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Synthesis of Protected (±)- α- and ß-Carba-psicofuranose

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Abstract: Protected racemic α- and ß-psicofuranose were synthesized from a non-carbohydrate precursor which is available in both enantiomeric forms.

INTRODUCTION

Carbocyclic analogues of sugars have attracted considerable attention as potential inhibitors of carbohydrate metabolism. While the corresponding *carba*-pyranoses have been extensively studied,[1] the five-membered *carba*-furanoses have received less attention. Both *carba*-ß-D-ribofuranose[2,3] and *carba*-ß-L-arabinofuranose[4,5] have been reported and, more recently, the synthesis of *carba*-ß-D-fructofuranose was described as the first example of a *carba*-ketofuranose.[6,7]

In the course of our ongoing efforts toward the synthesis of carbocyclic nucleoside analogues,[8] particularly those with a neplanocin A type cyclopentene "glycon" moiety,[9] we set out to develop an approach to carbocyclic five-memberd sugars possessing a tertiary hydroxyl function capable of generating the requisite cyclopentene upon dehydration. The selected targets represent carbocyclic analogues of psicofuranoses which are isomeric to the aforementioned ketohexose, *carba*-fructofuranose.

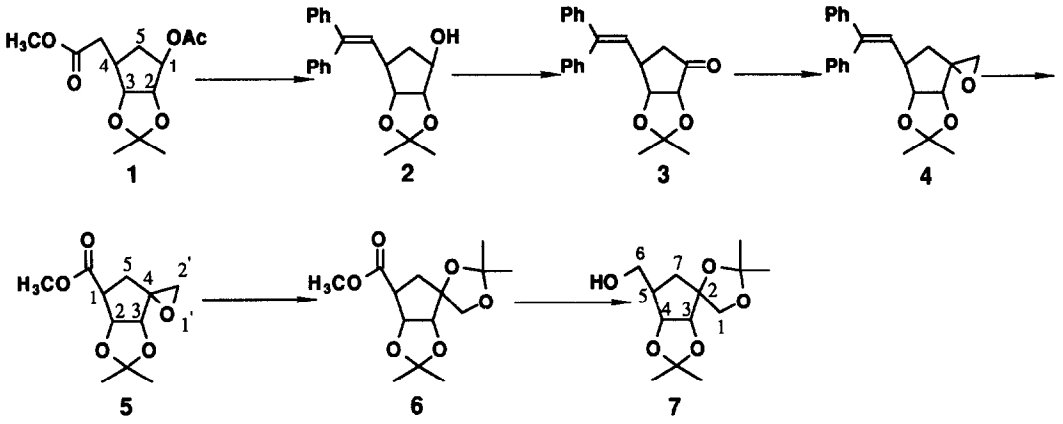
In order not to limit the synthesis to one particular enantiomer, compound (±)-**1** was chosen as starting material. This compound is accessible in five steps from norbornenol[4] from which both enantiomers are available in good yield and in high enantiomeric excess following enzymatic resolution.[10] Therefore, facile access is available to either enantiomer should one prove to be of biological interest.

CHEMISTRY

The required one-carbon shortening of the ester side chain in **1** was performed via a Barbier-Wieland-type degradation in order to preserve the ester function in the resulting side chain (compounds **5**, **9**, and **14**). This ester function provides a key branching point from which either carbocyclic psicofuranose nucleosides or carbocyclic C-nucleosides can be synthesized depending on the enantiomer used.

Grignard reaction of **1** with phenylmagnesium bromide required excess reagent due to the presence of the additional acetate ester function which underwent cleavage during the reaction. Anhydrous $CuSO_4$ mediated dehydration[11] of the unisolated tertiary alcohol intermediate gave the diphenylvinyl cyclopentanol **2**, which was transformed into ketone **3** by Swern oxidation (Scheme 1).

