Flexible Molecules with Defined Shape, XII[+]

Conformation Control in Open-Chain Compounds with up to Six Rotatable Bonds

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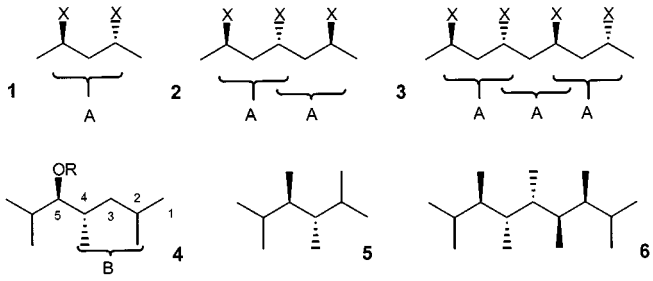
Substituent patterns on 1,3,5...-polyoxygenated-2,4,6...-polymethylated alkane chains, which preferentially adopt a fully extended backbone conformation, have been identified. This is demonstrated by analysis of the vicinal H,H-coupling constants along the backbones of compounds **19**, **23**, and **24**.

We showed in the preceeding paper[1] that 2,4-disubstituted pentanes **1** adopt mainly two backbone conformations, and that the conformer equilibrium may be shifted towards the conformation in which the carbon backbone is fully extended when the substitutents X are electronegative groups such as chlorine or phthalimido.



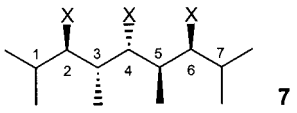
A combination of such 2,4-disubstituted pentane units, e.g. going from **1** to **2** or **3** should in principle result in larger flexible structures with a preference for the fully extended conformation. But even if the *local* conformational preferences in each of the segments A remain the same in going from **1** to **2** or **3**, the *overall* conformational preference for molecule **2** or **3** having four to six rotatable backbone bonds, will be significant only if the *local* conformational preferences in each of the segments A exceed 95%. The data reported previously[1] for compounds **1** with X = Cl or phthalimido show that this is not the case.

Therefore, conformation control in larger open chain structures would have to rely on effects other than or in addition to the polar and steric effects which control the conformation in the model compounds **1**.

Higher conformation control in local backbone segments may be achieved[2] if any undesired conformation is minimized by destabilizing interactions such as *syn*-pentane interactions. An example is given by **4**, in which the local conformer preference in segment B amounts to 7:1 due to the presence and relative configuration of the C-5 substituent. More precisely, it is the *anti* relative configuration of the (oxygen) substituent at C-5 and the methyl group at C-4 which destabilizes one of the two low energy backbone conformations in segment B of **4**.

This led us to consider multisubstituted carbon chains of the type **6**, which should have more pronounced conformational preferences. Structure **6** can also be derived by superposition of two building blocks **5** which have been calculated to possess a conformational preference of 80%.[3] MM3* calculations, however, indicate that the conformational preference for **6** is less than expected.

The problem is that multisubstitution creates a large number of *gauche* arrangements which destabilize all conformations, including the desired ground-state conformation. While such *gauche* interactions are an integral feature of the substitution pattern in **5**, higher conformational preferences should result if substituents − other than methyl groups − are chosen which, for steric or electronic reasons, prefer to occupy the positions lateral to the main chain.[1] This led us to the structures **7** which are hybrids of **2** and **6**. MM3* calculations suggest that carbon backbones **7** should indeed have high *overall* conformational preferences when the substituents X are an oxygen, halogen or an sp^2-hybridized carbon or nitrogen atom. In the case of **7a** (X = OCH_3) the poor results are a consequence of the fact that these molecules become sterically overcrowded: The *O*-methyl groups suffer *syn*-pentane interactions with



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% preference to populate the fully extended conformation according to MM3* calculations, only bonds from C-2 to C-6 are considered.

	a	b	c	d	e	f	g	h
X =	OCH_3	OAc	Cl	Br	vinyl	phenyl	PhthN	CN
	13	49	89	91	77	96	98	53

[+] Part XI: Ref.[1]

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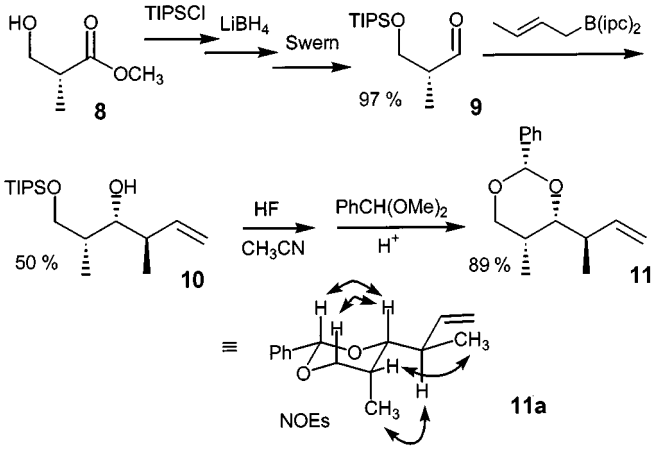
  1434−193X/99/1111−2929 $ 17.50+.50/0

the remainder of the skeleton. The low conformational preference calculated for **7b** is surprising and, as will be shown below, is a likely consequence of an inappropriate parameterization of the force field used for acetates.

The chloro compound **7c** would be a good candidate to demonstrate this type of design by comparison of its conformational preference with that of **2** (X = Cl). However, considering synthetic accessibility, as well as the chances for conformational analysis by NMR, we chose to study compound **19**, which is related to **7b**.

Synthesis

The synthesis of **19** proceeded in a linear fashion. The β-hydroxyisobutyrate **8** was converted into the TIPS-protected aldehyde **9** over three steps in a total yield of 97%. Crotylboration[4] of the aldehyde **9** proceeded with a 93:7 diastereoselectivity, and furnished the homoallylic alcohol **10** in 50% yield after chromatographic purification. The relative configuration of the alcohol **10** was secured by cleavage of the TIPS group (93%) and conversion into the benzylidene acetal **11** (96%). NOE data and coupling constants of the latter (cf. **11a**) clearly indicate that the shown structure is correct.



