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Synthesis of polyhydroxylated carbo-bicyclic compounds from sugar allyltins

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ABSTRACT

A highly functionalized polyhydroxylated dienoaldehyde, readily obtained from a D-glucose allyltin, served as a convenient precursor for a variety of configurationally different carbo-bicyclic polyols available in a free (deprotected) form. The activity of the free polyols against glycosidases was also tested.

1. Introduction

Sugar chirons[1] are particularly useful in the synthesis of polyhydroxylated carbo- and hetero cyclic derivatives. These compounds can be regarded as sugar mimics;[2] because of their similarity to 'normal' sugars, they efficiently block specific enzymes.[3] The synthesis and application of bicyclic derivatives are also a subject of interest.[4]

Previously we have proposed a general, convenient methodology for the preparation of enantiomerically pure carbo-bicyclic systems, such as **1**, from sugar allyltins.[5] These organometallics undergo a controlled fragmentation to dienoaldehydes **2** with an *E*-geometry across the internal double bond, regardless of the *E*- or *Z*-configuration of the starting allyltin.[6] Such dienoaldehydes are converted into hydrindane or decalin derivatives **3** or **4** respectively (see Fig. 1). We have already reported on the stereoselective functionalization of a bicyclic skeleton of intermediate **4**, which provided a number of bicyclic derivatives containing oxygen, nitrogen, phosphorus, or sulfur functionalities (see Fig. 2).[7]

Although the direct oxidation of the allylic position in **3** and **4** was not possible, we could perform this transformation indirectly. Opening of the oxirane ring in **8** (α and β) with selenium species followed by oxidative work-up afforded olefins **7** and **9** respectively; the latter were then converted into fully hydroxylated derivatives.[7]

Herein we report a concise approach to fully functionalized bicyclic derivatives with a hydrindane skeleton.

2. Results and discussion

The conversion of the hydrindane scaffold of **12** into an all-hydroxylated derivative requires functionalization of the double bond, oxidation of the allylic position, and finally cleavage of the C5–C5′ bond. We have reported that the introduction of two hydroxyl groups (via *cis*- or *trans*-di-hydroxylation) at the C2-C3 positions, as well as the azide, is possible.[5,7,8] However, the problem of the cleavage of the *exo*-carbon–carbon bond still remains unsolved (Fig. 3).

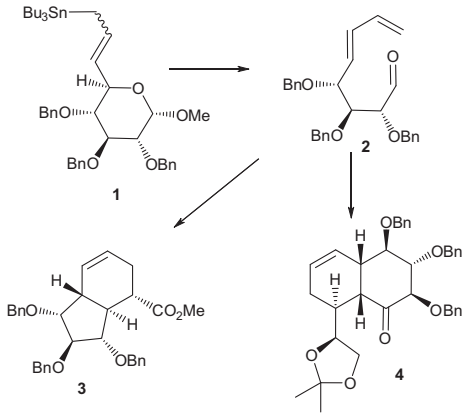

Figure 1. Synthesis of polyhydroxylated bicyclic compounds from D-*gluco*-configurated allyltin **1**.

The most convenient route to cleave the C5–C5′-bond in a highly stereoselective manner is, undoubtedly, the Baeyer–Villiger oxidation of ketone **12′**, which can be prepared from the parent ester in a few synthetic steps (route ***a***). The introduction of a keto-function in the cyclization step (route ***b***) would significantly reduce the number of synthetic steps (Fig. 4).

2.1. Synthesis of bicyclo[4.3.0]nonenes with a ketone pendant at the C5 position

The reaction of dienoaldehyde **2** with phosphonate **13** under mild PTC conditions[9] afforded triene **14**, which underwent

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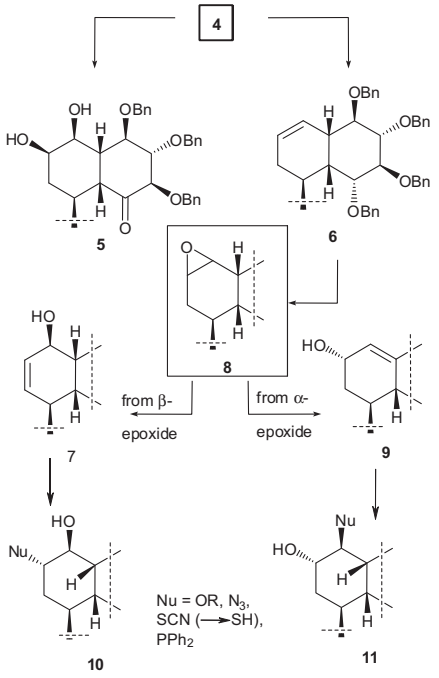


Figure 2. Synthesis of highly functionalized decalins.

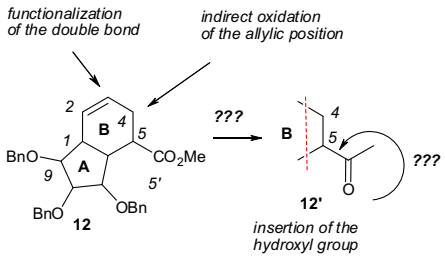


Figure 3. Functionalization of the hydrindane skeleton.

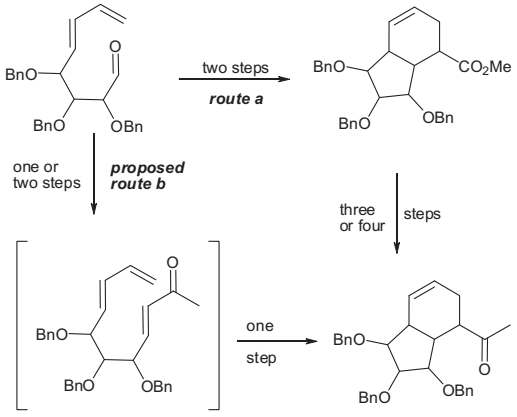
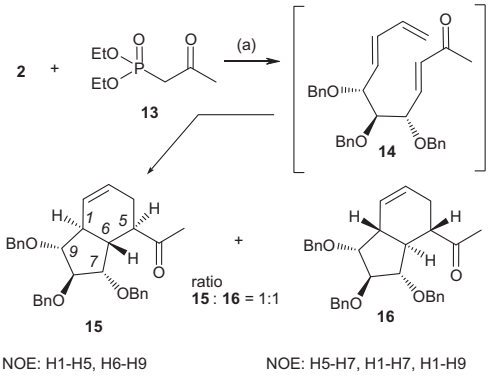


Figure 4. Route to bicyclic derivatives with the C-acetate pendant.

spontaneous cyclization to give two stereoisomeric bicyclic derivatives **15** and **16** in equal amounts (Scheme 1).

The structure of both stereoisomers was determined from the NOESY spectra; the most important interactions are shown in Scheme 1. The *trans*-relationship between the H-5 and H-6 protons in both adducts **15** and **16** unequivocally confirmed the (expected)



Scheme 1. Reagents: (a) K_2CO_3, 18-crown-6, toluene rt.

E-geometry across the newly formed double bond in the intermediate triene **14**.

The *trans*-junction between both rings in **15** and **16** can be explained by assuming the (preferred) *endo*-transition state of the Diels–Alder reaction (Fig. 5).

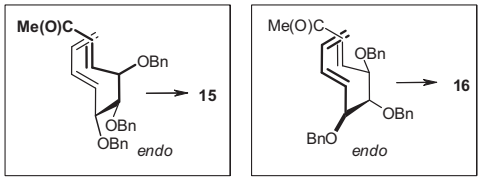


Figure 5. The exo-transition states leading to bicycle **15** and **16**.

2.2. Functionalization of the double bond in cycloadduct 15

Two methods, *cis*- and *trans*-di-hydroxylation were used to functionalize the double bond in the cycloadducts. Catalytic osmylation of olefin **15** provided two stereoisomeric diols **17** and **18** in 96% yield and in a 1:1.3 ratio. Epoxidation of **15** afforded an inseparable mixture of both epoxides **20**, which were converted by basic hydrolysis into a single stereoisomeric diol **19**. This *trans*-di-hydroxylation could be carried out more effectively in a one pot two-step process, consisting of oxidation of the double bond with 30% hydrogen peroxide in formic acid followed by opening of the oxirane ring, without isolation of the epoxide (see Scheme 2).

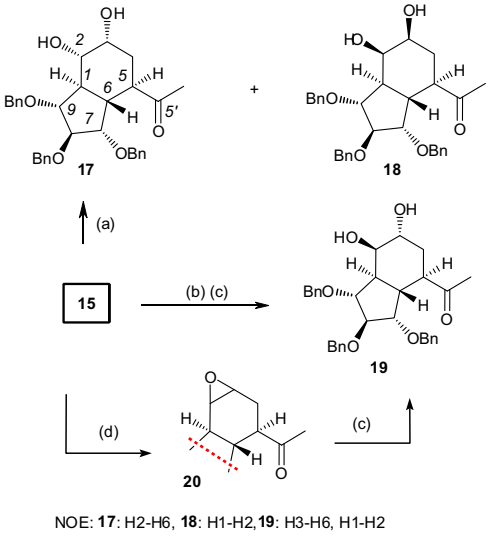
The configurations of all three stereoisomers were proven by the NOESY NMR spectra; the most important correlations are shown in Scheme 2.

The next step in the functionalization of the skeleton of **15** consisted of the cleavage of the *exo*-C5-C5′ bond. This was carried out by a Baeyer–Villiger oxidation, which is known to proceed with the retention of the configuration.[10] The reaction of diols **17**–**19** under standard conditions (MCPBA, Na_2HPO_4),[11] although not very efficient, allowed us to obtain the corresponding acetates **21–23** in rather moderate yields. A much better yield was obtained when stronger peracids were used; thus derivative **24**, upon treatment with TFAA/H_2O_2, provided 55% of the corresponding acetate **25** (Scheme 3).

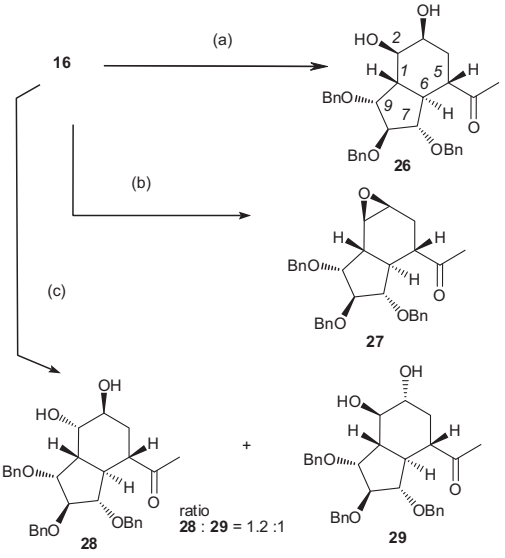
In the NOESY spectra of **21–23**, the interaction between the H1 and H5 resonances was observed, which proved that the configuration at the C5 center remained—as expected—unchanged.

