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Synthesis of carba-β-D- and L-idopyranosides by rearrangement of unsaturated sugars

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Abstract

The triisobutylaluminium- (TIBAL) and titanium(IV)-promoted conversions of 6-deoxyhex-5-enopyranosides into highly functionalised cyclohexane derivatives provide intermediates for the synthesis of enantiomerically pure carba-sugars. The preparation of enantiomerically pure methyl carba-β-D-idopyranoside **1**, methyl carba-β-L-idopyranoside **2** and 5′a-carbadisaccharide **3** is reported. © 2000 Elsevier Science Ltd. All rights reserved.

1. Introduction

Complex oligosaccharides are currently emerging as promising therapeutic agents.[1–4] A possible drawback of such drugs is their vulnerability towards in vivo degradation by glycosidases and this has prompted the search for non-hydrolysable oligosaccharide mimetics. Carba-sugars[5] are carbocyclic sugar mimetics in which the endocyclic oxygen atom of the sugar is replaced by a methylene group. As a consequence of this substitution, carba-sugars are hydrolytically stable analogues of their parent sugars and are of interest as tools for the elucidation of the (spatial) role of sugar hydroxyl groups in biological systems.[6] Furthermore, it is possible to substitute the pyranoid-ring oxygen of one sugar in an oligosaccharide with a methylene group, whilst retaining significant biological activity.[7] Carba-oligosaccharides as mimetics of biologically important systems are, therefore, attractive synthetic targets.

It is now well recognised that idose residues (as L-iduronic acid) play a crucial role in determining the biological activity of glycosaminoglycans.[8] The critical importance of L-iduronic acid in the antithrombin III binding sequence of heparin[9–11] and FGF-2 binding of heparan sulfate[12] has been specifically demonstrated. This has prompted us to explore the synthesis of carba-idopyranosyl derivatives in general.

Ogawa has reported the synthesis of racemic carba-β-idopyranose[13,14] based on cyclohexane derivatives from the Diels–Alder cycloaddition of furan and acrylic acid. Paulsen reported the synthesis of carba-α- and β-L-idopyranoses by anionic cyclisation of acyclic carbohydrates using an intramolecular

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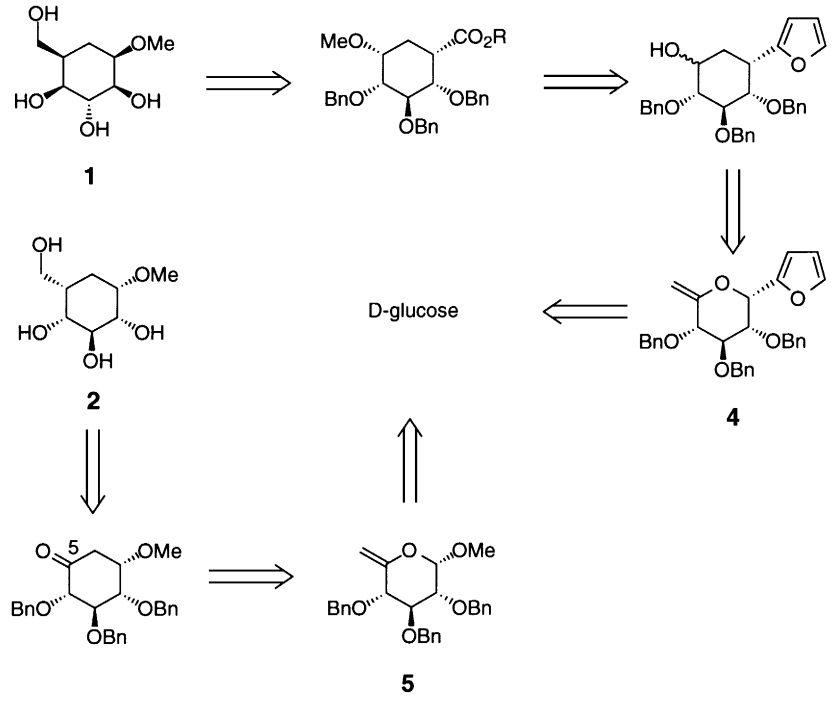
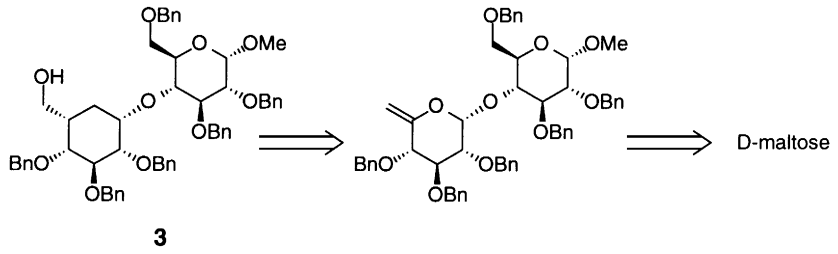
Horner–Emmons olefination.[15] A protected carba-β-D-idopyranose was obtained as a minor diastereomer by radical cyclisation of an acyclic carbohydrate.[16] Perhaps the most elegant syntheses of carba-β-L-idopyranose were provided by Ferrier[17] and Barton;[18] the direct rearrangement of 6-deoxyhex-5-enopyranoses into enantiomerically pure cyclohexanones (the so-called Ferrier-II reaction[19]) was followed by homologation to give the protected carba-sugars. This homologation strategy, coupled with our recent developments in the triisobutylaluminium- (TIBAL)[20–22] and titanium(IV)[23]-promoted conversion of carbohydrates into carbocycles[24] has led us to a novel and versatile synthesis of enantiomerically pure carba-idopyranosides. This paper reports: (i) the synthesis of both enantiomers of partially protected carba-β-D- **1** and L-idopyranosides **2** from D-glucose; and (ii) the synthesis of 5′a-carbadisaccharide **3** from D-maltose.

The synthesis of methyl carba-β-D-idopyranoside **1** requires carbocyclisation of unsaturated *C*-glycoside **4**, followed by unmasking of the carboxylic acid and reduction (Scheme 1). Synthesis of methyl carba-β-L-idopyranoside **2** requires carbocyclisation of the 6-deoxyhex-5-enopyranoside **5** followed by stereoselective introduction of the hydroxymethyl group at C-5; synthesis of the 5′a-carbadisaccharide **3** would follow an analogous strategy (Scheme 2).



Scheme 1.

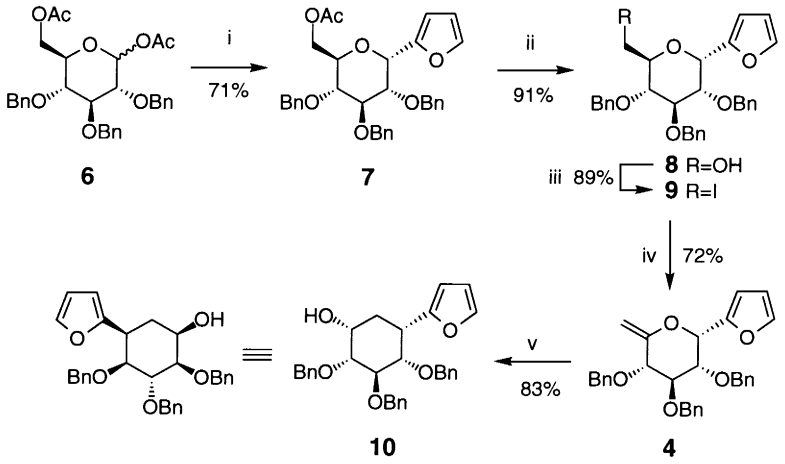


Scheme 2.

