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Chemoenzymatic synthesis of carbasugars from iodobenzene

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The versatile enantiopure *cis*-dihydrodiol metabolite **1**, formed by bacterial metabolism of iodobenzene, has been used for the synthesis of the pyranose carbasugars (pseudosugars) carba-β-D-altropyranose **2**, carba-α-L-galactopyranose **3**, carba-β-D-idopyranose **4** and carba-β-L-glucopyranose **5**. Substitution of the iodine atom by a carbomethoxy group, stereoselective catalytic hydrogenation of an α,β-unsaturated ester, and regioselective inversion of one or two allylic chiral centres are the key steps used in the synthesis of carbasugars **2**–**5**. The relative and absolute configurations of compounds **2**–**5** were established by a combination of stereochemical correlation, X-ray crystallography and ^{1}H-NMR spectroscopy.

Introduction

A wide range of *cis*-dihydrodiol metabolites has been reported as a result of toluene dioxygenase (TDO)-catalysed asymmetric dihydroxylation of monocyclic arene substrates, using mutant and recombinant strains of bacteria.[1–8] The constitutive mutant strain, *Pseudomonas putida* UV, has proved to be particularly successful and to date more than 50 enantiopure *cis*-dihydrodiol metabolites of mono-substituted benzene substrates have been isolated. The *cis*-dihydrodiol metabolite of fluorobenzene was exceptional – the only member of the series with a lower enantiomeric excess (ee) value (60–70%).[9] Although, enantiopure *cis*-dihydrodiols have been widely utilized in synthesis,[1–8] the majority of reports have focused on *cis*-dihydrodiols of toluene, chlorobenzene and bromobenzene as synthetic precursors. The *cis*-dihydrodiol derivative **1**, first reported in 1991 as a bacterial metabolite of iodobenzene,[10] is undoubtedly the most synthetically versatile *cis*-dihydrodiol derivative of the halogenated benzene substrates. However, owing to its commercial unavailability and less stable nature,[11] *cis*-dihydrodiol **1** has received relatively little attention as a synthetic precursor.[9,12–17] Having recently been able to produce large quantities of iodo-substituted benzene *cis*-dihydrodiols, during a single biotransformation, using in-house large-scale fermenters (100–150 L), a programme designed to exploit its particular advantages over other substituted *cis*-dihydrodiols has been undertaken.

One of the major advantages of *cis*-dihydrodiol **1** is the ease of replacement of the iodine atom by other atoms or groups by single-step substitution, using hydrogenolysis or Stille coupling (*e.g.* replacement by vinyl, ethynyl, alkyl, allyl, cyano, sulfanyl), without OH group protection, which has resulted in the availability of a much wider range of *cis*-dihydrodiols.[9] Furthermore, the relatively large steric requirements of the iodine atom, can be utilized to direct regio- and stereo-selectivity of TDO-catalysed *cis*-dihydroxylation of substituted iodobenzene substrates. This selectivity has facilitated the synthesis of new regio- and stereo-isomers of the *cis*- and *trans*-dihydrodiol isomers of iodobenzene.[13,17–21]

The synthetic advantages of iodobenzene *cis*-dihydrodiol **1**, allied to its improved availability, prompted this study to exploit its potential in the synthesis of four carbasugars (pseudosugars) **2**–**5** (Scheme 1). Owing to the structural similarities of pyranose carbasugars with normal sugars, but with resistance of carbasugars to ring-opening (mutatarotation) and enzyme-catalysed hydrolysis, there has been an increasing interest in their synthesis as potential enzyme inhibitors.[22] The antibiotic carba-α-D-galactopyranose *ent*-**3** is one of the few carba-monosaccharides to have been obtained entirely by bacterial enzyme-catalysed synthesis.[23] The carba-oligosaccharide fermentation product, acarbose, was also found to be an enzyme inhibitor.[24] Carba-α-DL-glucopyranose, obtained by chemical synthesis, was found to be an inhibitor of a glucokinase enzyme.[25] The chemical syntheses of all 16 racemic carbasugars, and most of the enantiopure members of the series, have been reviewed.[26,26] Prior to this study, few enantiopure carbasugars had been synthesized from benzene *cis*-dihydrodiol precursors.[15,28]

Results and discussion

The enantiopure metabolite of iodobenzene, *cis*-(1*S*,2*S*)-1,2-dihydroxy-1,2-dihydro-3-iodocyclohexa-1,3-diene **1**, obtained using the mutant bacterial strain *P. putida* UV4, contains two chiral centres whose absolute configurations are identical to those found at the C-3 and C-4 positions in the pyranose carbasugars carba-β-D-altropyranose **2** and carba-α-L-galactopyranose **3**. Protection of *cis*-diol **1**, as the (3a*S*,7a*S*)-acetonide derivative **6** (98% yield), followed by *cis*-dihydroxylation using a catalytic quantity of osmium tetroxide in the presence of *N*-methylmorpholine *N*-oxide in a solution of acetone–water afforded the (3a*S*,4*R*,5*R*,7a*S*)-diol acetonide isomer **7** exclusively (87% yield), as reported (Scheme 1).[16] Using similar conditions to those employed earlier for the palladium-catalysed carbonylation of vinyl iodides [$Pd(OAc)_2$/NaOAc/MeOH] under one atmosphere of carbon monooxide,[13] the *cis*-diol acetonide **7** was converted to the (3a*R*,6*R*,7*R*,7a*S*)-α,β-unsaturated ester **8** (81% yield). The overall yield of the key intermediate **8**, obtained by the four-step sequence (iodobenzene → **1**→ **6** → **7** → **8**), was >60%.

Catalytic hydrogenation of α,β-unsaturated ester **8** (H_2, Rh/Al_2O_3, EtOH), under pressure (55 psi), was found to occur preferentially from the less hindered face (*trans* to the acetonide group) to give compound **14** as the major component of an inseparable mixture of diastereoisomers (3a*R*,4*S*,6*R*,7*R*,7a*S*) **10** (35%) and (3a*R*,4*R*,6*R*,7*R*,7a*S*) **14** (65%) (Scheme 2). The mixture was converted, directly, to the corresponding dibenzoates **11**/**15** in order to effect a chromatographic separation by multiple-elution Preparative Layer Chromatography (PLC) (silica-gel, EtOAc–hexane). The less polar dibenzoate **11** (R_f 0.2) was a crystalline compound (28% yield) whose structure and stereochemistry were determined by NMR spectroscopic and X-ray crystallographic analysis. Based on the known absolute configuration of acetonide **6**, an X-ray crystal structure analysis

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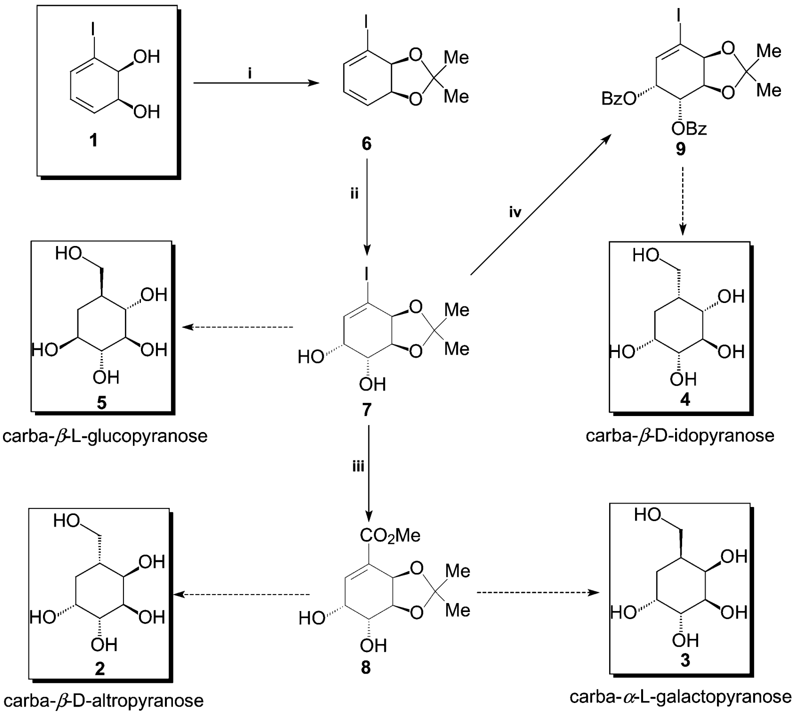
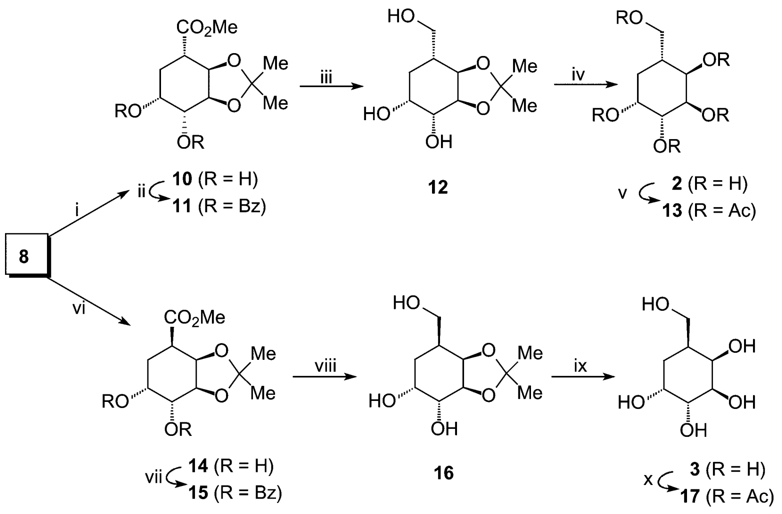


Scheme 1 *Reagents and conditions*: i 2,2-DMP (98%); ii OsO_4, Me_2CO, H_2O (87%); iii $Pd(OAc)_2$, CO, NaOAc, MeOH (81%); iv BzCl, C_6H_5N (95%).



Scheme 2 *Reagents and conditions*: i Rh/Al_2O_3, H_2; ii BzCl, C_5H_5N (28% from **8**); iii $LiAlH_4$ (74%); iv TFA (90%); v Ac_2O, C_5H_5N (78%); vi Rh/Al_2O_3, H_2; vii BzCl, C_5H_5N (56% from **8**); viii $LiAlH_4$ (76%); ix TFA (81%); x Ac_2O, C_5H_5N (84%).

showed that compound **11** had the (3a*R*,4*S*,6*R*,7*S*,7a*R*) absolute configuration (Fig. 1). The carbasugar ring had a pseudo-chair conformation with the carbomethoxy and benzoate groups *cis* to each other and *trans* to the acetonide group.

Reduction ($LiAlH_4$), of the three ester groups of compound (3a*R*,4*S*,6*R*,7*S*,7a*R*)-**11** yielded (3a*S*,4*R*,5*R*,7*R*,7a*R*)-acetonide triol **12** (74% yield). Acid-catalysed deprotection (TFA) gave (1*R*,2*R*,3*R*,4*R*,5*R*)-carba-β-D-altropyranose **2** ($[\alpha]_D$ + 44.3, 90% yield), which after purification by charcoal/Celite chromatography, was further characterized as the penta-acetate **13** ($[\alpha]_D$ −7.8, 78% yield, Scheme 2). Following a different approach, (1*S*,2*S*)-iodobenzene *cis*-dihydrodiol **1** had earlier been used as a precursor in an eight-stage synthesis of the penta-acetate derivative **13** of carba-β-D-altropyranose **2**.[15]

The absolute configurations at the five chiral centres, of dibenzoate **11** (Fig. 1), are identical to those found in the derived carbasugar **2**. Similarly, the X-ray crystal structure of compound **11** allowed the absolute configuration of the epimeric dibenzoate **15** to be rigorously assigned. A similar synthetic sequence was adopted, utilizing the more polar (3a*R*,4*R*,6*R*,7*S*,7a*R*)-dibenzoate **15** (R_f 0.15) as precursor to (3a*S*,4*R*,5*R*,7*S*,7a*R*)-acetonide triol **16** (76% yield),

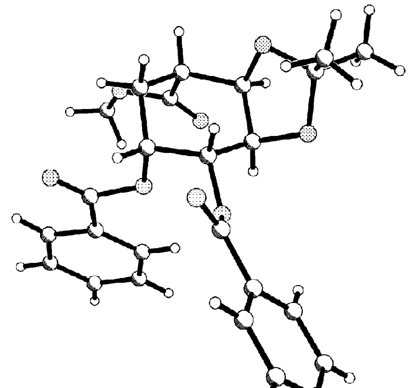
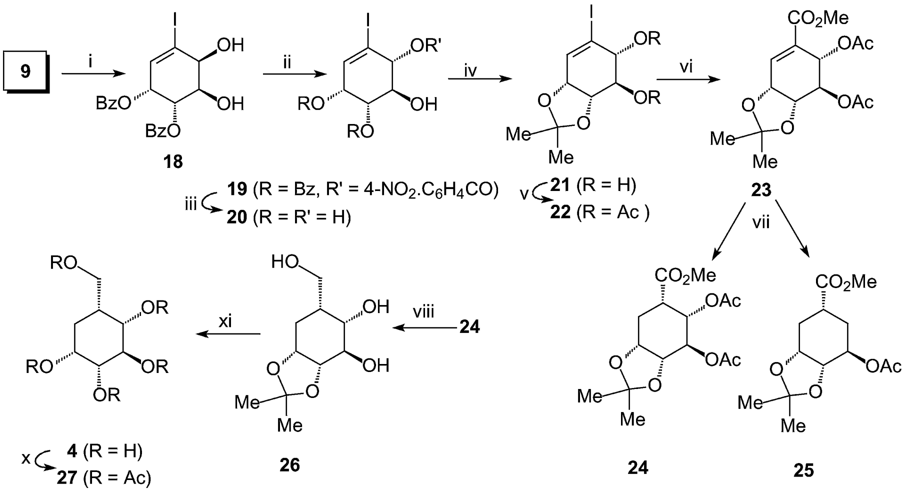


Fig. 1 X-Ray structure of dibenzoate (3a*R*,4*S*,6*R*,7*S*,7a*R*)-**11**.