2.3. Functionalization of the double bond in cycloadduct 16

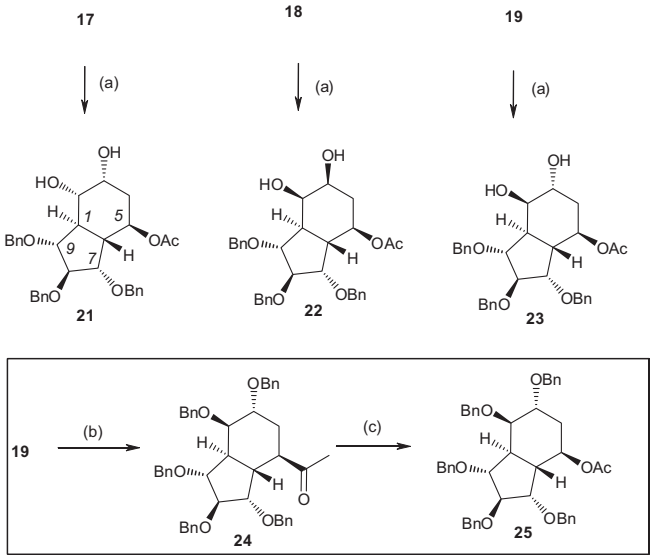
The same sequence of reactions was carried out on second stereoisomeric adduct **16**; this time, the opposite stereoselectivity



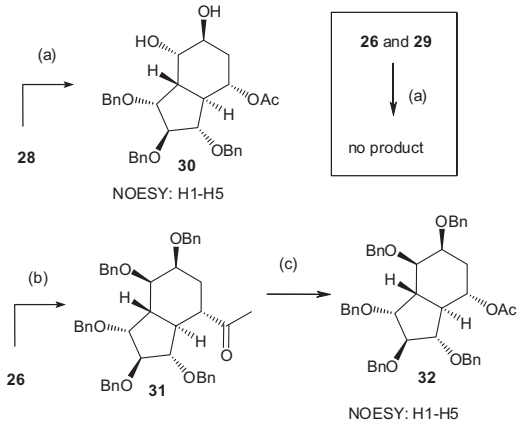
Scheme 2. Reagents: (a) OsO_4 (cat.), NMO, THF/*t*-BuOH/H_2O (v/v: 10/1/0.1); (b) HCO_2H, 30% H_2O_2; (c) MeOH, 10% NaOH (d) MCPBA.



Scheme 4. Reagents: (a) OsO_4 (cat.), NMO, THF/*t*-BuOH/H_2O (v/v: 10/1/0.1); (b) MCPBA, $NaHCO_3$; (c) (1) HCO_2H 30% H_2O_2; (2) MeOH, 10% $NaOH_{aq}$.



Scheme 3. Reagents: (a) MCPBA, Na_2HPO_4; (b) BnCl, NaOH; (c) TFAA, 50% H_2O_2.



Scheme 5. Reagents: (a) MCPBA, NaH_2PO_4; (b) BnCl, NaOH; (c) TFAA, 50% H_2O_2.

was noted. Osmylation of the double bond in **16** provided a single stereoisomeric diol **26**, while a one-pot *trans*-dihydroxylation gave two isomers **28** and **29** in a 1.2:1 ratio. Alternatively, epoxidation of olefin **16** provided a single oxirane **27**. The configurations of diols **26**, **28**, and **29** as well as epoxide **27** were determined by the NOESY spectra; the most important interactions are shown in Scheme 4.

Cleavage of the C5–C5′ bond via A Baeyer–Villiger reaction in the diols arising from cycloadduct **16** was much more difficult than those that originated from **15** (i.e., **17–19**; Scheme 3). Although diol **28** reacted as expected to provide acetate **30** in moderate yield, the other stereoisomers **26** and **29** did not undergo this process. Oxidation of diol **26**, however, could be performed 'indirectly' by protection of the free hydroxyls as benzyl ethers to **31** followed by a cleavage of the C5–C5′-bond with TFAA/H_2O_2 (Scheme 5).

2.4. Attempts to functionalize the C4 position of the bicyclic adducts

Although the direct allylic oxidation in adducts of type **3** or **4** (see Fig. 1) is not possible,[12] it can be performed indirectly, that is, by the formation of an epoxide followed by opening of the three membered ring with a selenium nucleophile and oxidative work-up according to Sharpless procedure.[8a,13]

However, opening of the oxirane ring in β-epoxide **27** with a selenium anion was unsuccessful. Attempts to introduce unsaturation at the C4–C5 position via elimination of a molecule of water from **34** did not give any positive results. Mesylate **33** was completely resistant toward basic elimination, although it underwent facile S_N2 displacement with the acetate ion to afford isomer **36-Ac**. On the other hand, xanthate **35** was only converted at high temperature to the 'wrong' olefin **37**, which had the double bond between the C5 and C6 atoms (Fig. 6).

Unsaturation at the C4–C5 position could be introduced, however, in another stereoisomeric structure derived from **15** as shown in Scheme 6.

Several of the prepared compounds were deprotected; derivatives: **41a**, **42a**, and **43a** were tested for the IR activity against four

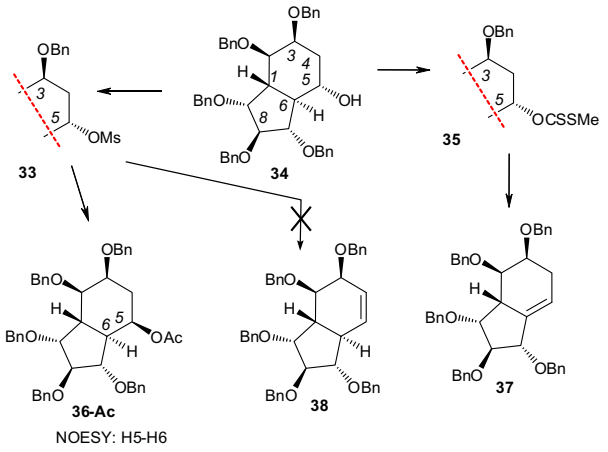
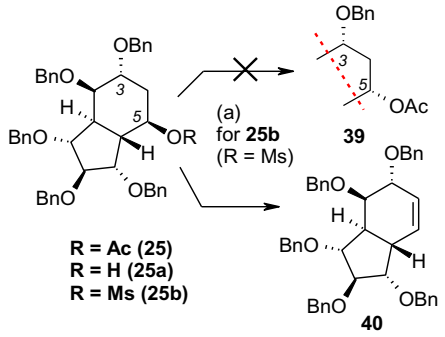


Figure 6. Attempts to functionalize the allylic position in **34**.



Scheme 6. Reagents: (a) CsOAc, DMF.

enzymes: α- and β-glucosidase, α-mannosidase, and α-fucosidase. The results are presented in Table 1; No significant activity was noted. (Fig. 7)

Table 1
Inhibition of the enzymes by bicyclic polyols (in %)

Compound	41a	42a	43a
c (mmol/l)	17.2	13.9	17.8
α-Glucosidase	15.3	12.6	3.3
β-Glucosidase	26.9	3.5	0
α-Mannosidase	10.1	22.8	11.7
α-Fucosidase	39.7	19.6	34.6

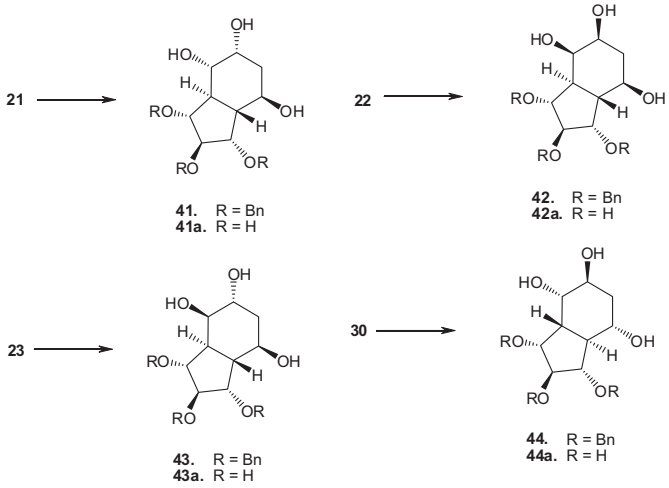


Figure 7. De-protected highly oxygenated hydrindanes.

3. Conclusion

We have presented a convenient route to a number of stereoisomeric, highly oxygenated derivatives with hydrindane skeleton. These compounds could be efficiently deprotected, however, none of these 'free' derivatives showed any significant activity against glycosidases.

4. Experimental

4.1. General methods

NMR spectra were recorded in $CDCl_3$ (unless otherwise stated) with a Varian AM-600 (600 MHz ^{1}H, 150 MHz ^{13}C) at room temperature. Chemical shifts (δ) are reported in ppm relative to Me_4Si (δ 0.00) for ^{1}H and residual chloroform (δ 77.00) for ^{13}C. All significant resonances were assigned by COSY (^{1}H–^{1}H), HSQC (^{1}H–^{13}C), and HMBC (^{1}H–^{13}C) correlations. Reagents were purchased from Sigma–Aldrich, Alfa Aesar or ABCR, and used without further purification. Commercial THF, CH_2Cl_2, and MeOH were dried over freshly activated (24 h at 250 °C) 3 Å molecular sieves for at least three days. Hexanes (65–80 °C fraction from petroleum) and EtOAc were purified by distillation. Other solvents were used without further purification. Thin-layer chromatography was carried out on silica gel 60 F_{254} (Merck). Mass spectra were recorded with an ESI/MS Mariner (PerSeptive Biosystem) mass spectrometer. Optical rotations were measured with a Jasco P 1020 polarimeter (sodium light) in chloroform ($c = 1$) at room temperature. The organic solutions were dried over $MgSO_4$.

4.2. Synthesis of derivatives of bicyclo[4.3.0]nonene

A mixture of (2*R*,3*S*,4*R*)-tri-*O*-benzyl-octa-5(*E*),7-diene-1-al[14] **2** (4.1 g, 9.25 mmol), phosphonate **13** (2.0 g, 10.2 mmol), K_2CO_3 (3.8 g, 27.8 mmol), and 18-crown-6 (30 mg) in toluene (100 mL) was stirred at rt for 24 h (TLC monitoring in hexane–ethyl acetate, 3:1). Water (30 mL) was then added, the organic phase was separated, and the aqueous phase extracted with ethyl acetate (25 mL). Combined organic solutions were washed with water and brine, dried, and concentrated. Crystallization of the residue from methanol afforded pure **16** (1.87 g); the mother liquors were concentrated and the product **15** was isolated by column chromatography (hexane–ethyl acetate, 12:1) as a colorless oil (1.95 g); overall yield was 86%.