2. Results and discussion

2.1. Synthesis of methyl carba-β-D-idopyranoside 1

Synthesis of the unsaturated *C*-glycoside **4** required the introduction of furan at C-1 of D-glucopyranose which was conveniently achieved by simple glycosylation of furan with 1,6-di-*O*-acetyl-2,3,4-tri-*O*-benzyl-D-glucopyranose **6**[25] in the presence of TMSOTf[26] to give the α-*C*-glycoside **7** in 71% yield. Standard deacetylation of **7** and iodination using Garegg's conditions[27] gave iodide **9** which underwent elimination with sodium hydride in DMF to afford the alkene **4** (58% yield from **7**). We recently reported that *C*-glycosides of 6-deoxyhex-5-enopyranoses undergo smooth TIBAL-mediated carbocyclisation provided that the aglycon is sufficiently electron-donating in nature.[22] Furan is known to stabilise α-carbocations[28] and we, therefore, anticipated that alkene **4** would undergo TIBAL-induced rearrangement. Indeed, when **4** was treated with TIBAL, the desired cyclohexane **10** was obtained as the major product in 83% yield (Scheme 3).



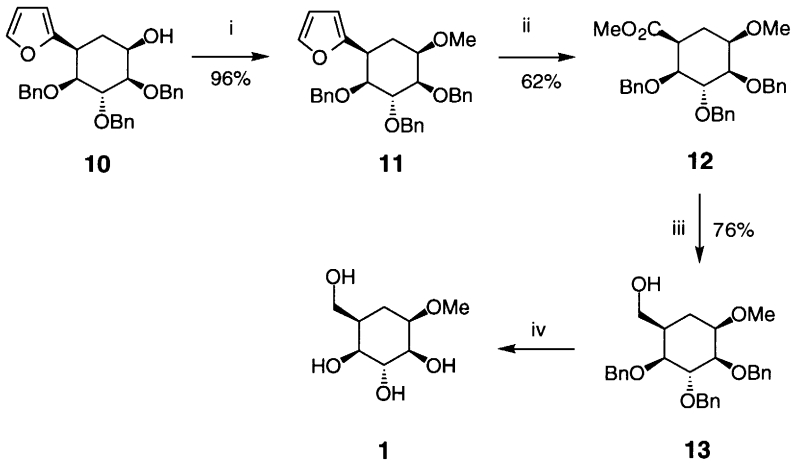
Scheme 3. (i) Furan, 4 Å molecular sieves, TMSOTf, CH_3CN, −40°C→−20°C; (ii) MeONa, MeOH, rt, 2 h; (iii) I_2, PPh_3, imidazole, toluene, 70°C, 30 min; (iv) NaH, DMF, rt, 2 h; (v) TIBAL, toluene, 50°C, 30 min

Methylation of alcohol **10** with methyl iodide in DMF containing sodium hydride gave the methyl ether **11** (96% yield). Oxidative cleavage of the furan **11** with ozone revealed the masked carboxylic acid which was immediately methylated to give the fully protected methyl carba-β-D-iduronate **12** in 62% yield. This, therefore, constitutes a new synthetic approach to the synthesis of carba-sugar analogues of iduronic acid. Reduction of the ester **12** with lithium aluminium hydride then gave methyl carba-β-D-idopyranoside **13** in 76% yield (Scheme 4).†

2.2. Synthesis of methyl carba-β-L-idopyranoside 2

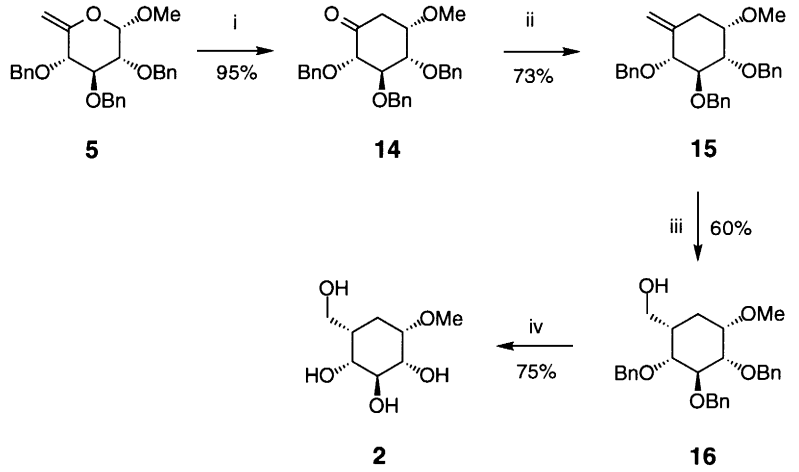
The ketone **14** was obtained in excellent yield by the Ti(IV)-promoted non-reductive rearrangement of the readily available 6-deoxyhex-5-enopyranoside **5** as previously reported.[23] Standard synthetic strategies[18] for one-carbon homologation of ketone **14** using Wittig reagents were unsuccessful due to preferential elimination of the methoxy group. However, exocyclic alkene **15** was obtained in 73% yield

† Hydrogenolysis of a small quantity of **13** afforded methyl carba-β-D-idoside **1** which showed identical ^1H and ^{13}C NMR spectra to its enantiomer **2**.



Scheme 4. (i) MeI, NaH, DMF, rt, 1 h; (ii) O_3, CH_2Cl_2, MeOH, −78°C, 15 min; then $KHCO_3$, MeI, DMF, rt, 5 h; (iii) $LiAlH_4$, Et_2O, rt, 4 h; (iv) H_2, Pd/C, MeOH, rt, 2 h

by methylenation of ketone **14** with the Tebbe reagent.[29] Hydroboration of alkene **15** with $BH_3 \cdot THF$ occurred from the less hindered β-face and after oxidative work-up with $NaOH/H_2O_2$ gave the protected methyl carba-β-L-idopyranoside **16** in 60% yield. Finally, debenzylation of **16** by hydrogenation over Pd/C afforded methyl carba-β-L-idopyranoside **2** in 75% yield (Scheme 5).

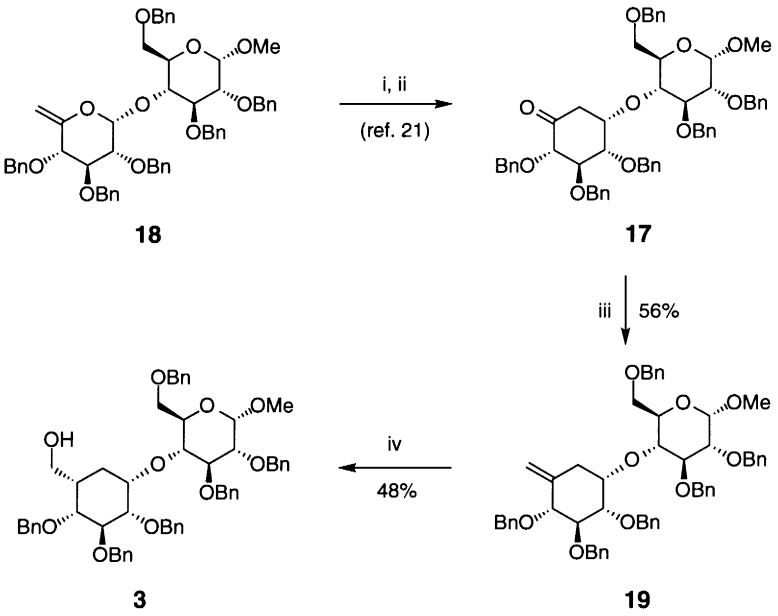


Scheme 5. (i) $Cl_3TiOiPr$, CH_2Cl_2, −78°C, 15 min (see Ref. 23); (ii) Tebbe reagent, toluene, THF, pyr., −45°C→rt; (iii) $BH_3 \cdot THF$, THF, rt, 1 h; then NaOH, H_2O_2, 0°C→rt, 1 h; (iv) H_2, Pd/C, MeOH, rt, 2 h

*2.3. Synthesis of 5′a-carbadisaccharide **3***

The key intermediate ketone **17** was obtained from methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4-tri-*O*-benzyl-6-deoxy-α-D-*xylo*-hex-5-enopyranosyl)-α-D-glucopyranoside **18** by TIBAL-promoted reductive rearrangement and oxidation with pyridinium chlorochromate (PCC) as previously reported.[21] Methylenation of ketone **17** with the Tebbe reagent gave the exocyclic alkene **19** in 56% yield, which underwent hydroboration with $BH_3 \cdot THF$ and subsequent oxidation with $NaOH/H_2O_2$ to give the protected 5′a-carbadisaccharide **3** in 48% isolated yield (Scheme 6). Analysis of vicinal coupling

constants in the ^{1}H NMR spectra for 5′a-carbadisaccharide **3** indicated that the carba-β-L-idopyranosyl ring adopted a $^1C_4$-conformation [all *trans*-diaxial couplings were observed for H5′a(ax): $J_{1',5'a(ax)}$ 11.3 and $J_{5',5'a(ax)}$=$J_{5'a(ax),5'a(eq)}$ 12.0 Hz].



