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Sugar allyltins in the synthesis of carbobicycles. Preparation of highly oxygenated enantiomerically pure decalins

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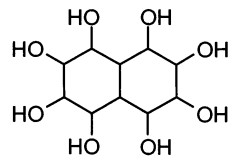
Abstract—Readily available unsaturated bicyclic ketones—obtained conveniently from sugar allyltins—are converted into highly oxygenated unsaturated decalins. The corresponding *cis*- and *trans*-diols resulting from oxidation of the double bond were obtained with 100% selectivity. Stereospecific introduction of nitrogen into the decalin system via azidation was also realized.

1. Introduction

Recently we elaborated a convenient route to sugar allyltin derivatives **1** from simple monosaccharides.[1–3] Irrespective of the (*E*)- or (*Z*)-configuration of the starting allyltin reagent 1,[2,3] these derivatives were converted into *trans*-dienoaldehydes **2** upon treatment with zinc chloride. Aldehydes **2** are useful starting materials for the preparation of bicyclo[4.3.0]nonene[4] **4** and bicyclo[4.4.0]decene[5] **3** systems.

Highly oxygenated bicyclo[4.3.0]nonanes and bicyclo[4.4.0]decanes are known to possess interesting biological activities. One of the stereoisomers of decalin **5** has shown potent and selective α-glucosidase inhibition at μM concentration against α- and β-glucosidases.[6] However, compounds of this type are available only in racemic form.[7]

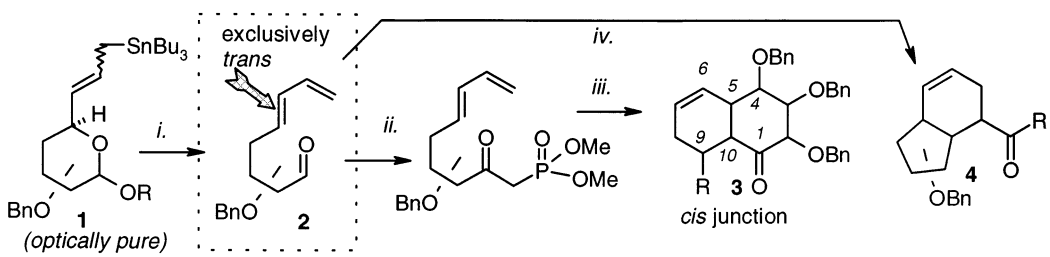


(±)-**5**

2. Results and discussion

The methodology shown in Scheme 1 opens a convenient route to enantiomerically pure carbobicyclic derivatives. Herein, a study on the functionalization of a decalin precursor obtained from sugar allyltin reagents is presented.

Decalone **6**[5] was selected as a model compound for this study. Reduction of **6** under standard conditions ($NaBH_4$) afforded alcohol **7** as a single stereoisomer.



Scheme 1. (i) Refs. 2 and 3: $ZnCl_2$, methylene chloride, rt, 2 h; (ii) Ref. 5: [O], then CH_2N_2, then $H_2C{=}P(O)(OMe)_2$; (iii) Ref. 5. RCHO, K_2CO_3, 18-crown-6, toluene, rt; (iv) Ref. 4.

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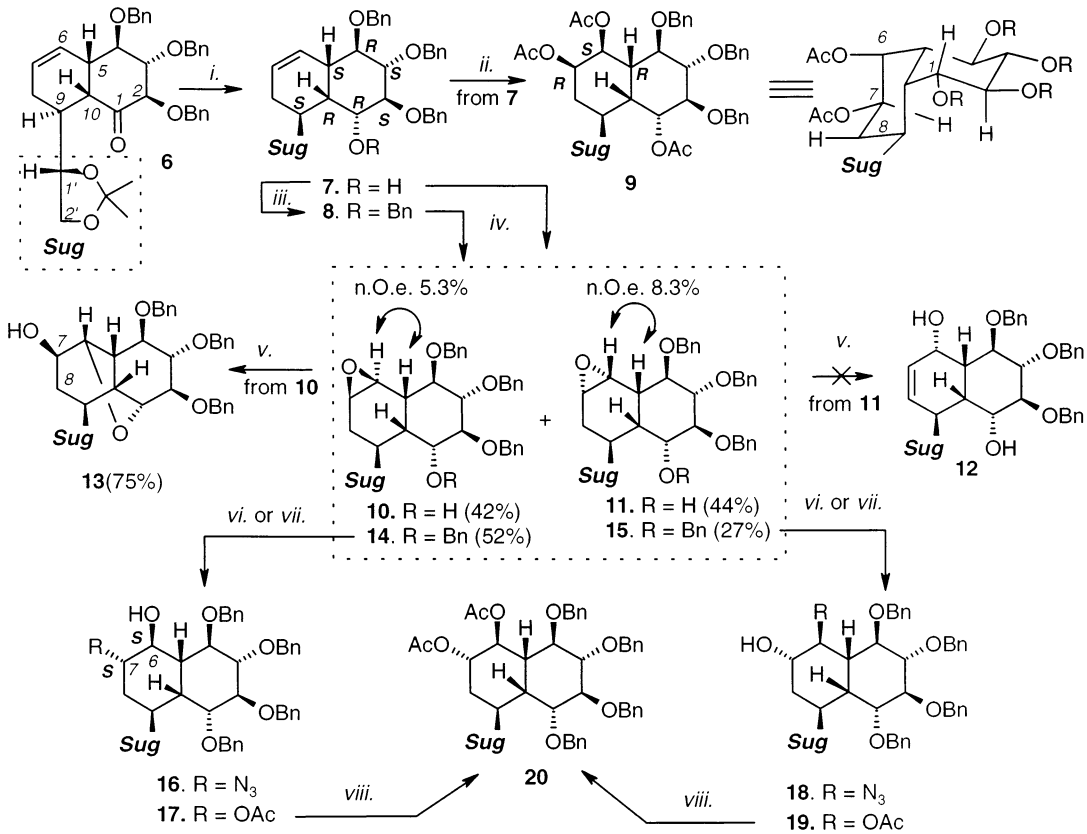
The configuration at the C(1) stereogenic center in **7** was easily assigned from the ^{1}H NMR spectrum of its acetate, in which the large coupling constant between C(1)H and C(2)H (C(1)H δ_H 5.05, dd, $J_{1,2}=8.7$, $J_{1,10}=3.5$ Hz) pointed unambiguously at the *trans* arrangement of these protons. Standard osmylation of the double bond[8] afforded (after acetylation) compound **9** again as a single isomer. The configuration of **9** was easily deduced from its ^{1}H NMR spectrum in which the large coupling constant $J_{7,8a}=12.1$ Hz was seen (Scheme 2).