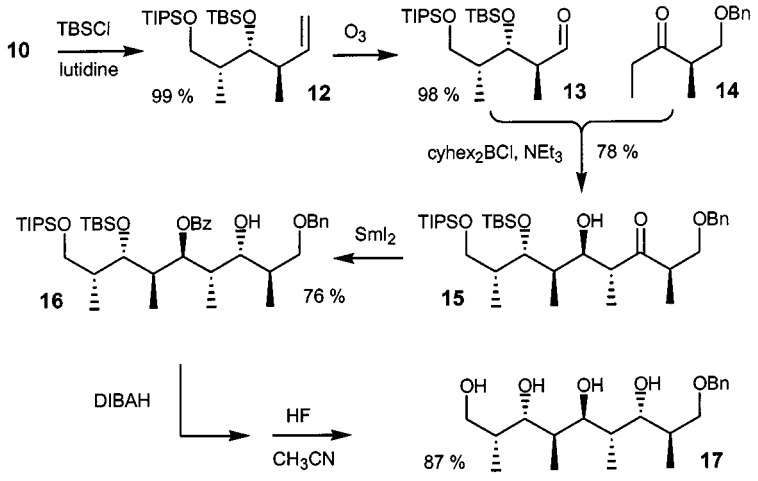
The homoallylic alcohol **10** was then protected with a TBS group (99%) and converted into the aldehyde **13** by ozonolysis (96%). The aldehyde **13** was combined with the boron enolate of ketone **14** following Paterson's methodology,[5] to furnish the aldol adduct **15** in 78% yield. The aldol product was subjected to Evans' samarium iodide catalysed *anti*-selective Tischtschenko reduction,[6] to yield 76% of the benzoate **16**.

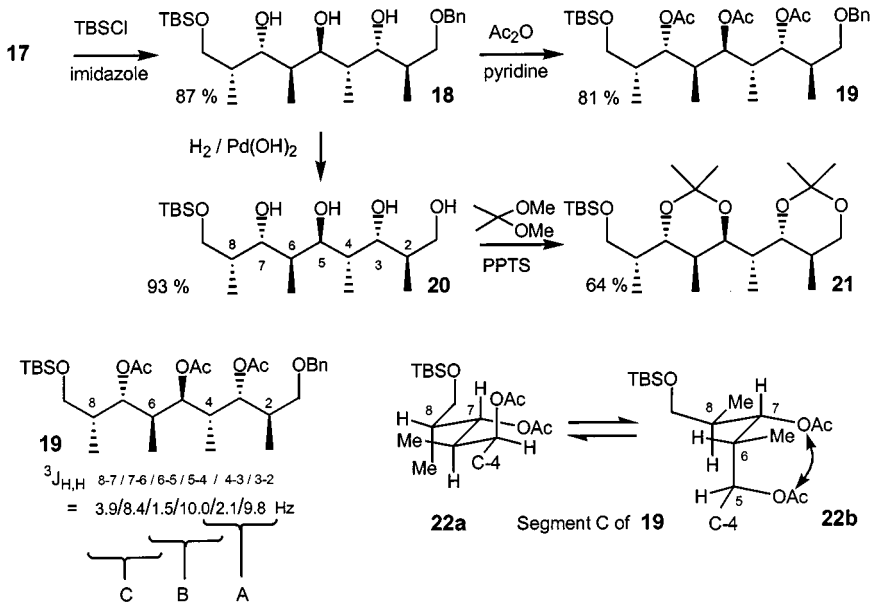
The benzoate **16** was reduced with DIBAH (87%) and the silyl groups were removed with hydrofluoric acid to give 99% of the tetraol **17**. While the latter is likely to possess a high conformational preference, severe overlap in the NMR-spectra did not allow for the determination of vicinal coupling constants. The tetraol **17** was therefore converted into the derivative **19** with differentiated protecting groups more amenable to conformational analysis. With this in mind, the primary hydroxyl group was selectively reprotected with TBDMS (87%) and the remaining hydroxyl groups were acetylated to give **19** in 81% yield.

Debenzylation of **18** (93%) and formation of the bisacetonide **21** (64%) permitted us to establish the relative configuration of the stereogenic centers created in the aldol addition.[7] One of the acetonides is in a twist boat conformation (δ_C = 23.8, 25.6, 100.5) and the other in a chair conformation (δ_C = 19.2, 29.9, 98.0). Since the terminal acetonide is always in a chair conformation, the twist boat conformation of the internal acetonide indicates the relative configuration at C-5 and C-7 as shown.

Compound **19** showed NMR spectra which allowed for the assignment of the individual hydrogen atoms at C-3, C-5, and C-7, and the determination of the vicinal coupling constants to these hydrogen atoms. Assignment of the coupling constants in segment C of **19** is tentative, since a definite assignment of the coupling constants for H7/H8 or H7/H6 was not possible. The coupling constants found for the segments A and B agree very well with those derived by calculating local conformer populations with the Macromodel[8] program

Judging from the alteration of the coupling constants,[9] the conformational preference in segment A and in segment B of **19** is at least 93:7. In segment C, it amounts to

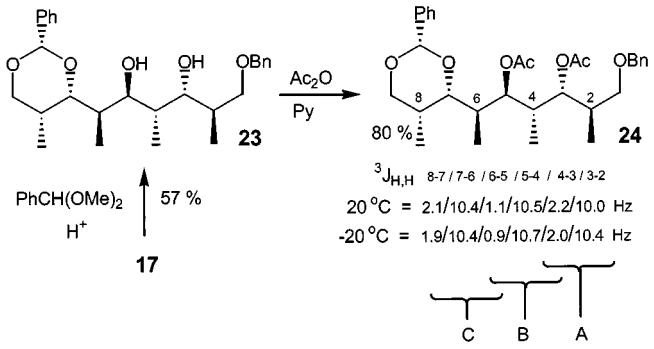




ca. 70:30. MM3* calculations suggest that the fully-extended conformation is the most stable one in segments A and B. For segment C (cf. **22**), the two lowest energy conformers are calculated to be **22a** and **22b**. The calculations suggest that the doubly-bent conformation **22b** is preferentially populated. This conformation implies a 1,3 parallel arrangement[10] of two acetoxy groups, a situation found in many crystal structures of peracetylated alditols.[11] Nevertheless, the idea behind the choice of compound **19**, which is to be studied here, was that the fully extended conformation should be the one which is considerably favored. Since the vicinal coupling constants indicated that one conformation is greatly favored, we had to ascertain whether this was the fully extended one or not. With this in mind, we determined the $^3J_{C,H}$ coupling constants between the hydrogens on the carbon at C-3, C-5, and C-7 substituted with acetoxy groups, and the carbon atoms of the four methyl groups. Each of the hydrogen resonances considered showed one small *and* one large ^3J coupling constant, to the carbon atoms of three methyl groups, the latter varying between 5.1 and 6.2 Hz. This being the case, it did not matter that the ^{13}C-NMR signals could not be assigned to the individual methyl groups. It is immediately clear that this pattern of $^3J_{C,H}$ coupling constants can arise only (cf. C-7-H in **22a**) if the main backbone of **19** is in an *all-trans* conformation. Therefore, in contrast to the MM3* calculation, segment C indeed adopts the fully extended conformation **22a** as the major conformer. All we can say at this point is that the MM3* calculations were unreliable for the calculation of the conformer preference in segment C. Perhaps the destabilizing interaction between two acetoxy groups in a 1,3-parallel arrangement (cf. **22b**) is underestimated in the MM3* force field. MM3* calculations of **1** (X = OAc) also predict a relatively high proportion (8%) of the conformer population having the acetoxy groups in a 1,3-parallel arrangement.