Scheme 6. (i) TIBAL, toluene, 50°C, 4 h; then PCC, DCM (see Ref. 21); (iii) Tebbe reagent, THF, pyr., −45°C→rt; (iv) BH_3·THF, THF, rt; then NaOH, H_2O_2, 0°C→rt

3. Conclusions

The synthesis of methyl carba-β-D-idopyranoside **1** from D-glucose highlights the use of furan as: (i) a suitable aglycon donor for the TIBAL-promoted rearrangement of alkene **4**; and (ii) a masked carboxylic acid. The synthetic strategy (Schemes 3 and 4) conveniently avoids the use of the more expensive L-glucose (following the synthetic strategy illustrated in Scheme 5, used for the enantiomeric D-idopyranoside **2**).

Preparation of carba-L-idopyranose **2** from D-glucose demonstrates the use of titanium(IV)-promoted conversion of carbohydrates into carbocycles.

This work establishes a new methodology for the synthesis of carba-sugar analogues of iduronic acid (**12** is a fully protected methyl carba-β-D-iduronate and **16** is a presursor of carba-L-iduronic acid).

This preparation of **3** completes the synthesis of a 5′a-carbadisaccharide using the direct TIBAL-promoted rearrangement of unsaturated disaccharide **18** as the key step. We are currently exploring the application of this methodology to the direct synthesis of carba-oligosaccharides as mimetics of biologically active heparin fragments.

4. Experimental

4.1. General

Melting points were recorded on a Büchi 510 apparatus and are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 digital polarimeter with a path length of 1 dm. Mass spectra were recorded on a Nermag R10-10 spectrometer, using chemical ionisation with ammonia. Elemental analyses were performed by the Service d'Analyse de l'Université Pierre et Marie Curie, 75252 Paris Cedex 05, France. NMR spectra were recorded on a Bruker AM-400 (400 and 100.6 MHz, for ^{1}H and ^{13}C, respectively) or a Bruker AC-250 (250 and 63 MHz, for ^{1}H and ^{13}C, respectively) using TMS as internal standard. TLC was performed on silica gel 60 F_{254} (Merck) and developed by charring with conc. H_2SO_4. Flash column chromatography was performed using silica gel 60 (230–400 mesh, Merck).

4.2. 2-(6-O-Acetyl-2,3,4-O-benzyl-α-D-glucopyranosyl)furan 7

1,6-*O*-Acetyl-2,3,4-*O*-benzyl-α,β-D-glucopyranose **6**[25] (1.5 g, 2.81 mmol) was dissolved in anhydrous acetonitrile (20 mL) containing 4 Å molecular sieves (3 g) and furan (0.65 mL, 8.43 mmol) at room temp. under argon. After stirring for 1 h, the mixture was cooled to −40°C and TMSOTf (0.69 mL, 3.37 mmol) was added dropwise. The mixture was then allowed to warm to −20°C when TLC (AcOEt:cyclohexane, 3:7) indicated completion of the reaction. Triethylamine (1 mL) was added and the mixture was warmed to room temp. and filtered (Celite®). DCM (250 mL) was added and then washed with water (2×50 mL). The solvent was removed in vacuo to afford a residue which was purified by flash chromatography (AcOEt:cyclohexane, 1:9) to give 2-(6-*O*-acetyl-2,3,4-*O*-benzyl-α-D-glucopyranosyl)furan **7** (1.08 g, 71%) as a colourless solid: mp 107°C (Et_2O/pentane); $[\alpha]_D^{20}$ +66 (*c* 1.0, $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 7.39 (d, 1H, $J_{A,B}$=1.8 Hz, H-A), 7.34–7.13 (m, 15H, H arom.), 6.47 (d, 1H, $J_{C,B}$=3.3 Hz, H-C), 6.28 (dd, 1H, H-B), 5.04 (d, 1H, $J_{1,2}$=6.4 Hz, H-1), 4.98 (d, 1H, *J*=10.7 Hz, -C*H*Ph), 4.82 (d, 1H, *J*=10.7 Hz, -C*H*Ph), 4.79 (d, 1H, *J*=10.7 Hz, -C*H*Ph), 4.60 (d, 1H, *J*=11.7 Hz, -C*H*Ph), 4.54 (d, 1H, *J*=11.7 Hz, -C*H*Ph), 4.49 (d, 1H, *J*=10.7 Hz, -C*H*Ph), 4.23–4.09 (m, 3H, H-3, H-6a, H-6b), 3.87 (dd, 1H, $J_{2,3}$=9.6 Hz, H-2), 3.60–3.52 (m, 1H, H-5), 3.49 (t, 1H, $J_{4,5}$=10.1 Hz, H-4), 1.95 (s, 3H, Ac); δ_C (63 MHz, $CDCl_3$) 170.7 (Ac), 150.3 (C-D), 142.9 (C-A), 138.6, 137.9, 137.8 (3×s, C-arom. quat.), 128.5–127.7 (15×d, Ph), 111.9 (C-C), 110.2 (C-B), 82.8 (C-3), 79.4 (C-2), 77.6 (C-5), 75.6, 75.1, 72.9 (3×t, *C*HPh), 71.6 (C-4), 70.0 (C-1), 63.3 (C-6), 20.9 (CH_3); *m/z* 560 $(M+NH_4)^+$; found: C, 72.90; H, 6.28; $C_{33}H_{34}O_7$ requires: C, 73.04; H, 6.31%.

4.3. 2-(2,3,4-O-Benzyl-α-D-glucopyranosyl)furan 8

A catalytic amount of sodium (20 mg) was added to a solution of **7** (765 mg, 1.41 mmol) in methanol (20 mL). After stirring at room temp. for 2 h, the solution was neutralised with IR 120 resin and filtered. The solvent was removed in vacuo and the residue was purified by flash chromatography (AcOEt:cyclohexane, 3:7) to afford 2-(2,3,4-*O*-benzyl-α-D-glucopyranosyl)furan **8** (640 mg, 91%) as a colourless oil: $[\alpha]_D^{20}$ +66 (*c* 1.2, $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 7.38 (d, 1H, $J_{A,B}$=1.5 Hz, H-A), 7.32–7.13 (m, 15H, H arom.), 6.47 (d, 1H, $J_{C,B}$=3.2 Hz, H-C), 6.28 (dd, 1H, H-B), 5.04 (d, 1H, $J_{1,2}$=6.5 Hz, H-1), 4.96 (d, 1H, *J*=10.9 Hz, -C*H*Ph), 4.82 (d, 1H, *J*=10.8 Hz, -C*H*Ph), 4.79 (d, 1H, *J*=11.1 Hz, -C*H*Ph), 4.60 (d, 1H, *J*=11.7 Hz, -C*H*Ph), 4.58 (d, 1H, *J*=10.9 Hz, -C*H*Ph), 4.56 (d, 1H, *J*=11.7 Hz, -C*H*Ph), 4.18 (t, 1H, $J_{3,4}$=9.4 Hz, $J_{3,2}$=9.4 Hz, H-3), 3.84 (dd, 1H, H-2), 3.75–3.52 (m, 2H, H-6a H-6b), 3.52 (t, 1H, $J_{4,5}$=9.3 Hz, H-4), 3.39 (dt, 1H, $J_{5,6}$=3.3 Hz, H-5), 1.67 (s, 1H, OH); δ_C (63 MHz, $CDCl_3$)