4.3. (1*R*),5*S*,6*S*,7*S*,8*S*,9*R*)-7,8,9-Tri-*O*-benzyl-5-methylcarbonyl-bicyclo[4,3,0]non-2-ene 15

$[\alpha]_D^{rt} = +43.8$ (c 1, $CHCl_3$); ^{1}H NMR δ: 5.97 (dd, J = 1.4, 9.8 Hz, 1H, H-2), 5.62 (m, 1H, H-3), 4.63 (m, 4H, 4 × OCH_2Ph), 4.50 (d, J = 11.5 Hz, 1H, OCH_2Ph), 4.34 (d, J = 11.5 Hz, 1H, OCH_2Ph), 3.96 (m, 2H, H-7 and H-8), 3.64 (dd, J = 3.9, 10.5 Hz, 1H, H-9), 3.12 (dt, J = 6.3, 11.2 Hz, 1H, H-5), 2.73 (m, 1H, H-1), 2.42 (m, 1H, H-4a), 2.12 (s, 3H, H-11), 2.06 (m, 1H, H-4b), 1.98 (m, 1H, H-6); ^{13}C NMR δ: 211.0 (C-10), 128.2 (C-2), 126.2 (C-3), 89.9, 81.2 (C-7 and C-8), 88.6 (C-9), 72.3, 71.7, 70.8 (3 × OCH_2Ph), 46.9 (C-5), 43.5 (C-6), 43.3 (C-1), 29.6 (C-4), 29.2 (C-11). HRMS (m/z) calcd for $C_{32}H_{34}O_4Na$ (M+Na$^+$) 505.2349, found 505.2343. Anal. Calcd for $C_{32}H_{34}O_4$: C, 79.64; H, 7.10. Found: C, 79.43; H: 7.05.

4.4. (1*S*,5*R*,6*R*,7*S*,8*S*,9*R*)-7,8,9-tri-*O*-benzyl-5-methylcarbonyl-bicyclo[4,3,0]non-2-ene 16

Mp = 127 °C; $[\alpha]_D^{rt} = +13.6$ (c 1, $CHCl_3$); ^{1}H NMR δ: 5.85 (m, 1H, H-2), 5.75 (m, 1H, H-3), 4.32–4.70 (m, 6H, 6 × OCH_2Ph), 3,93 (d, 1H,

J = 3.3 Hz, H-8), 3.82 (m, 1H, H-9), 3.70 (dd, 1H, J = 3.3, 9.7 Hz, 1H, H-7), 2.75 (m, 1H, H-5), 2.64 (m, 1H, H-6), 2.47 and 2.31 (2 × m, 2H, H-4), 2.40 (m, 1H, H-1), 2.12 (s, 3H, H-11); ^{13}C NMR δ: 211.2 (C-10), 127.6 (C-3), 125.8 (C-2), 89.4 (C-8), 88.5 (C-7), 80.7 (C-9), 72.2, 71.8, 71.0 (3 × OCH_2Ph), 53.7 (C-5), 44.5 (C-6), 43.5 (C-1), 28.5 (C-4), 27.6 (C-11). HRMS (m/z) calcd for $C_{32}H_{34}O_4Na$ (M+Na$^+$) 505.2339, found 505.2349. Anal. Calcd for $C_{32}H_{34}O_4$: C, 79.64; H, 7.10. Found: C, 79.36; H: 7.22.

4.5. The *cis*-dihydroxylation of bicyclo[4.3.0]nonene 15

To a solution of olefin **15** (0.85 g, 1.7 mmol) in THF (10 mL), *t*-butanol (1 mL), and water (0.1 mL), *N*-methylmorpholine-*N*-oxide (0.39 g, 2.1 mmol) was added followed by OsO_4 (0.1 mL of a 1% solution in *t*-butyl alcohol), and the mixture was stirred at rt until disappearance of the starting material (ca. 24 h; TLC monitoring in hexane–ethyl acetate, 1:1). Methanol (5 mL) was then added followed by saturated sodium thiosulfate (10 mL), and the mixture was stirred for 30 min. Next, it was filtered through Celite and partitioned between water (20 mL) and ethyl acetate (30 mL). The organic phase was separated and the aqueous phase extracted with EtOAc (2 × 50 mL). The combined organic solutions were washed with water and brine, dried, concentrated, and the products were isolated by column chromatography (methylene chloride–isopropanol, 97:3) to afford **17** (365 mg, 0.71 mmol, 41%) and **18** (482 mg, 0.93 mmol, 55%) as colorless oils.

4.6. (1*R*,2*S*,3*R*,5*S*,6*S*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-5-methyl-carbonyl-2,3-dihydroxybicyclo[4.3.0]nonane 17

$[\alpha]_D^{rt} = -29.5$ (c 1, $CHCl_3$); ^{1}H NMR (C_6D_6) δ: 4.61 (d, J = 11.7 Hz, 1H, OCH_2Ph), 4.48 (d, J = 11.7 Hz, 1H, OCH_2Ph), 4.45 (m, 2H, 2 × OCH_2Ph), 4.18 (m, 2H, 2 × OCH_2Ph), 4.07 (d, J = 5.0 Hz, 1H, H-9), 3.94 (d, J = 4.1 Hz, 1H, H-8), 3.86 (d, J = 4.1 Hz, 1H, H-7), 3.84 (m, 1H, H-3), 3.34 (m, 1H, H-5), 3.24 (m, 1H, H-2), 2.61 (m, 1H, H-1), 2.04 (dt, J = 13.9, 3.5 Hz, 1H, H-4a), 1.87 (ddd, J = 5.0, 10.8, 13.6 Hz, 1H, H-6),), 1.75 (s, 3H, H-11), 0.96 (m, 1H, H-4b); ^{13}C NMR (C_6D_6) δ: 209.8 (C-10), 90.1 (C-7), 89.7 (C-8), 81.7 (C-9), 76.4 (C-2), 72.2, 71.8, 71.2 (3 × OCH_2Ph), 68.5 (C-3), 43.8 (C-5), 43.2 (C-1, C-6), 33.4 (C-4), 28.4 (C-11). HRMS (m/z) calcd for $C_{32}H_{36}O_6Na$ (M+Na$^+$) 539.2400, found 539.2404. Anal. Calcd for $C_{32}H_{36}O_6$: C, 74.40; H, 7.02. Found: C, 74.43; H: 7.17.

4.7. (1*R*,2*R*,3*S*,5*S*,6*S*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-5-methyl-carbonyl-2,3-dihydroxybicyclo[4.3.0]nonane 18

Mp = 118 °C; $[\alpha]_D^{rt} = -15.6$ (c 1, $CHCl_3$); ^{1}H NMR (C_6D_6) δ: 4.63 (m, 2H, OCH_2Ph), 4.45 (d, J = 11.8 Hz, 1H, OCH_2Ph), 4.39 (d, J = 11.4 Hz, 1H, OCH_2Ph), 4.29 (d, J = 11.8 Hz, 1H, OCH_2Ph), 4.25 (m, 1H, H-9), 4.08 (d, J = 11.4 Hz, 1H, OCH_2Ph), 4.01 (m, 3H, H-2, H-7 and H-8), 3.23 (m, 1H, H-3), 2.57 (dt, J_d = 4.3, 11.3 Hz, 1H, H-5), 2.50 (m, 1H, H-6), 2.09 (m, 1H, H-1), 1.71 (s, 3H, H-11), 1.48 (m, 2H, H-4); ^{13}C NMR (C_6D_6) δ: 208.5 (C-10), 89.7 and 81.5 (C-7 and C-8), 84.8 (C-9), 72.6, 71.7, 71.1 (3 × OCH_2Ph), 72.0 (C-3), 68.4 (C-2), 48.1 (C-1), 47.6 (C-5), 38.2 (C-6), 31.2 (C-4), 28.1 (C-11). HRMS (m/z) calcd for $C_{32}H_{36}O_6Na$ (M+Na$^+$) 539.2404, found 539.2420. Anal. Calcd for $C_{32}H_{36}O_6$: C, 74.40; H, 7.02. Found: C, 74.31, H; 7.04.

4.8. Epoxidation of olefin 15

To a solution of olefin **15** (102 mg, 0,21 mmol) in methylene chloride (10 mL), *m*-chloroperbenzoic acid (135 mg, 0.42 mmol) was added and the mixture was stirred at rt for 30 min. (TLC monitoring in hexane–ethyl acetate, 3:1). Next, it was partitioned between methylene chloride (20 mL) and water (20 mL), and the organic phase was separated, washed with water (20 mL) and brine (20 mL), dried, and concentrated. The crude product was purified by column chromatography (hexane–ethyl acetate, 6:1) to afford an inseparable mixture of both stereoisomeric oxiranes.

4.9. (1*R*,5*S*,6*S*,7*S*,8*S*,9*R*)-7,8,9-Tri-*O*-benzyl-5-methylcarbonyl-2,3-epoxy-bicyclo [4.3.0]nonane 20

^{1}H NMR (C_6D_6) δ: 3.99–4.63 (m, 13.3H), 3.29 (d, J = 3.9 Hz, 1H), 3.10 (d, J = 2.7 Hz, 0.35H), 2.71(m, 2H), 2.61 (m, 0.7H), 2.41 (m, 2.7H), 2.31 (m, 2H), 2.01 (m, 0.7H), 1.69 (s, 3H, H-11), 1.66 (s, 1H, H-11'), 1.60 (m, 1.7H).

4.10. The *trans*-dihydroxylation of bicyclo[4.3.0]nonene 15

To a solution of the olefin **15** (750 mg, 1.5 mmol) in formic acid (25 mL), a 30% solution of H_2O_2 (0.45 mL) was added and the mixture was stirred at rt until disappearance of the starting material (30 min.). Formic acid was removed in vacuo, the residue was dissolved in methanol (30 mL) containing 10% aq. NaOH (10 mL), and the mixture was stirred until TLC (hexane–ethyl acetate, 1:1) showed the formation of a new product. It was then partitioned between methylene chloride (40 mL) and water (25 mL), the organic phase was separated, and the aqueous phase extracted with CH_2Cl_2 (2 × 30 mL). The combined organic solutions were washed with water and brine, dried, concentrated, and the product was purified by column chromatography (hexane–ethyl acetate, 1:1) to afford diol **19** (699 mg, 1.4 mmol, 90%) as a colorless oil.