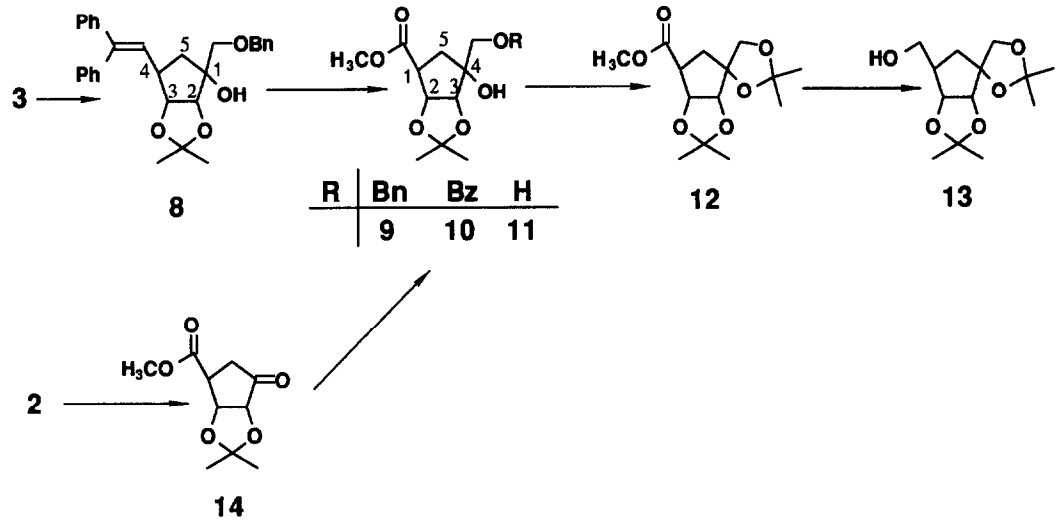
Scheme 1



The carbonyl function of this central intermediate underwent nucleophilic attack in a strictly regiospecific manner due to the high steric bias introduced by the isopropylidene group. Therefore, reaction of **3** with dimethylsulfoxonium ylide[12] gave the spirooxirane **4** which was then subjected to oxidative degradation with ruthenium tetroxide.[13] Esterification of the unisolated intermediate acid with diazomethane completed the final phase of the Barbier-Wieland degradation with the formation of the ester epoxide **5**. The epoxide ring in **5** was smoothly solvolyzed in acetone under acidic conditions and attack at the more highly substituted carbon position[14] resulted in the formation of **6**. Final reduction with lithium aluminum hydride provided *carba*-ß-psicofuranose **7** as an oil.

Several attempts to reverse the mode of opening of the epoxide ring in **5** under neutral and basic conditions failed giving only decomposition products. Therefore, another approach was developed to

Scheme 2



obtain the corresponding α-psicofuranose (Scheme 2). Addition of Johnson's benzyloxymethyl anion, generated *in situ* from the corresponding tri-n-butyltin precursor,[15] to cyclopentanone **3** led to the tertiary alcohol **8**. In the course of these experiments a simplified synthesis of this tin reagent was devised (see experimental). The resulting intermediate **8** was then subjected to the same type of oxidative degradation that was performed previously with compound **4**; however, in this instance, varying amounts of overoxidized product **10** were isolated depending on the duration of the reaction. Since the resulting mixture of **9** and **10** was not separable by preparative chromatography, the mixture was hydrogenated over palladium on carbon until the predominating benzyl-protected compound **9** was converted to diol **11**. At this stage, the mixture was resolved into its components. The benzoyl group in **10** could be removed by treatment with sodium methoxide in methanol to give the same diol **11**. In an attempt to circumvent the overoxidation problem, alcohol **2** was reacted with ruthenium tetroxide to give the methyl ester ketone **14** after esterification with diazomethane. This compound was reacted, in turn, with the benzyloxymethyl anion generated as before to give compound **9**.This route, however had the drawback of a low yield oxidation step, plus a multiplicity of byproducts formed from the reaction with the benzyloxymethyl anion. These byproducts possibly arose as a result of nucleophilic attack at the additional carbonyl (ester) function. The diol ester **11** obtained from both routes was converted by transacetalization with dimethoxypropane into the fully protected derivative **12** which upon reduction with LAH gave the desired isomeric carbocyclic α-psicofuranose as a crystalline solid.

EXPERIMENTAL

General. All chemical reagents were commercially available, dry solvents were used for all procedures and reactions were generally carried out under inert atmosphere. Melting points were determined on a Mel-Temp II apparatus, Laboratory Devices, USA, and are uncorrected. Silica gel column chromatography was performed on silica gel 60, 230-400 mesh (E. Merck), preparative TLC on Analtech plates (500 and 100 micron) and analytical TLC was performed on Merck silica gel 60 F_{254} aluminum sheets. Eluant compositions in volume : A = toluene/ethyl acetate 3:1; B = petroleum ether/ethyl acetate 3:1; C = petroleum ether/ethyl acetate 9:1; D = chloroform/methanol 9:1; E = toluene/ethyl acetate 9:1. Proton and carbon NMR spectra were recorded in $CDCl_3$ in a Varian XL-200 or a Bruker AC-250 instrument as indicated by the frequency noted for the individual spectra. Chemical shifts are expressed as δ values with reference to Me_4Si. In the carbon spectra the signs + and - refer to the peaks above or below the base line in the fully decoupled attached proton test (APT), the letters s, d, t, q indicate the multiplicity obtained by using distortionless enhancement by polarization transfer (DEPT). Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, GA. Mass spectra were recorded in a VG 7070 E mass spectrometer using fast atom bombardment (FAB) and either glycerol or 3-nitrobenzyl alcohol as matrix.