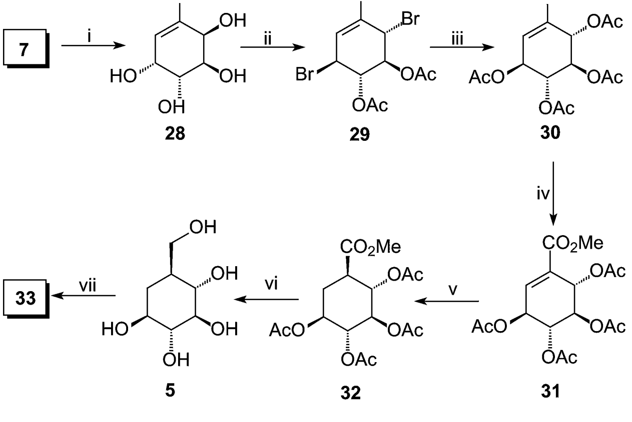
Scheme 3 *Reagents and conditions*: i HCl, MeOH (90%); ii PPh_3, DEAD, 4-$NO_2.C_6H_4CO_2H$ (70%); iii NaOH, MeOH (87%); iv 2,2-DMP, *p*-TSA (89%); v Ac_2O, C_5H_5N (95%); vi CO, $Pd(OAc)_2$, NaOAc, MeOH (87%); vii Rh/Al_2O_3, H_2, EtOH (40%), viii $LiAlH_4$, THF (81%); xi HCl, MeOH (79%), x Ac_2O, C_5H_5N (97%).

(1*R*,2*R*,3*R*,4*R*,5*S*)-carba-α-L-galactopyranose **3** ($[\alpha]_D$ −59.2, 81% yield), and (1*S*,2*R*,3*R*,4*R*,5*R*)-penta-acetate **17** ($[\alpha]_D$ −42.2, 84% yield; Scheme 2). Carbasugar **3** had earlier been synthesized in enantiopure form, and characterized as a penta-acetate **17**, using a different precursor and synthetic route.[28] Penta-acetates **13** and **17** were found to have comparable NMR and chiroptical data to the literature values.[15,28]

The synthesis of (1*R*,2*R*,3*R*,4*S*,5*R*)-carba-β-D-idopyranose **4**, from (1*S*,2*S*)-*cis*-dihydrodiol metabolite **1** (Schemes 1 and 3), required inversion of configuration at the C-2 chiral centre of compound **1**. This was achieved, indirectly, through the sequence **1** → **6** → **7** → **9** → **18** → **19** → **20** involving protection, dihydroxylation, protection, deprotection, inversion, and deprotection steps. Thus, treatment of the (3a*S*,4*R*,5*R*,7a*S*)-diol acetonide **7** with benzoyl chloride in pyridine gave (3a*R*,4*S*,5*R*,7a*S*)-dibenzoate **9** (95% yield, Scheme 1), which was, in turn, partially deprotected under acidic conditions to yield (1*S*,2*R*,5*S*,6*R*)-diol dibenzoate **18** (90% yield) (Scheme 3). Application of the Mitsunobu inversion procedure on diol **18** was found to occur, exclusively, at the allylic position, to give (1*R*,4*R*,5*S*,6*S*)-*p*-nitrobenzoate **19** (70% yield). Alkaline hydrolysis of triester **19** gave (1*R*,2*R*,3*S*,4*R*)-tetraol **20** (87% yield). The vicinal *cis*-diol moiety in intermediate **20** was protected by formation of (3a*S*,4*R*,5*R*,7a*R*)-acetonide **21** (89% yield), while the vicinal *trans*-diol group was protected as (3a*R*,4*S*,5*R*,7a*R*)-diacetate **22** (95% yield).

Palladium-catalysed carbonylation conditions (*cf.* **7** → **8**, Scheme 1) were employed to replace the iodine atom in compound **22** to give the required (3a*R*,6*S*,7*S*,7a*R*)-triester **23** (87% yield, Scheme 3). Catalytic hydrogenation of the alkene bond in compound **23**, under the conditions used earlier (**8** → **10** and **14**, Scheme 2), occurred from the less hindered face (*trans* to the acetonide and proximate ester groups) to yield (3a*R*,5*S*,6*S*,7*S*,7a*R*)-triester **24** (40% yield). Unfortunately, the hydrogenation of alkene **23** was accompanied by a competing hydrogenolysis reaction of the allylic acetyloxy group to give (3a*R*,5*S*,7*R*,7a*R*)-diester **25** (60% yield), which could be readily separated from the required triester **24** by chromatography. Reduction ($LiAlH_4$) of all three ester groups in compound **24** gave (3a*R*,4*R*,5*S*,6*R*,7a*R*)-triol **26** (81% yield), which was deprotected under acidic conditions to give the target molecule (1*R*,2*R*,3*R*,4*S*,5*R*)-carba-β-D-idopyranose **4** ($[\alpha]_D$ −6.1, 79% yield). This carbasugar was also characterized as the (1*R*,2*R*,3*R*,4*S*,5*R*)-penta-acetate **27** ($[\alpha]_D$ −14.0, 97% yield) (Scheme 3).

The last pyranose carbasugar, (1*S*,2*R*,3*R*,4*S*,5*S*)-carba-β-L-glucopyranose **5**, required the original (2*S*) absolute configuration to be inverted in the precursor, *cis*-1,2-dihydroxy-1,2-dihydro-3-iodocyclohexa-1,3-diene **1**. The first synthetic approach to carbasugar **5** involved inversion of configuration at two chiral allylic centres; a synthetic sequence involving concomitant inversion of configuration at these centres, in tetraol **28**, was developed (Scheme 4). Acid-catalysed deprotection, of *cis*-diol acetonide **7** (HCl/MeOH), gave (1*R*,2*R*,3*S*,4*S*)-*anti*-tetraol **28** (85% yield). Treatment of tetraol **28** with 1-bromocarbonyl-1-methylethyl acetate yielded the corresponding (1*S*,2*R*,5*S*,6*S*)-dibromo diacetoxy derivative **29** (87% yield), with inversion of configuration at both allylic chiral centres. The allylic bromine atoms in compound **29** were both replaced with acetate groups, with retention of configuration, using the Woodward–Winstein reaction conditions (AgOAc/AcOH/Ac_2O) to give (1*R*,2*S*,5*R*,6*S*)-tetra-acetate **30** (77% yield). Substitution of the iodine atom in compound **30** with a carbomethoxy group gave unsaturated (3*S*,4*R*,5*R*,6*S*)-tetra-acetate **31** (73% yield). Catalytic hydrogenation of compound **31** gave, exclusively, the saturated (1*R*,2*S*,3*R*,4*R*,5*S*)-tetra-acetate **32** (80% yield) as a crystalline compound. X-Ray crystal structure analysis of compound **32** showed that it exists in the chair conformation with the acetate and carbomethoxy groups all adopting equatorial positions and the overall structure having a (1*R*,2*S*,3*R*,4*R*,5*S*) absolute configuration, based on the known (1*S*) configuration of *cis*-dihydrodiol **1** (Fig. 2). The crystallographic asymmetric unit consists of two independent molecules which differ only in some torsion angles along the acetate and carbomethoxy side-chains.



Scheme 4 *Reagents and conditions*: i HCl/MeOH (85%); ii $AcOCMe_2$-COBr (87%); iii AgOAc/AcOH/Ac_2O (77%); iv $Pd(OAc)_2$, CO, NaOAc, THF, H_2O (73%); v Rh/Al_2O_3, H_2 (80%); vi $LiAlH_4$ (12%); vii Ac_2O (95%).

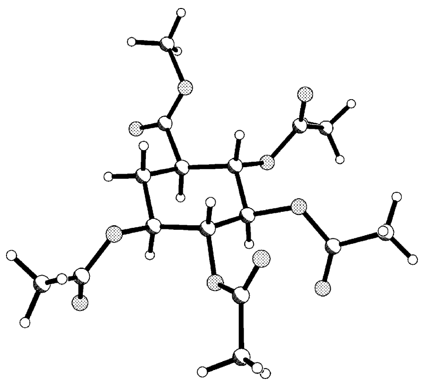


Fig. 2 X-Ray structure of (1*R*,2*S*,3*R*,4*R*,5*S*)-tetra-acetate **32**.

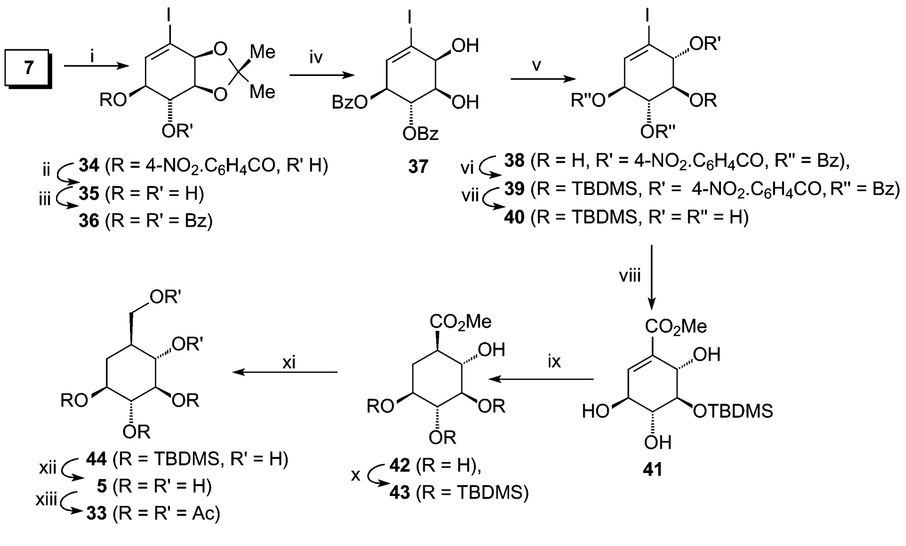
Reduction ($LiAlH_4$) of tetra-acetate **32** gave, after purification, the required (1*S*,2*R*,3*R*,4*S*,5*S*)-carba-β-L-glucopyranose **5** in low yield ($[\alpha]_D$ −6.1, 12%). Although the synthesis of carbasugar **5** from *cis*-dihydrodiol **1** was achieved in eight steps only, using the sequence shown in Scheme 4, a surprisingly low yield was obtained in the final step compared with similar reduction steps in the earlier carbasugar syntheses (**10** → **12**, **14** → **16**, **24** → **26**, Schemes 2 and 3).

In an attempt to obtain carbasugar **5** in a higher yield, an alternative synthetic strategy was developed. Two sequential Mitsunobu inversions, exclusively at the allylic alcohol centres, were the key steps of this synthesis (Scheme 5). Thus, employing the Mitsunobu conditions (*cf.* Scheme 3), the first allylic chiral centre in (3a*S*,4*R*,5*R*,7a*S*)-*cis*-diol acetonide **7** was inverted to give (3a*S*,4*S*,5*S*,7a*S*) 4-nitrobenzoate **34** (80% yield). Base-catalysed hydrolysis of ester **34** gave (3a*S*,4*R*,5*S*,7a*S*)-*trans*-diol acetonide **35** (82% yield), which was protected as the corresponding (3a*S*,4*S*,5*R*,7a*S*)-*trans*-dibenzoate acetonide **36** (93% yield). Removal of the acetonide protecting group from compound **36** under acidic conditions (HCl/MeOH) gave (1*S*,4*S*,5*R*,6*S*)-*cis*-diol dibenzoate **37** (86% yield). A further stereoselective Mitsunobu inversion at the second allylic chiral centre resulted in the formation of (1*R*,4*S*,5*S*,6*S*)-triester **38** (80% yield) which had the correct absolute configurations at the four chiral centres required for the synthesis of carba-β-L-glucopyranose **5** (Scheme 5).

The next phase of the synthesis involved the substitution of an iodine atom of a vinyl iodide with a carbomethoxy group, followed by a catalytic hydrogenation step, using similar conditions to those already discussed (*cf.* Schemes 1–3). In order to perform these steps in satisfactory yields with the required stereochemistry, several approaches were investigated. The optimal procedure involved protection of the free hydroxyl group of triester **38** as (1*R*,4*S*,5*R*,6*S*)-TBDMS ether **39** (93% yield) and deprotection *via* ester hydrolysis to give (1*S*,2*R*,3*S*,4*R*)-triol **40** (86% yield). The iodine atom in the latter compound was then replaced by a carbomethoxy group. The resulting α,β-unsaturated (3*S*,4*R*,5*R*,6*S*)-ester **41** (69% yield) was hydrogenated (H_2, Rh/Al_2O_3, EtOH) to give, exclusively, the saturated (1*R*,2*S*,3*R*,4*R*,5*S*)-ester **42** (80% yield). The 1*R* absolute configuration at the new chiral centre at C-1 in compound **42**, relative to the other chiral centres of known configuration, was established using ^{1}H-NMR spectroscopy. The coupling constant, between H-1 and H-2 hydrogens in hydrogenated ester **42** was found to be 10.0 Hz, which was similar to the coupling constant (11.0 Hz) found for the saturated methyl ester **32** whose stereochemistry was established by X-ray crystal structure analysis. Hence, a *trans* relationship between the methyl ester at C-1 and the adjacent hydroxyl at C-2 was established. Formation of (1*S*,2*S*,3*R*,4*R*,5*S*)-tri-TBDMS ester **43** (95% yield) followed by reduction ($LiAlH_4$) of the ester group gave partially protected alcohol derivative (1*S*,2*R*,3*R*,4*S*,5*S*)-tri-TBDMS ether **44** (82% yield) of the required pyranose carbasugar. Deprotection of compound **44** (HCl/MeOH) gave (1*S*,2*R*,3*R*,4*S*,5*S*)-carba-β-L-glucopyranose **5** ($[\alpha]_D$ −6.5, 78% yield) which was purified using a charcoal/Celite column and further characterized as (1*S*,2*S*,3*R*,4*R*,5*S*)-penta-acetate **33** ($[\alpha]_D$ −5.4, 97% yield). The chiroptical and spectroscopic data for compound **33** proved to be similar to that reported.[29]

Conclusion

Using the enantiopure (1*S*,2*S*)-*cis*-dihydrodiol metabolite of iodobenzene **1** as precursor, it has been possible to obtain the four pyranose carbasugars, carba-β-D-altrose **2**, carba-α-L-galactose **3**, carba-β-D-idose **4** and carba-β-L-glucose **5**. The opposite (1*R*,2*R*)-*cis*-dihydrodiol enantiomer of iodobenzene **1**, now available to us *via* chemoenzymatic routes, will allow the synthesis of the enantiomeric pseudosugars **2**, **3**, **4** and **5**. The synthetic methods thus described will allow 8 of the 32 possible pyranose carbasugars to be synthesized from the enantiomeric *cis*-dihydrodiol derivatives of iodobenzene. Chemoenzymatic methods have also recently been developed in our laboratories to produce all of the possible regioisomers and enantiomers of both *cis*- and *trans*-dihydrodiol metabolites from *cis*-dihydrodiol precursors, and this should allow the synthesis of an even wider range of carbasugars.



