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Synthesis of highly oxygenated bicyclo[4.3.0]nonanes from sugar allyltins: model transformations of the adduct derived from the D-mannose

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Abstract—Sugar allyltin, a derivative of the D-mannose, was converted in a few well-defined steps into the bicyclic precursor of fully oxygenated hydrindane. Selective transformations of this precursor into the bicyclic derivatives containing the azido functionality are presented. The previously assigned structure of the bicyclic skeleton is also corrected.

1. Introduction

Polyhydroxylated carbocyclic compounds are regarded as sugar mimics.[1] Different approaches are used to prepare such targets, involving mostly transformations of simple sugars (such as Ferrier-II rearrangement,[2] Sinaÿ 'molecular scissors',[3] RCM cyclization of sugar olefins[4] and others[1]). Much less is known, however, about the synthesis and properties of the bicyclic analogues, although the backbone is present in some natural products. For example, a highly oxygenated decalin skeleton can be found in the structure of macrolide antibiotics such as nargenicin A, the synthesis of which in enantiomerically pure form was realized by Roush.[5]

At the end of 1980s, Herczegh presented a route to polyhydroxylated bicyclic derivatives, which was based upon the standard transformations of simple monosaccharides.[6] A convenient route to the *racemic*, fully oxygenated bicyclo[4.3.0]nonanes and bicyclo[4.4.0]decanes was elaborated by Mehta and Ramesh, who found that such derivatives possess interesting anti-glucosidase activity.[7]

Over the past decade, we have presented a general approach to enantiomerically pure polyhydroxylated carbobicyclic compounds, based on the selective transformations of allyltin derivatives of simple monosaccharides; the idea is outlined in Figure 1. The synthesis is initiated from the corresponding dienoaldehydes **3** or **4** (obtained by a

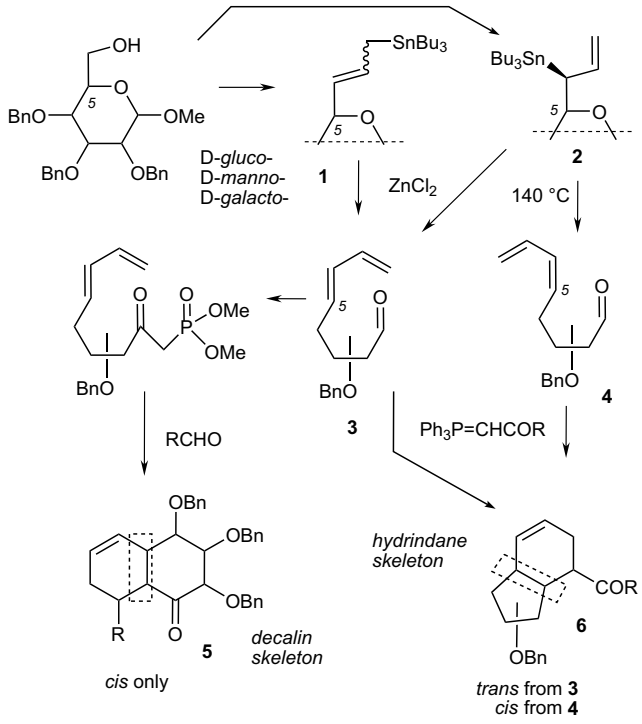

Figure 1. Convenient routes to highly oxygenated carbobicyclic derivatives. from sugar allyltins (Ref. 8).

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controlled fragmentation of the primary **1** or secondary **2** sugar allyltins), which are conveniently converted into the bicyclic precursors **5** and **6**.[8]

Appropriate functionalization of the allylic system in these precursors should afford the fully oxygenated derivatives including the analogues containing other than oxygen heteroatoms. The model study performed on precursors **7** and **8**, derived from the D-*gluco*-configurated sugar allyltin **1**, allowed us to obtain configurationally different products resulting from the oxidation of the double bond.[8,9] We also succeeded in the functionalization of the allylic position in these precursors,[10] although standard methods such as LDA-catalyzed isomerization of the corresponding epoxides failed[11] (Fig. 2).

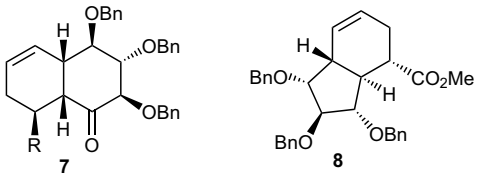


Figure 2. Decalin (**7**) and hydrindane (**8**) precursors obtained from the D-gluco-configurated sugar allyltin **1**.

Herein we report the functionalization of the hydrinadane skeleton of the precursor obtained from the D-*manno*-configurated sugar allyltin **9**.