4.11. (1*R*,2*R*,3*R*,5*S*,6*S*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-5-methyl-carbonyl-2,3-dihydroxybicyclo[4.3.0]nonane 19

$[\alpha]_D^{rt} = -2.3$ (c 1, $CHCl_3$); ^{1}H NMR (C_6D_6) δ: 4.63 (2H, 2 × OCH_2Ph), 4.42 (2H, 2 × OCH_2Ph), 3.86 (m, 1H, H-2), 4.28 (d, J = 11.7 Hz, 1H, OCH_2Ph), 4.24 (dd, J = 3.9 and 10.0 Hz, 1H, H-9), 4.14 (d, J = 11.7 Hz, 1H, OCH_2Ph), 4.06 (d, J = 5.2 Hz, 1H, H-7), 4.02 (d, J = 3.9 Hz, 1H, H-8), 3.68 (s, 1H, H-3), 3.26 (m, 1H, H-5), 2.69 (m, 1H, H-1), 2.47 (m, 1H, H-6), 1.78 (s, 3H, H-11), 1.66 (m, 2H, H-4); ^{13}C NMR (C_6D_6) δ: 210.8 (C-10), 89.4 (C-8), 85.3 (C-9), 81.9 (C-7), 72.5, 71.8, 71.1 (3 × OCH_2Ph), 70.3 (C-3), 68.6 (C-2), 44.9 (C-5), 43.7 (C-1), 38.6 (C-6), 30.6 (C-4), 28.3 (C-11). HRMS (m/z) calcd for $C_{32}H_{36}O_6Na$ (M+Na$^+$) 539.2404, found 539.2393. Anal. Calcd for $C_{32}H_{36}O_6$: C, 74.40; H, 7.02. Found: C, 74.25; H: 6.96.

4.12. Baeyer–Villiger oxidation of compounds 17, 18, 19, and 24; general procedure

To a solution of the corresponding ketone (1 mmol) in methylene chloride (30 mL), Na_2HPO_4 (213 mg, 1.5 mmol), and *m*-chloroperbenzoic acid (55% purity; 466 mg, 1.5 mmol) were added, the mixture was stirred at rt for 7 days, and then partitioned between water and CH_2Cl_2. The organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (30 mL). The combined organic solutions were washed with water and brine, dried, concentrated, and the products were isolated by column chromatography (hexane–ethyl acetate, 10:9).

4.13. (1*R*,2*S*,3*R*,5*S*,6*S*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-5-*O*-acetyl-2,3-dihydroxy-bicyclo[4.3.0]nonane 21

Obtained from **17** (103 mg, 0.19 mmol); yield: 24% (0.05 mmol, 26 mg). $[\alpha]_D^{rt} = -46.9$ (c 1, $CHCl_3$); ^{1}H NMR δ: 5.39 (dt, J = 4.7, 10.8 Hz, 1H, H-5), 4.37–4.59 (m, 6H, 6 × OCH_2Ph), 4.01 (m, 1H,

H-2), 3.88 (m, 2H, H-7 and H-8), 3.75 (d, J = 4.4 Hz, 1H, H-9), 3.60 (m, 1H, H-3), 2.55 (m, 2H, H-1 and H-4a), 1.94 (s, 3H, H-11), 1.27 (m, 1H, H-4b); ^{13}C NMR δ: 169.9 (C-10), 90.2, 88.1 (C-7 and C-8), 78.4 (C-9), 76.0 (C-3), 72.1, 71.8, 70.9 (3 × OCH$_2$Ph), 69.5 (C-2), 67.2 (C-5), 45.9 (C-6), 42.5 (C-1), 35.3 (C-4), 21.2 (C-11). HRMS (m/z) calcd for $C_{32}H_{36}O_7Na$ (M+Na$^+$) 555.2359, found 555.2364.

4.14. (1*R*,2*R*,3*S*,5*S*,6*S*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-5-*O*-acetyl-2,3-dihydroxy-bicyclo[4.3.0]nonane 22

Obtained from **18** (462 mg, 0,86 mmol); yield: 34% (0.29 mmol, 162 mg). $[\alpha]_D^{rt} = -51.3$; ^{1}H NMR δ: 5.01 (dt, J = 4.5, 10.9 Hz, 1H, H-5), 4.52–4.61 (m, 4H, 4 × OCH_2Ph), 4.46 (d, J = 11.8 Hz, 1H, OCH_2Ph), 4.36 (d, J = 12.2 Hz, 1H, OCH_2Ph), 4.03 (m, 2H, H-2 and H-7), 3.90 (d, J = 3.4 Hz, 1H, H-8), 3.73 (d, J = 4.3 Hz, 1H, H-9), 3.68 (m, 1H, H-3), 2.16 (m, 2H, H-4a and H-6), 2.09 (m, 1H, H-1), 1.92 (s, 3H, H-11), 1.58 (q, J = 11.5 Hz, 1H, H-4b); ^{13}C NMR δ: 170.3 (C-10), 88.5 (C-8), 84.1 (C-7), 78.1 (C-9), 72.2, 71.5, 70.5 (3 × OCH$_2$Ph), 70.3 (C-3), 67.9 (C-5), 67.4 (C-2), 45.6 (C-1), 40.8 (C-6), 33.6 (C-4), 21.2 (C-11). HRMS (m/z) calcd for $C_{32}H_{36}O_7Na$ (M+Na$^+$) 555.2359, found 555.2355.

4.15. (1*R*,2*R*,3*R*,5*S*,6*S*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-5-*O*-acetyl-2,3-dihydroxy-bicyclo[4.3.0]nonane 23

Obtained from **19** (110 mg, 0.21 mmol); yield: 28% (0.06 mmol, 32 mg). $[\alpha]_D^{rt} = -32.3$ (c 1, CHCl$_3$); ^{1}H NMR (C$_6$D$_6$) δ: 5.77 (dt, J = 4.5 and 11.2 Hz, 1H, H-5), 4.68 (s, 2H, 2 × OCH_2Ph), 4.48 (d, J = 12.4 Hz, 1H, OCH_2Ph), 4.42 (d, J = 11.7 Hz, 1H, OCH_2Ph), 4.39 (dd, J = 3.3, 9.7 Hz, 1H, C-9), 4.34 (d, J = 11.7 Hz, 1H, OCH_2Ph), 4.28 (d, J = 12.4 Hz, 1H, OCH_2Ph), 4.08 (d, J = 3.3 Hz, 1H, H-8), 4.03 (s, 1H, H-2), 3.95 (d, J = 4.5 Hz, 1H, H-7), 3.90 (m, 1H, H-3), 3.00 (m, 1H, H-1), 2.46 (m, 1H, H-6), 2.36 (m, 1H, H-4a), 1.85 (m, 1H, H-4b), 1.64 (s, 3H, H-11); ^{13}C NMR (C$_6$D$_6$) δ: 170.5 (C-10), 88.9 (C-8), 85.5 (C-9), 79.3 (C-7), 72.3, 71.6, 70.5 (3 × OCH$_2$Ph), 72.1 (C-3), 68.9 (C-5), 68.0 (C-2), 44.0 (C-1), 42.1 (C-6), 33.3 (C-4), 21.1 (C-11). HRMS (m/z) calcd for $C_{32}H_{36}O_7Na$ (M+Na$^+$) 555.2359, found 555.2354.

4.16. Preparation of protected derivative 25

Diol **19** (332 mg, 0.64 mmol), benzyl chloride (1.9 ml, 1.58 mmol), and Bu$_4$NBr (80 mg, 0.32 mmol) were dissolved in THF (15 mL) to which 50% aq. NaOH (15 mL) was added, and the mixture was vigorously stirred for 24 h at rt (until the disappearance of the starting material; TLC monitoring in hexane–ethyl acetate, 4:1). Next it was partitioned between water (20 mL) and ether (30 mL), the organic phase was separated, and the aqueous phase extracted with ether (2 × 20 mL). The combined organic solutions were washed with water (20 mL) and brine (20 mL), dried, concentrated, and the product was purified by column chromatography (hexane–ethyl acetate, 12:1) to afford compound **24** (223 mg, 0.32 mmol, 50%) as an oil.

4.17. (1*S*,2*R*,3*R*,5*R*,6*R*,7*S*,8*S*,9*R*)-2,3,7,8,9-Penta-*O*-benzyl-5-methyl-carbonyl-bicyclo[4.3.0]nonane 24

$[\alpha]_D^{rt} = -2.3$ (c 1, CHCl$_3$); ^{1}H NMR (C$_6$D$_6$) δ: 4.67 (d, J = 12.0 Hz, 1H, OCH_2Ph), 4.52 (m, 3H, 3 × OCH_2Ph), 4.37 (dd, J = 3.8, 9.9 Hz, 1H, H-9), 4.32 (d, J = 11.6 Hz, 1H, OCH_2Ph), 4.27 (m, 2H, 2 × OCH_2Ph), 4.22 (m, 3H, 3 × OCH_2Ph), 4.19 (d, J = 5.1 Hz, 1H, H-7), 4.12 (d, J = 3.8 Hz, 1H, H-8), 3.93 (t, J = 2.8 Hz, 1H, H-2), 3.65 (q, J = 2.8, 1H, H-3), 3.36 (m, 1H, H-5), 2.93 (ddd, J = 2.4, 9.7, 13.9 Hz, 1H, H-1), 2.70 (ddd, J = 5.1, 10.9, 13.9 Hz, 1H, H-6), 1.85 (dt, J = 13.4. 3.3 Hz, 1H, H-4a), 1.79 (s, 3H, H-11), 1.69 (dt, J = 2.6, 13.4 Hz, 1H, H-4b); ^{13}C NMR (C$_6$D$_6$) δ: 209.5 (C-10), 89.7 (C-8), 85.0 (C-9), 82.1 (C-7), 74.2 (C-3), 74.0 (C-2), 72.4, 72.2, 71.8, 71.2, 71.0 (5 × OCH$_2$Ph), 45.1 (C-5), 44.2 (C-1), 39.6 (C-6), 28.7 (C-4), 28.2 (C-11). HRMS (m/z) calcd for $C_{46}H_{48}O_6Na$ (M+Na$^+$) 719.3343, found 719.3342. Anal. Calcd for $C_{46}H_{48}O_6$: C, 79.28; H, 6.94. Found: C, 79.28; H. 6.73.

To a solution of **24** (105 mg, 0.2 mmol) in methylene chloride (15 mL), Na_2HPO_4 (60 mg, 0.4 mmol) and trifluoroacetic anhydride (0.1 mL, 0.4 mmol) were added followed by 50% aq. H_2O_2 (0.08 mL, 0.4 mmol). The mixture was stirred at room temperature for 24 h (TLC monitoring in hexane–ethyl acetate, 3:1) and partitioned between water (20 mL) and methylene chloride (15 mL). The organic phase was separated, washed with water (10 mL) and brine (10 mL), dried, concentrated, and product **25** was isolated by column chromatography (hexane–ethyl acetate, 12:1); yield 59 mg (0.09 mmol, 55%).

