Stereoselective Synthesis of Aminoacyl Hepto Glycosides: Synthetic Tools for Biochemical Interactions Studies

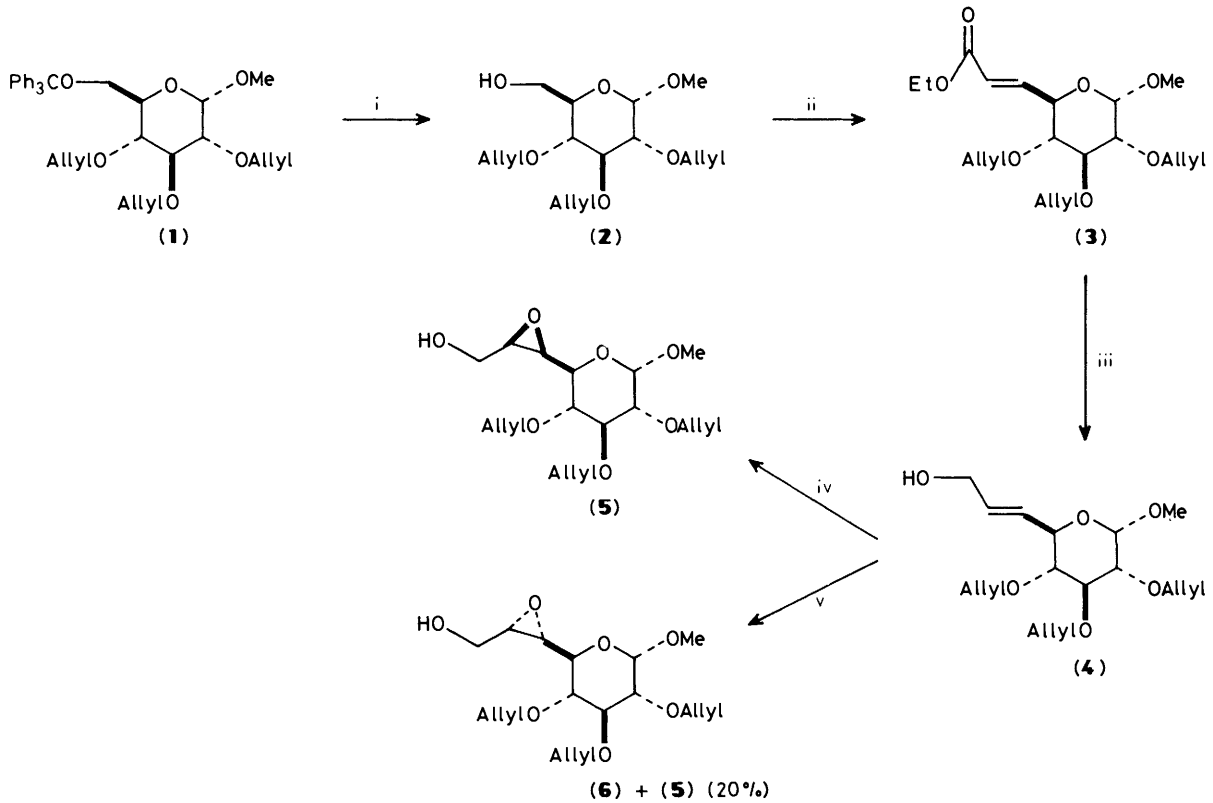
Michel Bessodes, Dimitri Komiotis, and Kostas Antonakis
Institut de Recherches Scientifiques sur le Cancer, BP 8-94802 Villejuif, France

The titanium-catalysed enantioselective epoxidation of allylic alcohols, and the regioselective opening of the resulting epoxide, have been successfully applied to the chiral synthesis of a terminal α-aminoacyl glycoside of biological importance. Limitation of this route has been evidenced as a consequence of the influence of the chiral centres of the sugar on the stereo- and regio-selectivities. This synthetic route offers a new entry to the important class of terminal α-aminoacyl sugars.

The leading concern in cancer chemotherapy is to elaborate more specific drugs that would consequently be expected to be less toxic for the tumour-bearing host. As a consequence of their great specificity, one would expect that linking biological macromolecules to targeting drugs would provide compounds of unique efficiency.[1] Recently the coupling of ketonucleosides with cancer-specific proteins have been reported.[2] In addition, amino and aminoacyl sugars are known to occur in many biologically active molecules.[3] Furthermore higher-carbon sugars have gained considerable attention in the past few years,[4] as they are important components of some antibiotics such as hikizimycin[5] or tunikamycin,[6] the latter having anticancer properties. These points as well as our current interest in the design of new antitumour drugs[7] led us to study the enantioselective synthesis of the terminal alpha amino acyl glycoside (**14**). Well aware of the importance of chirality in the specificity of drugs, we sought to design a synthetic route to compounds (**14**) that would be totally controlled stereochemically. Retrosynthetic analysis led us to choose the titanium-catalysed Sharpless epoxidation[8] as the chiral key step. From the different protecting groups assayed, the allyl ether was chosen for its inertness towards the different reaction conditions encountered along this synthesis. In addition it could be conveniently removed with specific reagents.[9]