Epoxidation using *m*-chloroperbenzoic acid was much less selective; two stereoisomeric oxiranes **10** and **11** were obtained in a 1:1 ratio (Scheme 2). The assignment of the configuration of both oxiranes was based on NOE experiments in ^{1}H NMR (see Scheme 2). Attempts to isomerize these epoxides to allylic alcohols (e.g. **12** from **11** or its C(6) epimer from **10**) with LDA[9] failed. Compound **11** was completely unreactive, but stereoisomer **10** underwent intramolecular opening of the oxirane ring (exclusively at C(6)) with the anion generated from C(1)OH to afford tricyclic compound **13** (Scheme 2).[†] Configuration of this derivative was assigned on the basis of the NMR spectrum of its acetate in which the ^{1}H–^{1}H correlations between the low-field signal of C(7)H ($\delta=$ 4.77) to both C(8)H were seen.

Since the free hydroxy group present in **10** or **11** induces undesired side reactions (e.g. formation of **13**) during functionalization of the oxirane ring, we decided to protect the 1-OH in **7** as its benzyl ether. Compound **8** obtained by standard benzylation of **7** was epoxidized (as described for **7**) to afford two stereoisomers **14** and **15** in 79% yield and in 2:1 ratio (Scheme 2). Configuration of these epoxides were assigned by comparison of their NMR spectra with the corresponding data for **10** and **11**. The most diagnostic were the $J_{5,6}$ coupling constant values assigned as 2.6 Hz (for **10** and **14**) and ca. 5 Hz (for **11** and **15**).

Attempts to izomerize these epoxides (having protected C(1)OH group) into allylic alcohols failed; both oxiranes were unreactive towards LDA.

Opening of the oxirane ring in both epoxides **14** and **15** was highly stereoselective. Attack of the azide anion on **14** afforded exclusively compound **16**, while the same reaction performed on **15** gave **18** as a single isomer. The configurations of both azides (precursors of amines) were easily assigned from the ^{1}H NMR spectra of acetylated products; the C(6)H resonance in **16-Ac** was observed at $\delta=5.35$ ppm, while that in **18-Ac** at $\delta=4.23$ ppm.



Scheme 2. (i) $NaBH_4$, THF/MeOH, 93%; (ii) OsO_4, NMO (cat.), then Ac_2O, 74%; (iii) BnBr, NaH, DMF, 93%; (iv). MCPBA; (v) LDA, THF, −78 to 0°C, then Ac_2O; (vi) NaN_3, DMF; (vii) AcONa, AcOH, DMF, 100°C, 20 h; (viii) Ac_2O.

[†] This result pointed unequivocally to a *trans*-relationship between the oxirane ring and the C(1)OH group in **11**, thus proving assignment of the configuration based on NOE experiments.

Reaction of the epoxides with acetate anion was more complex. Treatment of **14** with AcONa/AcOH[10] provided 66% of the *trans* isomer **17** and 17% of the monoacetate, which was identified as **19**! Final proof for this structure came from the acetylation experiment performed on both regioisomers—the same di-acetate **20** was obtained. Formation of compound **19** during opening of the oxirane ring in **14** might be explained by a migration of the acetate group from the O-7 to O-6 position. This assumption was verified experimentally; treatment of either pure **17** or pure **19** under the reaction conditions (AcONa/AcOH, 100°C, 20 h) led to a mixture of both compounds. Treatment of epoxide **15** with acetate afforded also both isomers **19** and **17**, which were converted into diacetate **20** by simple acetylation in 79% overall yield. No formation of the alternative (6*R*,7*R*) isomer was observed (Scheme 2).

The high selectivity observed in the opening of the oxirane ring in **14** and **15** may be explained by the preferred axial attack of the nucleophile, as presented in Fig. 1.

In the light of these results, formation of the tricyclic compound **13** deserves discussion. Attack of the free hydroxy group (at C(1)) occurring on the C(6) position (and not C(7), as in the intermolecular opening of the oxirane ring in **14**) results, most likely, from the different arrangement of reacting centers during such intramolecular process.