4.18. (1*S*,2*R*,3*R*,5*R*,6*R*,7*S*,8*S*,9*R*)-2,3,7,8,9-Penta-*O*-benzyl-5-*O*-acetyl-bicyclo [4.3.0] nonane 25

$[\alpha]_D^{rt} = -36.5$ (c 1, CHCl$_3$); ^{1}H NMR (C$_6$D$_6$) δ: 5.87 (dt, J = 4.4, 11.0 Hz, 1H, H-5), 4.63 (d, J = 12.0 Hz, 1H, OCH_2Ph), 4.51 (m, 3H, 3 × OCH_2Ph), 4.44 (d, J = 11.6 Hz, 1H, OCH_2Ph), 4.39 (dd, J = 3.2, 9.7 Hz, 1H, H-9), 4.31 (m, 3H, 3 × OCH_2Ph), 4.23 (d, J = 11.7 Hz, 1H, OCH_2Ph), 4.14 (d, J = 12.0 Hz, 1H, OCH_2Ph), 4.09 (d, J = 3.4 Hz, 1H, H-8), 4.01 (d, J = 4.5 Hz, 1H, H-7), 3.88 (t, J = 2.9 Hz, 1H, H-2), 3.73 (q, J = 2.9 Hz, 1H, H-3) 3.15 ddd, J = 2.7, 9.7, 13.9 Hz, 1H, H-1), 2.64 (dt, J = 13.2, 3.8 Hz, 1H, H-4a), 2.55 (ddd, J = 4.5, 11.0, 13.9 Hz, 1H, H-6), 1.73 (m, 4H, H-4b and H-11); ^{13}C NMR (C$_6$D$_6$) δ: 169.7 (C-10), 89.2 (C-8), 85.1 (C-9), 79.2 (C-7), 74.9 (C-2), 74.1 (C-3), 72.3, 72.1, 71.7, 70.8, 70.6 (5 × OCH$_2$Ph), 68.5 (C-5), 44.3 (C-1), 43.1 (C-6), 30.4 (C-4), 21.1 (C-11). HRMS (m/z) calcd for $C_{46}H_{48}O_7Na$ (M+Na$^+$) 735.3292, found 735.3308. Anal. Calcd for $C_{46}H_{48}O_7$: C, 77.50; H, 6.79. Found: C, 77.51; H, 6.56.

4.19. The *cis*-dihydroxylation of olefin 16

Catalytic osmylation of **16** (1.36 g, 2,8 mmol), performed analogously to the oxidation of **15**, afforded diol **26**, which was isolated by column chromatography (hexane–ethyl acetate, 1:1) as a colorless oil (1.27 g, 2.46 mmol, 88%).

4.20. (1*S*,2*R*,3*S*,5*R*,6*R*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-5-methyl-carbonyl-2,3-dihydroxybicyclo[4.3.0]none 26

^{1}H NMR δ: 4.70 (d, J = 11.9 Hz, 1H, OCH_2Ph), 4.51 m, 2H, 2 × OCH_2Ph), 4.45 d, J = 11.6 Hz, 1H, OCH_2Ph), 4.39 (m, 2H, 2 × OCH_2Ph), 4.07 (m, 1H, H-3), 3.95 (dd, J = 3.0, 10.6 Hz, 1H, H-2), 3.87 (m, 2H, H-8 and H-9), 3.74 (m, 1H, H-7), 2.71 (m, J = 3.6, 12.2 Hz, 1H, H-5), 2.19 (m, 1H, H-6), 2.06 (s, 3H, H-11), 2.01 (m, 1H, H-1), 1.94 (m, J = 3.6, 14.2 Hz, 1H, H-4a), 1.62 (ddd, J = 14.2, 12.2, 2.4, 1H, H-4b); ^{13}C NMR δ: 211.2 (C-10), 89.6 (C-7), 88.2 and 79.2 (C-8 and C-9), 71.8, 71.7, 71.0 (3 × OCH$_2$Ph), 69.6 (C-2), 69.3 (C-3), 49.2 (C-5), 45.9 (C-6), 44.2 (C-1), 33.8 (C-4), 29.1 (C-11). HRMS (m/z) calcd for $C_{32}H_{36}O_6Na$ (M+Na$^+$) 539.2404, found 539.2388.

4.21. Epoxidation of olefin 16

Treatment of **16** (103 mg, 0,21 mmol) with MCPBA, as described for the epoxidation of **15**, afforded **27** (87 mg, 0.18 mmol, 84%).

4.22. (1*S*,2*R*,3*S*,5*R*,6*R*,7*S*,8*S*,9*R*)-7,8,9-Tri-*O*-benzyl-5-methylocarbonyl-2,3-epoxy bicyclo[4,3,0]nonane 27

$[\alpha]_D^{rt} = -12.5$ (c 1, CHCl$_3$); ^{1}H NMR (C$_6$D$_6$) δ: 4.50 (d, J = 11.64, 1H, OCH_2Ph), 4.44 (m, 1H, OCH_2Ph), 4.35 (d, J = 12.9, 1H, OCH_2Ph),

4.15(dd, J = 11.9 and 16.2, 2H, 2 × OCH_2Ph), 3.84 (d, J = 3.4, 1H, H8), 3.64 (d, J = 4.7, 1H, H-7), 3.58 (dd, J = 3.4, 9.7, 1H, H-9), 3.36 (d, J = 3.9, 1H, H-2), 2.87 (s, 1H, H-3), 2.33 (dt, J = 4.7, 11.3, 1H, H-5), 2.25 (m, 1H, H-1), 1.89 (m, 1H, H-4a), 1.83 (dd, J = 4.7, 13.4, 1H, H-6), 1.77 (s, 3H, H-11), 1.70 (m, 1H, H-4b); ^{13}C NMR (C_6D_6) δ: 208.1 (C-10), 88.7 (C-8), 87.8 (C-9), 81.0 (C-7), 72.2, 71.6, 71.0 (3 × OCH_2Ph), 52.6 (C-3), 51.9 (C-2), 49.5 (C-5), 44.7 (C-6), 44.5 (C-1), 28.8 (C-11), 27.7 (C-4).HRMS (m/z) calcd for $C_{32}H_{34}O_5Na$ (M+Na^+) 521.4376, found 521.4370.

4.23. The *trans*-dihydroxylation of bicyclo[4.3.0]nonene 16

This reaction was carried out starting from **16** (1.0 g, 2 mmol) analogously to the *trans*-dihydroxylation of **15**. The products **28** (436 mg, 0.84 mmol, 42%) and **29** (368 mg, 0.71 mmol, 36%) were isolated by column chromatography (methylene chloride–methanol, 97:3) as colorless oils.

4.24. (1*S*,2*S*,3*S*,5*R*,6*R*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-5-methylcarbonyl-2,3-dihydroxybicyclo[4.3.0]nonane 28

$[\alpha]_D^{rt} = +32.9$ (c 1, $CHCl_3$); ^{1}H NMR (C_6D_6) δ: 4.52 (d, J = 11.4 Hz, 1H, OCH_2Ph), 4.43 (d, J = 11.4 Hz, 1H, OCH_2Ph), 4.32 (m, 3H, 3 × OCH_2Ph), 4.20 (m, 2H, H-2 and OCH_2Ph), 3.91 (m, 1H, H-3), 3.83 (m, 2H, H-8 and H-9), 3.78 (dd, J = 9.3, 3.8 Hz, 1H, H-7), 2.94 (m, 1H, H-6), 2.81 (m, 1H, H-5), 2.19 (m, 2H, H-1 and H-4a), 1.97 (s, 3H, H-11), 1.45 (m, 1H, H-4b); ^{13}C NMR δ: 209.8 (C-10), 90.4 (C-7), 88.5 and 88.2 (C-8 and C-9), 72.5, 71.6, 70.9 (3 × OCH_2Ph), 71.0 (C-2), 69.3 (C-3), 52.2 (C-5), 41.6 (C-1), 40.9 (C-6), 30.6 (C-4), 27.3 (C-11). HRMS (m/z) calcd for $C_{32}H_{36}O_6Na$ (M+Na^+) 539.2404, found 539.2404. Anal. Calcd for $C_{32}H_{36}O_6$: C, 74.40; H, 7.02. Found: C, 74.34; H, 7.17.

4.25. (1*S*,2*R*,3*S*,5*R*,6*R*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-5-methylcarbonyl-2,3-dihydroxybicyclo[4.3.0]nonane 29

$[\alpha]_D^{rt} = +14.8$ (c 1, $CHCl_3$); ^{1}H NMR δ: 4.69 (d, J = 12, 1H Hz, OCH_2Ph), 4.54 (d, J = 12 Hz, 1H, OCH_2Ph), 4.48 (d, J = 11.4 Hz, 1H, OCH_2Ph), 4.24 (d, J = 11.4 Hz, 1H, OCH_2Ph), 4.36 (m, 2H, 2 × OCH_2Ph), 3.89 (m, 2H, H-8 and H-9), 3.75 (~t, J = 9.5 Hz, 1H, H-2), 3.65 (m, 1H, H-7), 3.47 (m, 1H, H-3), 2.33 (m, 2H, H-5 and H-6), 2.06 (s, 3H, H-11), 1.96 (m, 1H, H-4a), 1.63 (m, 2H, H-1 and H-4b); ^{13}C NMR δ: 209.9 (C-10), 89.1 (C-7), 89.0 and 78.6 (C-8 and C-9), 74.8 (C-3), 73.0 (C-2), 72.1, 71.7, 71.3 (3 × OCH_2Ph), 53.7 and 46.1 (C-5 and C-6), 48.8 (C-1), 35.2 (C-4), 27.8 (C-11). HRMS (m/z) calcd for $C_{32}H_{36}O_6Na$ (M+Na^+) 539.2404, found 539.2408.

4.26. (1*S*,2*S*,3*S*,5*R*,6*R*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-5-*O*-acetyl-2,3-dihydroxy-bicyclo[4.3.0]nonane 30

This compound was obtained from **28** (435 mg, 0.83 mmol) according to the general procedure for the Baeyer–Villiger oxidation (with MCPBA); yield: 28% (0.23 mmol, 115 mg). $[\alpha]_D^{rt} = +23.2$ (c 1, $CHCl_3$); ^{1}H NMR (C_6D_6) δ: 5.54 (m, 1H, H-5), 4.30 (m, 3H, 3 × OCH_2Ph), 4.20 (m, 2H, H-7 and OCH_2Ph), 4.12 (m, 1H, H-2), 4.03 (d, J = 11.9 Hz, 1H, OCH_2Ph), 3.94 (m, 1H, H-3), 3.86 (d, J = 3.1 Hz, 1H, H-8), 3.8 (d, J = 4.9 Hz, 1H, H-9), 3.94 (m, 1H, H-6), 2.35 (ddd, J = 1.8, 4.9, 14.1 Hz), 2.24 (m, 1H, H-4a), 1.87 (m, 1H, H-4b), 1.68 (s, 3H, H-11); ^{13}C NMR (C_6D_6) δ: 170.4 (C-10), 90.7 (C-7), 88.6 (C-8), 84.8 (C-9), 72.7 (C-5), 72.4, 71.6, 70.7 (3 × OCH_2Ph), 70.9 (C-3), 70.6 (C-2), 44.0 (C-6), 41.4 (C-1), 34.2 (C-4), 21.09 (C-11). HRMS (m/z) calcd for $C_{32}H_{36}O_7Na$ (M+Na^+) 555.2359, found 555.2344. Anal. Calcd for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81. Found: C, 71.94; H, 6.91.