Results and Discussion

The tri-allyl ether (**2**) (Scheme 1), obtained in three steps from methyl glucoside by selective tritylation, allylation in dimethyl sulphoxide (DMSO)–KOH,[10] and detritylation with



Scheme 1. *Reagents and solvents:* i, HCO_2H, Et_2O; ii, $(COCl)_2$, DMSO; then $Ph_3P{=}CHCO_2Et$; iii, DIBAL, Et_2O; iv, Bu'OOH, (−)-DIPT; v, Bu'OOH, (+)-DIPT

formic acid,[11] was transformed into the unsaturated ester (**3**) in a one-pot, two-step reaction. T.l.c. and n.m.r. data for this compound confirmed the presence of only the *E* isomer. Di-isobutylaluminium hydride (DIBAL) selective reduction of the ester group gave the corresponding allylic alcohol (**4**). It should be noted that the allylic alcohol should be kept under nitrogen, since 30% of the corresponding aldehyde was isolated after only one month of shelf storage. The titanium-catalysed epoxidation of (**4**) in the presence of D-di-isopropyl tartrate (DIPT),[8] gave only one product, (**5**), as was shown by ^1H and ^{13}C n.m.r., whereas the same reaction performed in the presence of L-di-isopropyl tartrate gave an inseparable mixture of epoxides (**6**) and (**5**). N.m.r. studies of this mixture provided evidence that the ratio of the two products was 80:20 and that the minor

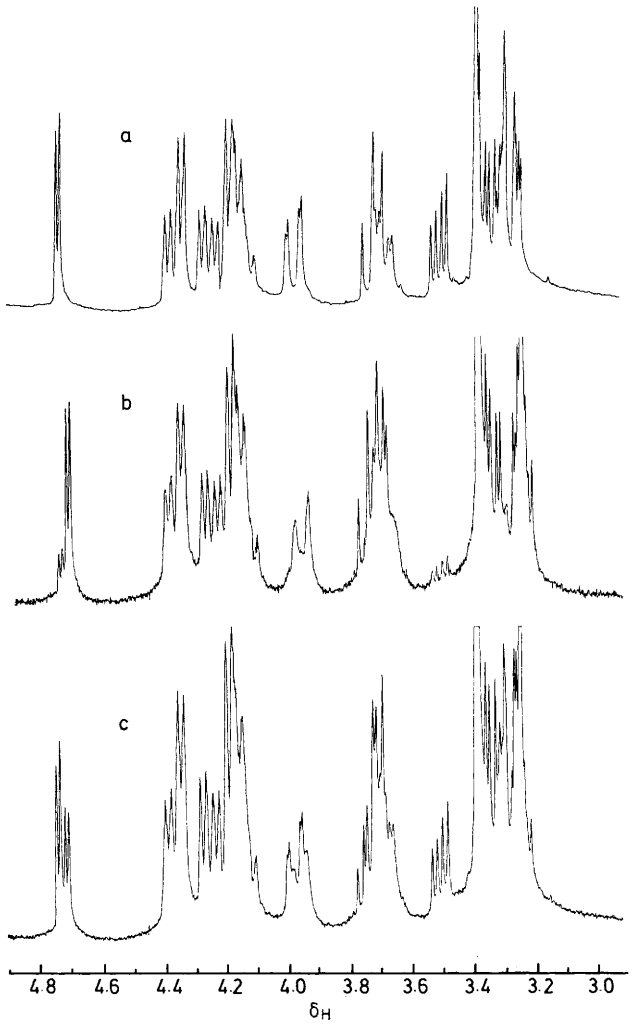
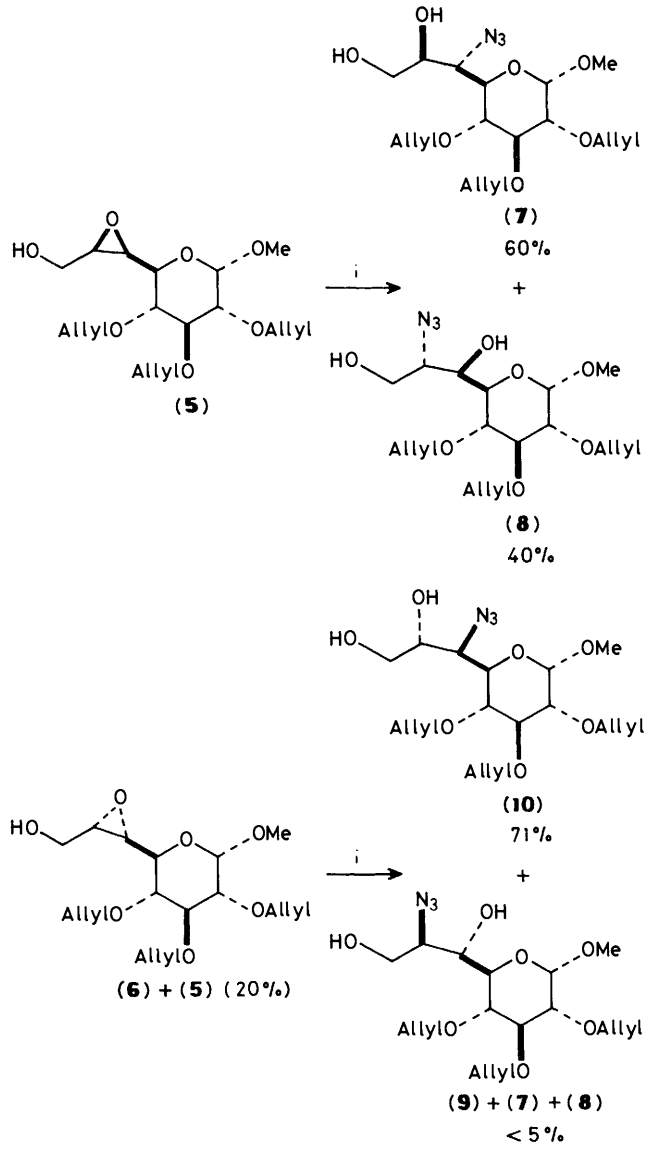