150.3 (C-D), 142.7 (C-A), 138.6, 137.9, 137.8 (3×s, C-arom. quat.), 128.3–127.5 (15×d, Ph), 111.5 (C-C), 110.0 (C-B), 82.5 (C-3), 79.4 (C-2), 77.7 (C-5), 75.4, 75.0, 73.5 (3×t, *C*HPh), 72.8 (C-4), 69.8 (C-1), 62.0 (C-6); *m/z* 518 $(M+NH_4)^+$; found: C, 74.32; H, 6.49; $C_{31}H_{32}O_6$ requires: C, 74.38; H, 6.44%.

*4.4. 2-(2,3,4-*O*-Benzyl-6-deoxy-6-iodo-α-*D*-glucopyranosyl)furan **9***

Imidazole (0.21 g, 3.07 mmol), triphenylphosphine (0.40 g, 1.53 mmol) and iodine (0.29 g, 1.13 mmol) were added to a solution of alcohol **8** (512 mg, 1.02 mmol) in anhydrous toluene (5 mL) at room temp. under argon. After stirring at 70°C for 30 min, TLC (AcOEt:cyclohexane, 1:2) indicated completion of the reaction. The reaction mixture was cooled to room temp. and saturated sodium thiosulfate (5 mL) was added. After stirring for 5 min, AcOEt (25 mL) was added and the organic layer was then washed with water (15 mL), dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (AcOEt:cyclohexane, 8:92) to afford 2-(2,3,4-*O*-benzyl-6-deoxy-6-iodo-α-D-glucopyranosyl)furan **9** (556 mg, 89%) as a colourless oil which was used immediately: δ_H (250 MHz, $CDCl_3$) 7.38 (d, 1H, $J_{A,B}$=1.7 Hz, H-A), 7.29–7.11 (m, 15H, H arom.), 6.47 (d, 1H, $J_{C,B}$=3.2 Hz, H-C), 6.28 (dd, 1H, H-B), 5.08 (d, 1H, $J_{1,2}$=6.5 Hz, H-1), 4.96 (d, 1H, *J*=10.9 Hz, -C*H*Ph), 4.90 (d, 1H, *J*=10.8 Hz, -C*H*Ph), 4.77 (d, 1H, *J*=10.8 Hz, -C*H*Ph), 4.69 (d, 1H, *J*=10.7 Hz, -C*H*Ph), 4.59 (d, 1H, *J*=11.7 Hz, -C*H*Ph), 4.51 (d, 1H, *J*=11.7 Hz, -C*H*Ph), 4.22 (t, 1H, $J_{3,4}$=$J_{3,2}$=9.1 Hz, H-3), 3.86 (dd, 1H, H-2), 3.42 (t, 1H, $J_{4,5}$=9.1 Hz, H-4), 3.33 (d, 2H, $J_{6,5}$=3.5 Hz, H-6), 3.05 (dt, 1H, H-5); δ_C (63 MHz, $CDCl_3$) 150.5 (C-D), 142.9 (C-A), 138.6, 138.1, 137.9 (3×s, C-arom. quat.), 128.5–127.7 (15×d, Ph), 111.8 (C-C), 110.2 (C-B), 82.4 (C-3), 81.7 (C-2), 79.6 (C-5), 75.6, 75.5, 73.0 (3×t, *C*HPh), 71.4 (C-4), 69.9 (C-1), 8.9 (C-6); *m/z* 628 $(M+NH_4)^+$.

*4.5. 2-(2,3,4-Tri-*O*-benzyl-6-deoxy-α-*D*-xylo-hex-5-enopyranosyl)furan **4***

Sodium hydride (350 mg, 8.7 mmol, 60% in mineral oil) was added to a vigorously stirred solution of iodide **9** (533 mg, 0.87 mmol) in anhydrous DMF (5 mL) at room temp. After 2 h, TLC (toluene:AcOEt, 98:2) indicated completion of the reaction. The reaction mixture was cooled to 0°C and methanol (30 mL) was added dropwise. The solvent was removed in vacuo and the residue was partitioned between DCM (50 mL) and water (50 mL). The aqueous layer was extracted with DCM (2×50 mL) and the combined extracts were washed with brine (50 mL), dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (toluene:AcOEt, 9:1) to afford 2-(2,3,4-tri-*O*-benzyl-6-deoxy-α-D-*xylo*-hex-5-enopyranosyl)furan **4** (302 mg, 72%), as a colourless oil: $[\alpha]_D^{20}$ −42 (*c* 1.3, $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 7.34–7.13 (m, 16H, H arom.+H-A), 6.39 (d, 1H, $J_{C,B}$=3.4 Hz, H-C), 6.28 (dd, 1H, $J_{B,A}$=1.8 Hz, H-B), 5.12 (d, 1H, $J_{1,2}$=4.8 Hz, H-1), 4.72 (d, 1H, *J*=11.4 Hz, -C*H*Ph), 4.69 (s, 2H, -CH_2Ph), 4.64 (d, 1H, *J*=11.9 Hz, -C*H*Ph), 4.61 (s, 1H, H-6a), 4.55 (s, 1H, H-6b), 4.54 (d, 1H, *J*=10.8 Hz, -C*H*Ph), 4.49 (d, 1H, *J*=10.8 Hz, -C*H*Ph), 4.01–3.82 (m, 3H, H-2, H-3, H-4); δ_C (63 MHz, $CDCl_3$) 154.5 (C-5), 142.3–110.0 (22C arom.), 94.2 (C-6), 81.0, 78.9, 78.2, 74.4, 73.7, 72.6, 71.9; *m/z* 500 $(M+NH_4)^+$; found: C, 77.08; H, 6.36; $C_{31}H_{30}O_5$ requires: C, 77.15; H, 6.27%.

*4.6. 2-[1D-(1,2,4,5/3)-2,3,4-Tri-*O*-benzyl-2,3,4,5-tetrahydroxy-cyclohexyl]furan **10***

TIBAL (2.1 mL, 2.1 mmol, 1 M in toluene) was added to a stirred solution of **4** (200 mg, 0.41 mmol) in anhydrous toluene (2 mL) at room temp. under argon. The mixture was heated at 50°C for 30 min, when TLC (AcOEt:cyclohexane, 3:7) indicated completion of the reaction. The mixture was cooled to room temp. and water (5 mL) was added dropwise over 15 min. AcOEt (5 mL) was added and the aqueous