2. Results and discussion

2.1. Determination of the configuration of the IMDA product of 11

In 1997, we reported on the selective intramolecular Diels–Alder (IMDA) reaction of trienes originated from sugar allyltins, derived from three simple monosaccharides: D-glucose, D-mannose, and D-galactose.[12] The (1*S*,5*R*,6*R*)-configuration was assigned to the main stereoisomer of the Diels–Alder cyclization of triene **11** (**12**: originated from the D-*manno*-allyltin **9**). However, subsequent studies on the functionalization of this bicyclic adduct indicated that the assignment based on the NOE (6%) between the H-6 and H-9 protons was not correct. The diagnostic signals of the H-9 and H-7 protons were observed almost at the same field (δ 3.72 and 3.75) and the NOE effect was assigned incorrectly to the H-9 and not to H-7.[12]

A comprehensive NMR study performed on derivative **14** (prepared from the main adduct of the IMDA reaction of **11** by standard methods) indicated that the (1*R*,5*S*,6*S*)-configuration should be assigned to the main product of cyclization of triene **11**, that is, compound **13** (not **12**) was formed in this intramolecular Diels–Alder reaction (Fig. 3).

The assignment of the relative configuration of the protons in **14** was carried out by the analysis of different NMR experiments taken in $CDCl_3$. The correct ^1H and ^{13}C NMR chemical shift assignments were possible based on

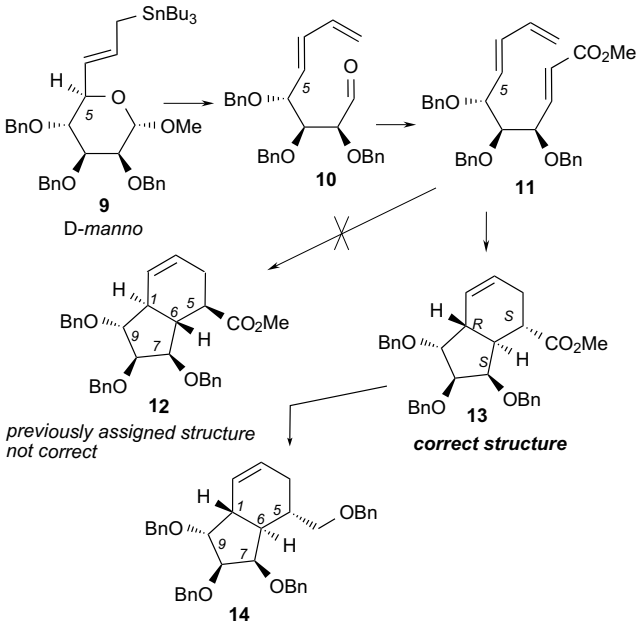


Figure 3. The assignment of the configuration of the main product of the cyclization of triene **11**.

Table 1. The ^1H and ^{13}C NMR chemical shifts for **14** in $CDCl_3$ solution at 303 K

$^1H/^{13}C$ resonances	Chemical shift (ppm.)
H1/C1	2.92 (m)/43.1
H2/C2	5.89 (dd) [1.6, 10.0 Hz]/126.2
H3/C3	5.66 (m)/127.7
H4a,H4e/C4	2.02 (m), 2.30 (m)/29.9
H5/C5	2.34 (m)/34.1
H5′,H5″/C5′	3.27 (dd) [6.2, 9.1 Hz], 3.40 (dd) [3.9, 9.1 Hz]/73.2
H6/C6	1.78 (ddd) [3.3, 11.1, 14.2 Hz]/44.3
H7/C7	4.04 (t)/77.6
H8/C8	3.96 (dd) [2.1, 4.6 Hz]/90.3
H9/C9	3.99 (dd) [2.1, 6.7 Hz]/83.0
–OCH_2Ph at C5′	4.36 (d), 4.44 (d) [12.1 Hz]/73.0
–OCH_2Ph at C7	4.40 (d), 4.80 (d) [11.6 Hz]/73.7
–OCH_2Ph at C8	4.57 (dd)/72.2
–OCH_2Ph at C9	4.53 (s)/71.5

the 2D gradient-selected HSQC and HMBC experiments and are collected in Table 1. Knowing the assignments of the ^1H NMR signals (Table 1), five protons (H1, H2, H3, one of H4, and H6) were chosen and irradiated in the NOE differential experiment.

The strongest NOE effects observed in the NOE differential spectra were for H1, H2, and H6 protons, which is presented in Figure 4. Irradiation of the hydrogen H2 led to the observation of the NOE at H1 (4.0%), H9 (1.1%), and H3 (7.0%). Irradiation of the H1 proton resulted in the following NOE effects: H9 (9.0%) and H2 (4.0%), whereas after saturation of the H6 proton, the NOE effects were observable only at H7 (3.5%) and H8 (3.5%). Analysis of the above-mentioned NOE effects observed for **14**, confirmed the *trans*-configuration of H1 and H6 protons as presented in Figure 4.

