.7, H2), 4.65 (d, $J_{4,5}$ 8.3, H4), 4.72 (d, $J_{1',2'}$ 4.0, H2′), 4.81 (d, $J_{1'',2''}$ 4.4, H2″), 5.88 (d, H1′), 5.91 (d, H1″), 6.04 (d, H1), 8.82, 9.23 (2H, 2 br s, NH). δ_C (75.5 MHz) 25.09–27.25 (CH_3), 52.46 (CO_2CH_3), 65.22, 66.40, 68.04 (C6, C6′, C6″), 67.93, 69.99, 70.39 (C3, C3′, C3″), 73.30, 73.53, 74.18, 79.09, 81.70, 81.92, 82.15, 86.15, 87.52 (C2, C2′, C2″, C4, C4′, C4″, C5, C5′, C5″), 104.50, 104.60, 105.07 (C1, C1′, C1″), 108.42, 109.67, 109.75, 111.27, 112.74, 113.21 (6C, OCO), 167.10, 167.19, 171.09 (3C, CO_2CH_3, NCO). *m/z* (FAB) 888.3983, $[M+H]^+$ requires 888.3977.

*[(3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-*C*-carboxy-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexose, Amide with (3S)-3-Amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-3-*C*-methoxycarbonyl-α-D-*ribo*-hexose **2**] **22***

The azido ester dipeptide **18** in MeOH was treated with hydrogen and palladium on activated charcoal as for the azide **4** to yield the amino ester tetrapeptide **22** as a glass (97%), $[\alpha]_D$ +81.6°. δ_H (partial, 300 MHz) 1.21–1.58 (48H, m, CH_3), 3.75 (s, CO_2CH_3), 4.56 (d, $J_{4,5}$ 8.4, H4), 4.67 (d, $J_{4',5'}$ 5.3, H4′), 4.81 (d, $J_{4'',5''}$ 8.6, H4″), 4.92 (d, $J_{1,2}$ 3.5, H2), 5.17 (d, $J_{1',2'}$ 4.0, H2′), 5.24 (d, $J_{1'',2''}$ 3.7, H2″), 5.87 (d, H1″), 5.99 (d, $J_{1''',2'''}$ 3.4, H1‴), 6.01 (d, H1), 5.17, 6.13 (d, H1′), 8.15, 8.58, 8.99 (3H, 3 br s, NH). δ_C (75.5 MHz) 25.28–26.90 (CH_3), 52.51 (CO_2CH_3), 66.61, 67.06, 67.31, 67.93 (C6, C6′, C6″, C6‴), 67.58, 70.36, 70.44, 71.94 (C3, C3′, C3″, C3‴), 72.09, 73.01, 73.64, 74.03, 80.83, 82.40, 82.51, 82.65, 83.29, 84.80, 85.69, 87.52 (C2, C2′, C2″, C2‴, C4, C4′, C4″, C4‴, C5, C5′, C5″, C5‴), 104.75, 105.09, 105.44, 106.93 (C1, C1′, C1″, C1‴), 109.04, 109.62, 109.83, 110.04, 111.71, 112.62, 112.70, 113.32 (8C, OCO), 165.55, 166.45, 168.08, 169.94 (4C, CO_2CH_3, NCO). *m/z* (FAB) 1173.5112, $[M+H]^+$ requires 1173.5190.

*[(3S)-3-Amino-3-C-carboxy-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-hexose, Amide with (3S)-3-Amino-3-C-carboxy-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-hexose, Amide with (3S)-3-Amino-3-C-carboxy-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-hexose, Amide with (3S)-3-Amino-3-C-carboxy-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-ribo-hexose, Amide with (3S)-3-Amino-3-deoxy-1,2:5,6-di-O-isopropylidene-3-C-methoxycarbonyl-α-D-ribo-hexose 2] **23***