4.27. (1*S*,2*R*,3*S*,5*R*,6*R*,7*S*,8*R*,9*R*)-2,3,7,8,9-Penta-*O*-benzyl-5-methylcarbonyl-bicyclo[4.3.0]nonane (31)

Diol **26** (367 mg, 0.71 mmol) was di-benzylated according to the procedure used for the preparation of **24** from **19**; yield of **31**: 250 mg (0.36 mmol, 50%). ^{1}H NMR δ: 4.32–4.69 (m, 10H,10 × OCH_2Ph), 4.03 (d, J = 4.2 Hz, 1H, H-2), 3.86 (m, 1H, H3), 3.78 (m, 1H, H-7), 3.76 (m, 1H, H-9), 2.72 (dt, J = 3.3 Hz, 12.2, 1H, H-5), 2.41 (m, 1H, H-1), 2.01 (dt, J = 14.3, 3.3 Hz, 1H, H-6), 2.06 (3H, H-11), 2.27 (m, 1H, H-4a), 1.46 (m, 1H, H-4b); ^{13}C NMR δ: 211.3 (C-10), 89.8 (C-9), 87.9 (C-8), 80.0 (C-2), 78.2 (C-7), 72.6 (C-3), 71.8, 71.6, 71.4, 71.0, 70.9 (5 × OCH_2Ph), 49.6 (C-5), 46.4 (C-6), 43.7 (C-1), 31.5 (C-4), 29.0 (C-11). HRMS (m/z) calcd for $C_{46}H_{48}O_6Na$ (M+Na^+) 719.3343, found 719.3348.

4.28. (1*S*,2*R*,3*S*,5*R*,6*R*,7*S*,8*R*,9*R*)-2,3,7,8,9-Penta-*O*-benzyl-5-*O*-acetyl-bicyclo [4.3.0]nonane 32

Treatment of **31** (250 mg, 0.36 mmol) with TFAA/50% H_2O_2 (as described for **24**) afforded **32** (149 mg, 0.21 mmol, 58%). $[\alpha]_D^{rt} = +46.5$ (c 1, $CHCl_3$); ^{1}H NMR (C_6D_6) δ: 5.59 (dt, J = 4.4, 10.9 Hz, 1H, H-5), 4.55 (d, J = 11.4 Hz, 1H, OCH_2Ph), 4.49 (m, 3H, 3 × OCH_2Ph), 4.41 (d, J = 12.4 Hz, 1H, OCH_2Ph), 4.36 (d, J = 11.8 Hz, 1H, OCH_2Ph), 4.31 (d, J = 11.8 Hz, 1H, OCH_2Ph), 4.26 (d, J = 11.8 Hz, 1H, OCH_2Ph), 4.21 (m, 2H, H-7 and OCH_2Ph), 4.09 (d, J = 11.8, 1H, OCH_2Ph), 4.05 (d, J = 4.2, 1H, H-9), 3.93 (d, J = 2.9 Hz, 1H, H-8), 3.68 (m, 1H, H-3), 3.65 (dd, J = 2.5, 10.7 Hz, 1H, H-2), 2.83 (ddd, J = 4.43, 10.7, 13.7 Hz, 1H, H-1), 2.48 (m, 1H, H-6), 2.22 (m, 1H, H-4a), 1.67 (s, 3H, H-11), 1.22 (m, 1H, H-4b); ^{13}C NMR (C_6D_6) δ: 170.1 (C-5), 90.7 (C-7), 88.8 (C-8), 80.6 (C-9), 78.8 (C-2), 73.5 (C-3), 71.7 (C-5), 72.4, 71.8, 71.6, 71.1, 70.9 (5 × OCH_2Ph), 48.7 (C-6), 43.4 (C-1), 35.1 (C-4), 21.1 (C-11). HRMS (m/z) calcd for $C_{46}H_{48}O_7Na$ (M+Na^+) 735.3292, found 735.3314. Anal. Calcd for $C_{46}H_{48}O_7$: C, 77.50; H, 6.79. Found: C, 77.23; H, 7.09.

4.29. Hydrolysis of the acetates in the Baeyer–Villiger products; general procedure

To a solution of the corresponding acetate (1 mmoL) in methanol (20 mL) a 10% solution of NaOH aq. (5 mL) was added, and the mixture was stirred at rt until the disappearance of the starting material (ca. 1 h; TLC monitoring in methylene chloride–methanol, 30:1). The mixture was concentrated to ca. 1/3 volume and partitioned between methylene chloride (30 mL) and water (15 mL). The organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (10 mL). The combined organic solutions were washed with water (10 mL), dried, concentrated, and the product was isolated by column chromatography (CH_2Cl_2–methanol, 30:1).

4.30. (1*R*,2*S*,3*R*,5*S*,6*S*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-2,3,5-trihydroxy-bicyclo[4.3.0] nonane 41

Obtained from **21** (107 mg, 0.21 mmol); yield: 90% (0.19 mmol, 87 mg). $[\alpha]_D^{rt} = -30.7$ (c 1, $CHCl_3$); ^{1}H NMR δ: 4.72 (d, J = 12.1, 1H, OCH_2Ph), 4.48–4.63 (m, 4H, 4 × OCH_2Ph), 4.38 (d, J = 11.4 Hz, 1H, OCH_2Ph), 4.32 (dt, J = 4.6, 10.7 Hz, 1H, H-5), 3.99 (m, 1H, H-3), 3.90 (m, 2H, H-7 and H-8), 3.87 (dd, J = 3.8 and 9.8 Hz, 1H, H-9), 3.57 (dd, J = 2.9, 10.4 Hz, 1H, H-2), 2.44 (m, 1H, H-1), 2.27 (m, 1H, H-4a), 1.53 (m, 1H, H-6), 1.36 (m, 1H, H-4b); ^{13}C NMR δ: 90.1 (C-9), 89.3, 79.2 (C-7 and C-8), 76.2 (C-2), 72.1, 71.9, 71.3 (3 × OCH_2Ph), 69.7 (C-3), 63.9 (C-5), 48.8 (C-6), 42.4 (C-1), 38.8 (C-4). HRMS (m/z) calcd for $C_{30}H_{34}O_6Na$ (M+Na^+) 513.2253, found 513.2250. Anal. Calcd for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99. Found.: C, 73.53; H: 7.10.

4.31. (1*R*,2*R*,3*S*,5*S*,6*S*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-2,3,5-trihydroxybicyclo[4.3.0] nonane 42

Obtained from **22** (149 mg, 0.28 mmol); yield: 70% (0.20 mmol, 96 mg). $[\alpha]_D^{rt} = -33.1$ (*c* 1, $CHCl_3$); ^1H NMR δ: 4.46–4.67 (m, 6H, 6 × OC*H*$_2$Ph), 4.38 (d, *J* = 11.4 Hz, 1H, OC*H*$_2$Ph), 4.02 (m, 2H, H-2 and H-7), 3.88–3.94 (m, 3H, H-5, H-8, H-9), 3.64 (m, 1H, H-3), 1.92–2.04 (m, 3H, H-1, H-6, H-4a), 1.56 (m, 1H, H-4b); ^{13}C NMR (150 MHz) δ: 89.4, 78.9, 65.6 (C-5, C-8 and C-9), 83.9 (C-7), 72.2, 71.6, 70.8 (3 × OCH$_2$Ph), 70.8 (C-3), 67.6 (C-2), 45.6, 44.1 (C-1, C-6), 37.4 (C-4). HRMS (*m*/*z*) calcd. for $C_{30}H_{34}O_6Na$ (M+Na$^+$) 513.2253, found 513.2255.

4.32. (1*R*,2*R*,3*R*,5*S*,6*S*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-2,3,5-trihydroxybicyclo [4.3.0]nonane 43

Obtained from **23** (117 mg, 0.21 mmol); yield: 80% (0.17 mmol, 86 mg). $[\alpha]_D^{rt} = -13.1$ (*c* 1, $CHCl_3$); ^1H NMR δ: 4.69 (d, *J* = 12.1 Hz, 1H, OC*H*$_2$Ph), 4.63 (d, *J* = 11.9 Hz, 1H, OC*H*$_2$Ph), 4.52 (m, 3H, 3 × OC*H*$_2$Ph), 4.46 (d, *J* = 11.6, 1H, OC*H*$_2$Ph), 4.19 (dt, *J* = 4.5, 10.9 Hz, 1H, H-3), 4.52 (m, 3H, H-7, H-8, H-9), 3.83 (m, 1H, H-5), 2.42 (m, 1H, H-6), 1.96 (m, 1H, H-4a), 1.84 (m, 1H, H-1), 1.64 (m, 1H, H-4b); ^{13}C NMR δ: 89.2, 84.2, 79.3 (C-7, C-8 and C-9), 72.1, 71.7, 70.9 (C-2, 3 × OCH$_2$Ph), 68.1 (C-5), 64.6 (C-3), 44.7 (C-1), 43.3 (C-6), 36.3 (C-4). HRMS (*m*/*z*) calcd for $C_{30}H_{34}O_6Na$ (M+Na$^+$) 513.2253, found 513.2252.

4.33. (1*S*,2*S*,3*S*,5*R*,6*R*,7*S*,8*R*,9*R*)-7,8,9-Tri-*O*-benzyl-2,3,5-trihydroxybicyclo[4.3.0] nonane 44

Obtained from **30** (110 mg, 0.21 mmol); yield: 91% (0.19 mmol, 92 mg). $[\alpha]_D^{rt} = +19.9$ (*c* 1, $CHCl_3$); ^1H NMR δ: 4.48–4.74 (m, 6H, 6 × OC*H*$_2$Ph), 4.08 (d, *J* = 5.1 Hz, 1H, H-7), 4.05 (m, 1H, H-2), 4.01 (m,1H, H-3), 3.93 (d, *J* = 3.6, 1H, H-8), 3.87 (m, 2H, H-5 and H-9), 2.44 (m, 1H, H-6), 2.08 (ddd, *J* = 1.8, 4.9, 14.0 Hz, 1H, H-1), 1.95 (m, 1H, H-4a), 1.82 (m, 1H, H-4b); ^{13}C NMR δ: 90.2 (C-9), 88.4 (C-8), 84.7 (C-8), 72.1, 71.9, 70.9 (3 × OCH$_2$Ph), 71.1 (C-3 and C-5), 70.3 (C-2), 44.9 (C-6), 40.3 (C-1), 36.2 (C-4). HRMS (*m*/*z*) calcd for $C_{30}H_{34}O_6Na$ (M+Na$^+$) 513.2253, found 513.2250. Anal. Calcd for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99. Found: C, 73.18; H, 6.99.