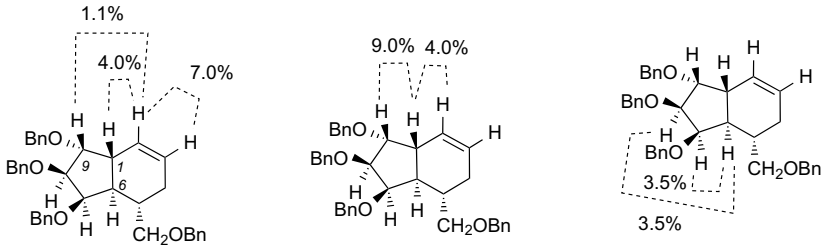


Figure 4. The ^{1}H NMR NOE effects for **14**.

Further confirmation of the relative stereochemistry of the bicyclic scaffold came from the spectra of the products of its transformations, that is, compounds **17**–**21** (Fig. 5). In all the spectra, the respective NOE cross peaks between H1–H9, H1–H5, and H6–H7 (and/or H8) were observed.

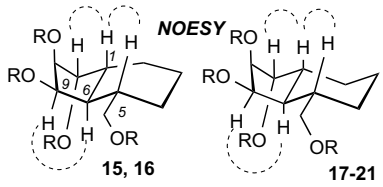


Figure 5. The NOESY correlations in the bicyclic scaffold.

2.2. Functionalization of the bicyclic skeleton in 14

Functionalization of the bicyclic skeleton leading to the fully oxygenated derivatives can be performed by the oxidation of the C-4 position followed by the oxidation of the C2–C3 double bond. Since the direct allylic oxidation in such complex derivatives proved not to be possible,[†] this goal can be realized by the transformation of the corresponding epoxides (prepared from the parent olefin) either by their conversion into the allylic alcohols (via opening of the three-membered ring with the selenide anion followed by oxidative work-up[‡]), or by opening of the three-membered ring with a suitable nucleophile and further transformation of the product(s). Herein we report the synthesis and functionalization of the carbobicyclic skeleton **14** derived from the D-mannose, which should open a convenient route to bicyclic derivatives with the amino functionalities (Scheme 1).

Standard epoxidation of olefin **14** with *m*-chloroperbenzoic acid afforded two epoxides **15** and **16** in 88% yield and in a 5:4 ratio. The configuration of these products was assigned from the advanced NMR experiments. The NOE cross peaks between the H1 and H2 in the spectrum of the minor epoxide **16** indicated a *cis*-arrangement of these two protons, thus confirming the (2*S*,3*R*)-configuration of this epoxide. Consequently the main product **15** was assigned as (2*R*,3*S*)-configuration.

Opening of the epoxide ring in **15** with sodium azide under standard conditions (THF, aq EtOH, NaN_3) provided three products. Two of them, **17** and **18**, proved to be the corresponding azides. The third product isolated from this reaction turned to be the *trans*-diol to which structure **19** was assigned; it was identical in all respect to the main stereoisomer formed in the reaction of **15** with water under acidic conditions.

The structure of the main stereoisomeric azide **17** was established on the basis of the NMR experiments performed on its acetate **17-Ac** (see Fig. 6).

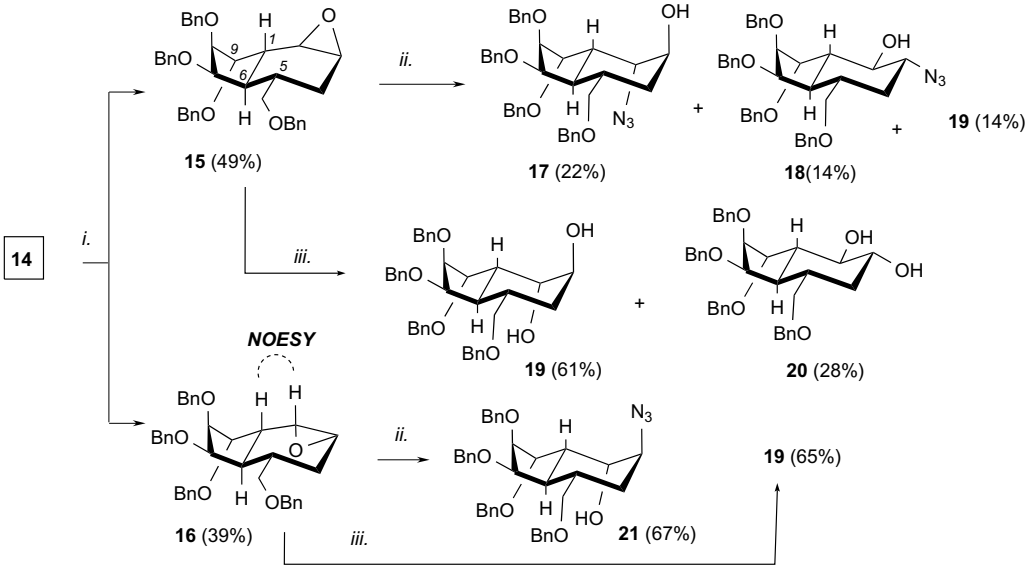
The signal resonating at the lowest field in the ^{1}H NMR spectrum of **17-Ac** (δ 4.98 ppm) correlated to two high field H-4 protons (δ 1.81 and 1.63 ppm) and to the signal at δ 71.39 ppm in the ^{13}C NMR spectrum, which strongly indicated at the presence of the acetoxyl group at the C-3 position. Therefore, the opening of the three-membered ring had to occur at the C-2 position, thus yielding compound **17**. This was proved further by the occurence of the cross peak between the H1 and H2 in the NOESY spectrum, which indicated the *cis*-arrangement of these protons. Consequently the alternative derivative resulting from the opening of the three-membered ring at the C-3 position had the structure depicted by formula **18**.