The conformational preference in segments A and B of **19** are high, because there is an *anti* arrangement between the acetoxy group on C-7 and the methyl group on C-6 which controls the conformation in segment B, and the acetoxy group on C-5 and the methyl group at C-4 which controls segment A. There is no such situation, namely the *syn* configuration at C-5 and C-6, to control the local conformation in segment C, which in turn has a lower conformational preference. If the oxygen atom at C-9 could be held in an arrangement antiperiplanar to the methyl group at C-8, conformational control in segment C, and, in consequence along the whole molecular backbone of **19** could be further improved.

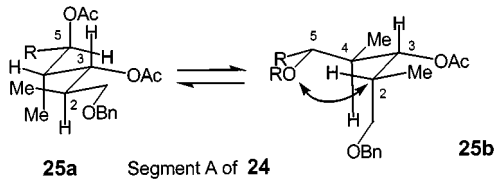
This can be achieved, for instance, if the C-9 and C-7 oxo functionalities are contained in a ring. For this reason we envisaged the benzylidene acetal **24** for further study. To access compound **24** the tetraol **17** was allowed to react with one equivalent of benzaldehyde dimethyl acetal and *p*-toluenesulfonic acid to furnish the monobenzylidene acetal **23** in 57% yield. The latter was acetylated to give **24** in 80% yield.

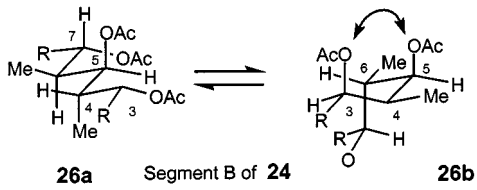


In the NMR spectrum of **24**, all relevant $^3J_{H,H}$ coupling constants could be determined. They showed a rather small temperature dependence, indicating[12] that to a large ex-

tent, **24** as a whole adopts a single conformation. The coupling constants measured at −20°C correspond within ±0.2 Hz with those calculated by Macromodel[8] for the fully extended conformation. While most of the individual coupling contants could be assigned without difficulty, those between H-2 and H-3, and H-4 and H-3 could not be assigned, because the ^{1}H-NMR signals of H-2 and H-4 overlapped.

Macromodel[8] calculations were then applied to arrive at population-averaged $^3J_{H,H}$ coupling constants, including the low energy (< 10 kJ over the lowest energy conformer) conformers of **24**. The coupling constants predicted in this manner (2.1, 10.6, 6.0, 5.9, 9.4 and 2.5 Hz) differ largely from those determined experimentally. Moreover, Macromodel predicts in segment B of **24**, a preference for the doubly bent conformer **26b**, whereas we were confident that the fully extended conformation **26a** should prevail. For this reason, we made a detailed evaluation of the preferred local conformations in each of the dimethylpentane segments of **24**. The conformation in segment C is unambiguously defined by the ring and by the coupling constant H-6/H-7 of 10.4 Hz.

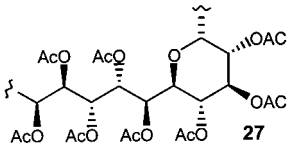




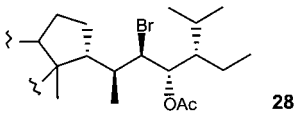
The two lowest energy conformers of segment A are shown as **25a** and **25b**. H-3 has NOE interactions with H-4 and CH_3-2, cf. **25a**, but not to H-2 and CH_3-4, as would be required by conformation **25b**. From this we conclude that the local conformation **25a** prevails in segment A, in line with the MM3* calculations. Contrary to MM3* calculations is the situation in segment B:

MM3* predicts **26b** to be more stable than **26a** by 5.4 kJ.mol^{-1}, whereas the coupling constants measured unambiguously show that conformation **26a** is by far the predominant one! Clearly, this is a warning that MM3* may give correct conformer geometries,[13] but may fail with respect to conformer energies in highly oxygenated systems such as **19** or **24**.

Overall, the conformational preferences recorded for compound **24** prove the validity of our concept in conformation design, which relies on the substituent pattern present in **7**. In fact, a large difference in coupling constants (equivalent to a high backbone conformational preference) has been noted with the related compounds **27**[14] and **28**.[15]

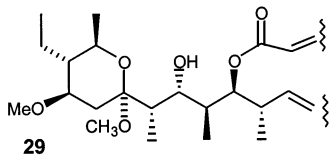


$^3J_{H,H}$ = 1.0/9.5/1.6/9.8/2.2/9.8 Hz

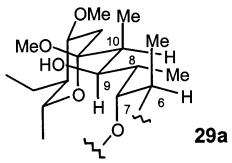


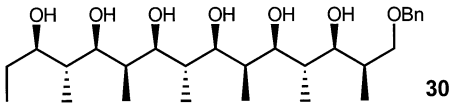
$^3J_{H,H}$ = 9.8/ <1/10.1/1.7 Hz

Moreover, a substituent pattern corresponding to **7** is found in elayomycin[16] (cf. **29**) and the related antibiotics bafilomycin,[17] hygrolidin,[18] and concanamycin.[16][19] Here, the preferred conformer is additionally stabilized by an intramolecular hydrogen bond. It is therefore of interest to investigate to what extent hydrogen bonding reinforces or counteracts backbone-based conformational preferences. A reinforcement of a backbone conformation has recently been reported by Paterson[20] in the case of the polyol **30**, in which the hydroxyl groups are on the same side of the carbon chain.



20 °C: $^3J_{H,H}$ = 4 / 11 / 2 / 10 Hz





Compound **30** has been found to have a marked tendency to adopt a fully hydrogen-bonded, fully extended backbone conformation. MM2 calculations suggest that these hydrogen bonds deform the backbone slightly, so as to give the chain a distinct curvature, similar to the one calculated for isotactic polyvinyl alcohol.[21] Due to almost complete signal overlap in **30**, local conformer preferences in the individual backbone segments could not be determined. In contrast to the polyol **30**, the hydroxyl groups in the diol **23** are on alternate sides of the carbon backbone. The diagnostic

coupling constants of **23**, as well as their temperature dependence are very similar to that of the diacetate **24**. This shows that the conformer population in segment B of **23** is not changed into the direction of a conformation corresponding to **26b**, a conformation that would allow for intramolecular hydrogen bonding between the hydroxy groups at C-3 and C-5. The backbone conformational preference is therefore a dominant feature in these compounds.