4.34. Removal of the benzyl groups from partially protected derivatives. Preparation of bicyclic hexa-ols

To a solution of the corresponding benzylated derivative (0.2 mmol), 10% Pd/C was added (~60 mg) and the heterogeneous mixture was placed in an autoclave under H_2 pressure (20 bar). After 3 h, the autoclave was decompressed and the mixture was filtered through Celite and concentrated.

4.35. (1*R*,2*S*,3*R*,5*S*,6*S*,7*S*,8*R*,9*R*)-2,3,5,7,8,9-Hexahydroxybicyclo-[4.3.0]nonane 41a

Debenzylation of **41** (80 mg, 0.16 mmol) afforded free derivative **41a** (32 mg; 90%). $[\alpha]_D^{rt} = -51.8$ (*c* 1, $CHCl_3$); ^1H NMR (D_2O) δ: 3.53–3.92 (m, 6H, H-2, H-3, H-5, H-7, H-8, H-9), 1.98-2.07 (m, 2H, H-4a and H-1 or H-6) and 1.37–1.47(m, 2H, H-4b and H-1 or H-6); ^{13}C NMR (D_2O) δ: 86.6, 83.1, 75.6, 75.1, 71,0, 63,8 (C-2, C-3, C-5, C-7, C-8, C-9), 49.3, 43.8 (C-1 and C-6), 39.4 (C-4). HRMS (*m*/*z*) calcd for $C_9H_{16}O_6Na$ (M+Na$^+$) 243.0845, found 243.0842.

4.36. (1*R*,2*R*,3*S*,5*S*,6*S*,7*S*,8*R*,9*R*)-2,3,5,7,8,9-Hexahydroxybicyclo-[4.3.0]nonane 42a

Debenzylation of **42** (96 mg, 0.20 mmol) afforded free derivative **42a** (37 mg; 86%). $[\alpha]_D^{rt} = -34.3$ (*c* 1, $CHCl_3$); ^1H NMR (D_2O) δ: 3.53–3.88 (m, 6H, H-2, H-3, H-5, H-7, H-8, H-9), 1.87 (m, 1H, H-4a), 1.65 (m, 2H, H-1 and H-6), 1.46 (m, 1H, H-4b); ^{13}C NMR (D_2O) δ: 86.9, 77.3, 74.8, 70.4, 66.8, 65.3 (C-2, C-3, C-5, C-7, C-8, C-9), 46.1, 43.4 (C-1 and C-6), 36.2 (C-4). HRMS (*m*/*z*) calcd for $C_9H_{16}O_6Na$ (M+Na$^+$) 243.0845, found 243.0839.

4.37. (1*R*,2*R*,3*R*,5*S*,6*S*,7*S*,8*R*,9*R*)-2,3,5,7,8,9-Hexahydroxybicyclo-[4.3.0]nonane 43a

Debenzylation of **43** (80 mg, 0.16 mmol) afforded free derivative **43a** (33 mg; 92%). $[\alpha]_D^{rt} = -2.4$ (*c* 1, $CHCl_3$); ^1H NMR (D_2O) δ: 3.88–3.92 (m, 3H, H-3, H-5, H-7), 3.71–3.77 (m, 3H, H-2, H-8, H-9), 2.01 (m, 1H, H-1), 1.88 (m, 1H, H-4a), 1.67 (m, 1H, H-6), 1.53 (m, 1H, H-4b); ^{13}C NMR (D_2O) δ: 86.9, 86.5, 77.7, 75.3, 71.2, 66.8, 64.3 (C-2, C-3, C-5, C-7, C-8, C-9), 44.0 (C-1), 43.9 (C-6), 35.5 (C-4). HRMS (*m*/*z*) calcd for $C_9H_{16}O_6Na$ (M+Na$^+$) 243.0845, found 243.0842.

4.38. (1*S*,2*S*,3*S*,5*R*,6*R*,7*S*,8*R*,9*R*)-2,3,5,7,8,9-Hexahydroxybicyclo-[4.3.0]nonane 44a

Debenzylation of **44** (69 mg, 0.20 mmol) afforded free derivative **44a** (30 mg; 95%). $[\alpha]_D^{rt} = +14.8$ (*c* 1, $CHCl_3$); ^1H NMR (D_2O) δ: 3.66–3.99 (m, 6H, H-2, H-3, H-5, H-7, H-8, H-9), 2.01 (m, 1H, H-1), 1.83 (m, 2H, H-6 and H-4a), 1.58 (m, 1H, H-4b); ^{13}C NMR (D_2O) δ: 86.5, 82.6, 78.5, 70.9, 70.7, 70.1 (C-6, C-2, C-3, C-5, C-7, C-8, C-9), 46.2 (C-1), 40.2 (C-6), 36.0 (C-4). HRMS (*m*/*z*) calcd for $C_9H_{16}O_6Na$ (M+Na$^+$) 243.0845, found 243.0843.

4.39. (1*S*,2*R*,3*S*,5*S*,6*R*,7*S*,8*R*,9*R*)-2,3,7,8,9-Penta-*O*-benzyl-5-hydroxybicyclo[4.3.0] nonane 36

Compound **36-Ac** (33 mg, 0.05 mmol) was converted, according to the general procedure for hydrolysis, into **36** isolated (29 mg, 92%) by column chromatography (hexane–ethyl acetate, 5:1). $[\alpha]_D^{rt} = +45.6$ (*c* 1, $CHCl_3$); ^1H NMR (C_6D_6) δ: 4.74 (m, 2H, 2 × OC*H*$_2$Ph), 4.55 (m, 3H, H-7 and 2 × OC*H*$_2$Ph), 4.50 (d, *J* = 12.0, 1H, OC*H*$_2$Ph), 4.40 (m, 2H, 2 × OC*H*$_2$Ph), 4.35 (m, 3H, 3 × OC*H*$_2$Ph), 4.24 (m, 2H, H-5 and H-9), 4.14 (d, *J* = 3.5 Hz, 1H, H-8), 3.76 (d, *J* = 10.1 Hz, 1H, O*H*), 3.72, (m, 1H, H-3), 3.64 (dd, *J* = 2.6, 10.9 Hz, 1H, H-2), 2.87 (ddd, *J* = 4.8, 11.1, 13.8 Hz, 1H, H-1), 2.33 (ddd, *J* = 2.4, 9.4, 13.8 Hz, 1H, H-6), 2.11 (dt, *J* = 14.9, 3.1 Hz, 1H, H-4a), 0.97 (m, 1H, H-4b); ^{13}C NMR (C_6D_6) δ: 88.6 (C-8), 85.9 (C-7), 81.3 (C-9), 79.1 (C-2), 75.5 (C-3), 72.9, 72.4, 71.2, 70.8, 70.6 (5 × OCH$_2$Ph), 65.7 (C-5), 50.2 (C-6), 39.0 (C-1), 34.6 (C-4). LR-MS (*m*/*z*) for $C_{44}H_{46}O_6Na$ (M+Na$^+$) 693.4. Anal. calcd for $C_{44}H_{46}O_6$: C, 78.78; H, 6.91. Found: C, 78.83; H, 6.99.

4.40. (1*S*,2*R*,3*R*,5*R*,6*R*,7*S*,8*S*,9*R*)-2,3,7,8,9-Penta-*O*-benzylo-5-hydroxy-bicyclo [4.3.0]nonane 25a

Compound **25** (62 mg, 0.05 mmol) hydrolyzed according to the general procedure afforded **25a** (45 mg, 75%) as an oil. $[\alpha]_D^{rt} = -18.0$ (*c* 1, $CHCl_3$); ^1H NMR (C_6D_6) δ: 4.61 (d, *J* = 12.0 Hz, 1H, OC*H*$_2$Ph), 4.49 (d, *J* = 12.0 Hz, 1H, OC*H*$_2$Ph), 4.41 (m, 3H, H-5 and 2 × OC*H*$_2$Ph), 4.31 (dd, *J* = 3.6, 9.9 Hz, 1H, H-9), 4.24 (m, 3H, 3 × OC*H*$_2$Ph), 4.15 (m, 2H, 2 × OC*H*$_2$Ph), 4.08 (d, *J* = 3.6 Hz, 1H, H-8), 4.03 (d, *J* = 4.8 Hz, 1H, H-7), 3.82 (m, 1H, H-2), 3.63 (m, 1H, H-3), 2.90 (ddd, *J* = 2.6, 9.9, 13.8 Hz, 1H, H-1), 2.14 (ddd, *J* = 4.8, 10.3, 13.8 Hz, 1H, H-6), 2.07 (dt, *J* = 13.5, 3.8 Hz, 1H, H-4a), 1.62 (m, 1H, H-4b); ^{13}C NMR (C_6D_6) δ: 89.9 (C-7), 84.7 (C-9), 79.9 (C-8), 75.4 (C-3), 73.5 (C-2), 72.0, 71.7, 71.4, 70.8, 70.6 (5 × OCH$_2$Ph), 64.7 (C-5), 46.0 (C-6), 43.9 (C-1), 34.6 (C-4). HRMS (*m*/*z*) calcd for $C_{44}H_{46}O_6Na$ (M+Na$^+$) 693.3186, found 693.3187. Anal. calcd for $C_{44}H_{46}O_6$: C, 78.78; H, 6.91. Found: C, 78.88; H, 6.69.