Scheme 5 *Reagents and conditions*: i PPh_3, DEAD, 4-$NO_2.C_6H_4CO_2H$ (80%); ii K_2CO_3, MeOH (82%); iii BzCl, C_5H_5N (93%); iv HCl, MeOH (86%); v PPh_3, DEAD, 4-$NO_2.C_6H_4CO_2H$ (80%); vi TBDMSTf (93%); vii NaOH, MeOH (86%); viii CO, $Pd(OAc)_2$, NaOAc, THF, H_2O (69%); ix Rh/Al_2O_3, H_2 (80%); x TBDMSTf (95%); xi $LiAlH_4$ (82%); xii TBAF, THF (78%); xiii Ac_2O, C_5H_5N (97%).

Experimental

^{1}H-NMR spectra were recorded at 300 MHz (Bruker Avance DPX-300) and at 500 MHz (Bruker Avance DRX-500). Chemical shifts (δ) are reported in ppm relative to $SiMe_4$ and coupling constants (J) are given in Hz. Mass spectra were recorded at 70 eV on a VG Autospec Mass Spectrometer, using a heated inlet system. Accurate molecular weights were determined by the peak matching method with perfluorokerosene as standard. Elemental microanalyses were obtained on a Perkin-Elmer 2400 CHN microanalyser. Optical rotation ($[\alpha]_D$) measurements were carried out with a Perkin-Elmer 214 polarimeter at ambient temperature (*ca.* 20 °C) and are expressed in units of 10^{-1} deg cm^2 g^{-1}. Flash column chromatography and PLC were preformed on Merck Kieselgel type (250–400 mesh) and PF $_{254/366}$ respectively. Merck Kieselgel 60F$_{254}$ analytical plates were used for TLC.

(3a*S*,7a*S*)-4-Iodo-2,2-dimethyl-3a,7a-dihydro-1,3-benzodioxole 6

To a stirred solution (0 °C) of *cis*-(1*S*,2*S*)-1,2-dihydroxy-3-iodocyclohexa-3,5-diene **1** (0.9 g, 3.8 mmol) in a mixture of acetone (5 cm^3) and 2,2-dimethoxypropane (5 cm^3) was added *p*-toluenesulfonic acid (0.075 g) and the reaction mixture was allowed to warm to room temperature. When the starting material had reacted completely (*ca.* 4 h, TLC analysis), the solvents were removed under reduced pressure, the residual material extracted with Et_2O (50 cm^3), and the ether extract washed with water (2 × 15 cm^3). The dried extract (Na_2SO_4) was evaporated and the crude product obtained was purified by flash column chromatography, to furnish the acetonide derivative **6** as colourless, viscous oil (1.03 g, 98%); (R_f 0.26, 10% diethyl ether in hexane); $[\alpha]_D$ +122 (c 0.97, $CHCl_3$); (Found: M$^+$, 278.0010; $C_9H_{11}{}^{127}IO_2$ requires 278.0009); δ_H (300 MHz, $CDCl_3$) 1.43, 1.45 [3H × 2, s, –C(Me)$_2$], 4.64 (1H, dd, $J_{7a,3a}$ 8.0, $J_{7a,7}$ 4.0, 7a-H), 4.73 (1H, d, $J_{3a,7a}$ 8.0, 3a-H), 5.78 (1H, dd, $J_{6,7}$ 10.0, $J_{6,5}$ 6.2, 6-H), 6.00 (1H, dd, $J_{7,6}$ 10.0, $J_{7,7a}$ 4.0, 7-H), 6.66 (1H, d, $J_{5,6}$ 6.2, 5-H); m/z (EI) 278 (M$^+$, 14%), 163 (34), 248 (12), 209 (54), 167 (22), 145 (24), 112 (87), 99 (23), 72 (10), 51 (17), 43 (100).

(3a*S*,4*R*,5*R*,7a*S*)-7-Iodo-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxole-4,5-diol 7

A solution of acetonide **6** (0.8 g, 2.88 mmol) in a mixture of acetone and water (5 : 1, 25 cm^3) containing *N*-methylmorpholine *N*-oxide (0.8 g) was treated with a catalytic amount of osmium tetroxide. The reaction mixture was allowed to stir at ambient temperature (12 h) and then a saturated solution of sodium metabisulfite (1 cm^3) was added; it was further stirred for an hour. The solvents were removed *in vacuo*, a saturated solution of sodium chloride (25 cm^3) added to the residue and the mixture extracted with EtOAc (3 × 25 cm^3). The combined organic extracts were dried (Na_2SO_4), the solvent evaporated, and the crude product obtained was purified by flash column chromatography (50% EtOAc in hexane) to furnish acetonide diol **7** as a white, crystalline solid (0.78 g, 87%); mp 139–141 °C; (R_f 0.35, 50% EtOAc in hexane); $[\alpha]_D$ +28 (c 0.62, $CHCl_3$); (Found: M$^+$, 311.9857; $C_9H_{13}{}^{127}IO_4$ requires 311.9860); δ_H (500 MHz, $CHCl_3$) 1.40, 1.44 [3H × 2, s, –C(Me)$_2$], 4.25 (1H, dd, $J_{4,3a}$ 6.5, $J_{4,5}$ 3.5, 4-H), 4.36 (1H, dd, $J_{5,4}$ 3.5, $J_{5,6}$ 3.2, 5-H), 4.42 (1H, dd, $J_{3a,4}$ 6.5, $J_{3a,7a}$ 5.4, 3a-H), 4.65 (1H, d, $J_{7a,3a}$ 5.4, 7a-H), 6.43 (1H, d, $J_{6,5}$ 3.2, 6-H); m/z (EI) 312 (M$^+$, 3%), 254 (75), 212 (100), 109 (54), 85 (71), 81 (59), 57 (87), 39 (72), 29 (78).

Methyl (3a*R*,6*R*,7*R*,7a*S*)-6,7-dihydroxy-2,2-dimethyl-3a,6,7,7a-tetrahydro-1,3-benzodioxole-4-carboxylate 8

Palladium(II) acetate (0.018 g, 5 mol%) was added to a solution of acetonide diol **7** (0.5 g, 1.60 mmol) and NaOAc·3H_2O (0.88 g, 6.4 mmol) in methanol (25 cm^3). The reaction mixture was stirred at room temperature under an atmosphere of carbon monoxide until all of the starting material had reacted (*ca.* 6 h). Removal of the solvent from the reaction mixture under reduced pressure and purification of the EtOAc-soluble portion of the crude product by PLC (60% EtOAc in hexane) yielded α,β-unsaturated methyl ester **8** as a white, crystalline solid (0.32 g, 81%); mp 144–146 °C, (lit.[30] 143–145 °C); (R_f 0.2, 60% EtOAc in hexane); $[\alpha]_D$ −39 (c 0.6, $CHCl_3$), (lit.[30] $[\alpha]_D$ −41); δ_H (500 MHz, $CDCl_3$) 1.36, 1.41 [3H × 2, s, –C(Me)$_2$], 2.78 (1H, d, J 3.7, –OH), 2.89 (1H, d, J 7.0, –OH), 3.82 (3H, s, –OMe), 4.25 (1H, dd, J 7.0, J 3.5, 7-H), 4.48 (1H, m, 7a-H), 4.52 (1H, br s, 6-H), 5.04 (1H, dd, $J_{3a,7a}$ 5.8, $J_{3a,5}$ 1.2, 3a-H), 6.87 (1H, dd, $J_{5,6}$ 2.6, $J_{5,3a}$ 1.3, 5-H).

Hydrogenation of compound 8

A solution of α,β-unsaturated methyl ester **8** (0.4 g, 1.64 mmol) in ethanol (20 cm^3) was stirred under an atmosphere of H_2 (55 psi for 20 h) in the presence of 5% Rh/Al_2O_3 catalyst (0.05 g). The catalyst was removed by filtration and the solvent distilled off to give the crude hydrogenated product as an inseparable mixture of diastereoisomers **10** and **14** (0.41 g). The mixture was converted (benzoyl chloride/pyridine) into the corresponding dibenzoates **11** and **15** which could be separated by multiple-elution PLC (15% EtOAc in hexane).

Methyl (3a*R*,4*S*,6*R*,7*S*,7a*R*)-6,7-di(benzoyloxy)-2,2-dimethylperhydro-1,3-benzodioxole-4-carboxylate 11

White, crystalline solid (0.21 g, 28%); mp 156–158 °C (from Et_2O–hexane); (R_f 0.2, 20% EtOAc in hexane); $[\alpha]_D$ −71 (c 0.42, $CHCl_3$); (Found C 66.0, H 5.61 $C_{25}H_{26}O_8$ requires C 66.1, H 5.8%); δ_H (500 MHz, $CDCl_3$) 1.42, 1.59 [3H × 2, s, –C(Me)$_2$], 2.34 (1H, ddd, J 14.5, J 6.0, J 3.0, 5-H), 2.55 (1H, m, 5′-H), 3.11 (1H, m 4-H), 3.46 (3H, s, –OMe), 4.60 (1H, dd, $J_{7a,7}$ 6.4, $J_{7a,3a}$ 5.0, 7a-H), 4.90 (1H, t, $J_{3a,4} = J_{3a,7}$ 5.0, 3a-H), 5.51 (1H, dd, $J_{7,7a}$ 6.4, $J_{7,6}$ 3.3, 7-H), 5.61 (1H, m, 6-H), 7.37–7.44 (4H, m, Ar–H), 7.54 (2H, m, Ar–H), 7.93 (2H, m, Ar–H), 7.99 (2H, m, Ar–H); δ_C (75 MHz, $CDCl_3$) 26.24, 26.47, 28.20, 41.05, 52.16, 69.78, 72.35, 73.99, 74.82, 109.44, 128.39, 128.46, 129.31, 129.40, 129.48, 129.60, 129.77, 129.82, 133.26, 133.32, 165.36, 165.70, 173.00 (×3).

Crystal data for 11. $C_{25}H_{26}O_8$, M = 454.5, orthorhombic, a = 6.622(2), b = 8.534(2), c = 39.364(13) Å, U = 2224.5(11) Å^3, T = 150(2) K, Mo-Kα radiation, λ = 0.71073 Å, space group $P2_12_12_1$ (no. 19), Z = 4, $F(000)$ = 960, D_x = 1.357 g cm^{-3}, μ = 0.101 mm^{-1}, Siemens P4 diffractometer, ω scans, scan range 1.0°, $4.1 < 2\theta < 50.0°$, measured/independent reflections: 3144/2889, direct methods solution, full matrix least squares refinement on $F_o{}^2$, anisotropic displacement parameters for most non-hydrogen atoms (two carbon atoms could not be refined anisotropically), hydrogens included at positions determined by the geometry of the molecule using the riding model, with isotropic vibration parameters, R_1 = 0.096 for 1108 data with $F_o > 4\sigma(F_o)$, 301 parameters, wR_2 = 0.260 (all data), GoF = 1.06, $\Delta\rho_{min,max} = -0.48/0.44$ e Å^{-3}.

CCDC reference number 262885. See http://www.rsc.org/suppdata/ob/b5/b502009c/ for crystallographic data in CIF or other electronic format.

Methyl (3a*R*,4*R*,6*R*,7*S*,7a*R*)-6,7-di(benzoyloxy)-2,2-dimethylperhydro-1,3-benzodioxole-4-carboxylate 15

White, crystalline solid (0.34 g, 56%); mp 154–155 °C (decomp.) (from Et_2O–hexane); (R_f 0.15, 20% EtOAc in hexane); $[\alpha]_D$ −131 (c 0.3, $CHCl_3$); (Found: C 66.0, H 5.7; $C_{25}H_{26}O_8$ requires C 66.1, H 5.8%); δ_H (500 MHz, $CDCl_3$) 1.40, 1.59 [3H × 2, s, –C(Me)$_2$], 2.31 (1H, dt, $J_{5,5'}$ 9.8, $J_{5,6} = J_{5,4}$ 4.9, 5-H), 2.41 (1H, m, 5′-H), 3.26 (1H, m, 4-H), 3.78 (3H, s, OMe), 4.56 (1H, dd, $J_{7a,7}$ 7.6, $J_{7a,3a}$ 4.7, 7a-H), 4.82 (1H, t, $J_{3a,4} = J_{3a,7a}$ 4.7, 3a-H), 5.34 (1H, dd, $J_{7,7a}$ 7.6, $J_{7,6}$ 2.6, 7-H), 5.72 (1 H, m, 6-H), 7.36 (2H, m, Ar–H), 7.46 (2H, m, Ar–H), 7.51 (1H, m, Ar–H), 7.58 (1H, m, Ar–H), 7.96 (4H, m, Ar–H); δ_C (75 MHz, $CDCl_3$) 25.44, 26.60, 28.33, 38.82, 52.68, 70.25, 73.97, 74.46, 76.29, 110.53, 128.52, 128.61, 128.70, 128.96, 129.15, 129.54, 129.97, 130.19, 133.53, 133.73, 165.64, 166.22, 171.81 (×3).