In summary, compound **24** has five backbone bonds capable of free rotation, but adopts (probably to an extent of > 90%) a single conformation. The compounds **19**, **23**, **24**, and **30** are related to natural products of polyketide biogenetic origin. This study of their conformational preferences allowed for a deeper insight into the conformational design achieved in an evolutionary process by nature. Based on these insights, the design of larger flexible backbone structures with a preferred conformation is in sight, given the fact that polymer-supported and partially automated synthesis of such structures is currently being developed.[22]

Experimental Section

All temperatures quoted are not corrected. − Reactions were carried out under dry nitrogen or argon. − Boiling range of petroleum ether: 40−60°C. − ^{1}H, ^{13}C NMR: Bruker AC 300, AM 400, and AMX 500. Spectra were recorded in $CDCl_3$ (99% D), which was also used as internal standard. Assignments are based on H,H- and C,H-COSY experiments and APT spectra. − Buffer of pH = 7: $NaH_2PO_4 \times 2\ H_2O$ (56.2 g) and $Na_2HPO_4 \times 2\ H_2O$ (213.3 g) in water (1.0 L). − Column chromatography: Silica gel Si60 (63−200 μm), E. Merck AG, Darmstadt. − Flash chromatography: Silica gel Si60 (40−63 μm), E. Merck AG, Darmstadt. − MPLC: 30 × 2 cm column with silica gel Si60 (15−25 μm), E. Merck AG, Darmstadt, 10 bar, detection by differential refractrometry (Knauer, Berlin).

1. Methyl (2*R*)-2-Methyl-3-(triisopropylsilyloxy)propanoate: To a solution of methyl (2*R*)-3-hydroxy-2-methylpropanoate (**8**, 4.0 g, 34 mmol) in dimethylformamide (68 mL) was added at room temperature chlorotriisopropylsilane (8.3 mL, 38.9 mmol), imidazole (3.2 g, 47 mmol) and 4-dimethylaminopyridine (0.6 g, 5 mmol). After stirring for 3 d at room temperature, water (150 mL) was added. The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 100 mL). The combined organic phases were washed with brine (100 mL), dried ($MgSO_4$) and concentrated. Flash chromatography of the residue (10.4 g) with pentane/*tert*-butyl methyl ether changing from 100:0 to 40:1 furnished 9.3 g (100%) of the product as a colorless oil. − $[\alpha]_D^{20} = -18.4$ (c = 5.302, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96−1.11 (m, 21 H), 1.14 (d, J = 7.0 Hz, 3 H), 2.65 (m, 1 H), 3.65 (s, 3 H), 3.75 (dd, J = 9.5 and 6.0 Hz, 1 H), 3.85 (dd, J = 9.5 and 6.7 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9, 13.4, 17.9, 42.7, 51.4, 65.7, 175.4. − $C_{14}H_{30}O_3Si$ (274.2): calcd. C 61.26, H 11.02; found C 61.25, H 11.14.

2. (2*R*)-2-Methyl-3-(triisopropylsilyloxy)propanol: $LiBH_4$ (0.86 g, 40 mmol) was added to a solution of methyl (2*R*)-2-methyl-3-(triisopropylsilyloxy)propanoate (7.26 g, 26.4 mmol) in ether (88 mL) at 0°C. The suspension was stirred for 2 d at room temperature. A 1:1 mixture of saturated aqueous NH_4Cl solution and $NaHCO_3$ solution (150 mL) was added, the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (100 mL). The combined organic phases were washed with brine (100 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue (6.7 g) using pentane/*tert*-butyl methyl ether changing from 100:1 to 4:1 furnished the product (6.52 g, 100%) as a colorless oil. − $[\alpha]_D^{20} = -9.1$ (c = 2.974, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (d, J = 7.0 Hz, 3 H), 1.05−1.19 (m, 21 H), 1.97 (m, 1 H), 3.01 (s, 1 H, OH), 3.60−3.66 (m, 3 H), 3.83 (dd, J = 9.7 and 4.2 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.8, 13.1, 17.9, 37.2, 68.5, 69.4. − $C_{13}H_{30}O_2Si$ (246.5): calcd. C 63.35, H 12.27; found C 63.18, H 12.44.

3. (2*R*)-2-Methyl-3-(triisopropylsilyloxy)propanal (9): A solution of dimethyl sulfoxide (0.87 mL, 12 mmol) in dichloromethane (2.3 mL) was added at −78°C to a solution of oxalyl chloride (0.52 mL, 6.1 mmol) in dichloromethane (6.0 mL). After stirring for 5 min, a solution of (2*R*)-2-methyl-3-(triisopropylsilyloxy)propanol (1.00 g, 4.06 mmol) in dichloromethane (8 mL) was added at −78°C. After stirring for 20 min, triethylamine (3.9 mL, 28 mmol) was added dropwise at this temperature. The solution was stirred for 20 min at −78°C, 15 min at −55°C and 45 min at 0°C. Semisaturated aqueous NH_4Cl solution (30 mL) was added, the phases were separated and the aqueous phase was extracted with dichloromethane (3 × 50 mL). The combined organic phases were washed with brine (50 mL), dried ($MgSO_4$), and concentrated. Column chromatography over silica gel of the residue (1.10 g) with pentane/*tert*-butyl methyl ether changing from 10:1 to 4:1 furnished **9** (960 mg, 97%) as a colorless oil which was used for the next reaction as obtained.

4. (3*R*,4*R*,5*R*)-4-Hydroxy-3,5-dimethyl-6-(triisopropylsilyloxy)-1-hexen-3-ol (10): *trans*-2-Butene (ca. 1.50 g, 26 mmol) was introduced at −78°C to a solution of potassium *tert*-butoxide (379 mg, 3.38 mmol) in THF (6.0 mL). After stirring for 15 min, *n*-butyllithium (1.54 M in hexane, 2.20 mL, 3.38 mmol) was added dropwise over 40 min at −78°C. The brown suspension was stirred for 15 min at −45°C and cooled to −78°C. (+)-*B*-methoxydiisopinocampheylborane (1.24 g, 3.9 mmol) was added dropwise over 30 min. The colorless solution was stirred for 45 min and cooled to −90°C. BF_3−diethyl ether (0.61 mL, 4.81 mmol) was added rapidly, followed by slow addition of **9** (764 mg, 3.13 mmol). The resulting viscous solution was stirred for 16 h at −90°C. After reaching room temperature, aqueous NaOH (3 M, 3.6 mL, 11 mmol) was added, the solution was brought to reflux and 30% aqueous H_2O_2 solution (1.5 mL) was added slowly. After refluxing for 5 h, saturated aqueous $NaHSO_3$ solution (30 mL) was added, the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 50 mL). The combined organic phases were washed with brine (50 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue (2.4 g) with pentane to pentane/*tert*-butyl methyl ether, 30:1, furnished 640 mg of a 13:1 diastereomeric mixture and 80 mg of a 4:1 diastereomeric mixture. These fractions were combined and subjected to a MPLC separation using petroleum ether/*tert*-butyl methyl ether, 16:1, to give **10** (466 mg, 50%) as a colorless oil. − $[\alpha]_D^{20} = +2.3$ (c = 6.870, $CHCl_3$). − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (d, J = 6.8 Hz, 3 H), 0.98 (d, J = 7.0 Hz, 3 H), 1.05−1.14 (m, 21 H), 1.81 (m, 1 H), 2.30 (m, 1 H), 2.78 (s, 1 H, OH), 3.58 (dd, J = 8.6 and 2.4 Hz, 1 H), 3.81 (m, 2 H), 5.10 (m, 2 H), 5.85 (ddd, J = 17.2, 10.3, and 8.2 Hz, 1 H). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.5, 11.8, 16.7, 17.9, 36.5, 41.7, 68.7, 76.9, 114.9. 142.1. − $C_{17}H_{36}O_2Si$ (300.6): calcd. C 67.94, H 12.07; found C 68.03, H 12.22.