Opening of the three-membered ring in the second epoxide **16** was highly regioselective and afforded only one azidoalcohol to which structure **21** was assigned on the basis of the NMR data. The signal of the carbon atom connected to the azido function (δ 61.09 ppm) correlated to the proton resonance occurring at δ 3.84, which displayed the cross peaks to both H-4 (δ 1.73 ppm) in the COSY spectrum. Therefore, the opening of the oxirane ring occurred at the C-3 position. This was further confirmed by the cross peak in the NOESY spectrum between the H1 and H2 protons in **21** (see Fig. 6).

The opening of the oxirane ring in either in **15** or **16** with the oxygen nucleophile provides two distereoisomeric *trans*-diols **19** and **20**. Reaction of the main epoxide **15** with water catalyzed by acid provided both *trans*-diols **19** and **20** in a 2:1 ratio. Reaction of the minor epoxide **16** under the same conditions furnished only one diol **19**. The structure of **19** and **20** was assigned from the NMR spectra of these diols. In the NOESY spectrum of **19**, the cross peak

[†] Similar to **14**, the bicyclic compound derived from the D-*gluco*-configurated allyltin did not undergo such an oxidation under a variety of conditions (see Ref. 11).

[‡] This strategy was successfully applied to the functionalization of configurationally different carbobicycles derived from sugar allyltins; see Ref. 10.



Scheme 1. Reagents and conditions: (i) MCPBA, CH_2Cl_2, rt, 2 h; (ii) THF, aqueous EtOH, NaN_3, reflux, 20 h; (iii) aqueous acetone, $HClO_4$ (cat.), 0 °C, 30 min.

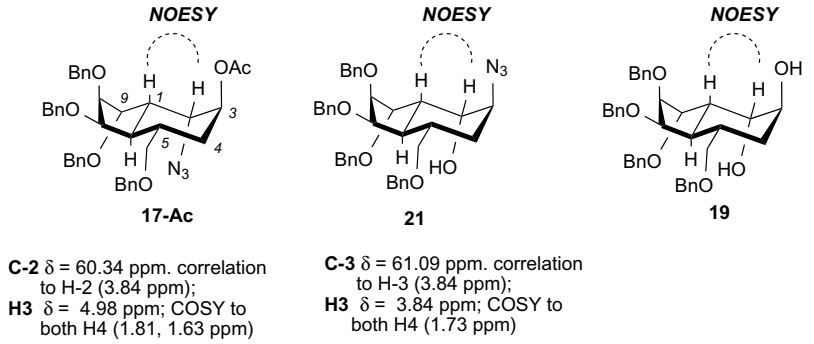


Figure 6. Assignment of the configuration of the products resulting from the opening of the oxirane ring.

between the H-1 and H-2 protons could be seen, while in the isomeric diol **20**, such a correlation is not possible. We have observed such a correlation between the H1 and H2 protons in the product resulting from the opening of epoxide **16** with water; thus the structure **19** can be safely assigned to this isomer.

Opening of the epoxide ring in **16** was highly selective and gave products azido-alcohol **21** or diol **19**, the stereochemistry of which could be predicted by the well-known Fürst-Plattner rule of the *trans* diaxial opening of the three-membered ring in cyclohexane derivatives.[13] We were, however, surprised that significant amounts of the *trans*-diequatorial products **18** and **20** were formed in the reaction of epoxide **15** with nucleophiles. We believe that this is due to the steric factors, since the C-2 position from 'the bottom part' is shielded by the neighboring five-membered ring.

3. Conclusion

The intramolecular Diels–Alder reaction of triene **11** derived form the D-mannose provided, as the major product, bicyclic derivative with the (1*R*,5*S*,6*S*)-configuration. The functionalization of the double bond was realized by epoxidation followed by the opening of the three-membered ring either with oxygen or nitrogen nucleophiles.