layer was extracted with AcOEt (2×10 mL). Combined extracts were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (cyclohexane:AcOEt, 9:1) to afford 2-[1D-(1,2,4,5/3)-2,3,4-tri-*O*-benzyl-2,3,4,5-tetrahydroxy-cyclohexyl]furan **10** (167 mg, 83%), as a colourless oil: $[\alpha]_D^{20}$ −7 (*c* 0.3, $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 7.32–6.99 (m, 16H, arom. H+H-A), 6.24 (dd, 1H, $J_{B,A}$=1.8 Hz, $J_{C,B}$=3.2 Hz, H-B), 6.24 (d, 1H, H-C), 4.57 (d, 1H, *J*=11.6 Hz, -C*H*Ph), 4.44 (d, 1H, *J*=12.0 Hz, -C*H*Ph), 4.36 (d, 1H, *J*=11.5 Hz, -C*H*Ph), 4.35 (d, 1H, *J*=12.0 Hz, -C*H*Ph), 4.15 (d, 1H, *J*=12.0 Hz, -C*H*Ph), 4.08 (d, 1H, *J*=12.0 Hz, -C*H*Ph), 3.90 (dddd, 1H, $J_{5,6a}$=12.0 Hz, $J_{5,OH}$=10.6 Hz, $J_{6b,5}$=3.8 Hz, $J_{5,4}$=2.7 Hz, H-5), 3.83–3.72 (m, 2H, H-2 H-3), 3.45 (br s, 1H, H-4), 3.18 (br d, 1H, $J_{1,6a}$=12.0 Hz, H-1), 2.39 (d, 1H, OH), 2.20 (q, 1H, $J_{6a,6b}$=12.0 Hz, H-6b), 1.84 (dt, 1H, $J_{1,6a}$=3.9 Hz, H-6a); δ_C (63 MHz, $CDCl_3$) 155.8 (C-D), 140.3 (C-A), 138.2, 137.8, 137.7 (3×s, C-arom. quat.), 128.3–127.7 (15×d, Ph), 110.2, 105.8 (C-C, C-B), 73.7, 72.4, 72.3, 72.3, 67.6, 35.5, 26.7; *m/z* 502 $(M+NH_4)^+$, 485 $(M+H)^+$; found: C, 75.75; H, 6.72; $C_{31}H_{32}O_5 \cdot \frac{1}{3}H_2O$ requires: C, 75.75; H, 6.90%.

*4.7. 2-[1D-(1,2,4,5/3)-2,3,4-Tri-*O*-benzyl-5-*O*-methyl-2,3,4,5-tetrahydroxy-cyclohexyl] furan **11***

Sodium hydride (17 mg, 0.42 mmol, 60% in mineral oil) was added to a vigorously stirred solution of **10** (101 mg, 0.21 mmol) and iodomethane (20 μL, 0.31 mmol) in anhydrous DMF (1 mL) at room temp. After 1 h, TLC (cyclohexane:AcOEt, 7:3) indicated completion of the reaction and methanol (5 mL) was added dropwise. The mixture was partitioned between Et_2O (10 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (3×10 mL) and the combined extracts dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (AcOEt:cyclohexane, 1:9), to afford 2-[1D-(1,2,4,5/3)-2,3,4-tri-*O*-benzyl-5-*O*-methyl-2,3,4,5-tetrahydroxy-cyclohexylfuran **11** (100 mg, 96%), as a colourless oil: $[\alpha]_D^{20}$ −12 (*c* 0.8, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.92–7.26 (m, 16H, arom. H+H-A), 6.37 (dd, 1H, $J_{B,A}$=1.8 Hz, $J_{C,B}$=3.2 Hz, H-B), 6.23 (d, 1H, H-C), 4.74 (s, 1H, -C*H*Ph), 4.68 (d, 1H, *J*=12.3 Hz, -C*H*Ph), 4.65 (d, 1H, *J*=12.3 Hz, -C*H*Ph), 4.55 (d, 1H, *J*=11.5 Hz, -C*H*Ph), 4.47 (d, 1H, *J*=11.6 Hz, -C*H*Ph), 4.29 (s, 1H, -C*H*Ph), 3.93 (t, 1H, $J_{3,2}$=$J_{2,4}$=3.8 Hz, H-3), 3.87–3.82 (m, 2H, H-2 H-4), 3.62 (dt, 1H, $J_{5,6a}$=10.7 Hz, $J_{5,4}$=$J_{5,6b}$=3.5 Hz, H-5), 3.34 (s, 3H, OMe), 3.28 (dt, 1H, $J_{1,6a}$=11.7 Hz, $J_{1,2}$=$J_{1,6b}$=3.3 Hz, H-1), 2.49 (q, 1H, $J_{6a,6b}$=11.7 Hz, H-6a), 1.94–1.86 (m, 1H, H-6b); δ_C (100 MHz, $CDCl_3$) 156.0 (C-D), 140.3 (C-A), 138.8, 138.6, 138.0 (3×s, C-arom. quat.), 129.7–127.0 (15×d, Ph), 110.4, 106.0 (C-C, C-B), 77.8, 72.8, 72.3, 72.0, 56.3, 36.2, 23.1; *m/z* 499 $(M+H)^+$; found: C, 77.03; H, 6.92; $C_{32}H_{34}O_5$ requires: C, 77.08; H, 6.87%.

*4.8. Methyl (carba-5a methyl 2,3,4-tri-*O*-benzyl-β-D-idopyranosyl)uronate **12***

Ozone gas was bubbled through a solution of furan **11** (92 mg, 0.18 mmol) in MeOH (3 mL) and CH_2Cl_2 (6 mL) at −78°C until the solution remained blue in colour. Oxygen was then bubbled through the solution for 1 min and then DMS (50 μL) was added. The solution was allowed to warm to room temp. and the solvent was removed in vacuo. The residue was dissolved in DMF (3 mL), and MeI (59 μL, 0.95 mmol) and $KHCO_3$ (111 mg, 1.11 mmol) were added. After stirring for 5 h at room temp., TLC (cyclohexane:AcOEt, 7:3) indicated completion of the reaction. The solvent was removed in vacuo and the residue was partitioned between CH_2Cl_2 (5 mL) and water (5 mL). The organic layer was dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (AcOEt:cyclohexane, 15:85), to afford methyl (carba-5a methyl 2,3,4-tri-*O*-benzyl-β-D-idopyranosyl)uronate **12** (56 mg, 62%), as a colourless oil: $[\alpha]_D^{20}$ −14 (*c* 0.5, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.40–7.26 (m, 15H, H arom.), 4.73 (d, 1H, *J*=12.3 Hz, -C*H*Ph), 4.63 (d, 1H, *J*=12.3 Hz, -C*H*Ph), 4.62 (d, 1H, *J*=12.0 Hz, -C*H*Ph), 4.58 (d, 1H, *J*=11.7 Hz, -C*H*Ph), 4.55 (d, 1H, *J*=11.7 Hz, -C*H*Ph), 4.48

(d, 1H, *J*=12.0 Hz, -C*H*Ph), 3.99 (br s, 1H, H-3), 3.88 (br s, 1H, H-2), 3.74 (br s, 1H, H-4), 3.69 (s, 3H, OMe), 3.50 (dt, 1H, $J_{5,6a}$=10.3 Hz, $J_{5,4}$=$J_{5,6b}$=3.3 Hz, H-5), 3.37 (s, 3H, OMe), 2.84 (dt, 1H, $J_{1,6a}$=10.8 Hz, $J_{1,2}$=$J_{1,6b}$=3.8 Hz, H-1), 2.49 (td, 1H, $J_{6a,6b}$=12.3 Hz, H-6a), 1.94–1.86 (m, 1H, H-6b); δ_C (100 MHz, $CDCl_3$) 173.0 (CO_2Me), 138.8, 138.4, 138.0 (3×s, C-arom. quat.), 128.4–127.3 (15×d, Ph), 77.6 (C-5), 76.3 (C-2), 73.1, 72.8, 72.3 (3×t, CH_2Ph), 56.6, 51.6 (2×OMe), 42.5 (C-1), 26.9 (C-6); *m/z* 491 $(M+H)^+$; found: C, 77.03; H, 6.92; $C_{30}H_{34}O_6$ requires: C, 77.08; H, 6.87%.