***rel*-(1*R*, 2*S*, 3*R*, 4*R*)-2,3-O-isopropylidene-4-(2,2-diphenylvinyl)cyclopentane-1-ol (2)**

A 3.0 M solution of phenylmagnesiumbromide in ether (47 mL, 141 mmol) was placed in a flask equipped with a reflux condenser and a solution of **1** (5.315 g, 19.52 mmol) in ether (50 mL) was added at a rate sufficient to hold the mixture to a gentle reflux. After the addition was completed the turbid solution was heated to reflux for 2 h and then hydrolyzed by the cautious addition of saturated NH_4Cl solution (50 mL). The ether layer was separated, the aqueous phase extracted with ether (2x70 mL), and the combined organic layers were dried and evaporated *in vacuo*. The residue was subjected to column chromatography (eluant A). The more polar fractions containing the crude product were pooled and evaporated to dryness to leave an oily residue.

A solution of this product in toluene (100 mL) was treated with anhydrous $CuSO_4$ (5.0 g) and

heated to reflux for 3.5 h while the liberated water was removed by means of a Dean-Stark trap. The solvent was removed after filtration over a pad of Celite and the residue was purified by column chromatography (eluant B) to give 3.60 g (54.8% over 2 steps) of the title compound as an highly viscous oil. An analytical sample was obtained by recrystallisation from ether/petroleum ether, mp 110-11°C. ^{1}H-NMR (200 MHz) δ 1.28 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.50 - 2.30 (m, 2H, CH_2-5), 2.05 (m, 1H, OH), 2.90 (m, 1H, H-4), 4.19 (m, 1H, H-1), 4.47 - 4.61 (m, 2H, H-2, H-3), 6.13 (d, J=10.7 Hz, 1H, vinyl-CH), 7.19 - 7.42 (m, 10H, Ph); ^{13}C-NMR: APT (50 MHz) δ 24.51 (-), 26.69 (-), 39.42 (+), 44.84 (-), 77.29 (-), 85.77 (-), 87.52 (-), 111.11 (+), 127.05 (-), 127.37 (-), 128.04 (-), 128.16 (-), 130.05 (-), 130.77 (-), 139.55 (+), 142.08 (+), 142.44 (+). Anal. Calcd. for $C_{22}H_{24}O_3$: C, 78.54; H, 7.24. Found: C, 78.61; H, 7.24.

***rel*-(2*R*, 3*R*, 4*R*)-2,3-O-isopropylidene-4-(2,2-diphenylvinyl)cyclopentan-1-one (3)**

A mixture of dimethyl sulfoxide (0.43 mL, 9.8 mmol) and CH_2Cl_2 (2.5 mL) was added dropwise to a cooled (-78°C) stirred solution of oxalyl chloride (0.43 mL, 4.9 mmol) in CH_2Cl_2 and stirring was continued until the evolution of gas ceased. A solution of **2** (1.360 g, 4.04 mmol) in CH_2Cl_2 (4 mL) was added slowly not allowing the temperature to rise above -65°C and stirring was continued for an additional 30 min, followed by quenching with triethylamine (1.8 mL). The reaction mixture was partitioned between water and CH_2Cl_2, the organic layers were dried, evaporated, and the residue subjected to column chromatography (eluant B) to give 1.165 g (86.2%) **3** as an oil which crystallized slowly on seeding. An analytical sample was recrystallized from petroleum ether, mp 91-2°C. ^{1}H-NMR: (200 MHz) δ 1.35 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 2.20 (m, 1H, H-5a), 2.80 (dd, J_1=18.4 Hz, J_2=8.4 Hz, 1H, H-5b), 3.26 (m, 1H, H-4), 4.37 (d, J=5.4 Hz, 1H, H-2), 4.66 (dd, J_1=5.4 Hz, J_2<1Hz, 1H, H-3), 5.72 (d, J=10.9 Hz, 1H, vinyl-CH), 7.18 - 7.50 (m, 10H, Ph); ^{13}C-NMR: APT (50 MHz) δ 25.03 (-), 26.79 (-), 37.67 (-), 41.35 (+), 78.40 (-), 82.25 (-), 112.48 (+), 127.20 (-), 127.34 (-), 127.60 (-), 127.69 (-), 128.22 (-), 128.48 (-), 129.58 (-), 138.86 (+), 141.53 (+), 144.45 (+), 213.14 (+). Anal. Calcd. for $C_{22}H_{22}O_3$: C, 79.02; H, 6.63. Found: C, 79.06; H, 6.66.