4. Experimental

4.1. General

The NMR spectra were recorded in $CDCl_3$ at 303 K with a Bruker DRX Avance 500 spectrometer equipped with a TBI 50SB H-C/BB-D-05 Z-G probehead, operating at 500.133 and 125.773 MHz for ^1H and ^{13}C, respectively (internal Me_4Si). The assignment of the ^1H and ^{13}C NMR signals was made using the results of the 2D methods including COSY, ^1H–^{13}C gradient-selected heteronuclear single quantum correlation (HSQC), heteronuclear multi bond correlation (HMBC), and DEPT. The relative configurations of the protons were determined based on NOESY and/or NOE differential experiments. The ^1H- and ^{13}C-aromatic resonances occurring at the typical δ values were omitted for simplicity. Mass spectra were

recorded with an ESI/MS Mariner (PerSeptive Biosystem) mass spectrometer. Optical rotations were measured with a Digital Jasco polarimeter DIP-360 ($\lambda = 589$ nm) for solutions in $CHCl_3$ (*c* 1) at room temperature. Column chromatography was performed on silica gel (Merck, 70–230 or 230–400 mesh). Methylene chloride was distilled from CaH_2 and THF from potassium prior to use. Organic solutions were dried over anhydrous magnesium sulfate.

4.2. (1*R*,5*R*,6*R*,7*R*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-5-benzyloxymethyl-bicyclo[4.3.0]non-2-ene 14

To a stirred suspension of $LiAlH_4$ (1.5 equiv, 3.62 mmol, 137.4 mg) in dry THF (10 mL) under an argon atmosphere, a solution of ester **13**[13] (1.2 g, 2.41 mmol) in THF (5 mL) was added dropwise at 0 °C. After 20 min, the cooling bath was removed and stirring was continued at rt for another 2 h. The excess of hydride was decomposed by the careful addition of water and the mixture was partitioned between 5% H_2SO_4 (10 mL) and ethyl acetate (15 mL). The organic layer was separated, washed with water, dried, and concentrated to afford the crude alcohol (963 mg, 85%), which was used in the next step without further purification.

To a vigorously stirred solution of this alcohol (456 mg, 0.97 mmol) in CH_2Cl_2 (30 mL), THF (10 mL), and aqueous 50% $NaOH_{aq}$ (20 mL), benzyl chloride (10 equiv, 9.70 mmol, 1.11 mL) was added, followed by tetrabutylammonium bromide (1 equiv, 0.97 mmol, 312 mg). After 48 h of vigorous stirring, the mixture was partitioned between water (30 mL) and CH_2Cl_2 (40 mL), the organic phase was separated, washed with water until neutrality and the aqueous one was extracted twice with CH_2Cl_2. Combined organic layers were dried, and concentrated, and the product was purified by column chromatography (hexane–ethyl acetate, 98:2) to afford **14** as an amorphous solid (418 mg, 77%). $[\alpha]_D = +46.2$; HRMS *m*/*z*: 583.28072 [$C_{38}H_{40}O_4Na$ ($M+Na^+$) requires 583.28188]. The NMR data are presented in Table 1.

4.3. Epoxidation of compound 14

To a solution of olefin **14** (1 g, 1.78 mmol) in CH_2Cl_2 (30 mL), MCPBA (55%, 1.3 equiv, 730 mg) was added and the mixture was stirred for 2 h at room temperature. Then it was diluted with CH_2Cl_2 (15 mL), washed with 2% aq NaOH, water, and brine. The organic phase was dried, and concentrated, and the products were isolated by column chromatography (hexane–ethyl acetate, 96:4 and then 9:1). Isolated first was epoxide **15** (503 mg, 49%) and then **16** (402 mg, 39%).

4.4. (1*S*,2*R*,3*S*,5*R*,6*R*,7*R*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-2,3-epoxy-5-benzyloxymethyl-bicyclo[4.3.0]nonane 15

$[\alpha]_D = +43.9$ (*c* 1, $CHCl_3$); HRMS *m*/*z*: 599.27527 [$C_{38}H_{40}O_5Na$ ($M+Na^+$) requires 599.27680]; ^1H NMR: δ 4.29–4.80 (8H, 4 × OCH_2Ph), 4.11 (dd, $J_{8,9}$ 1.8, $J_{1,9}$ 7.0, H-9), 3.92 (m, H-8), 3.91 (m, H-7), 3.46 (d, $J_{2,3}$ 3.9, H-2), 3.27 (2H, ~d, CH_2OBn), 3.18 (m, H-3), 2.42 (dd, $J_{1,6}$ 13.9, H-1), 2.24 (dd, $J_{4,5}$ 4.8, J_{gem} 15.0, H_{eq}-4), 1.89 (m, H-5), 1.74 (ddd, $J_{3,4}$ 2.5, $J_{4,5}$ 11.4, H_{ax}-4), 1.54 (ddd,$J_{6,7}$ 3.0, $J_{5,6}$ 10.9, H-6); ^{13}C NMR: δ 89.90 (C-8), 82.62 (C-9), 76.48 (C-7), 73.61, 72.91, 72.32, 71.46 (4 × O*C*H_2Ph), 71.88 (*C*H_2OBn), 53.43 (C-3), 52.77 (C-2), 43.15 (C-6), 42.94 (C-1), 31.43 (C-5), 28.61 (C-4). NOESY (diagnostic): H-1/H-9, H-6/H-7, and/or H-8.