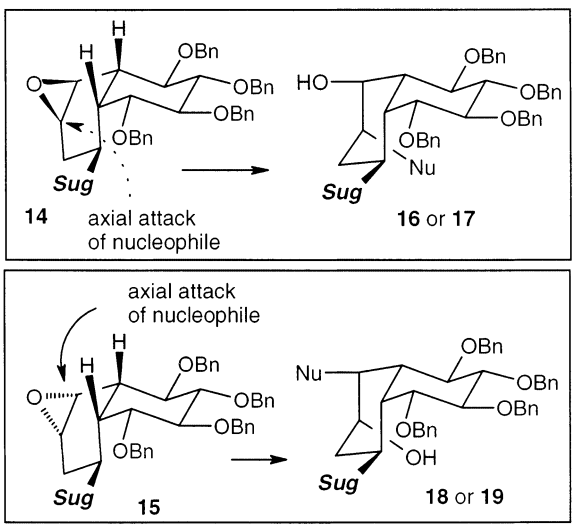


Figure 1. The preferred attack of the nucleophile on stereoisomeric epoxides.

Deprotection of such highly oxygenated, enantiomerically pure decalins was possible in good overall yield as exemplified by conversion of compound **9** into the octaacetate **22** (Scheme 3).

The isopropylidene group was removed with sulfuric acid and the resulting diol was acetylated to afford pentaacetate **21** in 83% yield. This compound was subjected to hydrogenation over Pd/C in the presence of catalytic amounts of acetic acid (without the acid the benzyl blocks were stable towards hydrogenation) and the resulting product was acetylated affording octaacetate **22** in 90% yield (75% overall from **9**).

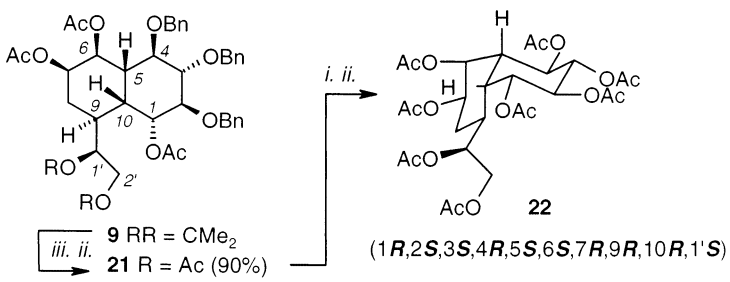
3. Conclusions

Optically pure decalins such as **6** are easily prepared from sugar allyltin derivatives. These compounds contain synthetically useful units which can be transformed into polyhydroxy decalins with very high selectivity. The stereospecific introduction of nitrogen is also possible. Deprotection of such highly oxygenated decalins can be performed easily and in good yields under standard conditions. Further work on the transformation of bicyclic precursors obtained from sugar allyltins and their biological evaluation is currently in progress.

4. Experimental

4.1. General

NMR spectra were recorded with a Bruker AM 500 spectrometer for solutions in $CDCl_3$ (internal Me_4Si) unless otherwise stated. All resonances were assigned by COSY (^1H–^1H and ^1H–^{13}C) and DEPT correlations. The relative configurations of the protons were determined by NOE or NOESY experiments. Mass spectra (ESI) were recorded with a PE SCIEX API 365 or Mariner PerSeptive Biosystems apparatus. Specific rotations were measured with a JASCO DIP Digital Polarimeter using chloroform solutions ($c \sim 1.5$) at room temperature. Column chromatography was performed on silica gel (Merck, 70–230 and 230–400 mesh). Organic solutions were dried over anhydrous sodium sulfate. (2*R*,3*S*,4*R*,5*S*,9*S*,10*R*)-{1-Keto-2,3,4-



Scheme 3. (i) 1. THF/H_2O, H_2SO_4, reflux, 12 h; (ii) Ac_2O/py; (iii) H_2/Pd, AcOEt/EtOH, cat. AcOH, rt, overnight.

tri-benzyloxy-6,7-ene-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin **6** was prepared according to Ref. 5.

4.2. Functionalization of the carbonyl group in 6

4.2.1. (1*R*,2*S*,3*S*,4*R*,5*S*,9*S*,10*R*)-{1-Hydroxy-2,3,4-tri-benzyloxy-6,7-ene-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin 7. Ketone **6** (150 mg, 0.26 mmol) was dissolved in MeOH (6 mL), THF (5 mL) and water (3 mL) and the mixture treated with sodium borohydride (15 mg, 1.5 equiv.) and stirred at room temperature for 30 min. The mixture was concentrated, the crude product was extracted with ethyl acetate and purified by column chromatography (hexane:ethyl acetate, 5:1) to afford **7** as an oil (140 mg, 93%). HRMS *m*/*z*: 593.2928 [$C_{36}H_{42}O_6Na$ (M+Na$^+$) requires 593.2874]. Anal. calcd for $C_{36}H_{42}O_6$: C, 75.76; H, 7.42. Found: C, 75.52; H, 7.22%.

Compound **7** was further characterized as its acetate derivative. $[\alpha]_D=+91.5$; ^{1}H NMR δ: 5.89 (m, H-6), 5.71 (m, H-7), 5.05 (dd, $J_{1,10}$ 3.5, $J_{1,2}$ 8.7, H-1), 4.35 (m, H-1′), 3.87 (dd, $J_{1',2'}$ 6.6, $J_{2',2'a}$ 8.2, H-2′), 3.85 (dd, $J_{2,3}$ 8.3, H-2), 3.65 (dd, $J_{3,4}$ 9.4, H-3), 3.60 (dd, $J_{1',2'a}$ 6.5, H-2′a), 3.57 (t, $J_{4,5}$ 9.4, H-4), 2.41 (m, H-5), 2.21 and 1.76 (2×m, both H-8), 2.15 (m, H-9 and H-10), 1.96 (CH_3CO_2), 1.43 and 1.33 [$C(CH_3)_2$]; ^{13}C NMR δ: 169.9 (C=O), 128.1 (C-6), 126.4 (C-7), 108.5 [$C(CH_3)_2$], 86.5 (C-3), 83.7 (C-4), 80.4 (C-2), 76.2 (C-1′), 75.5, 75.3 and 74.2 (3×CH_2Ph), 75.3 (C-1), 65.9 (C-2′), 39.4 (C-5), 37.5 and 36.0 (C-9,10), 26.3 and 24.9 [$C(CH_3)_2$], 25.8 (C-8), 21.3 (CH_3CO_2).