5. (3*R*,4*R*,5*R*)-4,6-Dihydroxy-3,5-dimethyl-1-hexene: A solution of HF in acetonitrile (5%, 2.4 mL) was added to **10** (143 mg, 0.48 mmol) at room temperature. After 45 min, saturated $NaHCO_3$

solution (10 mL) was added, the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (5 × 30 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue (90 mg) with pentane/*tert*-butyl methyl ether changing from 1:1 to 0:1 furnished the product (64 mg, 93%) as a colorless solid, m.p. 54°C. − $[\alpha]_D^{20} = -6.7$ ($c = 1.200$, $CHCl_3$). − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (d, J = 7.0 Hz, 3 H), 0.97 (d, J = 6.7 Hz, 3 H), 1.85 (m, 1 H), 2.17−2.32 (m, 2 H, OH), 2.83 (s, 1 H, OH), 3.51 (dd, J = 9.0 and 2.5 Hz, 1 H), 3.68 (dd, J = 10.7 and 5.7 Hz, 1 H), 3.74 (dd, J = 10.7 and 4.3 Hz, 1 H), 5.15 (m, 2 H), 5.72 (ddd, J = 16.9, 10.4, and 8.8 Hz, 1 H). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.9, 16.4, 35.8, 42.4, 67.5, 76.2, 116.5, 141.4. − $C_8H_{16}O_2$ (144.2): calcd. C 66.63, H 11.18; found C 66.63, H 11.30.

6. (2*S*,4*R*,5*R*)-5-Methyl-4-[(1*R*)-1-methyl-2-propenyl]-2-phenyl-1,3-dioxane (11): Benzaldehyde dimethyl acetal (52 μL, 0.35 mmol) and *p*-toluenesulfonic acid (ca. 5 mg) were added to a solution of (3*R*,4*R*,5*R*)-4,6-dihydroxy-3,5-dimethyl-1-hexene (48 mg, 0.33 mmol) in THF (1.7 mL). After 1 d at room temperature, saturated aqueous $NaHCO_3$ solution (5 mL) and *tert*-butyl methyl ether (10 mL) were added. The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 70 mL). The combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue (85 mg) with pentane to pentane/*tert*-butyl methyl ether, 100:1, furnished **11** (74 mg, 96%) as a colorless oil. − $[\alpha]_D^{20} = +58.1$ (c = 1.025, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.97 (d, J = 6.9 Hz, 3 H), 1.18 (d, J = 6.9 Hz, 3 H), 1.68 (m, 1 H), 2.40 (m, 1 H), 3.57 (dd, J = 10.0 and 2.2 Hz, 1 H), 4.05 (m, 2 H), 5.00−5.11 (m, 2 H), 5.47 (s, 1 H), 5.98 (ddd, J = 17.4, 10.5, and 6.6 Hz, 1 H), 7.30−7.36 (m, 3 H), 7.47−7.50 (m, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.9, 14.3, 30.1, 38.5, 73.9, 83.7, 101.5, 113.8, 125.9, 128.1, 128.5, 139.0, 141.5. − $C_{15}H_{20}O_2$ (232.3): calcd. C 77.55, H 8.68; found C 77.49, H 8.75.

7. (3*R*,4*R*,5*R*)-4-(*tert*-Butyldimethylsilyloxy)-3,5-dimethyl-6-(triisopropylsilyloxy)hexene (12): Lutidine (0.31 mL, 2.7 mmol) and *tert*-butyldimethylsilyl triflate (0.48 mL, 2.2 mmol) were added sequentially to a solution of **10** (500 mg, 1.66 mmol) in dichloromethane (8.3 mL) at 0°C. After 30 min at 0°C, and 1 h at room temperature, the mixture was recooled to 0°C and methanol (0.5 mL) was added. Silica gel (2.0 g) was added and the suspension was concentrated in vacuo. The residue was eluted by flash chromatography with pentane to give **12** (680 mg, 99%) as a colorless oil. − $[\alpha]_D^{20} = -1.2$ (c = 9.740, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 (s, 3 H), 0.04 (s, 3 H), 0.85 (d, J = 6.9 Hz, 3 H), 0.88 (s, 9 H), 0.99 (d, J = 7.0 Hz, 3 H), 1.04 (m, 21 H), 1.77 (m, 1 H), 2.34 (m, 1 H), 3.43 (dd, J = 9.7 and 6.6 Hz, 1 H), 3.54 (dd, J = 9.7 and 7.1 Hz, 1 H), 3.72 (dd, J = 5.0 and 3.2 Hz, 1 H), 4.96 (m, 2 H), 5.83 (ddd, J = 17.3, 10.3, and 7.7 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.0, −3.7, 11.9, 12.1, 17.1, 18.1, 18.4, 26.2, 39.6, 43.1, 66.3, 75.3, 113.9, 142.2. − $C_{23}H_{50}O_2Si_2$ (414.8): calcd. C 66.60, H 12.15; found C 66.60, H 12.15.

8. (2*S*,3*S*,4*R*)-3-*tert*-Butyldimethylsilyloxy-2,4-dimethyl-5-(triisopropylsilyloxy)pentanal (13): A stream of ozone was introduced to a solution of **12** (1.015 g, 2.45 mmol) in dichloromethane (12.3 mL) at −78°C until the blue color persisted. Excess ozone was removed with a stream of oxygen. Triphenylphosphane (706 mg, 2.69 mmol) was added and the solution was allowed to reach room temperature. A solution of *tert*-butyl hydroperoxide (5 M in dichloromethane, 0.33 mL, 1.60 mmol) was added to oxidize the excess triphenylphosphane. Silica gel (5.0 g) was added and the suspension was concentrated. The crude product was purified by filtration through silica gel with pentane/*tert*-butyl methyl ether varying from 50:1 to 20:1. This resulted in **13** (996 mg, 98%) as a colorless oil which was used for the next reaction as obtained.