4.5. (1*S*,2*S*,3*R*,5*R*,6*R*,7*R*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-2,3-epoxy-5-benzyloxymethyl-bicyclo[4.3.0]nonane 16

$[\alpha]_D = +35.3$ (*c* 1, $CHCl_3$); HRMS *m*/*z*: 599.2773 [$C_{38}H_{40}O_5Na$ ($M+Na^+$) requires 599.27680]; ^1H NMR: δ 4.27–4.87 (8H, 4 × OCH_2Ph), 4.14 (dd, $J_{8,9}$ 2.8, $J_{1,9}$ 7.1, H-9), 3.91–3.94 (2H, m, H-7 and H-8), 3.7 (d, $J_{2,3}$ 4.1, H-2), 3.26 (dd *J* 4.2, J_{gem} 9.0, one of CH_2OBn), 3.11 (dd, *J* 6.8, one of CH_2OBn), 3.08 (dd, $J_{3,4eq}$ 4.7, H-3), 2.67 (dd, $J_{1.6}$ 12.9, H-1), 2.14 (m, H_{eq}-4), 2.00 (m, H-5), 1.86 (m, H-6), 1.78 (dd, $J_{4,5}$ 10.6 J_{gem} 15.6, H_{ax}-4); ^{13}C NMR: δ 83.11 (C-9), 90.49 and 77.46 (C-7 and C-8), 73.61, 72.98, 72.85, 72.30, 71.75 (4 × O*C*H_2Ph and *C*H_2OBn), 52.65 (C-2), 50.25 (C-3), 43.99 (C-1), 39.07 (C-6), 32.98 (C-5), 27.30 (C-4). NOESY (diagnostic): H-1/H-2, H-1/H-9, H-3/H_{eq}-4, H-6/H-7, and/or H-8.

4.6. Reaction of epoxide 15 with sodium azide

To a solution of epoxide **15** (105 mg, 0.182 mmol) in THF (3.5 mL), ethanol (10 mL), and water (3 mL), NaN_3 (1.25 mmol, 81 mg) and NH_4Cl (1.55 mmol, 83 mg) were added, and the mixture was boiled under reflux for 20 h. It was then cooled to rt, diluted with AcOEt (10 mL), washed with water (10 mL), and brine, dried, concentrated, and the products were isolated by column chromatography (hexane–ethyl acetate, 92:8, 84:16, and then 60:40) to afford **18** (16 mg, 14%), **17** (25 mg, 22%), and diol **19** (15 mg, 14%).

4.7. Reaction of epoxide 16 with sodium azide

To a solution of epoxide **16** (62 mg, 0.108 mmol) in THF (2 mL), ethanol (4 mL), and water (0.5 mL), NaN_3 (1.3 equiv, 0.140 mmol, 9 mg), and NH_4Cl (1.5 equiv, 0.170 mmol, 9 mg) were added, and the mixture was boiled under reflux for 20 h. Then it was cooled to rt, diluted with AcOEt (10 mL), washed with water (4 mL), and brine, dried, concentrated, and the product **21** (45 mg, 67%) was isolated by column chromatography (hexane–ethyl acetate, 96:4).

4.8. Reaction of epoxide 15 with water

To a cooled to 0 °C solution of **15** (70 mg, 121.4 μmol) in acetone (10 mL) and water (0.5 mL), $HClO_4$ (3 drops of a 35% solution in water) was added, and the mixture was stirred for 30 min at 0 °C. Then it was quenched with aqueous Na_2CO_3 and the mixture was partitioned between water (10 mL) and AcOEt (15 mL). The organic phase was separated, dried, concentrated, and the products were isolated by column chromatography (hexane–ethyl acetate, 84:16 and 36:24) to afford **19** (44 mg, 61%) and **20** (20 mg, 28%).

4.9. Reaction of epoxide 16 with water

Reaction of epoxide **16** (40 mg, 0.07 mmol) under the same conditions as described in Section 4.8. afforded diol **19** in 65% yield.

4.10. Characteristics of the products of the ring opening reactions of epoxides 15 and 16

4.10.1. (1*S*,2*S*,3*S*,5*R*,6*R*,7*R*,8*R*,9*R*)-2-Azido-2-deoxy-3-hydroxy-7,8,9-tri-*O*-benzyl-5-benzyloxymethyl-bicyclo[4.3.0]nonane 17. $[\alpha]_D = +6.5$ (*c* 1, $CHCl_3$); HRMS *m*/*z*: 642.29110 [$C_{38}H_{41}N_3O_5Na$ ($M+Na^+$) requires 642.29384].