***rel*-(1*R*, 2*R*, 3*R*, 4*R*)-2,3-O-isopropylidene-4-(2,2-diphenylvinyl)cyclopentane-1-spiro-oxirane (4)**

A suspension of sodium hydride in oil (0.402 g, 80%, 13.38 mmol) and trimethylsulfonium iodide (2.949 g, 13.40 mmol, 1.2 eq.) was placed in a 250 mL flask under inert atmosphere. After addition of DMSO (25 mL) and stirring until the evolution of gas ceased, a solution of **3** (3.734 g, 11.166 mmol) in DMSO (10 mL) was added slowly. The mixture was allowed to react for 1 h at room temperature and partitioned between ether (250 mL) and water (100 mL). The organic layer was separated, dried and concentrated to a small volume *in vacuo* and cooled to give a first crop of crystalline **4**. A second crop could be obtained by concentrating the mother liquor further to give a combined yield of 3.496 g (89.9%) of the title compound as colorless crystals. An analytical sample was recrystallized from ether, mp 125-26.5°C. ^{1}H-NMR: (250 MHz) δ 1.28 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.44 (m, 1H, H-5a), 2.54 (dd, J_1=14.0 Hz, J_2=6.9 Hz, 1H, H-5b), 2.86 (A of AB, J_{AB}=4.5 Hz, 1H, H-2'$_a$), 3.00 (B of AB, J_{AB}=4.5 Hz, 1H, H-2'$_b$), 3.08 (m, 1H, H-4), 4.33 (dd, J_1=5.6 Hz, J_2=0.6 Hz, 1H, H-3), 4.66 (d, J=5.6 Hz, 1H, H-2), 6.07 (d, J=11.1 Hz, vinyl-CH), 7.17-7.42 (m, 10H, Ph); ^{13}C-NMR: DEPT (62.5 MHz) δ 24.30 (q), 26.42 (q), 35.62 (t), 44.25 (d), 47.41 (t), 65.64 (s), 84.68 (d), 85.55 (d), 110.78 (s), 127.18 (d), 127.23 (d), 127.39 (d), 128.08 (d), 128.32 (d), 128.65 (d), 129.85 (d), 139.50 (s), 142.11 (s), 142.74 (s). Anal. Calcd. for $C_{23}H_{24}O_3$: C, 79.28; H, 6.94. Found: C, 79.19; H, 6.98.

***rel*-(1*S*, 2*R*, 3*R*, 4*R*)-2,3-O-isopropylidene-4-spirooxirane-1-cyclopentaneacetic acid methyl ester (5)**

Epoxide **4** (3.319 g, 9.525 mmol) was dissolved in a 1:1 mixture of acetonitrile and carbon tetrachloride (40 mL). Sodium periodate (12.0 g) and 30 mL of a solution containing 2 mg/mL of ruthenium

trichloride hydrate were added. After stirring efficiently at room temperature for 2.5 h, sufficient water was added to dissolve the precipitated sodium iodate and the mixture was extracted with CH_2Cl_2 (3x70 mL). The combined organic layers were carefully dried and evaporated *in vacuo* . The black residue was treated with ether (100 mL) and the precipitated ruthenium salts were removed by filtration over Celite to give an almost colorless solution which was treated with an ether solution of diazomethane until no more acid could be detected on tlc (eluant D). Column chromatography (first eluant C until the benzophenone is eluted, then B) after removal of the solvent gave 1.186 g (54.6%) of the title compound **5** as an oil which crystallized on storage. An analytical sample was recrystallized from petroleum ether, mp 46-7.5°C. ^{1}H-NMR: (250 MHz) δ 1.28 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.84 (m, 1H, H-5_a), 2.62 (dd, J_1=14.4 Hz, J_2=8.5 Hz, 1H, H-5_b), 2.84 (A of AB, J_{AB}=4.5 Hz, 1H, H-2'$_a$), 2.97 (B of AB, J_{AB}=4.5Hz, 1H, H-2'$_b$), 3.07 (m, 1H, H-1), 3.70 (s, 3H, OCH_3), 4.26 (dd, J_1=5.7 Hz, J_2=1.0 Hz, 1H, H-2) 5.06 (d, J=5.7 Hz, 1H, H-3); ^{13}C-NMR: DEPT (62.5 MHz) δ 24.19 (q), 26.43 (q), 32.64 (t), 47.41 (t), 48.43 (d), 52.22 (q), 65.02 (s), 81.59 (d), 84.30 (d), 111.13 (s), 173.12 (s). Anal. Calcd. for $C_{11}H_{16}O_5$: C, 57.89; H, 7.07. Found: C, 57.89; H, 7.06.