(3a*S*,4*R*,5*R*,7*R*,7a*R*)-7-Hydroxymethyl-2,2-dimethylperhydro-1,3-benzodioxole-4,5-diol 12

A solution of dibenzoate **11** (0.28 g, 0.62 mmol) in anhydrous THF (10 cm^3) was treated with $LiAlH_4$ powder (0.08 g, 2.1 mmol). After refluxing the reaction mixture (12 h) under anhydrous conditions it was cooled in an ice bath and quenched by the addition of a THF–water mixture. The precipitated inorganic material was removed by filtration, the filtrate was dried (Na_2SO_4) and concentrated *in vacuo* to yield the crude product as an oil. Purification by flash column chromatography (10% MeOH in $CHCl_3$) afforded the partially protected carbasugar **12** as colourless oil (0.10 g, 74%); (R_f 0.35, 10% MeOH in $CHCl_3$); $[\alpha]_D$ +46 (*c* 0.47, MeOH); (Found: $M^+ - Me$, 203.0924; $C_9H_{15}O_5$ requires 203.0919); δ_H (500 MHz, acetone-d_6) 1.26, 1.38 [3H × 2, s, –C(Me)$_2$], 1.57 (1H, m, 6-H), 1.67–1.76 (2H, m, 7-H, 6′-H), 3.49 (1H, m, 1-H), 3.54 (2H, br s, 4-H, OH), 3.65 (3H, m, 1′-H, 2 × –OH), 3.97 (2H, m, 3a-H, 5-H), 4.16 (1H, dd, $J_{7a,3a}$ 5.3, $J_{7a,7}$ 3.7, 7a-H); δ_C (75 MHz, acetone-d_6) 26.75, 29.10, 42.37, 64.88, 69.72, 71.80, 75.75, 79.65 (×2), 108.85; *m/z* (EI) 203 ($M^+ - Me$, 78%), 143 (18), 125 (45), 95 (52), 79 (57), 71 (47), 59 (62), 57 (57), 43 (100), 29 (82).

(3a*S*,4*R*,5*R*,7*S*,7a*R*)-7-Hydroxymethyl-2,2-dimethylperhydro-1,3-benzodioxole-4,5-diol 16

Partially protected carbasugar **16** was similarly obtained from dibenzoate **15** (0.3 g, 0.66 mmol) as compound **11** → **12**. Purification by PLC (10% MeOH in $CHCl_3$) gave protected pseudosugar **16** as a colourless oil (0.11 g, 76%); (R_f 0.37, 10% MeOH in $CHCl_3$); $[\alpha]_D$ −47 (*c* 0.67, MeOH); (Found: $M^+ - Me$, 203.0914; $C_9H_{15}O_5$ requires 203.0919); δ_H (500 MHz, acetone-d_6) 1.22, 1.34 [3H × 2, s, –C(Me)$_2$], 1.43 (1H, dt, $J_{6,6'}$ 13.2, $J_{6,5} = J_{6,7}$ 2.8, 6-H), 1.66 (1H, m, 6′-H), 2.34 (1H, m, 7-H), 3.48 (4H, m, 4-H, 1-H, 2 × –OH), 3.62 (2H, m, 1′-H, –OH), 3.91 (1H, m, 5-H), 3.96 (1H, dd, $J_{3a,7a}$ 4.9, $J_{3a,4}$ 6.9, 3a-H), 4.29 (1H, t, $J_{7a,3a} = J_{7a,7}$ 4.9, 7a-H); δ_C (75 MHz, acetone-d_6) 26.94, 28.99, 35.48, 64.87, 70.19, 75.00, 75.87, 80.70 (×2), 109.06; *m/z* (EI) 203 ($M^+ - Me$, 88%), 185 (10), 143 (12), 125 (56), 107 (38), 95 (54), 83 (63), 79 (74), 59 (78), 43 (100), 29 (79).

(1*R*,2*R*,3*R*,4*R*,5*R*)-5-(Hydroxymethyl)cyclohexane-1,2,3,4-tetraol (carba-β-D-altropyranose) 2

Protected carbasugar **12** (0.05 g, 0.25 mmol) was dissolved in a mixture of TFA–THF–H_2O (0.5 : 4 : 1; 2 cm^3) and the solution was kept at 50 °C (2 h). The reaction mixture was then allowed to stir at room temperature overnight. The solvents were removed under reduced pressure and the crude product purified by charcoal–celite (1 : 1, v/v) column chromatography (water → 5% ethanol in water) to yield carba-β-D-altropyranose **2** as a colourless syrup (0.04 g, 90%); $[\alpha]_D$ +44.3 (*c* 0.44, MeOH), (lit.[31] −49.5, for the enantiomer); (Found: $M^+ - 2H_2O$, 142.0624; $C_7H_{10}O_3$ requires 142.0629); δ_H (500 MHz, D_2O) 1.59 (1H, q, $J_{7',7} = J_{7',5} = J_{7',1}$ 12.1, 7′-H), 1.84 (1H, m, 7-H), 1.96 (1H, m, 5-H), 3.67 (2H, m, 3-H, 6-H), 3.79 (2H, m, 4-H, 6′-H), 4.04 (2H, m, 1-H, 2-H); δ_C (75 MHz, D_2O) 28.79, 37.91, 63.58, 67.35, 68.65, 72.64, 73.05; *m/z* (EI) 142 ($M^+ - 2H_2O$, 18%), 124 (11), 116 (16), 111 (25), 86 (68), 83 (55), 73 (100).

[(1*R*,2*R*,3*R*,4*R*,5*R*)-2,3,4,5-Tetra(acetyloxy)cyclohexyl]methyl acetate (carba-β-D-altropyranose penta-acetate) 13

Carba-β-D-altropyranose **2** (0.03 g, 0.17 mmol) was converted to penta-acetate **13** by reacting it with acetic anhydride in pyridine at room temperature. The crude product was purified by column chromatography (hexane → 50% Et_2O in hexane) to yield penta-acetate **13** as a colourless oil (0.05 g, 78%); $[\alpha]_D$ −7.8 (*c* 1.43, $CHCl_3$), (lit.[15] $[\alpha]_D$ −8.1); δ_H (300 MHz, $CDCl_3$) 1.83 (1H, q, $J_{6,6'} = J_{6,5} = J_{6,1}$ 11.4, 6-H), 1.98 (1H, m, 6′-H), 2.01, 2.02, 2.07, 2.11, 2.14 (3H each, s, 5 × –$OCOCH_3$), 2.35 (1H, m, 1-H), 4.08 (2H, d, *J* 5.8, 7-H, 7′-H), 5.08 (1H, dd, $J_{2,1}$ 10.59, $J_{2,3}$ 3.0, 2-H), 5.20 (1H, m, 5-H), 5.27 (1H, m, 4-H), 5.34 (1H, dd, $J_{3,4}$ 4.89, $J_{3,2}$ 3.0, 3-H).

(1*R*,2*R*,3*R*,4*R*,5*S*)-5-(Hydroxymethyl)cyclohexane-1,2,3,4-tetraol (carba-α-L-galactopyranose) 3

Carbasugar **16** (0.13 g, 0.62 mmol) was deprotected (as compound **12** → **2**) to yield carba-α-L-galactopyranose **3** as a white solid (0.09 g, 81%); mp 162–163 °C (MeOH), (lit.[28] 161.5–162.5 °C); $[\alpha]_D$ −59.2 (*c* 0.76, H_2O), (lit.[28] $[\alpha]_D$ +66.3 for the enantiomer); (Found: $M^+ - 2H_2O$, 142.0632; $C_7H_{10}O_3$ requires 142.0630; δ_H (500 MHz, D_2O) 1.60 (1H, m, 7′-H), 1.72 (1H, dt, $J_{7,5} = J_{7,1}$ 3.7, $J_{7,7'}$ 14.5, 7a-H), 2.06 (1H, m, 5-H), 3.56 (1H, dd, $J_{6,6'}$ 11, $J_{6,5}$ 6.4, 6-H), 3.70 (1H, dd, $J_{6',6}$ 11, $J_{6',5}$ 7.9, 6′-H), 3.76 (2H, t, *J* 1.1, 2-H, 3-H), 4.15 (2H, m, 1-H, 4-H); δ_C (75 MHz, D_2O) 27.90, 36.55, 62.88, 69.39, 70.36, 71.35, 71.53; *m/z* (EI) 142 ($M^+ - 2 \times H_2O$, 15%), 124 (10), 116 (14), 111 (26), 86 (62), 83 (53), 73 (100), 57 (52).

[(1*S*,2*R*,3*R*,4*R*,5*R*)-2,3,4,5-Tetra(acetyloxy)cyclohexyl]methyl acetate (carba-α-L-galactopyranose penta-acetate) 17

Carba-α-L-galactopyranose **3** (0.04 g, 0.25 mmol) was converted (acetic anhydride–pyridine) to the penta-acetate **17** as a white solid (0.08 g, 84%); mp 145–146 °C (Et_2O–hexane); (lit.[28] 143–144 °C); $[\alpha]_D$ −42.2 (*c* 0.49, $CHCl_3$), (lit.[28] $[\alpha]_D$ +43.2 for the enantiomer); (Found M^+ 388.1360; $C_{17}H_{24}O_{10}$ requires 388.1369; δ_H (500 MHz, $CDCl_3$) 1.77 (2H, m, *J* 10.2, *J* 3.0, 6-H, 6′-H), 1.99, 2.01, 2.04 (3H each, s, 3 × –$OCOCH_3$), 2.11 (6H, s, 2 × –$OCOCH_3$), 2.46 (1H, m, 1-H), 3.88 (1H, dd, $J_{7,7'}$ 11, $J_{7,1}$ 5.7, 7-H), 3.96 (1H, dd, $J_{7',7}$ 11, $J_{7',1}$ 9.3, 7′-H), 5.18 (1H, dd, $J_{4,3}$ 10.9, $J_{4,5}$ 2.9, 4-H), 5.23 (1H, dd, $J_{3,4}$ 10.9, $J_{3,2}$ 2.6, 3-H), 5.52 (1H, q, $J_{5,4} = J_{5,6} = J_{5,6'}$ 2.9, 5-H), 5.58 (1H, t, $J_{2,3} = J_{2,1}$ 2.6, 2-H); δ_C (75 MHz, $CDCl_3$) 20.40, 20.42, 20.45, 20.67, 20.73, 26.33, 32.89, 62.61, 67.93, 67.95, 69.03, 69.30, 169.69, 169.72, 169.81, 169.98, 170.47; *m/z* (EI) 388 (M^+, 12%), 329 (15), 268 (21), 243 (45), 226 (37), 166 (74), 124 (75), 43 (100).

(3a*R*,4*S*,5*R*,7a*S*)-5-(Benzoyloxy)-7-iodo-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-5-yl benzoate 9

A solution of diol acetonide **7** (2.3 g, 7.4 mmol) in pyridine (1 cm^3) was treated with benzoyl chloride (2.5 g, 17.6 mmol); the reaction mixture was left at room temperature overnight. Pyridine was removed under reduced pressure and the residue taken up in EtOAc (70 cm^3). The EtOAc extract was washed with 5% aq. $NaHCO_3$ solution (2 × 40 cm^3), dried (Na_2SO_4) and concentrated (rotary evaporator) to give the crude dibenzoate **9** as a cream-coloured solid. Crystallization afforded dibenzoate **9** as a white, crystalline solid (3.5 g, 95%); mp 94–95 °C (MeOH); (R_f 0.25, 15% Et_2O in hexane); $[\alpha]_D$ −70.0 (*c* 0.86, $CHCl_3$); (Found: C 52.9, H 4.0; $C_{23}H_{21}{}^{127}IO_6$ requires C 53.1, H 4.0%); δ_H (500 MHz, $CDCl_3$) 1.44, 1.53 [3H each, s, –C(Me)$_2$], 4.62 (1H, dd, $J_{3a,7a}$ 5.4, $J_{3a,4}$ 6.0, 3a-H), 4.82 (1H, d, $J_{7a,3a}$ 5.4, 7a-H), 5.80 (1H, dd, $J_{4,3a}$ 6.0, $J_{4,5}$ 3.7, 4-H), 5.87 (1H, d, $J_{5,6} = J_{5,4}$ 3.7, 5-H), 6.63 (1H, d, $J_{6,5}$ 3.7, 6-H), 7.35–7.58 (6H, m, Ar–H), 7.91–8.00 (4H, m, Ar–H); δ_C (125 MHz, $CDCl_3$) 26.25, 27.65, 68.67, 69.47, 73.96, 78.84, 101.39, 110.69, 128.44, 128.53, 129.35, 129.39, 129.77, 129.87, 133.37, 133.47, 134.65, 134.79, 135.22, 135.49, 136.01, 165.36, 165.54; *m/z* (EI) 520 (M^+, 6%), 504 (2), 398 (5), 341 (6), 336 (11), 213 (7), 105 (100), 147 (12), 78 (6), 43 (21).

(1*S*,2*R*,5*S*,6*R*)-2-(Benzoyloxy)-5,6-dihydroxy-4-iodo-3-cyclohexenyl benzoate 18

To a solution of acetonide **9** (0.4 g, 0.8 mmol) in MeOH (20 cm^3), a HCl solution (1.5 M, 1 cm^3) was added and the reaction mixture kept at 50 °C until completion of the reaction (*ca.*

4 h, TLC analysis). Removal of the solvents from the reaction mixture using a rotary evaporator and crystallization of the residue gave white crystals of diol dibenzoate **18** (0.33 g, 90%); mp 85–87 °C (from MeOH); (R_f 0.23, 35% EtOAc in hexane); $[\alpha]_D$ −142 (*c* 0.58, $CHCl_3$); (Found: M^+ 480.0094; $C_{20}H_{17}{}^{127}IO_6$ requires 480.0070); δ_H (500 MHz, $CDCl_3$), 4.50 (1H, dd, $J_{6,1}$ 8.9, $J_{6,5}$ 3.7, 6-H), 4.57 (1H, d, $J_{5,6}$ 3.5, 5-H), 5.72 (1H, dd, $J_{1,6}$ 8.9, $J_{1,2}$ 4.0, 1-H), 5.85 (1H, dd, $J_{2,3}$ 4.4, $J_{2,1}$ 4.0, 2-H), 6.65 (1H, d, $J_{3,2}$ 4.4, 3-H), 7.36–7.46 (4H, m, Ar–H), 7.52–7.99 (6H, m, Ar–H); δ_C (125 MHz, $CDCl_3$) 68.26, 69.03, 69.52, 74.40, 105.32, 128.47, 128.50, 129.30, 129.79, 129.84, 130.12, 131.02, 131.34, 131.56, 131.88, 132.11, 133.45, 133.90, 165.52, 166.28; *m/z* (EI) 480 (M^+, 23%), 401 (21), 367 (42), 335 (65), 236 (79), 205 (35), 169 (43), 149 (97), 136 (42), 122 (100), 105 (27), 31 (99).