4.2.2. (1*R*,2*S*,3*S*,4*R*,5*S*,9*S*,10*R*)-{1-2,3,4-Tetra-benzyl-oxy-6,7-ene-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}-decalin 8. Benzylation (BnBr, NaH, DMF) of alcohol **7** afforded 90% of **8** which was isolated as an oil by column chromatography (hexane:ethyl acetate, 8:1); $[\alpha]_D=+87.8$; ^{1}H NMR δ: 5.89 (m, H-6), 5.75 (m, H-7), 4.77 (m, H-1′), 3.87 (dd, $J_{1,2}$ 9.6, $J_{2,3}$ 8.6, H-2), 3.76 (dd, $J_{1',2'}$ 7.1, $J_{2',2'a}$ 8.6, H-2′), 3.62 (dd, $J_{1',2'a}$ 5.4, H-2′), 3.57 (m, H-3,4), 3.53 (dd, $J_{1,10}$ 4.3, H-1), 2.32 (m, H-8), 2.22 (m, H-5, H-9), 1.95 (ddd, $J_{9,10}$ 11.2, $J_{5,10}$ 4.8, H-10), 1.81 (m, H-8a), 1.41 and 1.25 [$C(CH_3)_2$]; ^{13}C NMR δ: 128.3–127.3 (C-6,7 and C arom.), 107.9 [$C(CH_3)_2$], 86.8, 84.6, 82.9, 82.1 and 75.7 (C-1,2,3,4,1′), 75.6, 75.5, 75.3 and 74.4 (4×CH_2Ph), 65.0 (C-2′), 40.4, 39.4 and 35.2 (C-5,9,10), 26.0 and 24.2 [$C(CH_3)_2$], 25.8 (C-8). Anal. calcd for $C_{43}H_{48}O_6$: C, 78.15; H, 7.32. Found: C, 78.10; H, 7.43%.

4.3. *cis*-Hydroxylation of 7: (1*R*,2*S*,3*S*,4*R*,5*R*,6*S*,7*R*,9*S*,10*R*)-{1,6,7-tri-hydroxy-2,3,4-tri-benzyloxy-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin 9

Olefin **7** (155 mg, 0.26 mmol) was dissolved in THF (5 mL), *tert*-butanol (0.2 mL) and water (0.05 mL) to which *N*-methyl morpholine *N*-oxide (80 mg) and osmium tetraoxide (0.2 mL of a ca. 2% solution in toluene) were added. The mixture was stirred for 24 h at room temperature and partitioned between brine and ethyl acetate. The product was isolated by column chromatography (hexane:ethyl acetate, 1:6); yield of **9** 121 mg (74%); HRMS [ESI] *m*/*z*: 627.2997 [$C_{36}H_{44}O_8Na$ (M+Na$^+$) requires 627. 2928]. Anal. calcd for $C_{36}H_{44}O_8$: C, 71.50; H, 7.33. Found: C, 71.23; H, 7.40%.

This compound was further characterized as its tri-acetate derivative: $[\alpha]_D=-13.7$; ^{1}H NMR δ: 5.71 ($J_{5,6}\sim$ 3 Hz, H-6), 5.04 (ddd, $J_{6,7}$ 3.1, $J_{7,8}$ 4.5, $J_{7,8a}$ 12.1, H-7), 4.93 (dd, $J_{1,10}$ 3.9, $J_{1,2}$ 10.8, H-1), 4.61 (m, H-1′), 3.81 (dd, $J_{2,3}$ 9.0, H-2), 3.73 (m, H-4, 2′,2′a), 3.59 (dd, $J_{3,4}$ 8.8, H-3), 2.22 (m, H-9), 2.08 (m, H-5,8,10), 2.08, 1.98 and 1.94 (3×CH_3CO_2), 1.53 (m, H-8a), 1.44 and 1.34 [$C(CH_3)_2$]; ^{13}C NMR δ: 170.0, 169.6 and 169.4 (3×C=O), 108.6 [$C(CH_3)_2$], 87.2, 78.7, 78.0, 74.4, 74.3, 68.7, 67.6 (C-1,2,3,4,6,7,1′), 75.7, 75.5 and 75.2 (3×CH_2Ph), 63.9 (C-2′), 44.4, 36.5 and 35.7 (C-5,9,10), 25.9 and 24.5 [$C(CH_3)_2$], 24.7 (C-8), 21.2, 21.0 and 20.9 (3×CH_3CO_2).

4.4. Epoxidation reaction of unsaturated decalins

4.4.1. Reaction of 7 with *m*-chloroperbenzoic acid. To a solution of olefin **7** (770 mg, 1.35 mmol) in methylene chloride (30 mL) was added MCPBA (500 mg, 85% purity, 2.7 mmol) and the mixture was kept at room temperature for 24 h. Ether (100 mL) was added, the organic layer was washed with 0.5% NaOH, water, dried, concentrated, and the products **10** (330 mg, 42%) and **11** (350 mg, 44%) were isolated by column chromatography (hexane:ethyl acetate, 4:1→2:1).