4.9. *Carba-5a methyl 2,3,4-tri*-O-*benzyl*-β-D-*idopyranoside* ***13***

$LiAlH_4$ (4 mg, 0.1 mmol) was added to a solution of ester **12** (18 mg, 0.04 mmol) in Et_2O (1 mL) at 0°C. After stirring at room temp. for 4 h, TLC (cyclohexane:AcOEt, 7:3) indicated completion of the reaction. The mixture was cooled to 0°C and quenched by the dropwise addition of water (5 mL). The aqueous layer was extracted with AcOEt (3×20 mL), washed with brine (2×10 mL) and the combined extracts were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (AcOEt:cyclohexane, 3:7), to afford carba-5a methyl 2,3,4-tri-*O*-benzyl-β-D-idopyranoside **13** (13 mg, 76%), as a colourless oil: $[\alpha]_D^{20}$ −3 (*c* 0.3, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.41–7.30 (m, 15H, H arom.), 4.83 (d, 1H, *J*=11.0 Hz, -C*H*Ph), 4.77 (d, 1H, *J*=11.5 Hz, -C*H*Ph), 4.76 (d, 1H, *J*=11.0 Hz, -C*H*Ph), 4.74 (s, 2H, -CH_2Ph), 4.61 (d, 1H, *J*=11.6 Hz, -C*H*Ph), 4.06 (t, 1H, $J_{3,2}$=$J_{3,4}$=7.5 Hz, H-3), 3.99 (ddd, 1H, $J_{6a,6b}$=11.6 Hz, *J*=7.0 Hz, *J*=3.5 Hz, H-6a), 3.69 (ddd, 1H, *J*=8.3 Hz, *J*=4.1 Hz, H-6b), 3.66 (dd, 1H, $J_{4,5}$=5.2 Hz, H-4), 3.58 (dt, 1H, $J_{1,5aa}$=5.8 Hz, $J_{1,5ab}$=$J_{1,2}$=2.9 Hz, H-1), 3.53 (dd, 1H, H-2), 3.44 (s, 3H, OMe), 2.30–2.23 (m, 1H, H-5), 2.07 (dt, 1H, $J_{5aa,5ab}$=14.4 Hz, $J_{1,5aa}$=$J_{5,5aa}$=5.8 Hz, H-5aa), 1.47 (ddd, 1H, $J_{5,5ab}$=4.9 Hz, H-5ab); δ_C (100 MHz, $CDCl_3$) 138.7, 138.6, 138.2 (3×s, C-arom. quat.), 128.4–127.6 (15×d, Ph), 77.3, 74.9, 73.0, 72.9, 64.5, 57.5, 38.9, 26.0; *m/z* 480 $(M+NH_4)^+$; found: C, 75.30; H, 7.22; $C_{29}H_{34}O_5$ requires: C, 75.29; H, 7.41%.

4.10. *Carba-5a methyl 2,3,4-tri*-O-*benzyl-6-deoxy*-α-D-xylo-*hex-5-enopyranoside* ***15***

Pyridine (25 μL) and then Tebbe reagent[29] (5 mL, 5 mmol, 1.0 M in toluene) [prepared from titanocene dichloride (6.2 g, 24.9 mmol) and trimethylaluminium (26 mL, 52 mmol, 2.0 M in toluene)] were added to a solution of ketone **14**[23] (750 mg, 1.68 mmol) in anhydrous toluene (3.5 mL) and THF (1.5 mL) at −45°C under argon. After stirring for 1 h at −45°C, 1 h at 0°C and finally, 30 min at room temp., TLC (cyclohexane:AcOEt, 5:1) indicated completion of the reaction. The reaction mixture was cooled to 0°C and aqueous sodium hydroxide (1 mL, 15%) was cautiously added dropwise. The mixture was warmed to room temp. and diluted with CH_2Cl_2 (100 mL). After stirring for 15 min the mixture was filtered through Celite® and $MgSO_4$ washing with CH_2Cl_2 (2×50 mL). The solvent was removed in vacuo and the residue was purified by flash chromatography (AcOEt:cyclohexane, 1:6) to afford carba-5a methyl 2,3,4-tri-*O*-benzyl-6-deoxy-α-D-*xylo*-hex-5-enopyranoside **15** (545 mg, 73%), as a white solid: mp 84°C (Et_2O/pentane); $[\alpha]_D^{20}$ −45 (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.90–7.43 (m, 15H, H arom.), 5.33 (d, 1H, $J_{6a,6b}$=1.4 Hz, H-6a), 4.99 (d, 1H, H-6b), 4.90 (s, 2H, -CH_2Ph), 4.81 (d, 1H, *J*=12.2 Hz, -C*H*Ph), 4.79 (d, 1H, *J*=12.1 Hz, -C*H*Ph), 4.76 (d, 1H, *J*=12.5 Hz, -C*H*Ph), 4.75 (d, 1H, *J*=11.5 Hz, -C*H*Ph), 3.91–3.89 (m, 2H, H-3, H-4), 3.63 (ddd, 1H, $J_{1,5aa}$=4.2 Hz, $J_{1,5ab}$=2.0 Hz, $J_{1,2}$=3.0 Hz, H-1), 3.55 (dd, 1H, $J_{2,3}$=9.0 Hz, H-2), 3.42 (s, 3H, OMe), 2.71 (dd, 1H, $J_{5aa,5ab}$=14.2 Hz, H-5aa), 1.96 (dd, 1H, H-5ab); δ_C (100 MHz, $CDCl_3$) 140.7 (C-5), 139.0, 138.6 (3×s, C-arom. quat.), 128.3–127.4 (15×d, Ph), 110.9 (C-6), 83.3, 82.9 (C-3,C-4), 82.2 (C-2), 76.0 (C-1), 75.7, 73.6, 72.7 (3×t, CH_2Ph), 56.7 (CH_3); *m/z* 462 $(M+NH_4)^+$, 445 $(M+H)^+$; found: C, 78.28; H, 7.28; $C_{29}H_{32}O_4$ requires: C, 78.34; H, 7.25%.

4.11. *Carba-5a methyl 2,3,4-tri*-O-*benzyl-β*-L-*idopyranoside* **16**

$BH_3 \cdot THF$ (0.45 mL, 0.45 mmol, 1.0 M in THF) was added to a solution of **15** (100 mg, 0.22 mmol) in anhydrous THF (1 mL) at room temp. under argon. After 1 h, TLC (cyclohexane:AcOEt, 3:1) indicated completion of the reaction. Ethanol (1.5 mL), NaOH (0.4 mL, 3 M) and aqueous hydrogen peroxide (0.3 mL, 30%) were added and the mixture was stirred for 1 h at room temp., when TLC (cyclohexane:AcOEt, 3:1) indicated complete oxidation. The reaction mixture was poured into ice-water (10 mL) and stirred for 5 min. The aqueous layer was extracted with CH_2Cl_2 (3×15 mL) and the combined extracts were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (AcOEt:cyclohexane, 3:7) to afford carba-5a methyl 2,3,4-tri-*O*-benzyl-β-L-idopyranoside **16** (62 mg, 60%), as a colourless oil: $[\alpha]_D^{20}$ +4 (*c* 0.6, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.41–7.30 (m, 15H, H arom.), 4.83 (d, 1H, *J*=11.0 Hz, -C*H*Ph), 4.77 (d, 1H, *J*=11.5 Hz, -C*H*Ph), 4.76 (d, 1H, *J*=11.0 Hz, -C*H*Ph), 4.74 (s, 2H, -CH_2Ph), 4.61 (d, 1H, *J*=11.6 Hz, -C*H*Ph), 4.06 (t, 1H, $J_{3,2}=J_{3,4}$=7.5 Hz, H-3), 3.99 (ddd, 1H, $J_{6a,6b}$=11.6 Hz, *J*=7.0 Hz, *J*=3.5 Hz, H-6a), 3.69 (ddd, 1H, *J*=8.3 Hz, *J*=4.1 Hz, H-6b), 3.66 (dd, 1H, $J_{4,5}$=5.2 Hz, H-4), 3.58 (dt, 1H, $J_{1,5aa}$=5.8 Hz, $J_{1,5ab}=J_{1,2}$=2.9 Hz, H-1), 3.53 (dd, 1H, H-2), 3.44 (s, 3H, OMe), 2.30–2.23 (m, 1H, H-5), 2.07 (dt, 1H, $J_{5aa,5ab}$=14.4 Hz, $J_{1,5aa}=J_{5,5aa}$=5.8 Hz, H-5aa), 1.47 (ddd, 1H, $J_{5,5ab}$=4.9 Hz, H-5ab); δ_C (100 MHz, $CDCl_3$) 138.7, 138.6, 138.2 (3×s, C-arom. quat.), 128.4–127.6 (15×d, Ph), 77.3, 74.9, 73.0, 72.9, 64.5, 57.5, 38.9, 26.0; *m/z* 480 $(M+NH_4)^+$; found: C, 78.21; H, 7.51; $C_{29}H_{34}O_5$ requires: C, 75.29; H, 7.41%.