rel-(1*S*, 2*R*, 3*R*, 4*S*)-2,3-O-isopropylidene-4-spiro-5'-(2',2'-dimethyl-1',3'-dioxolane)-1-cyclopentane-acetic acid methyl ester (6)

A solution of epoxide **5** (407 mg, 1.783 mmol) in reagent grade acetone (10 mL) was treated with 5 drops of etherial HBF_4 (54%) and stirred at room temperature for 1.5 h. The reaction was quenched by the addition of triethylamine (0.1 mL) and the solvents were removed *in vacuo*. The crude material was purified by chromatography (eluant C) to give 397 mg (77.8%) of **6** as an oil which crystallized on storage, mp 57-9°C. ^{1}H-NMR: (250 MHz) δ 1.28 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 2.19 (m, 2H, CH_2-5), 2.80 (d, J=7.7 Hz, 1H, H-1), 3.66 (s, 3H, OCH_3), 3.80 (A of AB, J_{AB}=9.0 Hz, 1H, H-4'$_a$), 4.16 (B of AB, J_{AB}=9.0 Hz, 1H, H-4'$_b$), 4.35 (d, J=5.7 Hz, 1H, H-3), 5.18 (d, J=5.7 Hz, 1H, H-2); ^{13}C-NMR: DEPT (62.5 MHz) δ 23.98 (q), 26.28 (q), 26.48 (q), 26.51 (q), 36.57 (t), 48.38 (d), 51.74 (q), 68.33 (t), 81.49 (d), 84.98 (d), 88.46 (s), 110.16 (s), 110.69 (s), 172.98 (s). Anal. Calcd. for $C_{14}H_{22}O_6$: C, 58.73; H, 7.47. Found: C, 58.84; H, 7.74.

(±)-*carba*-(1,2:3,4-di-O-isopropylidene)-ß-psicofuranose (7)

A suspension of lithium aluminum hydride (10 mg, 0.263 mmol) in ether (3 mL) was treated with a solution of methyl ester **6** (63 mg, 0.220 mmol) in ether (2 mL). The reaction was quenched by cautious addition of saturated NH_4Cl solution after stirring at room temperature for 45 min. The ether layer was separated, evaporated and the residue was purified by preparative tlc (eluant D) to yield **7** (54 mg, 95.0%) as an oil. ^{1}H-NMR: (250 MHz) δ 1.25 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.37 (s, 6H, 2xCH_3), 1.65 (m, 1H, H-7a), 2.20 (m, 2H, H-7b, H-5), 2.93 (br s, 1H, OH), 3.63 (br s, 2H, CH_2OH), 3.78 (A of AB, J_{AB}=9.2 Hz, 1H, H-1_a), 4.31 (B of AB, J_{AB}=9.2 Hz, 1H, H-1_b), 4.33 (dd, J_1=5.7 Hz, J_2=1.5 Hz, 1H, H-4), 4.68 (d, J=5.7 Hz, 1H, H-3); ^{13}C-NMR: DEPT (62.5 MHz) δ 23.96 (q), 26.43 (q), 26.52 (q), 26.63 (q), 46.28 (t), 64.39 (t), 68.82 (t), 83.26 (d), 86.03 (d), 89.19 (s), 110.25 (s), 110.42 (s). Anal. Calcd. for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.25.61; H, 8.55. FAB-MS (m/z): 259 (MH^+, 100)

Simplified preparation of tri-n-butylbenzyloxymethyltin

A solution of sodium benzylate in THF was prepared by addition of benzyl alcohol (5.255 g, 48.6 mmol) to a suspension of NaH (1.683 g, 80% in oil, 56.1 mmol) in THF (100 mL). One hour after the evolution of hydrogen ceased, tri-n-butylchloromethyltin[16] (12.379 g, 36.5 mmol) and tetrabutylammonium iodide (0.3 g) were added and the mixture was stirred at room temperature overnight. The excess of NaH was destroyed by slow addition of MeOH (5 mL) and the mixture was diluted with petroleum ether (500

mL) and washed with water (2x250 mL). The organic layer was dried, evaporated *in vacuo*, and distilled over a short Vigreux column to give 13.7 g (91.3%) of the title compound, $bp_{(0.05)}$ 130-5°C, lit.[16] $bp_{(0.03)}$ 140-4°C.