4.4.1.1. (1*R*,2*S*,3*S*,4*R*,5*R*,6*S*,7*R*,9*S*,10*R*)-{6,7-Anhydro-1-hydroxy-2,3,4-tri-benzyl oxy-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin 10. HRMS *m*/*z*: 609.2827 [$C_{36}H_{42}O_7Na$ (M+Na$^+$) requires 609.2823]. Anal. calcd for $C_{36}H_{42}O_7$: C, 73.70; H, 7.22. Found: C, 73.51; H, 7.28%. $[\alpha]_D=+68.4$; ^{1}H NMR δ: 4.24 (dd, $J_{1',2'}$ 6.3, H-1′), 3.97 (dd, $J_{2',2'a}$ 8.5, H-2′), 3.69–3.57 (m, H-2,3,4,2′a), 3.54 (m, H-1), 3.49 (d, $J_{1,OH}$ 5.8, OH), 3.44 (dd, $J_{5,6}$ 2.6, $J_{6,7}$ 4.0, H-6), 2.92 (t, $J_{6,7}=J_{7,8}$ 4.0, H-7), 2.28 (ddd, $J_{4,5}$ 11.0, $J_{5,10}$ 4.0, H-5), 2.01 (m, H-10), 1.91 (m, H-8), 1.85 (m, H-9), 1.61 (m, H-8a), 1.40 and 1.32 [$C(CH_3)_2$]. ^{13}C NMR δ: 108.8 [$C(CH_3)_2$], 87.3, 87.1, 79.2, 77.3 and 74.4 (C-1,2,3,4,1′), 75.8, 75.3 and 75.1 (3×CH_2Ph), 66.9 (C-2′), 53.6 and 51.0 (C-6,7), 39.2, 36.9 and 33.2 (C-5,9,10), 26.3 and 25.3 [$C(CH_3)_2$], 24.3 (C-8). NOE: H5-H6 (5.3%).

4.4.1.2. (1*R*,2*S*,3*S*,4*R*,5*R*,6*R*,7*S*,9*S*,10*R*)-{6,7-Anhydro-1-hydroxy-2,3,4-tri-benzyl oxy-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin 11. HRMS *m*/*z*: 609.2828 [$C_{36}H_{42}O_7Na$ (M+Na$^+$) requires 609.2823]. Anal. calcd for $C_{36}H_{42}O_7$: C, 73.70; H, 7.22. Found: C, 73.80; H, 7.42%. $[\alpha]_D=+35.8$; ^{1}H NMR δ: 4.14 (m, H-1′), 4.04 (dd, $J_{1',2'}$ 5.7, $J_{2',2'a}$ 8.4, H-2′), 3.97 (d, $J_{1,OH}$ 7.8, OH), 3.89 (dd, $J_{4,5}$ 9.9, $J_{3,4}$ 10.2, H-4), 3.67 (m, H-1,2), 3.58 (m, H-3,2′a), 3.42 (dd, $J_{5,6}$ 5.1, $J_{6,7}$ 4.0, H-6), 3.34 (m, H-7), 2.27 (m, H-5), 2.09 (m, H-8), 1.81 (m, H-9,10), 1.46 (m, H-8a), 1.39 and 1.35 [$C(CH_3)_2$]; ^{13}C NMR δ: 109.2 [$C(CH_3)_2$], 86.5, 81.5 (double intensity), 79.9, and 77.8 (C-1,2,3,4,1′), 67.9 (C-2′), 53.3 and 53.2 (C-6,7),

42.4, 38.0 and 32.9 (C-5,9,10), 28.3 (C-8), 26.4 and 25.8 [C(CH_3)$_2$]. NOE: H5-H6 (8.3%).

4.4.2. Reaction of 8 with *m*-chloroperbenzoic acid. This reaction was performed using the same procedure as used to prepare **7**. This afforded two products: **14** (52%) and **15** (27%).

4.4.2.1. (1*R*,2*S*,3*S*,4*R*,5*R*,6*S*,7*R*,9*S*,10*R*)-{6,7-Anhydro-1,2,3,4-tetra-benzyloxy-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin 14. HRMS m/z: 699.3312 [$C_{43}H_{48}O_7Na$ (M+Na$^+$) requires 699.3292]. Anal. calcd for $C_{43}H_{48}O_7$: C, 76.31; H, 7.15. Found: C, 76.34; H, 7.24. $[\alpha]_D=+70.5$; ^{1}H NMR δ: 4.71 (m, H-1′), 3.81 (dd, $J_{1,2}=J_{2,3}$ 9.0, H-2), 3.73–3.59 (m, H-3,4, both 2′), 3.39 (dd, $J_{1,10}$ 4.1, H-1), 3.24 (dd, $J_{5,6}$ 2.6, $J_{6,7}$ 3.6, H-6), 2.92 (dd, $J_{7,8}$ 3.8, H-7), 2.21 (ddd, $J_{4,5}$ 11.1, $J_{5,10}$ 4.2, H-5), 2.02 (m, H-8,9), 1.94 (ddd, $J_{9,10}$ 11.0, H-10), 1.73 (m, H-8a), 1.40 and 1.21 [C(CH_3)$_2$]; ^{13}C NMR δ: 107.9 [C(CH_3)$_2$], 87.3, 83.2, 81.9, 78.9 and 75.5 (C-1,2,3,4,5,1′), 75.6, 75.4, 75.1 and 74.1 (4×CH_2Ph), 64.7 (C-2′), 53.8 and 51.6 (C-6,7), 39.0, 34.0 and 32.8 (C-5,9,10), 25.9 and 24.1 [C(CH_3)$_2$], 22.6 (C-8).