Figure. ^1H N.m.r. spectra of the inseparable mixture of epoxides (**5**) and (**6**). a, (−)-DIPT, −20 °C; b, (+)-DIPT, −20 °C; c, (−)-DIPT, 0 °C

epoxide was compound (**5**) obtained previously with the D-ligand (Figure). Furthermore, when similar epoxidation of (**4**) was carried out at 0 °C with either tartrate, almost no stereoselectivity was obtained, thus confirming that the diastereofacial induction of the chiral epoxidizing reagent at −20 °C was larger than that of the chiral substrate. According to these observations the structures of the epoxides (**5**) and (**6**) could be securely assigned, on the basis of the Sharpless model.[12] Similar results were obtained with the tribenzyl analogue of (**4**), thus excluding a possible influence of the allyl protecting groups on the complexation of the chiral ligand.

In order to improve this ratio, different variations of the epoxidation procedure were attempted. Lowering the temperature to −40 °C increased the reaction time to 6 days without affecting the ratio of isomers. Also, the catalytic process recently described[13] was disappointing in this case, giving mostly the unsaturated aldehyde, as a consequence of the previously observed oxidizability of this compound. It was thus hypothesized that failure to improve the stereoselectivity was due to the chiral influence of the asymmetric centres of the sugar substrate. Indeed, in the case of the epoxidation with D-tartrate, total diastereofacial selectivity was obtained. Since the complexation of the D-ligand occurred on the opposite side of the allylic alcohol,[14] this result is in accord with the previously mentioned hypothesis.

The azido function was then introduced by a recently described regioselective epoxide-opening reaction[15] (Scheme 2). The high regioselectivity of this reaction has been shown to be induced by the titanium ligand in a similar way as for the epoxidations. It could therefore be expected, from our previous observations, that compound (**5**) would lead to poor regio-