9. (2*R*,4*R*,5*R*,6*R*,7*S*,8*R*)-1-Benzyloxy-7-*tert*-butyldimethylsilyloxy-5-hydroxy-2,4,6,8-tetramethyl-9-(triisopropylsilyloxy)-3-nonanone (15): Triethylamine (121 μL, 0.86 mmol) and (2*R*)-1-benzyloxy-2-methyl-3-pentanone (**14**)[23] (115 mg, 0.56 mmol) in ether (1 mL) were added sequentially to a solution of chlorodicyclohexylborane (165 μL, 0.76 mmol) in ether (1.45 mL) at 0°C. The resulting suspension was stirred for 2.5 h at 0°C and cooled to −78°C. A solution of the aldehyde **13** (212 mg, 0.51 mmol) in ether (1 mL) was added slowly and the suspension was stirred for 4.5 h at −78°C. After stirring for 16 h at −20°C pH7 buffer (10 mL) was added, the phases were separated and the aqueous phase was extracted with ether (3 × 30 mL). The solvents were removed in vacuo, methanol (5 mL) and pH7 buffer (5 mL) were added, followed by the dropwise addition of 30% aqueous H_2O_2 (5 mL) at 0°C. After stirring for 4 h at 0°C, pH7-buffer solution (10 mL) was added, the phases were separated and the aqueous phase was extracted with dichloromethane (3 × 50 mL). The combined organic phases were washed with brine (50 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue (330 mg) with pentane/*tert*-butyl methyl ether gradients from 50:1 to 10:1 furnished the product **15** (247 mg, 78%) and residual **14** (13 mg) as colorless liquids. For analysis a sample of **15** was rechromatographed. − $[\alpha]_D^{20} = -21.6$ (c = 1.325, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.09 (s, 3 H), 0.12 (s, 3 H), 0.91 (s, 9 H), 0.93−0.95 (m, 9 H), 1.05−1.08 (m, 24 H), 1.72 (m, 1 H), 1.96 (m, 1 H), 2.86 (m, 1 H), 3.08 (m, 1 H), 3.16 (s, 1 H, OH), 3.47 (dd, J = 8.9 and 5.2 Hz, 1 H), 3.59 (m, 2 H), 3.66 (dd, J = 8.8 and 8.1 Hz, 1 H), 3.93 (broad t, J = 5.0 Hz, 1 H), 4.15 (dd, J = 9.7 and 1.4 Hz, 1 H), 4.46 (d, J = 12.1 Hz, 1 H), 4.51 (d, J = 12.1 Hz, 1 H), 7.24−7.34 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −3.9, −3.8, 10.5, 12.3, 12.5, 12.8, 13.3, 18.0, 18.4, 26.2, 37.2, 39.4, 46.7, 49.3, 66.6, 72.5, 73.0, 73.3, 76.9, 127.5, 128.3, 138.1, 217.2. − $C_{35}H_{66}O_5Si_2$ (623.1): calcd. C 67.47, H 10.68; found C 67.28, H 10.41.

10. (2*R*,3*R*,4*S*,5*S*,6*R*,7*S*,8*R*)-5-Benzoyloxy-1-benzyloxy-7-*tert*-butyldimethylsilyloxy-2,4,6,8-tetramethyl-9-(triisopropylsilyloxy)-3-nonanol (16): A solution of samarium diiodide (0.1 M in THF, 1.3 mL, 0.13 mmol) was added dropwise at −10°C to a solution of **15** (274 mg, 0.44 mmol) and benzaldehyde (179 μL, 1.76 mmol) in THF (1.5 mL). The yellow solution was stirred for 2 h at −10°C. Saturated aqueous $NaHCO_3$ solution (5 mL) was added, the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 20 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$) and concentrated. Flash chromatography of the residue (330 mg) with pentane/*tert*-butyl methyl ether mixtures from 50:1 to 20:1 furnished **16** (244 mg, 76%) as a colorless oil. − $[\alpha]_D^{20} = +5.5$ (c = 1.485, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.05 (s, 3 H), 0.15 (s, 3 H), 0.82 (d, J = 6.9 Hz, 3 H), 0.88−0.96 (m, 36 H), 1.06 (d, J = 7.1 Hz, 3 H), 1.79 (m, 1 H), 1.96 (m, 2 H), 2.12 (m, 1 H), 3.38−3.58 (m, 5 H), 3.64 (dd, J = 8.8 and 3.8 Hz, 1 H), 3.85 (broad d, J = 7.6 Hz, 1 H), 4.40 (d, J = 12.0 Hz, 1 H), 4.48 (d, J = 12.1 Hz, 1 H), 5.34 (dd, J = 9.7 and 1.2 Hz, 1 H), 7.21 (m, 5 H), 7.43 (m, 2 H), 7.56 (m, 1 H), 8.04 (m, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.1, −3.7, 9.0, 9.9, 10.4, 11.9, 14.0, 17.9, 18.7, 26.4, 36.5, 36.9, 38.8, 39.9, 65.9, 71.2, 72.7, 73.1, 73.8, 77.3, 127.2, 127.4, 128.2, 128.4, 129.8, 130.1, 133.0, 138.8, 167.6. − $C_{42}H_{72}O_6Si_2$ (729.2): calcd. C 69.18, H 9.95; found C 69.03, H 9.81.

11. (2*R*,3*R*,4*S*,5*S*,6*R*,7*S*,8*R*)-1-Benzyloxy-7-*tert*-butyldimethylsilyloxy-2,4,6,8-tetramethyl-9-(triisopropylsilyloxy)-3,5-nonanediol: A

solution of diisobutylaluminium hydride (1.0 M in toluene, 1.99 mL, 1.99 mmol) was added dropwise at −78°C to a solution of **16** (242 mg, 0.33 mmol) in dichloromethane (1.70 mL). After stirring for 1.5 h at −78°C, ethyl acetate (2.0 mL) was added. The mixture was stirred for 20 min at −78°C and allowed to reach room temperature. Aqueous potassium sodium tartrate solution (1.0 M, 10 mL) was added and the phases were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (5 × 20 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue (240 mg) with pentane/*tert*-butyl methyl ether mixtures from 50:1 to 20:1 furnished the product (180 mg, 87%) as a colorless oil. − $[\alpha]_D^{20}$ = −19.7 (*c* = 9.820, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.10 (s, 3 H), 0.13 (s, 3 H), 0.79 (d, *J* = 6.8 Hz, 3 H), 0.80 (d, *J* = 6.9 Hz, 3 H), 0.92 (s, 9 H), 0.99 (d, *J* = 7.1 Hz, 3 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 1.04−1.08 (m, 21 H), 1.68 (m, 1 H), 1.80 (m, 1 H), 1.95−2.03 (m, 2 H), 3.53−3.61 (m, 5 H), 3.67 (s, 1 H, OH), 3.92−3.95 (m, 2 H), 4.02 (broad d, *J* = 9.0 Hz, 1 H), 4.47 (d, *J* = 11.8 Hz, 1 H), 4.54 (d, *J* = 11.8 Hz, 1 H), 7.23−7.32 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.0, −3.7, 9.0, 11.4, 11.9, 13.2, 13.4, 18.0, 18.3, 26.2, 36.1, 37.5, 37.6, 39.7, 66.6, 71.8, 73.5, 74.6, 76.8, 78.5, 127.6, 127.7, 128.3, 137.8. − $C_{35}H_{68}O_5Si_2$ (625.1): calcd. C 67.25, H 10.96; found C 67.05, H 10.72.