The azido ester dipeptide **19** in MeOH was treated with hydrogen and palladium on activated charcoal as for the azide **4** to yield the amino ester pentapeptide **23** as a glass (95%), mp >230°C (EtOAc/pentane), $[\alpha]_D$ +42.8°. δ_H (partial, 300 MHz) 1.20–1.63 (60H, m, CH_3), 3.72 (s, CO_2CH_3), 4.74 (d, $J_{4,5}$ 7.4, H4), 4.96 (d, $J_{1,2}$ 3.6, H2), 5.07 (d, $J_{1',2'}$ 3.8, H2′), 5.09 (d, $J_{1'',2''}$ 4.2, H2″), 5.17 (d, $J_{1''',2'''}$ 3.6, H2‴), 5.86 (d, $J_{1,2}$ 3.6, H1), 6.06–6.11 (m, H1′, H1″, H1‴), 6.13 (d, $J_{1'''',2''''}$ 3.6, H1⁗), 7.85, 8.07, 8.35, 8.68 (4H, 4 br s, NH). δ_C (75.5 MHz) 25.11–26.75 (CH_3), 52.58 (CO_2CH_3), 66.61, 66.73, 67.01, 67.47, 67.87 (C6, C6′, C6″, C6‴, C6⁗), 67.63, 69.84, 69.99, 70.03, 71.73 (C3, C3′, C3″, C3‴, C3⁗), 72.33, 72.85, 72.99, 73.51, 73.60, 82.41, 82.55, 82.93, 83.23, 83.43, 83.53, 83.70, 84.88, 85.25, 87.45 (C2, C2′, C2″, C2‴, C2⁗, C4, C4′, C4″, C4‴, C4⁗, C5, C5′, C5″, C5‴, C5⁗), 105.13, 105.91, 106.05, 106.50, 106.89 (C1, C1′, C1″, C1‴, C1⁗), 109.0, 109.29, 109.51, 109.75, 109.79, 111.86, 112.19, 112.53, 112.69, 113.25 (10C, OCO), 164.93, 165.26, 165.88, 167.98, 169.16 (5C, CO_2CH_3, NCO). *m/z* (FAB) 1458.6376, $[M+H]^+$ requires 1458.6402.

*Structure Determination of **4***

A full sphere of CCD area-detector diffractometer data (Bruker AXS instrument, ω-scans; monochromatic $Mo_{K\alpha}$ radiation, λ 0.7107$_3$ Å, $2\theta_{max}$ 75°; $T \approx 153$ K) was measured, yielding 31 788 reflections, these merging after 'empirical'/multiscan absorption correction (proprietary software) to 8290 independent (R_{int} 0.031; 'Friedel' data also merged, there being no non-trivial anomalous scatter), 6410 with $F > 4\sigma(F)$ considered 'observed' and used in the full-matrix least-squares refinement, refining anisotropic displacement parameter forms for C, N, and O; $(x, y, z, U_{iso})_H$ were also refined. Conventional residuals R, R_w at convergence were both 0.045. Neutral atom scattering factors were employed; computation was performed using the *Xtal 3.7* program system.[9] The configuration setting adopted was on the basis of the known chemistry. Pertinent results are given below and in Table 1 and Fig. 1. Full crystallographic details (excluding structure factor amplitudes) are deposited with the Cambridge Crystallography Data Centre (CCDC 226182).

Crystal data: $C_{27}H_{40}N_4O_{13}$, M628.6. Monoclinic, space group $P2_1$ (C_2^2, no. 4), a 10.3840(6), b 13.1090(7), c 11.3260(6) Å, β 96.921(1)°, V 1531 Å^3. $D_c(Z=2)$ 1.36$_4$ g cm^{-3}. μ_{Mo} 0.11 mm^{-1}; specimen: 0.32 × 0.25 × 0.18 mm^3; 'T'$_{min/max}$ 0.93. $|\Delta\rho_{max}|$ 0.36(3) e Å^{-3}.

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References

[1] A. Scaffidi, B. W. Skelton, R. V. Stick, A. H. White, *Aust. J. Chem.* **2004**, *57*, 723. doi:10.1071/CH04015.
[2] B. Neises, W. Steglich, *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 522. doi:10.1002/ANIE.197805221
[3] A. Hassner, V. Alexanian, *Tetrahedron Lett.* **1978**, 4475. doi:10.1016/S0040-4039(01)95256-6
[4] N. L. Hungerford, T. D. W. Claridge, M. P. Watterson, R. T. Aplin, A. Moreno, G. W. J. Fleet, *J. Chem. Soc., Perkin Trans. 1* **2000**, 3666. doi:10.1039/B002996N
[5] J. H. Brewster, C. J. Ciotti, *J. Am. Chem. Soc.* **1955**, *77*, 6214.
[6] O. David, W. J. N. Meester, H. Bieraugel, H. E. Schoemaker, H. Hiemstra, J. H. van Maarseveen, *Angew. Chem., Int. Ed.* **2003**, *42*, 4373. doi:10.1002/ANIE.200351930
[7] J. C. McAuliffe, R. V. Stick, *Aust. J. Chem.* **1997**, *50*, 193.
[8] G. S. Forman, A. Scaffidi, R. V. Stick, *Aust. J. Chem.* **2004**, *57*, 25. doi:10.1071/CH03214
[9] *The Xtal 3.7 System* (Eds S. R. Hall, D. J. du Boulay, R. Olthof-Hazekamp) **2002** (University of Western Australia: Perth).