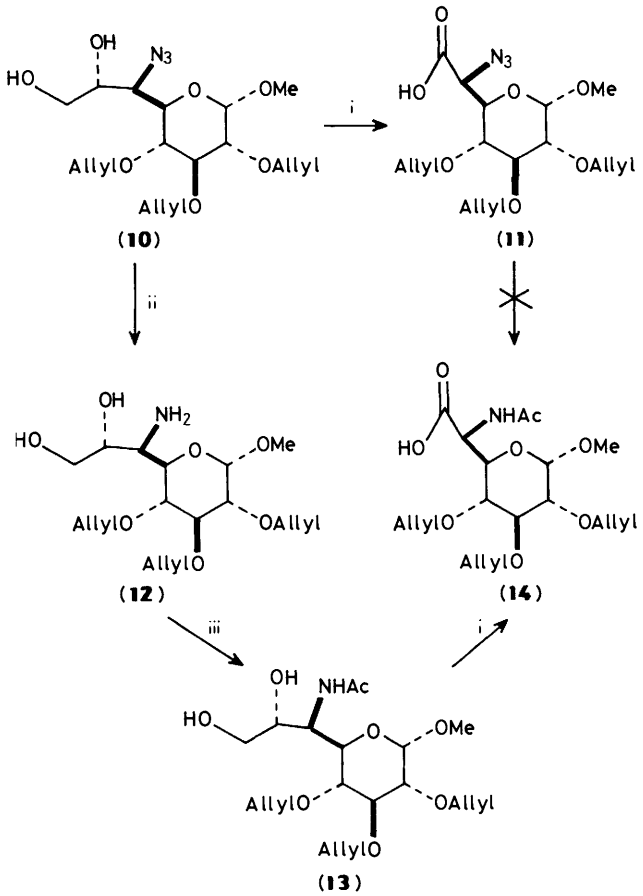


Scheme 2. *Reagents and solvent:* i, $Ti(N_3)_2(OPr^i)_2$, benzene

selective opening, because the complexation of the titanium ligand occurs on the same side as for the epoxidation of (**4**) with L-di-isopropyl tartrate, whereas opening of epoxide (**6**) should be more regioselective. Indeed, reaction of the unresolved mixture of epoxides (**5**) and (**6**) gave azide diols which were separated on a column to give a ratio of 71% (**10**) and 11% (**7**), (**8**), and (**9**). Since only compounds (**9**) and (**10**) corresponded to the opening of (**6**), and since only compound (**10**) could be cleaved by periodate, it could thus be deduced that the 1—3 regioselectivity in the opening of (**6**) was close to 80%. On the other hand when epoxide (**5**) was treated with the azide reagent in refluxing benzene a mixture of azide diols (**7**) and (**8**) was obtained first in the ratio of (**7**):(**8**) 40:60. Different attempts were made to improve the regioselectivity in the opening of epoxide (**5**). Increasing the temperature by the use of higher-boiling solvents (*i.e.* toluene) was not satisfactory due to solubility problems; however, when this reaction was performed in benzene at 120 °C in a sealed vessel the ratio was improved to 50:50. Lowering the concentration of the reactants proved to be more successful; the best ratio of (**7**) to (**8**) obtained was, however, limited to 60:40 for a concentration of 14 mM.[16] The ratio of azides was determined by the integrals of the n.m.r. spectra of the acetylated derivatives, measured at the acetyl resonance. Their structures were deduced from their susceptibility to periodate cleavage and from the deshielding effect observed on either proton 7-H or 6-H after acetylation of the free hydroxy groups. The stereochemistry at the opening site was deduced from the structures of the starting epoxides, since this type of reaction proceeds *via* an S_N2 mechanism.[17]

The oxidative degradation of diol (**10**) was then considered. The efficient $RuCl_3$–periodate reagent[18] was not suitable in this instance, on account of the presence of the allyl protecting groups. It was then suggested that the presence of Cr^{VI} salts could further oxidize the aldehyde formed by the periodate action, without affecting the double bonds of the allyl groups. Thus diol (**10**) was treated (Scheme 3) with a mixture of periodic acid and potassium dichromate to give the corresponding carboxylic acid (**11**) albeit in poor yield. Study of the reaction conditions showed that the problem resulted from the unstable aldehydo azide intermediate: indeed, increasing the ratio of chromic acid to periodic acid accelerated the aldehyde oxidation and raised the yield of the reaction. However, further difficulties in reducing the azide group prompted us to abandon this route.

The alternative was found by reduction of the azide diol (**10**), followed by specific acetylation of the resulting amine (**12**) with acetic anhydride–ethanol. This acetamido diol (**13**) was then oxidized using the procedure described earlier to give the acetamido acid (**14**).



Scheme 3. *Reagents and solvents:* i, H_5IO_6, $K_2Cr_2O_7$, aq. AcOH; ii, $LiAlH_4$, Et_2O; iii,, Ac_2O, MeOH

Experimental

Reactions were monitored by t.l.c., using plates purchased from Merck Co. (plastic sheets, Silicagel 60 F_{254}, 0.2 mm thickness), with various mixtures of solvents [A, EtOAc–hexane (3:7); B, EtOAc–hexane (7:3); C, CH_2Cl_2–acetone (85:15)]. The compounds were visualized by spraying a solution of 30% aqueous sulphuric acid, followed by charring with a heat gun. Purifications were obtained by flash chromatography on Chromagel (S.D.S., 60 Å, 200—400 mesh). Routine ^1H n.m.r. spectra were obtained with a Varian T-60 spectrometer. High-field ^1H and ^{13}C n.m.r. spectra were obtained with a Bruker MSL-300 spectrometer, for deuteriated chloroform solutions with tetramethylsilane as internal standard. Complete identification of the signals were possible by using homonuclear spin decoupling and 2D single-relay techniques.[19] Specific rotations were measured at room temperature on a Roussel-Jouan Quick Polarimeter at the Na-D line. Microanalyses were performed by the Centre National de Microanalyses du CNRS, Vernaison, France. Light petroleum refers to the fraction boiling in the range 40—60 °C.