(1*R*,4*R*,5*S*,6*S*)-4,5-Di(benzoyloxy)-6-hydroxy-2-iodo-2-cyclohexenyl 4-nitrobenzoate 19

To a suspension of diol dibenzoate **18** (0.5 g, 1 mmol) in dry benzene (10 cm^3) containing activated 3 Å molecular sieves (0.5 g) and triphenylphosphine (0.34 g, 1.3 mmol), DEAD (0.23 g, 1.32 mmol) was added drop-wise. After stirring the reaction mixture at room temperature (0.5 h), *p*-nitrobenzoic acid (0.2 g, 1.2 mmol) was added and the stirring continued (0.5 h); it was then refluxed at 90 °C (1.5 h). The molecular sieves were filtered off, the solvent was removed from the filtrate, and the crude product obtained was purified by column chromatography (10% EtOAc in hexane) to yield *p*-nitrobenzoate **19** as an off-white crystalline solid (0.44 g, 70%); mp 72 °C; (R_f 0.23, 35% EtOAc in hexane); $[\alpha]_D$ −37 (*c* 0.75, $CHCl_3$); (Found: C 51.25, H 3.01; $C_{27}H_{20}N^{127}IO_9$ requires C 51.51, H 3.18%); δ_H (500 MHz, $CDCl_3$) 4.66 (1H, dd, $J_{6,5}$ 9.0, $J_{6,1}$ 6.3, 6-H), 5.64 (1H, dd, $J_{5,6}$ 9.0, $J_{5,4}$ 4.4, 5-H), 5.88 (1H, dd, $J_{4,3}$ 4.8, $J_{4,5}$ 4.4, 4-H), 5.91 (1H, d, $J_{1,6}$ 6.3, 1-H), 6.87 (1H, d, $J_{3,4}$ 4.8, 3-H), 7.32–7.46 (10H, m, Ar–H), 7.91–8.05 (4H, m, Ar–H); δ_C (125 MHz, $CDCl_3$) 70.45, 71.12, 71.84, 79.98, 102.88, 125.32, 130.23, 130.34, 130.87, 131.01, 131.59, 132.59, 132.95, 133.04, 133.24, 134.56, 134.78, 134.99, 135.10, 135.33, 135.36, 136.36, 138.98, 152.50, 165.82, 167.28, 167.67; *m/z* (EI) 611 ($M^+ - H_2O$, 7%), 536 (67), 513 (21), 466 (12), 391 (64), 376 (77), 293 (6), 235 (6), 207 (15), 181 (77), 164 (36), 150 (100), 135 (18), 120 (32), 104 (67), 92 (36), 76 (62), 59 (48), 44 (34).

(1*R*,2*R*,3*S*,4*R*)-5-Iodo-5-cyclohexene-1,2,3,4-tetraol 20

To a solution of nitrobenzoate **19** (3.0 g, 4.8 mmol) in MeOH (50 cm^3), a 5% aq. NaOH solution (15 cm^3) was added. The reaction mixture was left at room temperature (2 h). The solvent was then removed under reduced pressure, and water (25 cm^3) added to the concentrate. The aqueous solution was acidified (2 M HCl), cooled, and the precipitated *p*-nitrobenzoic acid filtered off. The filtrate was concentrated under reduced pressure and the crude, syrupy material obtained was purified by column chromatography (EtOAc → 10% MeOH in EtOAc) to give tetraol **20** as colourless crystals (1.1 g, 87%); mp 145–147 °C (from acetone–MeOH); (R_f 0.23, 10% MeOH in $CHCl_3$); $[\alpha]_D$ −45 (*c* 0.46, MeOH); (Found: C 26.5, H 3.3; $C_6H_9{}^{127}IO_4$ requires C 26.4, H 3.3%); δ_H (500 MHz, CD_3OD) 3.54 (1H, dd, $J_{2,3}$ 10.6, $J_{2,1}$ 4.1, 2-H), 3.63 (1H, dd, $J_{4,3}$ 7.5, $J_{4,6}$ 1.6, 4-H), 3.83 (1H, dd, $J_{3,2}$ 10.6, $J_{3,4}$ 7.5, 3-H), 4.00 (1H, dd, $J_{1,6}$ 5.7, $J_{1,2}$ 4.1, 1-H), 6.53 (1H, dd, $J_{6,1}$ 5.7, $J_{6,4}$ 1.6, 6-H); δ_C (125 MHz, CD_3OD) 68.55, 70.67, 72.10, 76.95, 108.82, 138.01; *m/z* (EI) 272 (M^+, 2%), 217 (15), 199 (9), 188 (6), 170 (7), 152 (8), 149 (6), 129 (7), 113 (5), 91 (4), 81 (6), 70 (100), 55 (37), 32 (18).

(3a*S*,4*R*,5*R*,7a*R*)-6-Iodo-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxole-4,5-diol 21

Iodotetraol **20** (1 g, 3.7 mmol) was converted into acetonide diol **21** using the procedure described for the synthesis of acetonide **6**. Purification of the crude product by flash column chromatography (50% EtOAc in hexane) gave acetonide **21** as a white, crystalline compound (1.0 g, 89%); mp 165–167 °C ($CHCl_3$–hexane); (R_f 0.34, 50% EtOAc in hexane); $[\alpha]_D$ +15 (*c* 0.65, $CHCl_3$); (Found: C 34.5, H 4.2; $C_9H_{13}{}^{127}IO_4$ requires C 34.6, H 4.2%); δ_H (500 MHz, $CDCl_3$) 1.38, 1.50 [3H × 2, s, –C(Me)$_2$], 2.79 (1H, d, *J* 3.3, –OH), 2.93 (1H, d, *J* 6.7, –OH), 3.93 (1H, dd, $J_{4,3a}$ 7.3, $J_{4,5}$ 6.9, 4-H), 4.03 (1H, d, $J_{5,4}$ 6.9, 5-H), 4.25 (1H, dd, $J_{3a,4}$ 7.3, $J_{3a,7a}$ 6.2, 3a-H), 4.52 (1H, dd, $J_{7a,7}$ 3.9, $J_{7a,3a}$ 6.2, 7a-H), 6.56 (1H, dd, $J_{7,7a}$ 3.9, 7-H); δ_C (125 MHz, $CDCl_3$) 20.08, 28.07, 72.61, 73.97, 74.46, 76.28, 106.97, 111.04, 134.52; *m/z* (EI) 312 (M^+, 13%), 297 (42), 254 (26), 231 (14), 207 (65), 187 (12), 165 (45), 124 (18) 100 (76), 79 (67), 75 (60), 63 (41), 43 (100).

(3a*R*,4*S*,5*R*,7a*R*)-4-Acetyloxy-6-iodo-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-5-yl acetate 22

Acetonide diol **21** (0.1 g, 0.32 mmol) was acetylated (Ac_2O–pyridine) and the product purified by PLC (15% EtOAc in hexane) to give diacetate **22** as a white, crystalline solid (0.12 g, 95%); mp 135–137 °C (from MeOH); (R_f 0.41, 25% EtOAc in hexane); $[\alpha]_D$ −29 (*c* 0.58, $CHCl_3$); ν_{max} (cm^{-1}) 1753.6 (C=O), 1636.3 (C=C); (Found: C 39.3, H 4.3; $C_{13}H_{17}{}^{127}IO_6$ requires C 39.4, H 4.3%); δ_H (500 MHz, $CDCl_3$) 1.37, 1.51 [3H × 2, s, –C(Me)$_2$], 2.08, 2.14 (3H each, s, 2 × –OCOMe), 4.28 (1H, dd, $J_{3a,4}$ 8.6, $J_{3a,7a}$ 5.9, 3a-H), 4.50 (1H, dd, $J_{7a,3a}$ 5.9, $J_{7a,7}$ 4.5, 7a-H), 5.28 (1H, dd, $J_{4,3a}$ 8.6, $J_{4,5}$ 8.2, 4-H), 5.52 (1H, dd, $J_{5,4}$ 8.2, $J_{5,7}$ 2.0, 5-H), 6.69 (1H, dd, $J_{7,7a}$ 4.5, $J_{7,5}$ 2.0, 7-H); δ_C (125 MHz, $CDCl_3$) 20.86, 20.98, 26.34, 27.76, 71.29, 72.42, 73.77, 74.47, 101.74, 111.58, 135.93, 169.73, 170.04; *m/z* (EI) 381 (M^+ − Me, 15%), 279 (43), 269 (80), 237 (100), 236 (25), 227 (14), 207 (5), 169 (77), 152 (21), 127 (29), 110 (63), 109 (39), 81 (16), 69 (5).

Methyl (3a*R*,6*S*,7*S*,7a*R*)-6,7-di(acetyloxy)-2,2-dimethyl-3a,6,7,7a-tetrahydro-1,3-benzodioxole-5-carboxylate 23

α,β-Unsaturated methyl ester **23** was obtained from iododiacetate **22** (0.1 g, 0.25 mmol) using the palladium-catalyzed carbonylation reaction conditions employed for the synthesis of methyl ester **8**. Purification of the crude product by PLC (25% EtOAc in hexane) gave methyl ester **23** as a white solid. Crystallization of the crude product, from EtOH, yielded methyl ester **23** as colourless crystals (0.1 g, 87%); mp 102–105 °C (from EtOH); (R_f 0.36, 30% EtOAc–hexane); $[\alpha]_D$ +18 (*c* 0.65, $CHCl_3$); (Found: M^+ − Me, 313.0923; $C_{14}H_{17}O_8$ requires 313.0923); δ_H (500 MHz, $CDCl_3$) 1.38, 1.46 [3H × 2, s, –C(Me)$_2$], 2.04, 2.07 (3H each, s, 2 × –OCOMe), 3.78 (3H, s, –CO_2Me), 4.30 (1H, dd, $J_{7a,7}$ 5.7, $J_{7a,3a}$ 5.5, 7a-H), 4.72 (1H, dd, $J_{3a,7a}$ 5.5, $J_{3a,4}$ 4.0, 3a-H), 5.36 (1H, dd, $J_{7,7a}$ 5.7, $J_{7,6}$ 5.2, 7-H), 5.73 (1H, d, $J_{6,7}$ 5.2, 6-H), 7.00 (1H, d, $J_{4,3a}$ 4.0, 4-H); δ_C (125 MHz, $CDCl_3$) 20.78, 20.84, 26.22, 27.65, 52.26, 65.74, 69.87, 70.80, 72.81, 111.36, 129.76, 137.05, 164.89, 169.43, 169.88; *m/z* (EI) 313 (M^+ − Me, 90%), 298 (6), 225 (9), 212 (7), 211 (67), 179 (18), 169 (100), 168 (37), 141 (7), 139 (9), 137 (32), 136 (15), 109 (11), 69 (7), 59 (10).

Hydrogenation of methyl (3a*R*,6*S*,7*S*,7a*R*)-6,7-di(acetyloxy)-2,2-dimethyl-3a,6,7,7a-tetrahydro-1,3-benzodioxole-5-carboxylate 23

α,β-Unsaturated ester **23** (0.5 g, 1.5 mmol) was hydrogenated (H_2, 5% Rh/Al_2O_3, 35 psi, 10 h) in EtOH solution (15 cm^3). Purification and separation of the crude hydrogenated diastereoisomeric mixture by flash column chromatography (20% EtOAc in hexane → 30% EtOAc in hexane) gave pure samples of methyl esters **24** and **25**.

Methyl (3a*R*,5*S*,6*S*,7*S*,7a*R*)-6,7-di(acetyloxy)-2,2-dimethylperhydro-1,3-benzodioxole-5-carboxylate 24

The more polar methyl ester **24** formed white crystals (0.2 g, 40%); mp 120–121 °C (from EtOH); $[\alpha]_D$ −9 (*c* 0.70, $CHCl_3$); (Found: M^+ − Me, 315.0080; $C_{14}H_{19}O_8$ requires 315.0080); δ_H (500 MHz, $CDCl_3$) 1.32, 1.52 [3H each, s, –C(Me)$_2$], 2.11, 2.14

(3H × 2, s, 2 × –OCOMe), 2.13 (1H, ddd, $J_{4,5}$ 13.5, $J_{4,3a}$ 5.0, $J_{4,4'}$ 4.5, 4-H), 2.33–2.34 (1H, m, 4′-H), 2.90 (1 H, ddd, $J_{5,4}$ 13.5, $J_{5,6}$ 4.8, $J_{5,4'}$ 4.5, 5-H), 3.70 (3H, s, –CO$_2$Me), 4.04 (1H, dd, $J_{7a,7}$ = $J_{7a,3a}$ 5.2, 7a-H), 4.27 (1H, dd, $J_{3a,7a}$ 5.2, $J_{3a,4}$ 5.0, 3a-H), 5.08 (1H, ddd, $J_{7,6}$ 6.7, $J_{7,7a}$ 5.2, $J_{7,5}$ 1.5, 7-H), 5.68 (1H, dd, $J_{6,7}$ 6.7, $J_{6,5}$ 4.8, 6-H); δ_C (125 MHz, CDCl$_3$) 22.27, 22.37, 27.55, 27.60, 27.69, 41.08, 53.48, 70.74, 71.75, 74.11, 77.53, 111.15, 170.70, 171.03, 171.56; *m*/*z* (EI) 315 (M$^+$ − Me, 100%), 273 (6), 241 (10), 213 (19), 170 (13), 171 (29), 153 (59), 139 (8), 128 (6), 11 (10), 109 (14), 95 (11), 83 (8), 69 (6), 59 (15).