4.4.2.2. (1*R*,2*S*,3*S*,4*R*,5*R*,6*R*,7*S*,9*S*,10*R*)-{6,7-Anhydro-1,2,3,4-tetra-benzyloxy-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin 15. HRMS m/z: 699.3303 [$C_{43}H_{48}O_7Na$ (M+Na$^+$) requires 699.3292]. Anal. calcd for $C_{43}H_{48}O_7$: C, 76.31; H, 7.15. Found: C, 76.36; H, 7.05%. $[\alpha]_D=+42.3$; ^{1}H NMR δ: 4.66 (m, H-1′), 3.90 (dd, $J_{3,4}=J_{4,5}$ 10.2, H-4), 3.76 (dd, $J_{1,2}$ 10.2, $J_{2,3}$ 8.8, H-2), 3.70 (dd, $J_{1',2'}$ 7.1, $J_{2',2'a}$ 8.9, H-2′), 3.56 (m, H-3, 2′a), 3.42 (dd, $J_{1,10}$ 4.4, H-1), 3.37 (m, H-6,7), 2.42 (m, H-8), 2.15 (ddd, $J_{5,6}\sim J_{5,10}$ 5.0 Hz, H-5), 1.98 (m, H-9), 1.60 (m, H-8a), 1.42 and 1.23 [C(CH_3)$_2$]; ^{13}C NMR δ: 107.9 [C(CH_3)$_2$], 86.7, 81.7, 81.4, 79.9 and 75.3 (C-1,2,3,4,1′), 75.4, 75.3, 74.9 and 74.7 (4×CH_2Ph), 64.8 (C-2′), 53.9 and 53.0 (C-6,7), 39.9, 38.4 and 31.6 (C-5,9,10), 26.0 (C-8), 25.8 and 24.0 [C(CH_3)$_2$].

4.5. Attempts to isomerize epoxides with LDA

A solution of the epoxide: **10**, **11**, **14**, or **15** (ca. 0.25 mmol) in THF (15 mL) was cooled to −78°C under an argon atmosphere. LDA (6 equiv., of a 2 M solution in THF/heptane) was added at −78°C, the mixture was allowed to attain 0°C in 2 h, saturated ammonium chloride was added and the product was extracted with ethyl acetate. From reactions of **11**, **14**, and **15** only starting materials were recovered in almost quantitative yields. Only from reaction of **10** a new product **13** was obtained. It was characterized as acetate (75% yield from **10**), which was purified by column chromatography (hexane:ethyl acetate, 2:1→1:1).

4.5.1. (1*R*,2*S*,3*S*,4*R*,5*R*,6*R*,7*R*,9*S*,10*R*)-{7-*O*-Acetyl-1,6-anhydro-2,3,4-tri-benzyloxy-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin 13-Ac. HRMS m/z: 651.2943 [$C_{38}H_{44}O_8Na$ (M+Na$^+$) requires 651.2928]. Anal. calcd for $C_{38}H_{44}O_8$: C, 72.59; H, 7.05. Found: C, 72.55; H, 7.23%. $[\alpha]_D=-11.7$; ^{1}H NMR δ: 4.77 (m, H-7), 4.15 (m, H-1′), 3.97 (d, $J_{1,2}$ 2.6, H-1), 3.93 (m, H-6,2′), 3.59 (dd, $J_{2,3}=J_{3,4}$ 4.5, H-3), 3.47 (m, H-2,2′a), 3.44 (dd, $J_{4,5}<1$, H-4), 2.87 (d, $J_{9,10}$ 2.5, H-10), 2.61 (s, H-5), 1.97 (m, H-8), 1.96 (CH_3CO_2), 1.75 (m, H-9), 1.32 and 1.29 [C(CH_3)$_2$], 1.11 (m, H-8a); ^{13}C NMR δ: 169.7 (C=O), 109.3 [C(CH_3)$_2$], 81.9 (C-4), 81.5 (C-2), 80.5 (C-3), 79.7 (C-2), 77.6 (C-6), 76.5 (C-1′), 73.0, 71.6 and 71.0 (3×CH_2Ph), 71.2 (C-7), 68.8 (C-2′), 40.1 (C-9), 37.4 (C-5), 34.3 (C-10), 27.0 and 25.8 [C(CH_3)$_2$], 25.6 (C-8), 21.2 (CH_3CO_2). The strong ^{1}H–^{1}H correlations between H-7 (at $\delta=4.77$ ppm) and both H-8 (1.97 and 1.11 ppm) were observed in the COSY spectrum.