12. (2*R*,3*S*,4*S*,5*R*,6*S*,7*R*,8*R*)-9-Benzyloxy-1,3,5,7-tetrahydroxy-2,4,6,8-tetramethylnonane (17): HF in acetonitrile (5%, 2.0 mL) was added to a solution of (2*R*,3*R*,4*S*,5*S*,6*R*,7*S*,8*R*)-1-benzyloxy-7-*tert*-butyldimethylsilyloxy-2,4,6,8-tetramethyl-9-(triisopropylsilyloxy)-3,5-nonanediol (251 mg, 0.40 mmol). After stirring for 1 h, saturated aqueous $NaHCO_3$ solution (10 mL) was added and the phases were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (5 × 30 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), and concentrated to give **17** (154 mg, 87%) as a colorless solid which was used as obtained.

13. (2*R*,3*S*,4*S*,5*S*,6*S*,7*R*,8*R*)-9-Benzyloxy-1-*tert*-butyldimethylsilyloxy-2,4,6,8-tetramethyl-3,5,7-nonanetriol (18): Imidazole (42 mg, 0.62 mmol) was added to a solution of **16** (170 mg, 0.48 mmol) in DMF (1.6 mL). The solution was cooled to 0°C and a solution of *tert*-butylchlorodimethylsilane (76 mg, 0.50 mmol) in DMF (1.6 mL) was added slowly. After stirring for 2 h at 0°C and 16 h at room temperature, saturated aqueous $NaHCO_3$ solution (10 mL) was added and the phases were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (4 × 30 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether varying from 4:1 to 1:1 furnished **17** (195 mg, 87%) as a colorless solid, m.p. 71°C. − $[\alpha]_D^{20}$ = −18.2 (*c* = 1.050, $CHCl_3$). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.06 (s, 6 H), 0.81 (d, *J* = 6.9 Hz, 3 H), 0.85 (d, *J* = 6.9 Hz, 3 H), 0.87 (d, *J* = 7.0 Hz, 3 H), 0.89 (s, 9 H), 0.99 (d, *J* = 7.0 Hz, 3 H), 1.72−1.82 (m, 3 H), 2.02 (m, 1 H), 3.03 (s, 1 H, OH), 3.36 (s, 1 H, OH), 3.54−3.61 (m, 2 H), 3.67 (dd, *J* = 9.8 and 4.0 Hz, 1 H), 3.77 (m, 3 H), 3.91 (dd, *J* = 9.4 and 2.0 Hz, 1 H), 4.05 (dd, *J* = 8.9 and 1.3 Hz, 1 H), 4.51 (d, *J* = 11.8 Hz, 1 H), 4.54 (d, *J* = 11.8 Hz, 1 H), 7.26−7.34 (m, 5 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = −5.61, −5.58, 9.8, 10.2, 10.3, 13.3, 18.2, 25.9, 35.9, 36.7, 37.36, 37.44, 68.5, 72.3, 73.5, 75.7, 76.7, 76.9, 127.7, 127.8, 128.4, 137.7. − $C_{26}H_{48}O_5Si$ (468.8): calcd. C 66.62, H 10.32; found C 66.63, H 10.22.

14. (2*R*,3*S*,4*S*,5*S*,6*S*,7*R*,8*R*)-3,5,7-Triacetoxy-9-benzyloxy-1-*tert*-butyldimethylsilyloxy-2,4,6,8-tetramethylnonane (19): Acetic anhydride (58 μL, 0.62 mmol) and 4-(dimethylamino)pyridine (1 mg, 0.01 mmol) were added sequentially at room temperature to a solution of **18** (37 mg, 0.08 mmol) in dichloromethane (0.4 mL) and pyridine (0.1 mL). After 20 h, pH7-buffer solution (2 mL) was added, the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 20 mL). The combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue (60 mg) with pentane/*tert*-butyl methyl ether varying from 10:1 to 4:1 furnished **19** (38 mg, 81%) as a colorless oil. − $[\alpha]_D^{20}$ = +7.4 (*c* = 1.240, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.02 (s, 3 H), 0.03 (s, 3 H), 0.96 (d, *J* = 6.9 Hz, 3 H), 0.88 (s, 9 H), 0.91 (d, *J* = 7.0 Hz, 3 H), 0.96 (d, *J* = 6.9 Hz, 3 H), 0.97 (d, *J* = 6.8 Hz, 3 H), 1.94 (s, 3 H), 1.98 (s, 3 H), 2.01 (s, 3 H), 1.94−2.16 (m, 4 H), 3.22 (dd, *J* = 9.1 and 7.5 Hz, 1 H), 3.32 (dd, *J* = 9.9 and 7.1 Hz, 1 H), 3.40 (dd, *J* = 9.1 and 4.7 Hz, 1 H), 3.57 (dd, *J* = 9.9 and 5.4 Hz, 1 H), 4.43 (m, 2 H), 4.74 (dd, *J* = 8.4 and 3.9 Hz, 1 H), 4.77 (dd, *J* = 9.8 and 2.1 Hz, 1 H), 4.96 (dd, *J* = 10.0 and 1.5 Hz, 1 H), 7.24−7.33 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.5, −5.4, 10.0, 10.4, 11.1, 14.3, 18.2, 21.0, 21.1, 25.9, 35.57, 35.60, 36.3, 37.6, 66.0, 71.4, 73.20, 73.23, 73.3. 75.0, 127.5, 127.7, 128.3, 138.5, 170.2, 170.5, 171.0. − $C_{32}H_{54}O_8Si$ (594.9): calcd. C 64.61, H 9.15; found C 64.50, H 9.19.