***rel*-(1*R*,2*R*,3*R*,4*R*)-1-[(benzyloxy)methyl]-2,3-O-isopropylidene-4-(2,2-diphenylvinyl)-cyclopentane-1-ol (8)**

A cooled (-78°C) stirred solution of tri-n-butylbenzyloxymethyltin (1.270g, 3.08 mmol, 1.2 eq.) in THF (50 mL) was treated dropwise with a solution of n-BuLi (1.77 mL, 2.83 mmol, 1.6 N in hexane) over a period of 2 min. Stirring was continued for another 3 min followed by the dropwise addition of a solution of **3** (0.861 g, 2.57 mmol) in THF (3 mL) not allowing the temperature to exceed -65°C. The mixture was stirred for another 15 min at -78°C and then quenched by the rapid addition of a saturated NH_4Cl solution. The resulting mixture was extracted with ether (2x40 mL) and the combined ether layers were dried and evaporated. The residue was subjected to column chromatography (eluant E) to give 0.661 g of pure **8** as an oil and a number of fractions which contained **8** and some unreacted ketone **3**. These fractions were pooled, concentrated, redissolved in MeOH and treated with excess $NaBH_4$ for 30 min to convert unreacted **3** to the more polar alcohol. Concentration of the solution followed by partitioning between CH_2Cl_2 and water and a second chromatography gave an additional 86 mg of **8** bringing the total yield to 0.747 g (63.7%). ^{1}H-NMR: (200 MHz) δ 1.36 (s, 3H, CH_3), 1.47 s, 3H, CH_3), 1.60-2.00 (m, 2H, CH_2-5), 3.01 (br s, 1H, OH), 3.16 (m, 1H, H-4), 3.31 (A of AB, J_{AB}=9.46 Hz, 1H, Ha of C*H*$_2$OBn), 3.43 (B of AB, J_{AB}=9.46 Hz, 1H, Hb of C*H*$_2$OBn), 4.46 - 4.56 (m, 4H, H-2, H-3, C*H*$_2$Ph), 5.87 (d, J=10.2 Hz, 1H, vinyl-CH), 7.19 - 7.45 (m, 15H, Ph); ^{13}C-NMR: APT (50 MHz) δ 25.35 (-), 26.57 (-), 42.39 (+), 43.35 (-), 73.47 (+), 74.38 (+), 76.35 (+), 81.80 (-), 86.64 (-), 114.43 (+), 127.03 (-), 127.12 (-), 127.34 (-), 127.43 (-), 127.63 (-), 127.99 (-), 128.21 (-), 128.36 (-), 128.47 (–), 130.10 (-), 130.29 (-), 138.06 (+), 139.37 (+), 142.67 (+), 143.21 (+). Anal. Calcd. for $C_{30}H_{32}O_4$ (containing 3.7% SiO_2 from chromatography): C, 76.00.54; H, 6.80. Found: C, 75.95; H, 6.93.

***rel*-(1*S*,2*R*,3*R*,4*R*)-4-[(benzyloxy)methyl]-4-hydroxy-2,3-O-isopropylidene-1-cyclo-pentaneacetic acid methyl ester (9)**

A: From **8:** The tertiary alcohol **8** (0.747 g, 1.64 mmol) was dissolved in a 1:1 mixture of acetonitrile and carbon tetrachloride (25 mL). Sodium periodate (5.0 g) and 18.6 mL of a solution containing 2 mg/mL of ruthenium trichloride hydrate were added. After stirring efficiently at room temperature for 45 min, enough water was added to dissolve the precipitated sodium iodate and the mixture was extracted with CH_2Cl_2 (3x30 mL). The combined organic extract was carefully dried, evaporated *in vacuo*, and the black residue was treated with ether (100 mL). The precipitated ruthenium salts were removed by filtration over Celite and the almost colorless solution was treated with an ether solution of diazomethane until no more acid could be detected on tlc (eluant D). Column chromatography (first eluant C until the benzophenone is eluted, then B) after removal of the solvent gave 0.299 g of an oil containing mostly the title compound **9** and some (~10 %) **10** as estimated by ^{1}H-NMR. This mixture was used in the next step without further purification.

B: From **14:** Benzyloxymethyltin (0.580 g, 1.29 mmol, 1.2 eq. in 10 mL THF), n-butyl lithium (0.808 mL, 1.6 N in hexane) and **14** (0.252 g, 1.176 mmol, in 1.5 mL THF) were reacted as described for compound **8** and quenched with a large excess of saturated NH_4Cl solution (40 mL) to minimize side reactions. The mixture was extracted with ether (20 mL) and the residue left after the evaporation of the organic layer was subjected to chromatography (eluant B) to give 0.190 g (48%) of **9** as an oil.^{1}H-NMR: (200 MHz) δ 1.37 (s, 3H, CH_3), 1.56 (s, 3H, CH_3), 2.20 (m, 2H, CH_2-5), 3.02 (br s, 1H, OH), 3.19 (m, 1H, H-1), 3.35 (A of AB, J_{AB}=9.5 Hz, 1H, H_a of CH_2OBn), 3.41 (B of AB, J_{AB}=9.5 Hz, 1H, H_b of CH_2OBn),