This compound was characterized further as the acetate: ^1H NMR: δ 4.98 (dd, $J_{2,3}$ 3.0, $J_{3,4}$ 6.3, H-3), 4.35–4.75 (8H, 4 × OCH_2Ph), 4.18 (dd, $J_{8,9}$ 5.2, $J_{1,9}$ 9.3, H-9), 3.98 (~t, H-7), 3.88 (dd, $J_{7,8}$ 3.6, H-8), 3.84 (~t, H-2), 3.25 (dd, *J* 4.3, J_{gem} 9.1, one of CH_2OBn), 3.14 (dd, *J* 6.1, one of CH_2OBn), 2.60 (ddd, $J_{1,2}$ 2.3, $J_{1,6}$ 13.1, H-1), 2.10 (m, H-5), 2.04 (3H, s, CH_3CO), 1.92 (ddd, $J_{6,7}$ 3.0, $J_{5,6}$ 8.8, H-6), 1.81 (m, one of H-4), 1.63 (ddd, $J_{4,5}$ 12.6, J_{gem} 15.0, one of H-4); ^{13}C NMR: δ 169.97 (CH_3CO), 91.04 (C-8), 82.51 (C-9), 76.52 (C-7), 73.41, 73.16, 72.53, 72.37 (4 × O*C*H_2Ph and *C*H_2OBn), 71.39 (C-3), 60.34 (C-2), 40.84 (C-1), 40.34 (C-6), 32.87 (C-5), 28.85 (C-4), 21.33 (*C*H_3CO); IR *v* cm^{-1} (film): 2114 (strong, –N=N=N). NOESY (diagnostic): H-1/H-2, H-1/H-5, H-1/H-9, H-6/H-7, H-6/H-8.

4.10.2. (1*S*,2*R*,3*R*,5*R*,6*R*,7*R*,8*R*,9*R*)-3-Azido-3-deoxy-2-hydroxy-7,8,9-tri-*O*-benzyl-5-benzyloxymethyl-bicyclo[4.3.0]-nonane 18. $[\alpha]_D = +23.7$ (*c* 1, $CHCl_3$); HRMS *m*/*z*: 642.291460 [$C_{38}H_{41}N_3O_5Na$ ($M+Na^+$) requires 642.29384]. ^1H NMR: δ 4.33–4.78 (8H, 4 × OCH_2Ph), 4.12 (dd, $J_{8,9}$ 2.8, $J_{1,9}$ 7.2, H-9), 3.95 (~t, H-7), 3.90 (~t, H-8), 3.66 (~t, H-2), 3.32 (ddd, $J_{3,4eq}$ 4.7, $J_{2,3}$ 9.3, $J_{3,4ax}$ 13.9, H-3), 3.28 (dd, *J* 4.0, J_{gem} 9.1, one of CH_2OBn), 3.15 (dd, *J* 6.1, one of CH_2OBn), 2.25 (ddd, $J_{1,2}$ 10.6, $J_{1,6}$ 17.9 H-1), 2.14 (m, one of H-4), 2.01 (m, H-5), 1.60 (m, H-6), 1.32 (m, one of H-4); ^{13}C NMR: δ 89.87 (C-8), 81.77 (C-9), 76.87 (C-7), 73.65, 73.15, 72.29, 71.92, and 71.68 (4 × O*C*H_2Ph and *C*H_2OBn), 73.03 (C-2), 65.91 (C-3), 48.36 (C-1), 44.72 (C-6), 34.93 (C-5), 33.67 (C-4); IR *v* cm^{-1} (film): 2100 (strong, –N=N=N). NOESY (diagnostic): H-1/H-3, H-1/H-5, H-1/H-9, H-2/H-6, H-3/H-5, H-6/H-7.

4.10.3. (1*S*,2*S*,3*S*,5*R*,6*R*,7*R*,8*R*,9*R*)-2,3-Di-hydroxy-7,8,9-tri-*O*-benzyl-5-benzyloxymethyl-bicyclo[4.3.0]nonane 19. $[\alpha]_D = -1.3$ (*c* 1, $CHCl_3$); HRMS *m*/*z*: 617.28444 [$C_{38}H_{42}O_6Na$ ($M+Na^+$) requires 617.28736]. ^1H NMR: δ 4.38–4.75 (8H, 4 × OCH_2Ph), 4.26 (dd, $J_{8,9}$ 3.8, $J_{1,9}$ 8.3, H-9), 4.12 (~t, H-2), 4.05 (~t, H-7), 3.92 (dd, $J_{1,2}$ 2.9, $J_{3,4}$ 6.0, H-3), 3.86 (~t, H-8), 3.32 (dd, *J* 4.7, J_{gem} 9.1, one of CH_2OBn), 3.24 (dd, *J* 6.0, one of CH_2OBn), 2.65 (ddd, $J_{1,2}$ 2.0, $J_{1,6}$ 13.7, H-1), 2.25 (m, H-5), 2.00 (ddd, $J_{6,7}$ 3.0, $J_{5,6}$ 10.9, H-6), 1.71–1.74 (2H, m, both H-4); ^{13}C NMR: δ 90.52 (C-8), 85.80 (C-9), 76.91 (C-7), 73.47, 73.30, 73.04, 72.19, 72.01 (4 × O*C*H_2Ph and *C*H_2OBn), 70.39 (C-2), 69.59 (C-3), 41.14 (C-1), 40.13 (C-6), 31.63 (C-5), 31.40 (C-4). NOESY (diagnostic): H-1/H-2, H-1/H-5, H-1/H-9, H-6/H-7, H-6/H-8.