4.41. (1*S*,2*R*,3*R*,5*R*,6*R*,7*S*,8*S*,9*R*)-2,3,7,8,9-Penta-*O*-benzyl-5-*O*-mesyl-bicyclo [4.3.0]nonane 25b

To a cooled (0 °C) solution of alcohol **25a** (43 mg, 0.07 mmol) and triethylamine (0.01 mL, 0.15 mmol) in methylene chloride (10 mL), mesyl chloride (0.02 mL, 0.15 mmol) was added and the mixture was stirred for 2 h (TLC monitoring in hexane–ethyl acetate, 3:1). The mixture was then partitioned between water (30 mL) and methylene chloride (20 mL). The organic phase was separated, washed with water (15 mL), dried, concentrated, and the product (45 mg, 0.06 mmol, 92%) was isolated by column chromatography (hexane–ethyl acetate, 10:1) as an oil. $[\alpha]_D^{rt} = -7.4$ (*c* 1, $CHCl_3$); ^{1}H NMR δ: 5.51 (dt, *J* = 4.5, 10.9 Hz, 1H, H-5), 4.54 (m, 2H, 2 × OC*H*$_2$Ph), 4.45 (dd, *J* 8.8, 11.7 Hz, 2H, 2 × OC*H*$_2$Ph), 4.44 (d, *J* = 12.1 Hz, 1H, OC*H*$_2$Ph), 4.36 (m, 2H, 2 × OC*H*$_2$Ph), 4.33 (m, 4H, H-9, 3 × OC*H*$_2$Ph), 4.17 (dd, *J* = 4.3, 11.7 Hz, 2H, 2 × OC*H*$_2$Ph), 4.08 (d, *J* = 12.0 Hz, 1H, OC*H*$_2$Ph), 4.03 (m, 2H, H-7 and H-8), 3.79 (m, 1H, H-2), 3.64 (m, 1H, H-3), 3.07 (ddd, *J* = 2.6, 9.6, 13.8 Hz, 1H, H-1), 2.68 (dt, *J* = 13.4, 3.8 Hz, 1H, H-4a), 2.57 (ddd, *J* = 4.5, 10.6, 13.8 Hz, 1H, H-6), 2.31 (s, 3H, -OMs), 1.94 (m, 1H); ^{13}C NMR δ: 88.0, 80.3 (C-7, C-8), 85.0 (C-9), 76.7 (C-5), 75.0 (C-3), 73.5 (C-2), 72.3, 72.2, 71.7, 70.9, 70.8 (5 × OCH$_2$Ph), 44.7 (C-1), 43.7 (C-6), 37.7 (OMs), 32.3 (C-4); HRMS (*m*/*z*) calcd for $C_{45}H_{48}O_8SNa$ (M+Na$^+$) 771.2958, found 771.2965. Anal. calcd for $C_{45}H_{48}O_8S$: C, 72.17; H, 6.46. Found: C, 72.29; H. 6.43.

4.42. (1*S*,2*R*,3*S*,5*R*,6*R*,7*S*,8*R*,9*R*)-2,3,7,8,9-Penta-*O*-benzyl-5-*O*-mesyl-bicyclo[4.3.0] nonane 33

Alcohol **34** (100 mg, 0.15 mmol), converted into **33** (90 mg, 0.12 mmol, 81%) analogously to **25**, was purified by column chromatography (toluene–methanol, 19:1). $[\alpha]_D^{rt} = +47.8$ (*c* 1, $CHCl_3$); ^{1}H NMR (C_6D_6) δ: 5.08 (dt, *J* = 4.4, 10.9 Hz, 1H, H-5), 4.56 (m, 1H, OC*H*$_2$Ph), 4.50 (m, 2H, 2 × OC*H*$_2$Ph), 4.44 (d, *J* = 12.1 Hz, 1H, OC*H*$_2$Ph), 4.36 (m, 2H, 2 × OC*H*$_2$Ph), 4.30 (d, *J* = 11.7 Hz, 1H, OC*H*$_2$Ph), 4.21 (d, *J* = 11.7 Hz, OC*H*$_2$Ph), 4.12 (d, *J* = 4.2 Hz, 1H), 4.03 (dd, *J* = 2.6, 8.8 Hz, 1H), 3.95 (d, *J* = 2.6 Hz, 1H), 3.65 (m, 1H), 3.60 (dd, *J* = 2.6, 10.9 Hz, 1H), 2.78 (m, 1H), 2.63 (m, 2H), 2.21 (s, 3H, -OMs), 1.27 (m, 1H); ^{13}C NMR (C_6D_6) δ: 89.9, 87.6, 80.0,79.7, 77.8, 73.1 (C-2, C-3, C-5, C-7, C-8, C-9), 71.8, 71.4, 71.3, 70.8, 70.6 (5 × OCH$_2$Ph), 47.9, 43.5 (C-1, C-6), 37.2 (-OMs), 36.2 (C-4). HRMS (*m*/*z*) calcd for $C_{45}H_{48}O_8SNa$ (M+Na$^+$): 771.2962, found 771.2965.Anal. calcd for $C_{45}H_{48}O_8S$: C, 72.17; H, 6.46; S, 4.28. Found: C, 72.06; H, 6.32; S, 4.47.

4.43. (1*S*,2*R*,3*S*,5*S*,6*R*,7*S*,8*R*,9*R*)-2,3,7,8,9-Penta-*O*-benzyl-5-*O*-acetyl-bicyclo[4.3.0] nonane 36-Ac

A solution of mesylate **33** (50 mg, 0.07 mmol) and cesium acetate (14 mg, 0.08 mmol) in DMF (10 mL) was stirred at rt for 48 h (TLC monitoring in hexane–ethyl acetate, 3:1), and then partitioned between water (20 mL) and ether (30 mL). The organic phase was separated and the aqueous phase extracted with ether (2 × 10 mL). The combined organic solutions were washed with water and brine (5 mL each), dried, concentrated, and the crude product was isolated by column chromatography (hexane–ethyl acetate, 9:1) to afford **36-Ac** (35 mg, 0.05 mmol, 65%) as an oil. $[\alpha]_D^{rt} = +7.8$ (*c* 1, $CHCl_3$); ^{1}H NMR (C_6D_6) δ: 5.33 (m, 1H, H-5), 4.67 (d, *J* = 12.3, 1H, OC*H*$_2$Ph), 4.57 (m, 2H, 2 × OC*H*$_2$Ph), 4.50 (d, *J* = 11.6 Hz, 1H, OC*H*$_2$Ph), 4.39 (m, 4H, 4 × OC*H*$_2$Ph), 4.32 (d, *J* = 11.9 Hz, 1H, OC*H*$_2$Ph), 4.24 (d, *J* = 11.9 Hz, 1H, OC*H*$_2$Ph), 4.18 (m, 2H, H-7, H-9), 4.11 (d, *J* = 3.2 Hz, 1H, H-8), 3.66 (dd, J_1 = 3.2, 11.0 Hz, 1H, H-2), 3.62 (m, 1H, H-3), 3.05 (ddd, *J* = 4.5, 10.7, 13.7 Hz, 1H, H-1), 2.59 (dt, *J* = 15.8, 2.9 Hz, 1H, H-4a), 2.40 (ddd, *J* = 2.9, 9.7, 13.7 Hz, 1H, H-6), 1.55 (s, 3H, C(O)C*H*$_3$), 0.92 (m, 1H, H-4b); ^{13}C NMR (C_6D_6) δ: 170.36 (*C*(O)CH$_3$), 89.29 (C-8), 84.64, 81.01 (C-7 andC-9), 78.88 (C-2), 73.12 (C-3), 71.98, 71.74, 71.66, 71.21, 70.50 (5 × OCH$_2$Ph), 67.49 (C-5), 47.76 (C-6), 40.11 (C-1), 31.32 (C-4), 20.82 (C(O)*C*H$_3$). HRMS (*m*/*z*) calcd for $C_{46}H_{48}O_7Na$ (M+Na$^+$) 735.3292, found 735.3292. Anal. calcd for $C_{46}H_{48}O_7$: C, 77.50; H, 6.99. Found: C, 77.29; H; 6.93.

4.44. (1*S*,2*R*,3*S*,7*S*,8*R*,9*R*)-2,3,7,8,9-Penta-*O*-benzyl-bicyclo[4.3.0]-non-5,6-ene 37

To a solution of alcohol **34** (84 mg, 0.13 mmol) in THF (5 mL), sodium hydride (50% dispersion in mineral oil, 7 mg, 0.15 mmol) was added and the mixture was stirred at rt for 20 min. Carbon disulfide (0.05 mL, 0.65 mmol) was added and—after another 20 min, methyl iodide (0.04 mL, 0.65 mmol), and the mixture was stirred for 3 h at rt (TLC monitoring in hexane–ethyl acetate, 3:1). Next, it was partitioned between water (10 mL) and ethyl acetate (10 mL), the organic phase was separated, and the aqueous phase extracted with ethyl acetate (10 mL). The combined organic solutions were washed with water and brine (5 mL each), dried, and concentrated. Crude xanthate **35** was heated at 200 °C for 1 h (TLC monitoring in hexane–ethyl acetate, 3:1). After cooling to rt, the crude product was purified by column chromatography (hexane–ethyl acetate, 11:1) to afford olefin **37** (10 mg, 0.02 mmol, 12%) as an oil. ^{1}H NMR (C_6D_6) δ: 5.79 (m, 1H, H-5), 4.56 (m, 3H, 3 × OC*H*$_2$Ph), 4.46 (m, 4H, 4 × OC*H*$_2$Ph), 4.32 (m, 4H, 3 × OC*H*$_2$Ph and 1H), 4.21 (d, *J* = 5.6 Hz, 1H), 4.02 (m, 2H), 3.92 (s, 1H), 3.83 (m, 1H), 2.31 (m, 1H, H-4a), 1.92 (m, 1H, H-4b); ^{13}C NMR (C_6D_6) δ: 117.12 (C-5),86.90, 85.77, 81.82, 77.49, 72,74 (C-2, C-3, C-7, C-8, C-9), 71.87, 71.78, 71.43, 71.32, 70.83 (5 × OCH$_2$Ph), 44.21 (C-1), 31.13 (C-4). LR-MS (*m*/*z*) for $C_{44}H_{45}O_5Na$ (M+Na$^+$) 675.3.

4.45. (1*S*,2*R*,3*R*,6*R*,7*S*,8*S*,9*R*)-2,3,7,8,9-Penta-*O*-benzylbicyclo[4.3.0]-non-4,5-ene 40

To a solution of compound **25b** (33 mg, 0.04 mmol) in DMF (10 mL), CsOAc (14 mg, 0.08 mmol) was added and the mixture was stirred and heated at reflux for 48 h (TLC monitoring in hexane–ethyl acetate, 3:1). After cooling, it was partitioned between water (20 mL) and ether (30 mL), the organic phase was separated, and the aqueous phase extracted with ether (2 × 20 mL). The combined organic solutions were washed with water and brine (10 mL each), dried, concentrated, and the crude product was purified by column chromatography (hexane–ethyl acetate, 3:1) to afford **40** (14 mg, 45%) as an oil. ^{1}H NMR (C_6D_6) δ: 6.19 (d, *J* = 10.2, 1H), 5.88 (m, 1H), 4.65 (d, *J* = 12.1 Hz, 1H), 4.55 (d, *J* = 12.1 Hz, 1H), 4.43 (m, 3H), 4.33 (m, 6H), 4.17 (s, 1H), 4.15 (d, *J* = 3.7 Hz, 1H), 3.95 (m, 1H), 3.81 (d, *J* = 4.8 Hz), 3.05 (ddd, *J* = 2.1, 10.1, 12.7 Hz, 1H), 2.88 (m, 1H); ^{13}C NMR (C_6D_6) δ: 131.39, 126.77 (C-4 and C-5), 91.10, 84.38, 81.74, 75.18, 73.50 (C-2, C-3, C-7, C-8, C-9), 72.19, 71.83, 71.65, 71.34, 70.98 (5 × OCH$_2$Ph), 44.23, 38.76 (C-1 and C-6). HRMS (*m*/*z*) calcd for $C_{44}H_{44}O_5Na$ (M+Na$^+$) 675.3086, found 675.3082.

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