4.12. *Carba-5a methyl β*-L-*idopyranoside* **2**

10% Pd/C (10 mg) was added to a solution of **16** (126 mg, 27 mmol) in methanol (10 mL). After stirring for 2 h at room temp. under hydrogen (1.5 atm), TLC (AcOEt:*i*PrOH:H_2O, 3:3:1) indicated completion of the reaction. The mixture was filtered (Celite®) and the solvent was removed in vacuo. The residue was purified by flash chromatography (CH_2Cl_2:MeOH, 9:1) to afford carba-5a methyl β-L-idopyranoside **2** (39 mg, 75%), as a colourless oil: $[\alpha]_D^{20}$ +8.0 (*c* 2.0, MeOH); δ_H (400 MHz, CD_3OD) 4.17–4.12 (m, 1H, H-2 H-3), 3.97 (dd, 1H, $J_{3,4}$=5.1 Hz, $J_{4,5}$=2.8 Hz, H-4), 3.92 (dd, 1H, $J_{6a,6b}$=10.2 Hz, $J_{6a,5}$=7.1 Hz, H-6a), 3.73 (dd, 1H, $J_{5,6b}$=6.6 Hz, H-6b), 3.76–3.71 (m, 1H, H-1), 3.57 (s, 3H, OMe), 2.26–2.18 (m, 1H, H-5), 1.87–1.82 (m, 2H, H-5a); δ_C (100 MHz, CD_3OD) 79.3 (C-1), 72.7 (C-4), 72.5 (C-2+C-3), 64.8 (C-6), 56.7 (OMe), 40.0 (C-5), 24.3 (C-5a); *m/z* 210 $(M+NH_4)^+$, 193 $(M+H)^+$; found: C, 49.62; H, 8.68; $C_8H_{16}O_5$ requires: C, 49.99; H, 8.39%.

4.13. *Methyl 2,3,6-tri*-O-*benzyl-4*-O-*(carba-5a 2,3,4-tri*-O-*benzyl-6-deoxy-α*-D-xylo-*hex-5-enopyranosyl)-α*-D-*glucopyranoside* **19**

Pyridine (31 μL) and then Tebbe reagent[29] (0.19 mL, 0.19 mmol, 1.0 M in toluene) were added to a stirred solution of methyl 2,3,6-tri-*O*-benzyl-4-*O*-[1D-(1,2,4/3)-2,3,4-tri-*O*-benzyl-1,2,3,4-tetrahydroxy-cyclohex-5-onyl]-α-D-glucopyranoside **17**[21] (83 mg, 0.1 mmol) in anhydrous THF (3 mL) at −45°C under argon. The reaction mixture was warmed to room temp. over 15 min and after a further 1 h, TLC (cyclohexane:AcOEt, 4:1) indicated remaining starting material (R_f 0.2) and formation of product (R_f 0.35). The reaction mixture was cooled to −15°C and aqueous sodium hydroxide (0.5 mL, 3 M) was cautiously added dropwise. The mixture was warmed to room temp. and filtered through Celite® washing with Et_2O (10 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (3×15 mL) and AcOEt (15 mL) and then the combined extracts were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (eluent gradient, 15–20%

AcOEt in cyclohexane) to afford methyl 2,3,6-tri-*O*-benzyl-4-*O*-(carba-5a 2,3,4-tri-*O*-benzyl-6-deoxy-α-D-*xylo*-hex-5-enopyranosyl)-α-D-glucopyranoside **19** (46 mg, 56%; 77% based on recovered **17**), as a colourless oil: $[\alpha]_D^{20}$ +1.2 (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.38–7.25 (m, 30H, H arom.), 5.21 (br s, 1H, H-6′a), 5.04 (d, 1H, *J*=11.4 Hz, -C*H*Ph), 4.97 (br s, 1H, H-6′b), 4.79–4.62 (m, 10H, 9×-C*H*Ph, H-1), 4.60 (d, 1H, *J*=12.0 Hz, -C*H*Ph), 4.56 (d, 1H, *J*=12.2 Hz, -C*H*Ph), 4.46 (dt, 1H, $J_{1',5'aa}$=5.8 Hz, $J_{1',2'}=J_{1',5'ab}$=2.8 Hz, H-1′), 4.00 (t, 1H, $J_{2,3}=J_{3,4}$=9.0 Hz, H-3), 3.85 (ddd, 1H, $J_{4,5}$=9.8 Hz, $J_{5,6b}$=5.0 Hz, $J_{5,6a}$=2.0 Hz, H-5), 3.80–3.79 (m, 2H, H-3′, H-4′), 3.72 (dd, 1H, H-4), 3.70 (dd, 1H, H-6a), 3.65 (dd, 1H, $J_{6a,6b}$=10.6 Hz, H-6b), 3.60 (dd, 1H, $J_{1,2}$=3.5 Hz, H-2), 3.59–3.56 (br m, 1H, H-2′), 3.44 (s, 3H, OMe), 2.83 (br dd, 1H, $J_{5'aa,5'ab}$=14.3 Hz, H-5′aa), 2.02 (br d, 1H, H-5′ab); δ_C (100 MHz, $CDCl_3$) 141.1 (C-5′), 138.8, 138.7, 138.7, 138.6, 138.2, 138.0 (6×s, C-arom. quat.), 128.5–127.1 (30×d, Ph), 112.9 (C-6′), 97.6 (C-1), 82.2 (C-3), 81.9, 81.3 (C-3′, C-4′), 80.8 (C-2′), 80.4 (C-2), 74.6 (C-1′), 74.5, 74.4, 73.3, 73.3, 72.8, 72.7 (6×t, *C*H_2Ph), 72.6 (C-4), 69.8 (C-5), 69.7 (C-6), 55.1 (Me), 32.3 (C-5′a); *m/z* 894.5 ($M+NH_4^+$, 100%); found: C, 77.02; H, 7.27; $C_{56}H_{60}O_9$ requires: C, 76.68; H, 6.90%. Further elution afforded recovered **17** (23 mg).