4.6. Epoxide ring opening reactions with azide

4.6.1. (1*R*,2*S*,3*S*,4*R*,5*R*,6*S*,7*S*,9*S*,10*R*)-{7-Azido-6-acetoxy-1,2,3,4-tetra-benzyloxy-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin 16-Ac. Epoxide **15** (180 mg, 0.26 mmol) was dissolved in ethanol (15 mL), water (4 mL) and THF (4 mL). Sodium azide (120 mg, 1.8 mmol) and ammonium chloride (120 mg) were added, the mixture was heated under reflux for 24 h, cooled to rt and partitioned between brine and ethyl acetate. The organic layer was separated, washed with water, dried and concentrated, the crude product was acetylated under standard conditions and purified by column chromatography (hexane:ethyl acetate, 6:1) to afford **16-Ac** (180 mg, 89%) as an oil. HRMS m/z: 784.3565 [$C_{45}H_{51}N_3O_8Na$ (M+Na$^+$) requires 784.3568]. Anal. calcd for $C_{45}H_{51}N_3O_8$: C, 70.94; H, 6.75; N, 5.52. Found: C, 71.10; H, 6.74; N, 5.41%. $[\alpha]_D=+34.2$; ^{1}H NMR δ: 5.35 (t, $J_{5,6}=J_{6,7}\sim3$, H-6), 4.93–4.75 (m, CH_2Ph and C-1′), 4.11 (t, $J_{3,4}=J_{4,5}$ 9.1, H-4), 3.84 (m, H-2 and H-7), 3.78 (t, $J_{1',2'}=J_{2',2'a}$ 7.8, H-2′), 5.62 (dd, $J_{1',2'a}$ 5.6, H-2′a), 3.52 (t, $J_{2,3}$ 8.6, H-3), 3.41 (dd, $J_{1,2}$ 9.1, $J_{1,10}$ 3.4, H-1), 2.19 (m, H-8 and H-9), 2.02 (H-10 and CH_3CO_2), 1.91 (m, H-5), 1.50 (m, H-8a), 1.43 and 1.28 [C(CH_3)$_2$].

4.6.2. (1*R*,2*S*,3*S*,4*R*,5*R*,6*S*,7*S*,9*S*,10*R*)-{6-Azido-7-acetoxy-1,2,3,4-tetra-benzyloxy-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin 18-Ac. This compound was obtained from **15** analogously as described above in 67% yield. HRMS m/z: 784.3566 [$C_{45}H_{51}N_3O_8Na$ (M+Na$^+$) requires 784.3568]. Anal. calcd for $C_{45}H_{51}N_3O_8$: C, 70.94; H, 6.75; N, 5.52. Found: C, 70.94; H, 6.72; N, 5.31%. $[\alpha]_D=+10.7$; ^{1}H NMR δ: 5.08 (broad signal, H-7), 4.23 (t, $J_{5,6}=J_{6,7}$ 5.5, H-6), 4.07 (t, $J_{3,4}=J_{4,5}$ 8.2, H-4), 3.91 (m, H-2 and H-2′), 3.69 (m, H-3), 3.65 and 3.57 (2×m, H-1 and H-2′a), 2.20 and 1.61 (2×m, both H-8), 2.03 (m, H-5).

4.7. Opening of the oxirane ring with sodium acetate

4.7.1. Reaction of epoxide 14. Compound **14** (210 mg, 0.3 mmol) was dissolved in DMF (5 mL) to which sodium acetate (250 mg) and acetic acid (0.25 mL) were added and the mixture was heated at 100°C for 20 h. The mixture was partitioned between brine and ethyl acetate, the organic phase was separated, washed with water, dried and concentrated and the products were isolated by column chromatography (hexane:ethyl acetate, 4:1→3:1) to afford two monoalcohols which were identified as **17** (152 mg, 66%) and **19** (38 mg, 17%).

Each alcohol (**17** or **19**) was separately acetylated under standard conditions to afford the same product, peracetate **20** (purified by column chromatography in hexane:ethyl acetate, 6:1) in quantitative yield.

4.7.1.1. (1*R*,2*S*,3*S*,4*R*,5*R*,6*S*,7*S*,9*S*,10*R*)-{6-Acetoxy-7-hydroxy-2,3,4-tetra-benzyloxy-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin 17. ^{1}H NMR δ: 4.90 (m, H-7), 4.22 (m, H-6), 4.04 (t, $J_{3,4}=J_{4,5}$ 8.4, H-4), 3.88 (m, H-2′), 3.83 (dd, $J_{1,2}$ 6.8 $J_{2,3}$ 7.3 H-2), 3.67 (m, H-3), 3.59–3.55 (m, H-2′a and H-1), 2.06 (CH_3CO_2), 2.00 (M, H-5,8,10), 1.62 (m, H-8a), 1.38 and 1.28 [$C(CH_3)_2$].

4.7.1.2. (1*R*,2*S*,3*S*,4*R*,5*R*,6*S*,7*S*,9*S*,10*R*)-{7-Acetoxy-6-hydroxy-2,3,4-tetra-benzyloxy-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin 19. ^{1}H NMR δ: 5.31 (t, $J_{5,6}=J_{6,7}$ 3.2, H-6), 4.19 (H-4), 3.91 (H-7), 3.86 (t, $J_{1,2}=J_{2,3}$ 8.9, H-2), 3.77 (H-2′a), 3.61 (dd, $J_{1',2'}$ 6.0, $J_{2',2'a}$ 8.4, H-2′), 3.52 (dd, $J_{3,4}$ 8.6, H-3), 3.45 (m, H-1), 2.30 (m, H-9), 2.01 (H-8 and CH_3CO_2), 1.88 (m, H-5), 1.44 (m, H-8a), 1.40 and 1.27 [$C(CH_3)_2$].