Methyl 2,3,4-*Tri*-O-*allyl*-6-O-*trityl*-α-D-*glucopyranoside* (**1**).—To a solution of methyl 6-*O*-trityl-α-D-glucoside[20] (437 mg, 1 mmol) in DMSO (0.7 ml) were added allyl bromide (0.38 ml, 4.4 mmol) and powdered potassium hydroxide (1 g, 18 mmol) at 0 °C. The mixture was stirred for 1 h then diluted with ether (20 ml) and washed successively with saturated aq. sodium hydrogen sulphate and brine. It was then evaporated and the residue was flash chromatographed in a 1:9 mixture of ethyl acetate–hexane to yield *compound* (**1**) as a clear syrup (490 mg, 89%), R_F 0.72 (solvent A); $[\alpha]_D$ +53.75° (*c* 0.1 in $CHCl_3$) (Found: C, 75.5; H, 7.4. $C_{35}H_{40}O_6$ requires C, 75.5; H, 7.2%).

Methyl 2,3,4-*Tri*-O-*allyl*-α-D-*glucopyranoside* (**2**).—Compound (**1**) (556 mg, 1 mmol) was dissolved in a 3:2 mixture of formic acid–ether (5 ml), and the solution was stirred for 10 min. Ethyl acetate (50 ml) was added and the solution was washed successively with brine (×4), then with saturated aq. sodium hydrogen carbonate until neutral. The organic layer was dried over magnesium sulphate and evaporated. The residue was chromatographed on silica with solvent A to give *compound* (**2**) (280 mg, 90%) as an oil, R_F 0.2 (solvent A); $[\alpha]_D$ +112.5° (*c* 0.1 in $CHCl_3$); δ_H 6.02—5.85 (3 H, m, 3 × C*H*=CH_2), 5.32 (6 H, m, 3 × CH=CH_2), 4.75 (1 H, d, *J* 4.8 Hz 1-H), 4.40—4.10 (6 H, m, 3 × OCH_2), 3.85—3.70 (3 H, m, 3-H and 6-H_2), 6.30 (1 H, m, 5-H), 3.40 (3 H, s, OMe), 3.40—3.30 (2 H, m, 2- and 4-H), and

2.15 (1 H, s, OH) (Found: C, 61.2; H, 8.4. $C_{16}H_{26}O_6$ requires C, 61.2; H, 8.3%).

Ethyl [*methyl* (E)-2,3,4-*Tri*-O-*allyl*-6,7-*dideoxy*-α-D-gluco-*oct*-6-*enopyranoside*]*uronate* (**3**).—Oxalyl chloride (0.116 ml, 1.36 mmol) was dissolved under nitrogen in dichloromethane (10 ml) at —70 °C. DMSO (0.185 ml, 2.61 mmol) was added and the solution was stirred for 15 min. A solution of compound (**2**) (314 mg, 1 mmol) in dichloromethane (6 ml) was then added and the mixture was stirred for 20 min. Triethylamine (0.64 ml, 4.61 mmol) was added and the mixture was stirred for an additional 20 min. The temperature was then raised to −20 °C and a solution of ethyl triphenylphosphoranylidene acetate (1 g, 2.8 mmol) in dichloromethane (6 ml) was added. The solution was allowed to warm to room temperature and was then washed twice with brine, dried over magnesium sulphate, and concentrated. Flash chromatography in a 2:7 mixture of ethyl acetate–hexane gave *compound* (**3**) as a clear syrup (336 mg, 88%), R_F 0.7 (solvent A); $[\alpha]_D$ +24.73° (*c* 0.1 in $CHCl_3$); δ_H 7.04 (1 H, dd, *J* 15.7 Hz, 6-H), 6.14 (1 H, d, *J* 15.8 Hz, 7-H), 6.0—5.8 (3 H, m, 3 × C*H*=CH_2), 5.3—5.1 (6 H, m, 3 × CH=CH_2), 4.77 (1 H, d, *J* 3.4 Hz, 1-H), 4.4—4.0 (9 H, m, 4 × OCH_2, and 5-H), 3.75 (1 H, t, *J* 9.3 Hz, 3-H), 3.38 (3 H, s, OMe), 3.37 (1 H, dd, *J* 3.6 Hz, 2-H), 3.06 (1 H, t, *J* 9.6 Hz, 4-H), and 1.3 (3 H, t, *J* 7.1 Hz, Me) (Found: C, 63.3; H, 8.0. $C_{20}H_{30}O_7$ requires C, 62.8; H, 7.9%).