4.14. Methyl 2,3,6-tri-O-*benzyl-4*-O-*(carba-5a methyl 2,3,4-tri*-O-*benzyl-β*-L-*idopyranosyl)-α*-D-*glucopyranoside **3***

BH_3·THF (0.11 mL, 0.11 mmol, 1.0 M in THF) was added to a solution of **19** (47 mg, 0.054 mmol) in anhydrous THF (2 mL) at 0°C under argon and immediately warmed to room temp. After 1 h, TLC (cyclohexane:AcOEt, 4:1) indicated loss of starting material (R_f 0.4) and formation of product (R_f 0.1). Ethanol (0.4 mL) was added dropwise, followed by NaOH (0.1 mL, 3 M) and aqueous hydrogen peroxide (0.07 mL, 30%) and the mixture was stirred for 2 h at room temp., when TLC (cyclohexane:AcOEt, 3:1) indicated loss of starting material (R_f 0.25) and formation of a major product (R_f 0.3). Ice-water (10 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3×30 mL) and the combined extracts were dried ($MgSO_4$), filtered and the solvent was removed in vacuo. The residue was purified by flash chromatography (eluent gradient, 25–30% AcOEt in cyclohexane) to afford methyl 2,3,6-tri-*O*-benzyl-4-*O*-(carba-5a methyl 2,3,4-tri-*O*-benzyl-β-L-idopyranosyl)-α-D-glucopyranoside **3** (23 mg, 48%), as a colourless oil: $[\alpha]_D^{20}$ +33.3 (*c* 0.9, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.37–7.21 (m, 30H, H arom.), 4.99 (d, 1H, *J*=10.9 Hz, -C*H*Ph), 4.80–4.68 (m, 4H, 4×-C*H*Ph), 4.67 (d, 1H, $J_{1,2}$=3.7 Hz, H-1), 4.64–4.58 (m, 4H, 4×-C*H*Ph), 4.28 (dt, 1H, $J_{1',5'a(ax)}$=11.3 Hz, $J_{1',2'}=J_{1',5'a(eq)}$=3.5 Hz, H-1′), 4.22 (d, 1H, *J*=11.7 Hz, -C*H*Ph), 4.21 (d, 1H, *J*=12.7 Hz, -C*H*Ph), 4.06 (d, 1H, *J*=12.6 Hz, -C*H*Ph), 3.93 (t, 1H, $J_{2,3}=J_{3,4}$=9.0 Hz, H-3), 3.87 (br t, 1H, $J_{1',2'}=J_{2',3'}$=3.5 Hz, H-2′), 3.80 (dd, 1H, $J_{6a,6b}$=10.3 Hz, $J_{5,6a}$=3.0 Hz, H-6a), 3.77–3.71 (m, 4H, H-3′, H-4, H-5, H-6b), 3.58 (dd, 1H, H-2), 3.53–3.50 (m, 3H, H-4′, H-6′a, H-6′b), 3.46 (s, 3H, OMe), 1.97 (ddd, 1H, $J_{5',5'a(ax)}=J_{5'a(ax),5'a(eq)}$ 12.0 Hz, H-5′a(ax)), 1.90–1.83 (m, 1H, H-5′), 1.73 (ddd, 1H, $J_{5',5'a(eq)}$=3.5 Hz, H-5′a(eq)); δ_C (100 MHz, $CDCl_3$) 139.2, 138.6, 138.1, 138.0, 137.9, 137.9 (6×s, C-arom. quat.), 128.4–127.2 (30×d, Ph), 98.0 (C-1), 82.7 (C-3), 79.9 (C-2), 78.1 (C-1′), 76.9 (C-2′), 76.0 (C-4′), 75.4 (t, *C*H_2Ph), 74.1 (C-4), 73.4 (t, *C*H_2Ph), 73.3 (C-3′), 73.25, 73.2, 71.7, 71.1 (4×t, *C*H_2Ph), 70.0 (C-5), 68.7 (C-6), 64.9 (C-6′), 55.3 (Me), 37.8 (C-5′), 23.1 (C-5′a); *m/z* 912.4 ($M+NH_4^+$, 100%), 482.4 (22%); found: C, 75.00; H, 7.34; $C_{56}H_{62}O_{10}$ requires: C, 75.14; H, 6.98%.

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References

1. van Boeckel, C. A. A.; Petitou, M. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1671–1690.
2. Petitou, M.; Hérault, J.-P.; Bernat, A.; Driguez, P.-A.; Duchaussoy, P.; Lormeau, J.-C.; Herbert, J.-M. *Nature* **1999**, *398*, 417–422.
3. Sinaÿ, P. *Nature* **1999**, *398*, 377–378.
4. *Complex Carbohydrates in Drug Research*; Bock, K.; Claussen, H., Eds.; Munksgaard, 1994.
5. Suami, T.; Ogawa, S. *Adv. Carbohydr. Chem. Biochem.* **1990**, *48*, 21–90.
6. Suami, T.; Ogawa, S.; Takata, M.; Yasuda, K. *Chem. Lett.* **1985**, 719–722.
7. Tsuno, T.; Ikeda, C.; Numata, K.; Tomita, K.; Konishi, M.; Kawaguchi, H. *J. Antibiot.* **1986**, *39*, 1001–1003.
8. Casu, B.; Petitou, M.; Provasoli, M.; Sinaÿ, P. *Trends Biochem. Sci.* **1988**, *13*, 221–225.
9. Lindahl, U.; Bäckström, G.; Thunberg, L.; Leder, I. G. *Proc. Natl. Acad. Sci. USA* **1980**, *77*, 6551–6555.
10. Choay, J.; Lormeau, J.-C.; Petitou, M.; Sinaÿ, P.; Fareed, J. *Ann. New York Acad. Sci.* **1981**, *370*, 644–649.
11. Thunberg, L.; Bäckström, G.; Lindahl, U. *Carbohydr. Res.* **1982**, *100*, 393–410.
12. Kovensky, J.; Duchaussoy, P.; Bono, F.; Salmivirta, M.; Sizun, P.; Herbert, J.-M.; Petitou, M.; Sinaÿ, P. *Bioorg. Med. Chem.* **1999**, *7*, 1567–1580.
13. Ogawa, S.; Tsukiboshi, Y.; Iwasawa, Y.; Suami, T. *Carbohydr. Res.* **1985**, *136*, 77–89.
14. Ogawa, S.; Ara, M.; Kondoh, T.; Saitoh, M.; Masuda, R.; Toyokuni, T.; Suami, T. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1121–1126.
15. Paulsen, H.; von Deyn, W. *Liebigs Ann. Chem.* **1987**, 125–131.
16. Marco-Contelles, J.; Pozuelo, C.; Jimeno, M. L.; Martinez, L.; Martinez-Grau, A. *J. Org. Chem.* **1992**, *57*, 2625–2631.
17. Blattner, R.; Ferrier, R. J. *J. Chem. Soc., Chem. Commun.* **1987**, 1008–1009.
18. Barton, D. H. R.; Géro, S. D.; Cléophax, J.; Machado, A. S.; Quiclet-Sire, B. *J. Chem. Soc., Chem. Commun.* **1988**, 1184–1186.
19. Ferrier, R. J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1455–1458.
20. Das, S. K.; Mallet, J.-M.; Sinaÿ, P. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 493–496; *Angew. Chem*. **1997**, *109*, 513–516.
21. Pearce, A. J.; Sollogoub, M.; Mallet, J.-M.; Sinaÿ, P. *Eur. J. Org. Chem.* **1999**, 2103–2117.
22. Sollogoub, M.; Mallet, J.-M.; Sinaÿ, P. *Angew. Chem., Int. Ed. Engl.* **1999**, in press.
23. Sollogoub, M.; Mallet, J.-M.; Sinaÿ, P. *Tetrahedron Lett.* **1998**, *39*, 3471–3472.
24. Dalko, P. I.; Sinaÿ, P. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 773–777; *Angew. Chem*. **1999**, *111*, 819–823.
25. Frechet, J. M.; Schuerch, C. *J. Am. Chem. Soc.* **1972**, *94*, 604–609.
26. Dondoni, A.; Marra, A.; Scherrmann, M.-C. *Tetrahedron Lett.* **1993**, *34*, 7323–7326.
27. Garegg, P.; Samuelsson, B. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2866–2869.
28. Wennerberg, J.; Ek, F.; Hansson, A.; Frejd, T. *J. Org. Chem.* **1999**, *64*, 54–59.
29. Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611–3613.