4.7.1.3. (1*R*,2*S*,3*S*,4*R*,5*R*,6*S*,7*S*,9*S*,10*R*)-{6,7-Di-acetoxy-2,3,4-tetra-benzyloxy-9-[(1′*S*)-5,5-dimethyl-2,4-dioxolane-1′-yl]}decalin 20. HRMS (ESI) m/z: 801.3626 [$C_{47}H_{54}O_{10}Na$ ($M+Na^+$) requires 801.3609]. Anal. calcd for $C_{47}H_{54}O_{10}$: C, 72.37; H, 6.99. Found: C, 72.40; H, 7.15%. $[\alpha]_D=17.9$; ^{1}H NMR δ: 5.42 (m, H-6), 5.05 (m, H-7), 4.82 (m, H-1′), 4.03 (dd, $J_{4,5}$ 10.3, $J_{3,4}$ 8.8, H-4), 3.86 (t, $J_{1,2}=J_{2,3}$ 9.3, H-2), 3.79 (t, $J_{1',2'}=J_{2',2'a}$ 8.5, H-2′), 3.63 (dd, $J_{1',2'a}$ 5.7, H-2′a), 3.54 (dd, H-3), 3.43 (dd, $J_{1,10}$ 3.8, H-1), 2.18 (m, H-8,10), 2.05 and 2.03 (2×CH_3CO_2 and H-9), 1.96 (m, H-5), 1.46 (m, H-8a), 1.39 and 1.27 [$C(CH_3)_2$].

4.7.2. Reaction of epoxide 16. Epoxide **16** was treated with NaOAc and HOAc at 100°C for 4 h, as described in Section 4.7.1 to afford a mixture of **17** and **19** in the ratio ~1:1, which upon acetylation afforded 79% of diacetate **20** identical in all respect with the diacetate obtained from **14**.

4.8. Isomerization of monoacetates 17 and 19

Acetate **17** was treated with AcONa and HOAc in DMF, as described above for 4 h. In the post-reaction mixture the regioisomer **19** was detected; the ratio of **17** and **19** was estimated at 4:1.

4.9. Deprotection of 9, a synthesis of (1*R*,2*S*,3*S*,4*R*,5*S*,6*S*,7*R*,9*R*,10*R*,1′*S*)-1,2,34,6,7-hexa-acetoxy-9-C-(1′,2′-diacetoxy-1′-ethyl)decalin 22

Compound **9** (200 mg, 0.27 mmol) was dissolved in THF (20 mL) and water (6 mL) to which concentrated sulfuric acid (1 mL) was added. The mixture was heated under reflux for 12 h, cooled to rt and partitioned between ethyl acetate and brine. The organic phase was separated, washed with water, dried and concentrated, the residue was acetylated under standard conditions, and the product was purified by column chromatography (hexane:ethyl acetate, 3:1) to afford **21** (175 mg, 83%); HRMS [LSIMS] m/z: 797.3149 [$C_{43}H_{50}O_{13}Na$ ($M+Na^+$) requires 797.3149]; ^{13}C NMR δ: 170.6, 170.5, 170.1, 169.7 (double) (5×C=O), 86.9, 79.5 77.8, 75.4, 71.1, 68.5, 67.3 (C-1,2,3,4,6,7,1′), 61.9 (C-8), 44.4, 36.5, 35.7 (C-5,9,10), 25.9 (C-8), 21.2, 21.0, 20.8, 20.7, 20.6 (5×CH_3CO_2).

Compound **21** (140 mg, 0.18 mmol) was dissolved in ethyl acetate (15 mL) and ethanol (5 mL) to which a few drops of acetic acid were added. The mixture was subjected to hydrogenation over 10% Pd/C for 12 h, filtered, concentrated and the residue was acetylated under standard conditions. The crude product was purified by column chromatography (hexane:ethyl acetate, 1:1) to afford the desired octaacetate **22** in 90% yield; $[\alpha]_D=+10.3$; HRMS [LSIMS] m/z: 653.2050 [$C_{28}H_{38}O_{16}Na$ ($M+Na^+$) requires 653.2058]; Anal. calcd for $C_{28}H_{38}O_{16}$: C, 53.33; H, 6.07. Found: C, 53.50; H, 6.23; ^{1}H NMR δ: 5.76 (m, H-1′), 5.62 (dd, $J_{1,2}$ 10.6, $J_{2,3}$ 9.2, H-2), 5.33 (dd, $J_{3,4}$ 9.1, $J_{4,5}$ 11.9, H-4), 5.25 (t, $J_{5,6}=J_{6,7}$ 2.8, H-6), 5.08 (t, H-3), 5.06 (dd, $J_{1,10}$ 4.6, H-1), 4.99 (ddd, $J_{7,8}$ 4.4, $J_{7,8a}$ 11.9, H-7), 4.22 (dd, $J_{1',2'}$ 8.4, $J_{2',2'a}$ 12.1, H-2′), 4.12 (dd, $J_{1',2'a}$ 2.7, H-2′a), 2.41 (m, H-9 and H-10), 2.25 (ddd, $J_{5,10}$ 3.4, H-5), 2.13, 2.13, 2.10, 2.05, 2.03, 2.00, 1.99 and 1.97 (8×CH_3CO_2), 2.05 and 1.60 (2×m, both H-8); ^{13}C NMR δ: 170.5, 170.4, 169.9, 169.8, 169.7, 169.6, 169.5 and 169.2 (8×C=O), 73.9 (C-3), 72.6 (C-1), 71.0 (C-1′), 69.2 (C-2), 68.2 (C-4), 68.1 (C-7), 66.8 (C-6), 61.9 (C-2′), 42.4 (C-5), 35.8 (C-10), 35.5 (C-9), 25.9 (C-8), 21.0 (double), 20.8, 20.7, 20.6, 20.5, 20.4 (double) (8×CH_3CO_2).

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