Methyl (E)-2,3,4-*Tri*-O-*allyl*-6,7-*dideoxy*-α-D-gluco-*oct*-6-*enopyranoside* (**4**).—The ester (**3**) (382 mg, 1 mmol) was dissolved in ether (8 ml) and DIBAL (1M in hexane; 2.1 ml, 2.1 mmol) was added to the stirred solution at 0 °C. After this time two clear layers separated and ether (10 ml) was added. The mixture was then washed successively with saturated aq. sodium hydrogen carbonate and brine (×2). After evaporation the residual syrup was purified on a column [EtOAc–hexane 6:4)] to give *compound* (**4**) (323 mg, 95%) as an oil, R_F 0.5 (solvent B); $[\alpha]_D$ +98.1° (*c* 0.1 in $CHCl_3$); δ_H 6.05—5.7 (5 H, m, 3 × C*H*=CH_2, and 6- and 7-H), 5.3—5.1 (6 H, m, 3 × CH=CH_2), 4.73 (1 H, d, *J* 3.6 Hz, 1-H), 4.4—4.0 (9 H, m, 3 × OCH_2, 5-H, and 8-H_2), 3.7 (1 H, t, *J* 9.5 Hz, 3-H), 3.39 (3 H, s, OMe), 3.37 (1 H, dd, *J* 3.6, 9.7 Hz, 2-H), 3.06 (1 H, t, *J* 9.6 Hz, 4-H), and 1.82 (1 H, s, OH) (Found: C, 63.4; H, 8.3. $C_{18}H_{28}O_6$ requires C, 63.5; H, 8.2%).

Methyl 2,3,4-*Tri*-O-*allyl*-6,7-*anhydro*-α-D-threo-D-gluco-*octopyranoside* (**5**).—The allylic alcohol (**4**) (340 mg, 1 mmol) and D-di-isopropyl tartrate (304 mg, 1.3 mmol) were dissolved in dry dichloromethane (10 ml) and cooled under nitrogen to −23 °C. Titanium tetraisopropoxide (0.33 ml, 1.1 mmol) was added and the mixture was stirred for 15 min. t-Butyl hydroperoxide (3.2M in toluene; 0.4 ml, 1.28 mmol) was then added and the solution was left in the freezer (−25 °C) for 24 h, then allowed to warm to 0 °C and 10% aq. tartaric acid (4 ml) was added to the stirred mixture. After 30 min the mixture was diluted with dichloromethane (20 ml) and washed with water (×3). Concentration and column chromatography [EtPAc–hexane (6:4)] gave *compound* (**5**), which crystallized from dichloromethane–hexane (330 mg, 93%), m.p. 64 °C; R_F 0.42 (solvent B); $[\alpha]_D$ +116.9° (*c* 0.1 in $CHCl_3$); δ_H 6.0—5.8 (3 H, m, 3 × C*H*=CH_2), 5.4—5.1 (6 H, m, 3 × CH=CH_2), 4.74 (1 H, d, *J* 3 Hz, 1-H), 3.98 (1 H, m, 8-H), 3.75—3.65 (2 H, m, 3-H and 3-H′), 3.52 (1 H, dd, *J* 5.6, 12.5 Hz, 5-H), 3.39 (3 H, s, OMe), and 3.4—3.23 (4 H, m, 2-, 4-, 6-, and 7-H) (Found: C, 60.7; H, 7.9. $C_{18}H_{28}O_7$ requires C, 60.7; H, 7.9%).

Methyl 2,3,4-*Tri*-O-*allyl*-6,7-*anhydro*-β-L-threo-D-gluco-*octopyranoside* (**6**).—Epoxidation of compound (**4**) with L-di-isopropyl tartrate was performed according to the above procedure. The reaction time was 48 h, and purification of the reaction mixture by flash chromatography [EtOAc–hexane (6:4)] gave an oily mixture of epoxides (**5**) and (**6**) in the ratio 20:80 (338 mg, 95%), R_F 0.42 (solvent B); $[\alpha]_D$ +108.8° [(**5**) + (**6**); *c* 0.1 in $CHCl_3$]; δ_H 4.74 [d, *J* 3 Hz, 1-H of (**5**)], 4.71 [d, *J* 3 Hz, 1-H of (**6**)] (ratio of integrals at 4.74 and 4.71 20:80), 3.95 (1 H, m, 8-H), 3.75—3.60 (3 H, m, 3-H, and 8-H′), 3.39 (3 H, s, OMe), 3.4—3.23 (4 H, m, 2-, 4-, 6-, and 7-H) (Found: C, 59.3; H, 7.8. $C_{18}H_{28}O_7 \cdot \frac{1}{2}H_2O$ requires C, 59.2; H, 7.9%).