Methyl (3a*R*,5*S*,7*R*,7a*R*)-7-acetyloxy-2,2-dimethylperhydro-1,3-benzodioxole-5-carboxylate 25

The less polar methyl ester **25** was also obtained as a white, crystalline compound (0.25 g, 60%); mp 53–55 °C (from EtOH); $[\alpha]_D$ +8 (*c* 0.61, CHCl$_3$); (Found: M$^+$ 271.9988; C$_{13}$H$_{20}$O$_6$ requires 271.9985); δ_H (500 MHz, CDCl$_3$) 1.33, 1.48 [3H × 2, s, –C(Me)$_2$], 1.84–1.85 (1H, m, 6-H), 1.96–1.97 (1H, m, 4′-H), 2.07 (3 H, s, –OCOMe), 2.11–2.12 (2H, m, 4-H, 6′-H), 2.61–2.63 (1H, m, 5-H), 3.71 (3H, s, –CO$_2$Me), 3.99 (1H, dd, $J_{7a,3a}$ 5.0, $J_{7a,7}$ 4.2, 7a-H), 4.28 (1H, ddd, $J_{3a,4}$ 11.0, $J_{3a,4'}$ 5.4, $J_{3a,7a}$ 5.0, 3a-H), 5.33 (1H, dd, $J_{7,6}$ 9.3, $J_{7,7a}$ 4.2, 7-H); δ_C (125 MHz, CDCl$_3$) 21.16, 26.08, 27.66, 28.46, 29.03, 34.77, 51.96, 69.76, 72.79, 74.58, 110.30, 169.37, 170.20; *m*/*z* (EI) 272 (M$^+$, 24%), 213 (10), 143 (12), 132 (51), 109 (52), 81 (94), 53 (94), 51 (100), 29 (90).

(3a*S*,4*R*,5*S*,6*R*,7a*R*)-6-Hydroxymethyl-2,2-dimethylperhydro-1,3 -benzodioxole-4,5-diol 26

Reduction (LiAlH$_4$–THF, 0.08 g, 2 mmol) of methyl ester **24** (0.23 g, 0.68 mmol) and subsequent purification of the crude product by flash column chromatography (10% MeOH in CHCl$_3$) furnished protected carbasugar **26** as a colourless oil (0.12 g, 81%); $[\alpha]_D$ −7 (*c* 0.74, MeOH); (Found: M$^+$ − Me, 203.0910; C$_9$H$_{15}$O$_5$ requires 203.0919); δ_H (500 MHz, D$_2$O) 1.22, 1.28 [3H × 2, s, –C(Me)$_2$], 1.54–1.56 (2H, m, 7-H, 7′-H), 1.78–1.79 (1H, m, 6-H), 3.43–3.44 (1H, m, 1′-H), 3.55 (1H, dd, $J_{1,6}$ 7.0, $J_{1,1'}$ 5.4, 1-H), 3.68 (1H, dd, $J_{5,4}$ 7.1, $J_{5,6}$ 4.0, 5-H), 3.74 (1H, dd, $J_{4,3a}$ 11.0, $J_{4,5}$ 7.1, 4-H), 3.83 (1H, dd, $J_{7a,3a}$ 5.6, $J_{7a,7}$ 5.4, 7a-H), 4.11 (1H, $J_{3a,4}$ 11.0, $J_{3a,7a}$ 5.6, 3a-H); δ_C (125 MHz, CDCl$_3$) 21.00, 23.89, 24.00, 33.26, 62.11, 66.80, 72.02, 75.35, 77.23, 109.11; *m*/*z* (EI) 203 (M$^+$ − Me, 35%), 185 (24), 149 (6), 143 (11), 125 (23), 111 (15), 107 (17), 95 (39), 91 (6), 84 (31), 79 (60), 73 (40), 67 (52), 59 (88), 55 (100).

(1*R*,2*R*,3*R*,4*S*,5*R*)-5-Hydroxymethyl-cyclohexane-1,2,3,4-tetraol (carba-β-D-idopyranose) 4

Deprotection of acetonide group of carbasugar derivative **26** (0.08 g, 0.36 mmol) using the method described for the synthesis of compound **18**, followed by purification of the crude product by charcoal–Celite (1 : 1, v/v) column chromatography (water → 10% EtOH in water), afforded carba-β-D-idopyranose **4** as a colourless, viscous oil (0.05 g, 79%); $[\alpha]_D$ −6.1 (*c* 0.91, MeOH); (Found: M$^+$ 178.0846; C$_7$H$_{14}$O$_5$ requires 178.0841); δ_H (500 MHz, D$_2$O) 1.59–1.60 (1H, m, 6-H), 1.66–1.67 (1H, m, 6′-H), 2.03–2.04 (1H, m, 5-H), 3.60 (1H, dd, $J_{7,5}$ 11.0, $J_{7,7'}$ 6.4, 7-H), 3.66 (2H, m, 3-H, 7′-H), 3.74 (1H, dd, $J_{4,5} = J_{4,3}$ 4.3, 4-H), 3.90–3.91 (2H, m, 1-H, 2-H); δ_C (125 MHz, D$_2$O) 27.10, 38.70, 62.76, 68.31, 71.66, 72.90, 73.37, *m*/*z* (EI) 178 (M$^+$, 16%), 177 (100), 175 (72), 173 (32), 163 (17), 156 (14), 139 (27), 135 (32), 121 (47), 120 (14), 110 (9), 77 (8).

[(1*R*,2*R*,3*R*,4*S*,5*R*)-2,3,4,5-Tetra(acetyloxy)cyclohexyl]methyl acetate 27

Carba-β-D-idopyranose **4** (0.05 g, 0.03 mmol) was converted to penta-acetate **27** (Ac$_2$O–pyridine), a white, crystalline solid (0.11 g, 97%); mp 110–112 °C (from Et$_2$O–hexane); $[\alpha]_D$ −14.0 (*c* 0.50, CHCl$_3$); ν_{max} (cm^{-1}) 1747.8 (C=O); (Found: C 52.3, H 5.9; C$_{17}$H$_{24}$O$_{10}$ requires C 52.6, H 6.2%); δ_H (500 MHz, CDCl$_3$) 1.74 (1H, ddd, $J_{6,6'}$ 13.5, $J_{6,1}$ 4.0, $J_{6,5}$ 3.8, 6-H), 2.038, 2.040, 2.047, 2.049, 2.063 (3H each, s, 5 × –OCOMe), 2.05–2.06 (1H, m, 6′-H), 2.51–2.53 (1H, m, 1-H), 4.10–4.11 (1H, m, 7-H), 4.17 (1H, dd, $J_{7',1}$ 11.1, $J_{7',7}$ 7.7, 7′-H), 4.97–4.98 (1H, m, 5-H), 5.11 (1H, dd, $J_{4,3}$ 5.4, $J_{4,5}$ 3.5, 4-H), 5.22 (1H, dd, $J_{2,3}$ 5.0, $J_{2,1}$ 4.8, 2-H), 5.28 (1H, dd, $J_{3,4}$ 5.4, $J_{3,2}$ 5.0, 3-H); δ_C (125 MHz, CDCl$_3$) 20.70, 20.77, 20.80, 20.98, 21.12, 24.82, 34.85, 63.59, 68.14, 68.25, 68.43, 68.65, 168.91, 169.52, 169.62, 169.97, 170.73; *m*/*z* (EI) 388 (M$^+$, 14%), 329 (27), 287 (45), 268 (12), 243 (22), 209 (9), 167 (15), 132 (33), 101 (40), 61 (11), 43 (100).

(1*R*,2*R*,3*S*,4*S*)-5-Iodo-5-cyclohexene-1,2,3,4-tetraol 28

Iodotetraol **28** was obtained by acid-catalysed hydrolysis of acetonide diol **7** (0.5 g, 1.6 mmol) using the method described for the synthesis of benzoate diol **18**, as a white, crystalline solid (0.37 g, 85%); mp 160–162 °C (from MeOH–CHCl$_3$); (R_f 0.26, 10% MeOH in CHCl$_3$); $[\alpha]_D$ −82 (*c* 0.5, MeOH); (Found: M$^+$ 272.0913; C$_6$H$_9$^{127}IO$_4$ requires 272.0910); δ_H (500 MHz, D$_2$O) 3.96–3.97 (1H, m, 3-H), 4.10–4.11 (1H, m, 2-H), 4.26–4.27 (1H, m, 1-H), 4.48–4.49 (1H, m, 4-H), 6.54–6.55 (1H, m, 6-H); δ_C (125 MHz, D$_2$O) 67.83, 67.90, 68.73, 74.62, 103.00, 140.12; *m*/*z* (EI) 272 (M$^+$, 2%), 254 (17), 236 (22), 187 (5), 146 (2), 128 (4), 117 (8), 113 (17), 85 (31), 71 (74), 57 (79), 43 (100), 39 (17), 32 (13), 29 (27).

(1*S*,2*R*,5*S*,6*S*)-6-(Acetyloxy)-2,5-dibromo-3-iodo-3-cyclohexenyl acetate 29

To a solution of the iodotetraol **28** (0.8 g, 3 mmol) in dry acetonitrile (10 cm^3) at 0 °C under a nitrogen atmosphere was added drop-wise 1-bromocarbonyl-1-methylethyl acetate (1.37 g, 6.6 mmol). The reaction mixture was stirred at 0 °C (0.25 h) and then at room temperature (2 h). Most of the solvent was then removed under reduced pressure, the residue extracted with Et$_2$O (2 × 50 cm^3), the extract washed with 3% aq. NaHCO$_3$ (3 × 10 cm^3), dried (Na$_2$SO$_4$) and concentrated to give the crude *bis*-bromoacetate **29** as a light brown-coloured foam. Crystallization of the crude product afforded colourless crystals of *bis*-bromoacetate **29** (1.26 g, 87%); mp 70 °C (CHCl$_3$–hexane); $[\alpha]_D$ +75 (*c* 0.50, CHCl$_3$); (Found: M$^+$ 484.0101; C$_{10}$H$_{11}$^{127}I^{81}Br$_2$O$_4$ requires 484.0108); δ_H (500 MHz, CDCl$_3$) 2.11, 2.13 (3H each, s, 2 × –OCOMe), 4.60 (1H, $J_{5,6}$ 5.3, $J_{5,4}$ 3.4, 5-H), 4.73 (1H, d, $J_{2,1}$ 5.5, 2-H), 5.41 (1H, dd, $J_{1,6}$ 7.4, $J_{1,2}$ 5.5, 1-H), 5.53 (1H, dd, $J_{6,1}$ 7.4, $J_{6,5}$ 5.3, 6-H), 6.70 (1H, d, $J_{4,5}$ 3.4, 4-H); δ_C (125 MHz, CDCl$_3$) 20.70, 20.75, 44.00, 52.80, 70.34, 79.89, 98.90, 140.01, 169.20, 169.67, *m*/*z* (EI) 484 (M$^+$, 25%), 482 (47), 480 (26), 425 (32), 423 (12), 366 (19), 300 (10), 230 (21), 199 (57), 176 (38), 132 (5), 87 (54), 52 (40), 43 (100), 22 (10).

(1*R*,2*S*,5*R*,6*S*)-2,5,6-Tri(acetyloxy)-4-iodo-3-cyclohexenyl acetate 30

Silver acetate (0.4 g, 2.4 mmol) was added to a solution of *bis*-bromoacetate **29** (0.3 g, 0.6 mmol) in a mixture of dry AcOH (6 cm^3) and Ac$_2$O (0.6 cm^3). The reaction mixture was gently refluxed (1 h), cooled to room temperature and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and the crude product obtained was purified by PLC (25% EtOAc in hexane) to yield tetra-acetate **30** as a white, crystalline solid (0.09 g, 77%); mp 112–115 °C (from MeOH); (R_f 0.4, 25% EtOAc in hexane); $[\alpha]_D$ +49 (*c* 0.78, CHCl$_3$); (Found: C 38.2, H 4.0; C$_{14}$H$_{17}$^{127}IO$_8$ requires C 38.2, H 3.9%); δ_H (500 MHz, CDCl$_3$) 2.01, 2.03, 2.07, 2.12 (3H each, s, 4 × –OCOMe), 5.33 (1H, dd, $J_{6,1}$ 10.4, $J_{6,5}$ 7.4, 6-H), 5.38 (1H, dd, $J_{1,6}$ 10.4, $J_{1,2}$ 7.8, 1-H), 5.46 (1H, dd, $J_{2,1}$ 7.8, $J_{2,3}$ 2.4, 2-H), 5.71 (1H, dd, $J_{5,6}$ 7.4, $J_{5,3}$ 2.4, 5-H), 6.39 (1H, d, $J_{3,2}$ 2.4, 3-H); δ_C (125 MHz, CDCl$_3$) 20.51, 20.55, 20.74, 20.86, 70.45, 70.52, 72.09, 74.36, 97.81, 137.68, 169.53, 169.65, 169.80, 170.02; *m*/*z* (EI) 381 (M$^+$ − OAc, 4%), 338 (8), 313 (6), 271 (10), 237 (11), 212 (3), 168 (5), 151 (4), 127 (23), 110 (11), 81 (5), 43 (100).

Methyl (3*S*,4*R*,5*R*,6*S*)-3,4,5,6-tetra(acetyloxy)-1-cyclohexene-1-carboxylate 31

The palladium-catalyzed carbonylation reaction of iodotetra-acetate **30** (0.4 g, 0.9 mmol), as described for compound **8**, gave α,β-unsaturated methyl ester **31** as a white, crystalline solid (0.2 g, 73%); mp 122–124 °C (from MeOH); (R_f 0.45, 50% EtOAc in hexane); $[\alpha]_D$ +23 (*c* 0.68, $CHCl_3$); (Found: M^+ 372.0047; $C_{16}H_{20}O_{10}$ requires 372.0056); δ_H (500 MHz, $CDCl_3$) 2.04, 2.05, 2.07, 2.15 (3H each, s, 4 × –OCOMe), 3.76 (3H, s, $–CO_2Me$), 5.32–5.33 (2H, m, 4-H, 5-H), 5.68 (1H, dd, $J_{3,4}$ 4.1, $J_{3,2}$ 3.8, 3-H), 6.01 (1H, d, $J_{6,5}$ 4.1, 6-H), 6.79 (1H, d, $J_{2,3}$ 3.8, 2-H); δ_C (125 MHz, $CDCl_3$) 20.58, 20.64, 20.70, 20.74, 52.37, 69.02, 70.00, 70.33, 71.82, 130.18, 137.87, 156.61, 156.66, 156.73, 169.59, 169.86; *m*/*z* (EI) 372 (M^+, 2%), 341 (5), 313 (9), 210 (82), 169 (99), 139 (37), 125 (17), 109 (13), 81 (7), 43 (100).