3.68 (s, 3H, OCH_3), 4.51 (d, J=7.6 Hz, 1H, H-3), 4.56 (br s, 2H, CH_2Ph), 4.87 (dd, J_1=7.6 Hz, J_2=5.1 Hz, 1H, H-2), 7.20 - 7.30 (m, 5H, Ph); ^{13}C-NMR: APT (50 MHz) δ 24.84 (-), 26.35 (-), 38.23 (+), 47.81 (-), 52.03 (-), 73.49 (+), 73.91 (+), 81.41 (-), 82.46 (-), 114.57 (+), 127.62 (-), 128.28 (-), 128.37 (-), 137.87 (+), 174.11 (+). This compound was not further characterized and used as such in the next step.

rel-(1*S*,2*R*,3*R*,4*R*)-4-[(benzoyloxy)methyl]-4-hydroxy-2,3-O-isopropylidene-1-cyclo-pentaneacetic acid methyl ester (10) and _rel_-(1*S*,2*R*,3*R*,4*R*)-4-hydroxymethyl-4-hydroxy-2,3-O-isopropylidene-1-cyclopentaneacetic acid methyl ester (11)

The mixture of **9** and **10** from the experiment above (0.299 g) was hydrogenated in ethanol (30 mL) in the presence of 0.2 g of palladium on carbon (10%) at 3 bar for 3h; the catalyst was removed by filtration over a pad of celite and the solvent was evaporated *in vacuo*. The residue was subjected to column chromatography (first eluant B until the nonpolar benzoylated product eluted, then eluant D) to give 0.188 g (46.7% over 2 steps) of **11** and 40 mg (6.6 %) of **10** as colorless oils. **10:** ^{1}H-NMR: (250 MHz) δ 1.36 (s, 3H, CH_3), 1.56 (s, 3H, CH_3), 2.08 (m, 1H, H-5a), 2.36 (dd, J_1=13.6 Hz, J_2=7.3 Hz, 1H, H-5b), 3.15 (br s, 1H, OH), 3.25 (m, 1H, H-1), 3.70 (s, 3H, OCH_3), 4.22 (A of AB, J_{AB}=11.4 Hz, 1H, H_a of CH_2OBz), 4.28 (B of AB, J_{AB}=11.4 Hz, 1H, H_b of CH_2OBz), 4.51 (d, J=7.6 Hz, 1H, H-2), 4.92 (dd, J_1=7.6 Hz, J_2=5.2 Hz, 1H, H-3), 7.20-7.45 (m, 3H, Ph), 7.55 (m, 2H, Ph); ^{13}C-NMR: APT (50 MHz) δ 24.77 (-), 26.26 (-), 38.31 (+), 47.61 (-), 52.18 (-), 68.13 (+), 81.37 (-), 82.36 (-), 115.02 (+), 128.37 (-), 129.67 (-), 133.13 (-), 166.15 (+), 173.87 (+).

11: ^{1}H-NMR: (250 MHz) δ 1.29 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.93 (dd, J_1=13.8 Hz, J_2=9.7 Hz, 1H, H-5a), 2.21 (dd superimposed on br s, J_1=13.8 Hz, J_2=7.9 Hz, 2H, H-5b, OH), 3.12 (m, 2H, H-1,OH), 3.40 (dd, J_1=11.1 Hz, J_2=5.1 Hz, 1H, CH*H*O), 3.55 (dd, J_1=11.1 Hz, J_2=2.3 Hz, 1H, C*H*HO), 3.63 (s, 3H, OCH_3), 4.42 (d, J=7.2 Hz, 1H, H-3), 4.89 (dd, J_1=7.2 Hz, J_2=4.5 Hz, 1H, H-2); ^{13}C-NMR: APT (50 MHz) δ 24.51 (-), 26.15 (-), 37.64 (+), 47.32 (-), 52.01 (-), 66.98 (+), 78.17 (+), 81.17 (-), 82.25 (-), 114.03 (+), 173.90 (+). Anal. Calcd. for $C_{11}H_{18}O_6$ (containing 1.3% SiO_2 from chromatography): C, 52.95; H, 7.27. Found: C, 52.94; H, 7.26. High-res. FAB-MS: Calcd.: 247.1182, found: 247.1167.

rel-(1*S*,2*R*,3*R*,4*R*)-2,3-O-isopropylidene-4-spiro-5'-(2',2'-dimethyl-1',3'-dioxolane)-cyclopentaneacetic acid methyl ester (12)