Methyl 2,3,4-*Tri*-O-*allyl*-6-*azido*-6-*deoxy*-α-L-erythro-D-gluco-*octopyranoside* (**7**).—Titanium di-isopropoxide diazide[15] (300 mg, 1.2 mmol) was placed in a flame-dried round-bottom flask with benzene (CaH_2-dried; 60 ml) and the mixture was refluxed under nitrogen until dissolution occurred. A solution of epoxide (**5**) (356 mg, 1 mmol) in dry benzene (10 ml) was then added and the mixture was stirred for 15 min, then evaporated to dryness, and the residue was dissolved in ether (30 ml) and hydrolysed with 5% sulphuric acid during 1 h. The organic layer was then decanted and the aqueous phase was washed with ether (15 ml) (×4). The combined washings were evaporated under reduced pressure and the residue was fractionated [flash chromatography, dichloromethane–acetone (90:10)] to give azides (**7**) and (**8**) in the ratio 60:40 (340 mg, 85%) as an oil, R_F 0.51 (**7**), 0.47 (**8**); $[\alpha]_D$ +147.5° (**7**), +95.6° (**8**) (*c* 0.1 in $CHCl_3$); δ_H* (**7**) 6.0—5.8 (3 H, m, 3 × C*H*=CH_2), 5.4—5.1 (6 H, m, 3 × CH=CH_2 and 7-H), 4.75 (1 H, d, *J* 3.5 Hz, 1-H), 4.58 (1 H, dd, *J* 2, 12 Hz, 8-H), 4.43—4.10 (7 H, m, 3 × OCH_2 and 8-H′), 3.96 (1 H, m, 6-H), 3.84 (1 H, m, 5-H), 3.70 (1 H, t, *J* 9.5 Hz, 3-H), 3.46 (1 H, dd, *J* 3, 9.8 Hz, 4-H), 3.43 (3 H, s, OMe), and 3.33 (1 H, dd, *J* 3.6, 9.7 Hz, 2-H) (Found: C, 54.1; H, 7.4; N, 10.2. $C_{18}H_{29}N_3O_7$ requires C, 54.1; H, 7.3; N, 10.5%); δ_H (**8**) 6.0—5.8 (3 H, m, 3 × C*H*=CH_2), 5.4—5.1 (6 H, m, 3 × CH=CH_2), 4.78 (1 H, d, *J* 3.4 Hz, 1-H), 4.01 (2 H, m, 8-H), 3.82—3.73 (3 H, m, 3-, 5-, and 6-H), 3.58 (1 H, m, 7-H), 3.48—3.4 (4 H, m, 4-H and Me), and 3.32 (1 H, dd, *J* 3.5, 9.7 Hz, 2-H) (Found: C, 54.2; H, 7.3; N, 10.3%).

Methyl 2,3,4-*Tri*-O-*allyl*-6-*azido*-6-*deoxy*-α-D-erythro-D-gluco-*octopyranoside* (**10**).—The procedure was identical to that above. The product was crystallized from ethyl acetate–hexane to give compound (**10**) 83 mg; 71%), m.p. 81 °C; R_F 0.47 (solvent C); $[\alpha]_D$ +101.8° (*c* 0.1 in $CHCl_3$); δ_H* 5.40—5.15 (7 H, m, 3 × CH_2, and 7-H), 4.75—4.65 (2 H, m, 1- and 8-H), 4.5—4.1 (7 H, m, 3 × OCH_2 and 8-H′), 3.85 (1 H, m, 6-H), 3.75 (2 H, m, 3- and 5-H), 3.47 (1 H, t, *J* 9.5 Hz, 4-H), 3.38 (1 H, dd, *J* 3.5, 9.6 Hz, 2-H), and 3.32 (3 H, s, OMe) (Found: C, 54.2; H, 7.3; N, 10.3%).

Methyl 2,3,4-*Tri*-O-*allyl*-6-(R)-*azido*-6-*deoxy*-β-L-glycero-D-gluco-*heptopyranosiduronic Acid* (**11**).—To a solution of diol (**10**) (400 mg, 1 mmol) in 50% aq. acetic acid (6 ml) were added potassium dichromate (530 mg, 1.8 mmol) and periodic acid (500 mg, 2.2 mmol) all at once. The mixture was stirred at room temperature for 10 min and diluted with ethyl acetate (20 ml) and the organic phase was washed successively with saturated aq. sodium hydrogen sulphate (3 × 5 ml) and water (2 × 5 ml), dried over sodium sulphate, and evaporated to give a clear oil. Flash chromatography [CH_2Cl_2–acetone (1:1)] gave pure compound (**11**) (126 mg, 33%) as an oil, R_F 0.5 [CH_2Cl_2–acetone (1:1)]; $[\alpha]_D$ +141.3° (*c* 0.1 in $CHCl_3$); δ_H 6.0—5.8 (3 H, m, 3 × C*H*=CH_2), 5.4—5.1 (6 H, m, 3 × CH=CH_2), 4.74 (1 H, d, *J* 3.5 Hz, 1-H), 4.43—4.08 (8 H, m, 3 × OCH_2, and 5- and 6-H), 3.76 (1 H, t, *J* 9.3 Hz, 3-H), 3.49 (1 H, t, *J* 9.3 Hz, 4-H), 3.42—3.33 (4 H, m, OMe and 2-H). (Elemental analysis for this compound could not be obtained because of its instability).

* On account of the overlapping signals, the n.m.r. data of compounds (**7**) and (**10**) were taken from their acetylated derivatives.