Methyl (1*R*,2*S*,3*R*,4*R*,5*S*)-2,3,4,5-tetra(acetyloxy)cyclohexane-1-carboxylate 32

Catalytic hydrogenation of α,β-unsaturated methyl ester **31** (0.7 g, 1.8 mmol), as described for the synthesis of compound **24**, gave saturated methyl ester **32** as a white, crystalline solid (0.53 g, 80%); mp 139–141 °C (from EtOH); $[\alpha]_D$ +23 (*c* 0.68, $CHCl_3$); ν_{max} (cm^{-1}) 1736.3 (C=O); (Found: C 51.2, H 5.7; $C_{16}H_{22}O_{10}$ requires C 51.3, H 5.9%); δ_H (500 MHz, $CDCl_3$) 1.76 (1H, ddd, $J_{6,5}$ 12.0, $J_{6,6'}$ 4.6, $J_{6,1}$ 3.8, 6-H), 1.99, 2.01, 2.02, 2.03 (3H each, s, 4 × –OCOMe), 2.35 (1H, ddd, $J_{6',1}$ 14.0, $J_{6',5}$ 4.7, $J_{6',6}$ 4.6, 6′-H), 2.73 (1H, ddd, $J_{1,6'}$ 14.0, $J_{1,2}$ 11.0, $J_{1,6}$ 3.8, 1-H), 3.67 (3H, s, $–CO_2Me$), 4.91 (1H, ddd, $J_{5,6}$ 12.0, $J_{5,4}$ 9.8, $J_{5,6'}$ 4.7, 5-H), 5.10 (1H, dd, $J_{3,4}$ 9.8, $J_{3,2}$ 9.7, 3-H), 5.17 (1H, dd, $J_{4,3} = J_{4,5}$ 9.8, 4-H), 5.28 (1H, dd, $J_{2,1}$ 11.0, $J_{2,3}$ 9.7, 2-H); δ_C (125 MHz, $CDCl_3$) 20.53, 20.59, 20.67, 20.79, 29.04, 42.90, 50.52, 70.15, 71.21, 72.42, 72.69, 169.87, 169.94, 170.22, 170.45, 170.63; *m*/*z* (EI) 374 (M^+, 4%), 315 (5), 301 (15), 254 (9), 230 (14), 194 (8), 187 (16), 153 (27), 138 (24), 115 (12), 87 (8), 83 (15), 68 (23), 55 (11), 43 (100).

Crystal data for 32. $C_{16}H_{22}O_{10}$, $M = 374.3$, triclinic, $a = 5.871(3)$, $b = 9.395(4)$, $c = 16.257(7)$ Å, $\alpha = 87.59(1)$, $\beta = 86.43(1)$, $\gamma = 81.82(1)°$ $U = 885.4(7)$ Å^3, $T = 150(2)$ K, Mo-Kα radiation, $\lambda = 0.71073$ Å, space group *P*1 (no. 1), $Z = 2$, $F(000) = 396$, $D_x = 1.404$ g cm^{-3}, $\mu = 0.118$ mm^{-1}, Bruker CCD area detector diffractometer, ϕ and ω scan, $2.5 < 2\theta < 46.5°$, measured/independent reflections: 5440/4751, direct methods solution, full matrix least squares refinement on F_o^2, anisotropic displacement parameters for non-hydrogen atoms, all hydrogens located in difference Fourier but included at positions determined by the geometry of the molecule using the riding model, with isotropic vibration parameters, $R_1 = 0.067$ for 2995 data with $F_o > 4\sigma(F_o)$, 479 parameters, $wR_2 = 0.189$ (all data), GoF = 0.98, $\Delta\rho_{min,max} = -0.25/0.45$ e Å^{-3}.

CCDC reference number 262886. See http://www.rsc.org/suppdata/ob/b5/b502009c/ for crystallographic data in CIF or other electronic format.

(1*S*,2*R*,3*R*,4*S*,5*S*)-5-(Hydroxymethyl)cyclohexane-1,2,3,4-tetraol (carba-β-L-glucopyranose) 5

Reduction of methyl ester **32** (0.25 g, 0.67 mmol), as described for compound **26**, furnished a sample of crude carbasugar **5**. Purification of the product by charcoal–Celite (1 : 1, v/v) column chromatography (water → 5% EtOH in water) afforded carba-β-L-glucopyranose **5** as a colourless syrup (0.014 g, 12%); $[\alpha]_D$ −6.1 (*c* 0.70, MeOH); [lit.[32] $[\alpha]_D$ +6.7 (*c* 0.15, MeOH)]; (Found: $M^+ - H_2O$ 148.0034; $C_6H_{12}O_4$ requires 148.0060); *m*/*z* (EI) 160 ($M^+ - H_2O$, 26%), 142 (30), 112 (18), 97 (7), 82 (42), 56 (100), 43 (60), 23 (32).

[(1*S*,2*S*,3*R*,4*R*,5*S*)-2,3,4,5-Tetra-acetyloxycyclohexyl]methyl acetate 33

Carba-β-L-glucopyranose **5** (0.025 g, 0.14 mmol) was acetylated (Ac_2O–pyridine) to give carba-β-L-glucopyranose penta-acetate **33** as a colourless syrup (0.05 g, 95%); (Found: M^+ 388.1371; $C_{17}H_{24}O_{10}$ requires 388.1369); $[\alpha]_D$ −5.4 (*c* 0.71, $CHCl_3$), (lit.[29] $[\alpha]_D$ −7.4, $CHCl_3$); δ_H (500 MHz, MeOH) 1.54–1.55 (1H, m, 6-H), 2.04–2.05 (1H, m, 1-H), 1.99, 2.01, 2.03, 2.05, 2.06 (3H each, s, 5 × –OCOMe), 2.16–2.18 (1H, m, 6′-H), 3.94 (1H, dd, $J_{7,7'}$ 11.4, $J_{7,1}$ 3.2, 7-H), 4.08 (1H, dd, $J_{7',7}$ 11.4, $J_{7',1}$ 5.1, 7′-H), 4.92 (1H, ddd, $J_{5,6}$ 12.5, $J_{5,4}$ 9.5, $J_{5,6'}$ 4.9, 5-H), 5.03 (1H, dd, $J_{3,4} = J_{3,2}$ 9.5, 3-H), 5.10 (1H, dd, $J_{4,3} = J_{4,5}$ 9.5, 4-H), 5.16 (1H, dd, $J_{2,1} = J_{2,3}$ 9.7, 2-H); δ_C (125 MHz, $CDCl_3$) 20.53, 20.59, 20.72, 20.86, 21.13, 29.41, 36.35, 62.80, 70.59, 71.76, 72.74, 73.28, 169.80, 169.83, 169.90, 170.09, 170.69; *m*/*z* (EI) 388 (M^+, 9%), 329 (6), 307 (2), 286 (4), 243 (6), 227 (11), 226 (40), 208 (20), 183 (21), 166 (92), 142 (10), 141 (19), 128 (22), 125 (25), 124 (100), 115 (16), 103 (13), 96 (32), 84 (60), 71 (17), 61 (5).

(3a*S*,4*S*,5*S*,7a*S*)-4-Hydroxy-7-iodo-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-5-yl 4-nitrobenzoate 34

Using Mitsunobu reaction conditions as described for the synthesis of *p*-nitrobenzoate **19**, acetonide diol **7** (0.2 g, 0.64 mmol) was converted to *p*-nitrobenzoate **34** as a white, crystalline solid (0.24 g, 80%); mp 77–80 °C (from EtOAc–hexane); (R_f 0.24, 30% EtOAc in hexane); $[\alpha]_D$ −3 (*c* 0.68, $CHCl_3$); (Found: $M^+ - Me$, 445.9739; $C_{15}H_{13}{}^{127}INO_7$ requires 445.9737); δ_H (500 MHz, $CDCl_3$) 1.45, 1.58 [3H × 2, s, $–C(Me)_2$], 4.03 (1H, dd, $J_{4,5} = J_{4,3a}$ 8.0, 4-H), 4.27 (1H, dd, $J_{3a,4}$ 8.0, $J_{3a,7a}$ 6.4, 3a-H), 4.75 (1H, d, $J_{7a,3a}$ 6.4, 7a-H), 5.47 (1H, dd, $J_{5,4}$ 8.0, $J_{5,6}$ 2.3, 5-H), 6.49 (1H, d, $J_{6,5}$ 2.3, 6-H), 8.21, 8.28 (4H, m, Ar–H); δ_C (125 MHz, $CDCl_3$), 26.38, 28.48, 70.99, 74.88, 77.19, 79.42, 79.70, 97.03, 111.18, 124.00, 131.37, 135.18, 138.42, 151.18, 164.64; *m*/*z* (EI) 446 ($M^+ - Me$, 17%), 294 (9), 236 (13), 228 (7), 166 (52), 150 (98), 120 (8), 117 (12), 110 (25), 106 (100), 91 (76), 81 (10), 76 (15), 65 (20).

(3a*S*,4*R*,5*S*,7a*S*)-7-Iodo-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxole-4,5-diol 35

A solution of *p*-nitrobenzoate **34** (0.5 g, 1.1 mmol) in MeOH (10 cm^3) was treated with aq. K_2CO_3 solution (0.3 g per 0.5 cm^3). The reaction mixture was heated at 40 °C until all the starting material had hydrolyzed (*ca.* 2 h, TLC analysis). The solvent was then removed under reduced pressure and the residue purified by flash column chromatography (50% EtOAc in hexane) to give *trans*-diol **35** as a white, crystalline solid (0.28 g, 82%); mp 135–137 °C (from EtOAc–hexane); (R_f 0.44, 50% EtOAc in hexane); $[\alpha]_D$ −5.0 (*c* 0.99, MeOH); (Found: M^+ 311.9866; $C_9H_{13}{}^{127}IO_4$ requires 311.9859); δ_H (500 MHz, $CDCl_3$) 1.28, 1.42 [3H × 2, s, $–C(Me)_2$], 3.76 (1H, dd, $J_{4,3a}$ 7.8, $J_{4,5}$ 7.5, 4-H), 4.04 (1H, dd, $J_{5,4}$ 7.5, $J_{5,6}$ 1.8, 5-H), 4.18 (1H, dd, $J_{3a,4}$ 7.8, $J_{3a,7a}$ 6.2, 3a-H), 4.69 (1H, d, $J_{7a,3a}$ 6.2, 7a-H), 6.54 (1H, d, $J_{6,5}$ 1.8, 6-H); δ_C (125 MHz, $CDCl_3$), 24.97, 27.00, 70.68, 71.81, 76.26, 78.33, 94.00, 109.54, 140.98; *m*/*z* (EI) 312 (M^+, 2%), 298 (5), 297 (59), 237 (6), 209 (8), 191 (5), 185 (9), 148 (12), 127 (5), 117 (17), 116 (55), 110 (42), 101 (26), 81 (15), 59 (100), 57 (6).

(3a*R*,4*S*,5*S*,7a*S*)-4-Benzoyloxy-7-iodo-2,2-dimethyl-3a,4,5,7a-tetrahydro-1,3-benzodioxol-5-yl benzoate 36

trans-Diol **35** (0.1 g, 0.32 mmol) was converted to dibenzoate **36** (PhCOCl–pyridine) as a white, crystalline solid (0.16 g, 93%); mp 108–109 °C (from MeOH); (R_f 0.26, 15% Et_2O–hexane); $[\alpha]_D$ +87 (*c* 0.67, $CHCl_3$); (Found C 52.75, H 4.25; $C_{23}H_{21}{}^{127}IO_6$ requires C 53.1, H 4.0%); δ_H (500 MHz, $CDCl_3$) 1.43, 1.62 [3H × 2, s, $–C(Me)_2$], 4.51 (1H, dd, $J_{3a,4}$ 8.0, $J_{3a,7a}$ 5.8, 3a-H), 4.83 (1H, d, $J_{7a,3a}$ 5.8, 7a-H), 5.61 (1H, dd, $J_{5,4}$ 8.0, $J_{5,6}$ 2.2, 5-H), 5.72 (1H, dd, $J_{4,5} = J_{4,3a}$ 8.0, 4-H), 6.60 (1H, d, $J_{6,5}$ 2.2, 6-H), 7.37–7.43 (4H, m, Ar–H), 7.50 (2H, m, Ar–H), 7.97–8.03 (4H, m, Ar–H);

δ_C (125 MHz, $CDCl_3$), 26.74, 28.23, 71.12, 71.99, 75.29, 79.93, 97.18, 111.57, 128.77, 128.85, 129.45, 129.80, 130.23, 130.25, 130.43, 130.75, 131.18, 133.45, 133.59, 133.78, 138.79, 165.89, 166.15; *m/z* (EI) 520 (M^+, 2%), 505 (5), 398 (30), 341 (4), 142 (37), 106 (38), 105 (100), 77 (68).

(1*S*,4*S*,5*R*,6*S*)-6-Benzoyloxy-4,5-dihydroxy-3-iodo-2-cyclohexenyl benzoate 37

Deprotection of the acetonide group of dibenzoate **36** (0.16 g, 0.3 mmol) using the procedure described for the synthesis of benzoate **18** gave *cis*-diol **37** as a colourless oil (0.125 g, 86%); (R_f 0.23, 30% EtOAc in hexane); $[\alpha]_D$ −23 (*c* 1.0, $CHCl_3$); (Found: $M^+ - H_2O$, 462.0021; $C_{20}H_{15}{}^{127}IO_5$ requires 462.0025); δ_H (500 MHz, $CDCl_3$) 4.06 (1H, dd, $J_{5,6}$ 8.6, $J_{5,4}$ 4.2, 5-H), 4.54 (1H, d, $J_{4,5}$ 4.2, 4-H), 5.74–5.76 (2H, m, 1-H, 6-H), 6.50 (1H, d, $J_{2,1}$ 2.3, 2-H), 7.39–7.48 (6H, m, Ar–H), 7.96–8.11 (4H, m, Ar–H); δ_C (125 MHz, $CDCl_3$) 70.45, 71.91, 73.62, 76.49, 94.41, 100.46, 128.85, 129.13, 129.45, 130.01, 130.78, 131.23, 131.78, 132.67, 133.33, 133.67, 134.04, 137.97, 167.90, 167.98; *m/z* (EI) 462 ($M^+ - H_2O$, 34%), 353 (27), 329 (7), 316 (13), 307 (8), 281 (5), 254 (41), 249 (18), 236 (36), 231 (52), 225 (93), 212 (39), 208 (100), 207 (23), 196 (7).