A solution containing diol **10** (0.114 g, 0.463 mmol), dimethoxy propane (5 mL), p-toluenesulfonic acid (20 mg) and CH_2Cl_2 (5 mL) was stirred for 30 min at room temperature, treated with NEt_3 (0.1 mL) and then evaporated. Column chromatography (eluant B) yielded 0.100mg (75.4%) of **12** as an oil. ^{1}H-NMR: (250 MHz) δ 1.30 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.99 (m, 1H, H-5a), 2.51 (dd, J_1=13.2 Hz, J_2=9.7 Hz, 1H, H-5b), 2.87 (m, 1H, H-1), 3.67 (s, 3H, OCH_3), 3.71 (s, 2H, CH_2O), 4.26 (d, J=5.6 Hz, 1H, H-3), 4.78 (dd, J_1=5.6 Hz, J_2=1.3 Hz, 1H, H-2); ^{13}C-NMR: DEPT (62.5 MHz) δ 24.73 (q), 26.16 (q), 26.67 (q), 26.87 (q), 34.80 (t), 47.19 (d), 52.12 (q), 72.08 (t), 81.07 (d), 82.80 (d), 86.31 (s), 109.74 (s), 86.31 (s), 174.11 (s). Anal. Calcd. for $C_{14}H_{22}O_6$: C, 58.73; H, 7.47. Found: C, 58.91; H, 7.59. FAB-MS (m/z): 287 (mH^+, 100).

(±)-_carba_-(1,2:3,4-di-O-isopropylidene)-α-psicofuranose (13)

A suspension of lithium aluminum hydride (30 mg, 0.791 mmol) in ether (4 mL) was treated with a solution of the methylester **12** (73 mg, 0.255 mmol) in ether (2 mL). The reaction was quenched by the cautious addition of saturated NH_4Cl solution after stirring at room temperature for 30 min. The ether layer was separated, evaporated, and the residue was purified by preparative tlc (eluant D) to yield **13** (35 mg, 53.1%) as an oil which crystallized on storage, mp 66-8°C. ^{1}H-NMR: (250 MHz) δ 1.31 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.57 (dd, J_1=12.8 Hz, J_2=4.8 Hz, 1H, H-7a), 2.28 (m,

1H, H-5), 2.37 (dd, J_1=12.8 Hz, J_2=9.1 Hz, 1H, H-7b), 3.50 (m, 2H, CH_2-6), 3.75 (A of AB, J_{AB}=8.7 Hz, 1H, H-1_a), 3.84 (B of AB, J_{AB}=8.7 Hz, 1H, H-1_b), 4.25 (d, J=5.9 Hz, 1H, H-3), 4.40 (dd, J_1=5.0 Hz, J_2=2.4 Hz, H-4); ^{13}C-NMR: DEPT (62.5 MHz) δ 25.17 (q), 26.37 (q), 26.76 (q), 26.80 (q), 35.65 (t), 45.21 (d), 64.08 (t), 72.72 (t), 81.95 (d), 83.62 (d), 86.40 (s), 109.79 (s), 112.46 (s). Anal. Calcd. for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.27; H, 8.47. FAB-MS (m/z): 259 (MH^+, 83).

***rel*-(1*S*, 2*R*, 3*R*)-2,3-O-isopropylidene-4-oxo-1-cyclopentaneacetic acid methyl ester (14)**

A mixture containing carbon tetrachloride (10 mL), acetonitrile (10 mL), an aqueous solution of $RuCl_3$ (15 ml, 2 mg/mL $RuCl_3$), cyclopentanol **2** (1.078 g, 3.20 mmol) and $NaIO_4$ (5.5 g) was stirred vigorously for 4 h at room temperature. After sufficient water had been added to dissolve the precipitated sodium iodate, the mixture was extracted with CH_2Cl_2 (3x50 mL each). The combined organic extract was treated as described for compound **5** and after column chromatography (eluant B) 0.148 g (21.5%) of **14** was obtained as an oil. An analytical sample was obtained by Kugelrohr distillation (0.05 mbar, oven temp. 110°C) to give **14** as an colorless oil which crystallized on storage, mp 38-40°C. ^{1}H-NMR: (200 MHz) δ 1.36 (s, 3H, CH_3), 1.44 (s, 3H, CH_3), 2.43 - 2.90 (m, 2H, CH_2-5), 3.33 (dd, J_1=9.2 Hz, J_2=2.5 Hz, 1H, H-1), 3.75 (s, 3H, OCH_3), 4.39 (d, J=5.3 Hz, 1H, H-3), 4.88 (d, J=5.3 Hz, 1H, H-2); ^{13}C-NMR: APT (50 MHz) δ 24.87 (-), 26.76 (-), 36.98 (+), 42.54 (-), 52.61 (-), 78.37 (-), 78.69 (-), 112.55 (+), 173.11 (+), 211.25 (+). Anal. Calcd. for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59. Found: C, 56.19; H, 6.56.

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