4.10.4. (1*S*,2*R*,3*R*,5*R*,6*R*,7*R*,8*R*,9*R*)-2,3-Di-hydroxy-7,8,9-tri-*O*-benzyl-5-benzyloxymethyl-bicyclo[4.3.0]nonane 20. $[\alpha]_D = +33.8$ (*c* 1, $CHCl_3$); HRMS *m*/*z*: 617.28769 [$C_{38}H_{42}O_6Na$ ($M+Na^+$) requires 617.28736]. ^1H NMR: δ 4.44–4.76 (8H, 4 × OCH_2Ph), 4.12 (dd, $J_{8,9}$ 3.0, $J_{1,9}$ 7.5, H-9), 3.99 (~t, H-7), 3.91 (~t, H-8), 3.60 (~t, H-2), 3.54 (ddd, $J_{3,4eq}$ 4.4, $J_{2,3}$ 8.7, $J_{3,4ax}$ 12.6, H-3), 3.29 (dd, *J* 4.4, J_{gem} 9.1, one of CH_2OBn), 3.19 (dd, *J* 5.9, one of CH_2OBn), 2.24 (ddd, $J_{1,2}$ 10.4, $J_{1,6}$ 13.2, H-1), 2.10 (ddd, $J_{3,4eq} = J_{4eq,5}$ 4.3, J_{gem} 12.7, H_{eq}-4), 2.02 (m, H-5), 1.63 (ddd, $J_{6,7}$ 3.2, $J_{5,6}$ 10.9, H-6), 1.30 (m, H_{ax}-4); ^{13}C NMR: δ 90.17 (C-8), 81.91 (C-9), 70.01 (C-7), 74.78 and 74.72 (C-2 and C-3), 73.57, 73.10, 72.25, 71.50 (4 × OCH_2Ph), 72.47 (*C*H_2OBn), 47.59 (C-1), 45.45 (C-6), 35.91 (C-4), 34.56 (C-5).

NOESY (diagnostic): H-1/H-3, H-1/H-9, H-2/H_{ax}-4, H-2/H-6, H-3/H_{eq}-4, H-3/H-5, H-6/H_{ax}-4, H-6/H-7, H-6/H-8.

4.10.5. (1*S*,2*S*,3*S*,5*R*,6*R*,7*R*,8*R*,9*R*)-3-Azido-3-deoxy-2-hydroxy-7,8,9-tri-*O*-benzyl-5-benzyloxymethyl-bicyclo[4,3,0]-nonane 21. $[\alpha]_D = -7.4$ (*c* 1, $CHCl_3$); HRMS *m*/*z*: 642.29403 [$C_{38}H_{41}N_3O_5Na$ ($M+Na^+$) requires 642.29384]. ^1H NMR: δ 4.28–4.67 (8H, 4 × OCH_2Ph), 4.17 (dd, $J_{8,9}$ 3.6, $J_{1,9}$ 8.2, H-9), 4.06 (m, H-2), 3.96 (~t, H-7), 3.78 (~t, H-8), 3.73 (m, H-3), 3.22 (dd, *J* 4.4, J_{gem} 9.2, one of CH_2OBn), 3.14 (dd, *J* 5.7, one of CH_2OBn), 2.46 (ddd, $J_{1,2}$ 1.4, $J_{1,6}$ 13.6, H-1), 2.07 (m, H-5), 1.95 (m, H-6), 1.73 (2H, m, both H-4); ^{13}C NMR: δ 90.25 (C-8), 85.60 (C-9), 76.66 (C-7), 73.55, 73.02, 72.27, 72.07 (4 × OCH_2Ph), 72.67 (*C*H_2OBn), 68.54 (C-2), 61.09 (C-3), 41.40 (C-1), 39.74 (C-6), 32.26 (C-5), 28.00(C-4). NOESY (diagnostic): H-1/H-2, H-1/H-5, H-1/H-9, H-6/H-7, H-6/H-8.

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