(1*R*,4*S*,5*S*,6*S*)-4,5-Di(benzoyloxy)-6-hydroxy-2-iodo-2-cyclohexenyl 4-nitrobenzoate 38

Employing the Mitsunobu reaction conditions as described for the synthesis of *p*-nitrobenzoate **19**, *cis*-diol **37** (0.05 g, 0.1 mmol) gave *p*-nitrobenzoate **38** as a white, crystalline solid (0.051 g, 80%); mp 108–111 °C (from EtOAc); (R_f 0.28, 20% EtOAc in hexane); $[\alpha]_D$ +125 (*c* 0.51, $CHCl_3$); (Found: M^+ 629.0259; $C_{27}H_{20}{}^{127}INO_9$ requires 629.0261); δ_H (500 MHz, $CDCl_3$) 4.32 (1H, dd, $J_{6,5}$ 10.6, $J_{6,1}$ 7.6, 6-H), 5.78 (1H, dd, $J_{5,6}$ 10.6, $J_{5,4}$ 8.2, 5-H), 5.91 (1H, dd, $J_{4,5}$ 8.7, $J_{4,3}$ 2.7, 4-H), 6.03 (1H, d, $J_{1,6}$ 7.6, 1-H), 6.68 (1H, d, $J_{3,4}$ 2.3, 3-H), 7.39, 7.42–7.56 (6H, m, Ar–H), 7.98–8.34 (8H, m, Ar–H); δ_C (125 MHz, $CDCl_3$) 72.20, 72.45, 73.50, 78.70, 97.80, 130.10, 130.78, 131.29, 131.34, 131.40, 131.47, 131.55, 132.45, 133.00, 133.12, 133.67, 134.11, 134.22, 134.49, 134.71, 134.77, 134.81, 135.56, 135.91, 164.96, 166.45, 167.50; *m/z* (EI) 629 (M^+, 12%), 508 (100), 510 (5), 502 (3), 463 (4), 386 (5), 341 (4), 308 (12), 289 (13), 222 (10), 198 (7), 154 (3), 100 (9), 67 (12), 43 (5).

(1*R*,4*S*,5*R*,6*S*)-4,5-Di(benzoyloxy)-6-[{1-(*tert*-butyl)-1,1-dimethyl}-oxy]-2-iodo-2-cyclohexenyl 4-nitrobenzoate 39

To a solution of *p*-nitrobenzoate **38** (0.13 g, 0.21 mmol) in dry CH_2Cl_2 (4 cm^3) containing 2,6-lutidine (0.07 g, 0.62 mmol) was added, under a nitrogen atmosphere, TBDMSTf (0.085 g, 0.32 mmol) at 0 °C. After stirring the reaction mixture at 0 °C (0.25 h) and then at room temperature (3 h), it was quenched by adding 5% aq. $NaHCO_3$ solution. The mixture was extracted with CH_2Cl_2 (2 × 20 cm^3), the organic extract washed with water and dried (Na_2SO_4). Purification of the residue, obtained after evaporation of CH_2Cl_2, by PLC (25% EtOAc in hexane) yielded the mono-TBDMS derivative **39** as a colourless, viscous oil (0.14 g, 93%); (R_f 0.20, 10% Et_2O in hexane); $[\alpha]_D$ +117 (*c* 0.61, $CHCl_3$); (Found: M^+ 742.9934; $C_{33}H_{34}{}^{127}INSiO_9$ requires 742.9933); δ_H (500 MHz, $CDCl_3$) 0.15, 0.17 [3H × 2, s, –Si(Me)$_2$], 0.68 [9H, s, –C(Me)$_3$], 4.41 (1H, dd, $J_{6,5}$ 8.1, $J_{6,1}$ 7.6, 6-H), 5.82–5.83 (2H, m, 4-H, 5-H), 6.06 (1H, d, $J_{1,6}$ 7.6, 1-H), 6.68 (1H, d, $J_{3,4}$ 2.0, 3-H), 7.26–7.53 (6H, m, Ar–H), 7.95–8.30 (8H, m, Ar–H); δ_C (125 MHz, $CDCl_3$) −4.47, −4.45, 15.12, 24.79, 25.25, 25.35, 71.20, 72.61, 72.76, 78.55, 99.23, 123.69, 133.42, 133.54, 133.56, 133.65, 133.66, 133.67, 133.99, 134.11, 134.24, 134.25, 134.37, 134.41, 134.66, 134.70, 134.72, 134.73, 134.74 137.89, 163.63, 163.93, 165.34; *m/z* (EI) 743 (M^+, 9%), 686 (14), 624 (27), 577 (16), 546 (12), 512 (53), 489 (17), 455 (13), 390 (17), 373 (5), 351 (80), 327 (7), 289 (14), 212 (10), 105 (100), 77 (17), 57 (15), 43 (28).

(1*S*,2*R*,3*S*,4*R*)-3-[1-(*tert*-Butyl)-1,1-dimethylsilyl]-5-iodo-5-cyclohexene-1,2,4-triol 40

To a solution of compound **39** (0.2 g, 0.27 mmol) in MeOH (20 cm^3), 5% aq. NaOH solution was added (3 cm^3). The reaction mixture was stirred at room temperature until all the starting material had hydrolysed (TLC analysis). The solvents were evaporated and the residue purified by flash column chromatography (60% EtOAc in hexane) to give the TBDMS triol **40** as a colourless, viscous oil (0.09 g, 86%); (R_f 0.49, 70% EtOAc in hexane); $[\alpha]_D$ +13 (*c* 0.69, MeOH); (Found: M^+ 386.0398; $C_{12}H_{23}{}^{127}IO_4Si$ requires 386.0410); δ_H (500 MHz, CD_3OD) 0.00, 0.04 [3H × 2, s, –Si(Me)$_2$], 0.77 [9H, s, –C(Me)$_3$], 3.16 (1 H, dd, $J_{2,3}$ 10.4, $J_{2,1}$ 8.0, 2-H), 3.23 (1H, dd, $J_{3,2}$ 10.4, $J_{3,4}$ 7.0, 3-H), 3.77 (1H, dd, $J_{1,2}$ 8.0, $J_{1,6}$ 2.1, 1-H), 3.91 (1H, dd, $J_{4,3}$ 7.0, $J_{4,6}$ 1.7, 4-H), 6.12 (1H, dd, $J_{6,1}$ 2.1, $J_{6,4}$ 1.7, 6-H), δ_C (125 MHz, CD_3OD) −4.72, −4.70, 17.88, 25.07, 25.24, 25.41, 72.38, 72.90, 75.07, 75.42, 103.32, 140.81, *m/z* (EI) 386 (M^+, 10%), 329 (3), 311 (6), 283 (4), 237 (5), 202 (6), 191 (10), 185 (15), 184 (48), 183 (17), 156 (19), 155 (8), 121 (26), 110 (28), 103 (32), 82 (15), 75 (100), 59 (7).

Methyl (3*S*,4*R*,5*R*,6*S*)-5-[{1-(*tert*-butyl)-1,1-dimethylsilyl}-oxy]-3,4,6-trihydroxy-1-cyclohexene-1-carboxylate 41

Palladium-catalyzed carbonylation of compound **40** (0.08 g, 0.2 mmol) using the procedure mentioned earlier yielded methyl ester **41** as a colourless, viscous oil (0.09 g, 69%); (R_f 0.40, 70% EtOAc in hexane); $[\alpha]_D$ +32 (*c* 0.57, MeOH); (Found: $M^+ - H_2O$, 300.0034; $C_{14}H_{24}O_5Si$ requires 300.0019); δ_H (500 MHz, CD_3OD) 0.04 [6H, s, –Si(Me)$_2$], 0.77 [9H, s, –C(Me)$_3$], 3.18 (1H, dd, $J_{4,5}$ 10.2, $J_{4,3}$ 8.0, 4-H), 3.32 (1H, dd, $J_{5,4}$ 10.2, $J_{5,6}$ 7.3, 5-H), 3.60 (3H, s, $-CO_2Me$), 3.81 (1H, dd, $J_{3,4}$ 8.0, $J_{3,2}$ 2.2, 3-H), 3.95 (1H, d, $J_{6,5}$ 7.3, 6-H), 6.30 (1H, d, $J_{2,3}$ 2.2, 2-H); δ_C (125 MHz, CD_3OD) −4.24, −4.22, 17.93, 25.24, 25.44, 25.83, 51.39, 70.33, 71.49, 75.52, 76.03, 103.80, 140.34, 167.13; *m/z* (EI) 300 ($M^+ - H_2O$, 34%), 285 (56), 243 (79), 208 (27), 176 (34), 124 (100), 91 (81), 76 (11), 43 (65), 29 (15).

Methyl (1*R*,2*S*,3*R*,4*R*,5*S*)-3-[{1-(*tert*-butyl)-1,1-dimethylsilyl}-oxy]-2,4,5-tri(hydroxyl)cyclohexane-1-carboxylate 42

α,β-Unsaturated methyl ester **41** (0.08 g, 0.25 mmol) was catalytically hydrogenated using the procedure described for the hydrogenation of compound **8** to give the saturated methyl ester **42** as a colourless syrup (0.07 g, 80%); $[\alpha]_D$ +18 (*c* 0.60, MeOH); (Found: $M^+ - H_2O$ 302.0942; $C_{14}H_{26}SiO_5$ requires 302.0951); δ_H (500 MHz, MeOH) 0.01 [6H, s, –Si(Me)$_2$], 0.78 [9H, s, –C(Me)$_3$], 1.38–1.39 (1H, m, 6-H), 1.79 (1H, ddd, $J_{6',1}$ 13.1, $J_{6',6} = J_{6',5}$ 4.2, 6′-H), 2.31 (1H, ddd, $J_{1,6'}$ 13.1, $J_{1,2}$ 10.0, $J_{1,6}$ 3.6, 1-H), 3.42 (3H, s, $-CO_2Me$), 3.03–3.04 (2H, m, 3-H, 4-H), 3.41–3.42 (2H, m, 2-H, 5-H); δ_C (125 MHz, $CDCl_3$) −4.26, 19.37, 26.66–26.75, 47.59, 52.81, 74.38, 75.17, 78.26, 79.23, 175.80; *m/z* (EI) 302 ($M^+ - H_2O$, 25%), 245 (34), 231 (10), 227 (24), 213 (25), 171 (19), 167 (12), 153 (10), 139 (46), 129 (18), 121 (16), 111 (19), 93 (18), 83 (13), 75 (100), 73 (43), 67 (11), 59 (18).

Methyl (1*R*,2*S*,3*R*,4*R*,5*S*)-3,4,5-tri[{1-(*tert*-butyl)-1,1-dimethylsilyl}oxy]-2-hydroxycyclohexane-1-carboxylate 43

Using the procedure described for the synthesis of compound **39**, methyl ester **42** (0.160 g, 0.5 mmol) was converted to the tri-TBDMS derivative **43**, a colourless syrup (0.250 g, 95%); $[\alpha]_D$ −4 (*c* 0.71, $CHCl_3$); (Found: M^+ 548.0084; $C_{26}H_{56}O_6Si_3$ requires 548.0080); δ_H (500 MHz, $CDCl_3$) 0.006, 0.01, 0.012 [6H, s, 3 × –Si(Me)$_2$], 0.78, 0.80, 0.81 [9H, s, 3 × –C(Me)$_3$], 1.79–1.80 (2H, m, *J* 9.2, 6-H, 6′-H), 2.60–2.61 (1H, m, 1-H), 3.59 (3H, s, $-CO_2Me$), 3.60–3.61 (1H, m, 3-H), 3.66–3.68 (1H, m, 4-H), 3.87–3.89 (1H, m, *J* 8.1, *J* 2.3, 5-H), 4.13–4.14 (1H, m, *J* 6.0, 2-H); δ_C (125 MHz, $CDCl_3$) −4.51, −4.47, −4.39, −4.35, −4.22, −4.11, 17.82, 17.87, 17.95, 23.45, 25.10, 25.22, 25.27, 25.56, 25.78, 25.81, 25.82, 25.98, 26.06, 40.02, 51.62, 73.36, 74.96, 78.59, 79.37, 174.94; m/z (EI) 548 (M^+, 2%), 474 (33), 473 (74), 415 (10), 399 (14), 341 (8), 267 (20), 245 (10), 209 (5), 189 (29), 171 (5), 148 (25), 147 (84), 133 (21), 115 (12), 105 (5), 89 (18), 84 (27), 73 (100).

(1*S*,2*R*,3*R*,4*S*,5*S*)-5-(Hydroxymethyl)cyclohexane-1,2,3,4-tetraol (carba-β-L-glucopyranose) 5

Compound **43** (0.080 g, 0.15 mmol) was reduced ($LiAlH_4$–THF) using the procedure described for the synthesis of compound **26** to give the protected carbasugar **44** as a colourless syrup; ^{1}H-NMR spectral data of the crude product were consistent with the structure. Deprotection of carbasugar **44** was carried out without purification. To a cooled solution (0 °C) of carbasugar **44** (0.1 g) in dry THF (1 cm^3), tetrabutylammonium fluoride solution (1.0 M solution in THF, 0.75 cm^3) was added. The reaction mixture was stirred at 0 °C (0.5 h) and then at room temperature (3 h). Removal of the solvent under reduced pressure afforded the crude, free carbasugar which, upon purification using charcoal–Celite (1 : 1, v/v) column chromatography (water → 10% EtOH in water), afforded carba-β-L-glucose **5** as a white powder (0.02 g, 82%); $[\alpha]_D$ −6.5 (c 0.50, MeOH). The spectral data of carbasugar **5** were identical to those reported in the literature.[32]

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