15. (4*S*,5*S*,6*S*)-4-[(1*R*)-2-*tert*-Butyldimethylsilyloxy-1-methylethyl]-6-{(1*S*)-1-[(4*R*,5*S*)-2,2,5-trimethyl-1,3-dioxan-4-yl]ethyl}-2,2,5-trimethyl-1,3-dioxane (21): Palladium hydroxide (5% on carbon, ca. 10 mg) was added to a solution of **18** (67 mg, 0.15 mmol) in methanol (1.0 mL) at room temperature. The mixture was stirred for 1 h under an atmosphere of hydrogen and was filtered through Kieselgur. The filtrate was concentrated and the residue (50 mg) was taken up in 2,2-dimethoxypropane (1.0 mL). Pyridinium *p*-toluenesulfonate (ca. 10 mg) was added and the mixture was stirred for 12 h at room temperature. pH7 buffer (3 mL) was added, and the phases were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 20 mL). The combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue (160 mg) with pentane/*tert*-butyl methyl ether = 100:1 furnished **21** (38 mg, 64%) as a colorless oil. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.04 (s, 6 H), 0.70 (d, *J* = 6.7 Hz, 3 H), 0.80 (d, *J* = 6.8 Hz, 3 H), 0.82 (d, *J* = 6.7 Hz, 3 H), 0.88 (d, *J* = 6.9 Hz, 3 H), 0.89 (s, 9 H), 1.26 (s, 3 H), 1.29 (s, 3 H), 1.35 (s, 3 H), 1.41 (s, 3 H), 1.64 (m, 1 H), 1.74 (m, 1 H), 1.81−1.90 (m, 2 H), 3.41 (dd, *J* = 7.7 and 3.0 Hz, 1 H), 3.44 (dd, *J* = 9.7 and 5.7 Hz, 1 H), 3.51 (dd, *J* = 9.7 and 7.8 Hz, 1 H), 3.52 (t, *J* = 11.3 Hz, 1 H), 3.67 (dd, *J* = 11.4 and 5.0 Hz, 1 H), 3.69 (dd, *J* = 10.8 and 4.3 Hz, 1 H), 3.85 (dd, *J* = 10.5 and 1.9 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.42, −5.39, 8.1, 10.9, 11.6, 12.3, 18.2, 19.2, 23.8, 25.6, 25.9, 29.9, 30.2, 33.4, 35.1, 39.3, 65.1, 66.4, 68.3, 72.1, 73.8, 98.0, 100.5. − The material obtained did not give a correct elemental analysis.

16. (2*S*,4*S*,5*R*)-4-[(1*R*,2*S*,3*S*,4*R*,5*R*)-6-Benzyloxy-2,4-dihydroxy-1,3,5-trimethylhexyl]-5-methyl-2-phenyl-1,3-dioxane (23): Benzaldehyde dimethylacetal (29 μL, 0.20 mmol) and *p*-toluenesulfonic acid (ca. 5 mg) were added to a solution of **17** (66 mg, 0.19 mmol) in THF (1.9 mL) at 0°C. After 2 h at this temperature, the mixture was held for 16 h at room temperature. Saturated aqueous $NaHCO_3$ solution (2 mL) and *tert*-butyl methyl ether (10 mL) were added and the phases were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 40 mL). The combined organic phases were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue (90 mg) with pentane/*tert*-butyl methyl ether mixtures from 10:1 to 1:1 furnished **23** (47 mg, 57%) as a colorless oil. − $[\alpha]_D^{20}$ = +1.5 (*c* = 1.765, $CHCl_3$). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.74 (d, *J* =

6.9 Hz, 3 H), 0.86 (d, J = 6.9 Hz, 6 H), 1.19 (d, J = 7.1 Hz, 3 H), 1.69 (m, 1 H), 1.75 (m, 1 H), 1.84 (m, 1 H), 2.02 (m, 1 H), 2.67 (s, 1 H, OH), 3.50 (t, J = 9.1 Hz, 1 H), 3.60 (dd, J = 9.1 and 4.0 Hz, 1 H), 3.89 (dd, J = 9.3 and 2.4 Hz, 1 H), 3.92 (s, 1 H, OH), 3.92 (dd, J = 10.0 and 2.2 Hz, 1 H), 4.03 (m, 1 H), 4.05 (dd, J = 11.1 and 1.5 Hz, 1 H), 4.10 (dd, J = 11.1 and 2.5 Hz, 1 H), 4.52 (s, 2 H), 5.51 (s, 1 H), 7.31−7.34 (m, 8 H), 7.47 (m, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 8.0, 10.0, 10.9, 13.0, 30.1, 35.8, 37.0, 37.6, 71.8, 73.5, 74.1, 76.6, 77.0, 80.7, 101.6, 126.1, 127.7, 127.8, 128.1, 128.48, 128.51, 137.5, 139.0. − $C_{27}H_{38}O_5$ (442.6): calcd. C 73.27, H 8.65; found C 73.02, H 8.69.

17. (2*S*,4*S*,5*R*)-4-[(1*S*,2*R*,3*S*,4*R*,5*R*)-2,4-Diacetoxy-6-benzyloxy-1,3,5-trimethylhexyl]-5-methyl-2-phenyl-1,3-dioxane (24): Acetic anhydride (58 μL, 0.62 mmol) and 4-dimethylaminopyridine (1 mg, 0.01 mmol) were added sequentially into a solution of **23** (35 mg, 0.08 mmol) in dichloromethane (0.4 mL) and pyridine (0.1 mL). After stirring for 20 h at room temperature, pH7-buffer solution (3 mL) was added, the phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 20 mL). The combined organic phases were washed with brine (5 mL), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue (45 mg) with pentane/*tert*-butyl methyl ether varying from 10:1 to 4:1 furnished **24** (33 mg, 80%) as a colorless oil. − $[\alpha]_D^{20}$ = +62.6 (c = 1.405, $CHCl_3$). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.81 (d, J = 7.1 Hz, 3 H), 0.92 (d, J = 6.9 Hz, 3 H), 0.98 (d, J = 6.8 Hz, 3 H), 1.14 (d, J = 6.9 Hz, 3 H), 1.60 (m, 1 H), 1.92 (m, 1 H), 1.93 (s, 3 H), 2.08 (s, 3 H), 2.02−2.10 (m, 2 H), 3.22 (dd, J = 9.1 and 7.3 Hz, 1 H), 3.41 (dd, J = 9.1 and 4.5 Hz, 1 H), 3.48 (dd, J = 10.4 and 2.1 Hz, 1 H), 4.05 (m, 2 H), 4.43 (m, 2 H), 4.88 (dd, J = 10.0 and 2.2 Hz, 1 H), 5.26 (dd, J = 10.5 and 1.1 Hz, 1 H), 5.42 (s, 1 H), 7.26−7.34 (m, 8 H), 7.60 (m, 2 H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = 7.5, 9.8, 10.5, 14.1, 20.9, 21.1, 30.0, 35.3, 35.9, 36.0, 71.9, 73.18, 73.23, 73.5. 73.7, 79.7, 101.2, 125.9, 127.4, 127.7, 127.9, 128.21, 128.24, 138.5, 139.1, 170.6, 171.0. − Molecular mass $C_{31}H_{42}O_7$: calcd. 526.293054; found M^+ 526.294403.

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