Methyl 2,3,4-*Tri*-O-*allyl*-6-*amino*-6-*deoxy*-α-D-erythro-D-gluco-*octopyranoside* (**12**).—Compound (**10**) (400 mg, 1 mmol) was dissolved in dry ether (20 ml), and the solution was cooled to 0 °C. Lithium aluminium hydride (104 mg, 2.7 mmol) was then added and the mixture was stirred for 30 min. Water (0.2 ml), 15% NaOH (0.4 ml), and water (0.2 ml) were then successively and cautiously added. The mixture was stirred until a white precipitate was deposited (15 min) and the mixture was filtered on Celite. After concentration of the filtrate the residue was chromatographed [EtOAc–EtOH (8:2)] and crystallization from ether–light petroleum gave crystalline *compound* (**12**) (306 mg, 82%), m.p. 78 °C; R_F 0.25 [EtOAc–EtOH (8:2)]; $[\alpha]_D$ +122.5° (*c* 0.1 in $CHCl_3$); δ_H 6.0—5.8 (3 H, m, 3 × C*H*=CH_2), 5.4—5.0 (6 H, m, 3 × CH=CH_2), 4.74 (1 H, d, *J* 3.2 Hz, 1-H), 4.42—4.12 (8 H, m, 3 × OCH_2, and 8-H_2), 3.85 (1 H, m, 5-H), 3.80 (2 H, m, 3- and 6-H), 3.67 (1 H, m, 2-H), 3.43 (3 H, s, OMe), 3.32 (2 H, m, 2- and 4-H) (Found: C, 57.9; H, 8.8; N, 3.7. $C_{18}H_{31}NO_7$ requires C, 57.9; H, 8.3; N, 3.8%).

Methyl 6-*Acetamido*-2,3,4-*tri*-O-*allyl*-6-*deoxy*-α-erythro-D-gluco-*octopyranoside* (**13**).—To a solution of compound (**12**) (373 mg, 1 mmol) in dry methanol (12 ml) was added acetic anhydride (0.15 ml, 1.6 mmol). After 30 min at room temperature the mixture was concentrated and the residue was crystallized from EtOAc–hexane to give the *amide* (**13**) (398 mg, 96%), m.p. 150 °C; R_F 0.57 [EtOAc–EtOH (8:2)]; $[\alpha]_D$ +57.5° (*c* 0.1 in $CHCl_3$); δ_H 6.0—5.8 (3 H, m, 3 × C*H*=CH_2), 5.4—5.2 (6 H, m, 3 × CH=CH_2), 4.4—4.0 (11 H, m, 3 × OCH_2, 8-H_2, and 5-, 6-, and 7-H), 4.74 (1 H, d, *J* 3.5 Hz, 1-H), 4.40—4.0 (11 H, m, 3 × OCH_2, 8-H_2, and 5-, 6-, and 7-H), 3.78 (1 H, t, *J* 9.2 Hz, 3-H), 3.42 (3 H, s, OMe), 3.32 (1 H, dd, *J* 3.6, 9.6 Hz, 2-H), 3.14 (1 H, t, *J* 9.5 Hz, 4-H), and 2.06 (3 H, s, NAc) (Found: C, 57.9; H, 7.9; N, 3.3. $C_{20}H_{33}NO_8$ requires C, 57.8; H, 8.0; N, 3.4%).

Methyl 6-*Acetamido*-2,3,4-*tri*-O-*allyl*-6-*deoxy*-α-D-gluco-*heptopyranosiduronic Acid* (**14**).—Compound (**13**) (415 mg, 1 mmol) was dissolved in a mixture of acetic acid (4.5 ml), water (6 ml), and acetone (1.5 ml) and was treated with periodic acid (708 mg, 3.1 mmol) and potassium dichromate (823 mg, 2.8 mmol) under the conditions described for compound (**11**). After work-up, compound (**14**) was crystallized from EtOAc–hexane (363 mg, 91%), m.p. 201 °C; R_F 0.26 [EtOAc–EtOH–AcOH (8:2:0.1)]; $[\alpha]_D$ +56.5° (*c* 0.1 in $CHCl_3$); δ_H 6.0—5.8 (3 H, m, 3 × C*H*=CH_2), 5.4—5.1 (6 H, m, 3 × CH=CH_2), 4.99 (1 H, dd, *J* 1.8, 9.6 Hz, 6-H), 4.75 (1 H, d, *J* 3.4 Hz, 1-H), 4.4—4.06 (m, 7 H, 3 × OCH_2 and 5-H), 3.66 (1 H, t, *J* 9.2 Hz, 3-H), 3.37—3.20 (5 H, m, OMe and 2- and 4-H), and 2.0 (3 H, s, NAc) (Found: C, 57.4; H, 8.0; N, 3.4. $C_{19}H_{29}NO_8$ requires C, 57.1; H, 7.3; N, 3.5%).

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