# Conformational Analysis of *oligo*-1,3-Dioxanylmethanes[‡]

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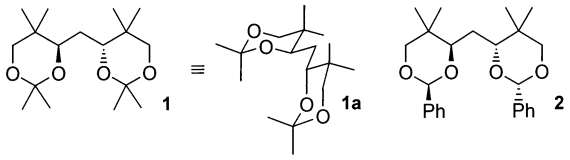
Stereoselective synthesis of a series of 1,3-dioxan-4-ylmethanes **1**–**9** has been achieved by use of solely substrate-based asymmetric induction. The simple $C_2$-symmetric bis(dioxanyl)methane **1** has a greater than 99% conformational preference at the two inter-ring bonds for the conformation **1a**. The homologous structures **3**–**9** contain up to five dioxanylmethane units, maintaining a high conformational preference in each of the bis(dioxanyl)methane units. Thus, these flexible compounds reach a conformational preference in excess of 90% over up to eight rotatable inter-ring bonds.



Nature has attained conformation "design" of flexible structures through evolution. This is evident in many bioactive natural products; examples are to be found in the flexible linker units between diverse parts of certain pharmacophore structures.[2] Conformation design of flexible structures therefore turns out to be a means to specify and separate distinct biological activities of multivalent drugs.[3] Conformation design becomes important in materials science as well, when conformation-dependent properties need to be optimised.[4,5] In these contexts, a modular approach to conformation design of larger flexible backbone structures appears attractive. Such an approach could rely on small modules; molecules possessing only one or two rotatable bonds and to a great extent populating a single conformation. A combination of several modules of this kind should then give rise to larger flexible molecules, which should, despite their higher number of rotatable bonds, nevertheless populate a single preferred conformation.

There is, however, an obvious limitation in such an approach. Consider a single module in which the conformational preference for population of the desired conformation is $x$ ($0 < x < 1$). In a larger molecule, arising out of a combination of $n$ modules, the overall preference to populate a single backbone conformation will be $x^n$. This means that the overall conformational preference one can attain will decrease exponentially with the number of modules that are combined. A sizeable conformational preference in molecules composed of $n > 1$ modules can therefore only be attained if the conformational preference in each module is approaching 1.0 (in practice, it should be greater than 0.98). To test the validity of this reasoning, we set out to study a set of compounds comprising combinations of up to four identical modules. In this manner we wanted to evaluate how far conformation design on a modular basis can be pushed in a real system.

The module chosen for our studies was that of the bis(dioxanyl)methanes **1** (cf. also **2**).[6] Compound **1**, for instance, would be expected to populate conformation **1a** with a very high preference, on the grounds that any 120° rotation about one of the inter-ring bonds would generate conformations that were destabilised by two simultaneous *syn*-pentane interactions. While such high-energy conformations relax into non-diamond-lattice-type conformations, they should nevertheless be destabilised by greater than 5 kcal[7] with respect to the most stable conformation **1a**.[8]




On this basis, the conformational preference in **1** should approach $x = 1.0$ and, hence, would augur well for endowing molecules such as **3**−**5**, products of combination of several modules of **1**, with large overall conformational preferences.

We report here on a study of such *oligo*-dioxanylmethanes. The study was extended to the arylidene acetals **6** and **8**, as well as the mixed acetals **7** and **9**, in order − among other reasons − to facilitate conformational analysis. This was based on the determination of vicinal $^3J_{H,H}$ constants along the backbone and therefore required that each of the relevant proton signals could be individually assigned and not be subject to severe signal overlap.

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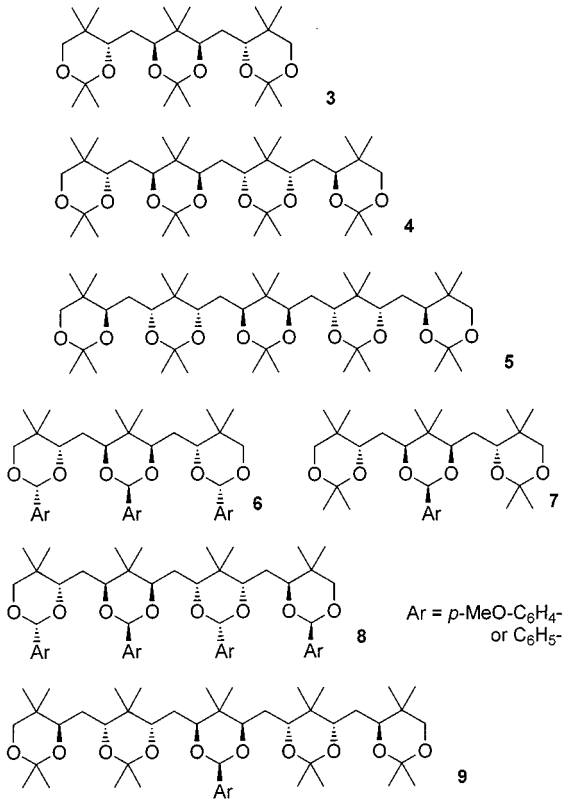
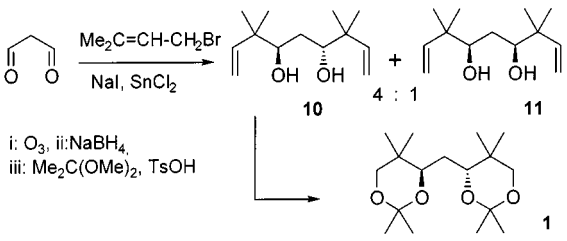


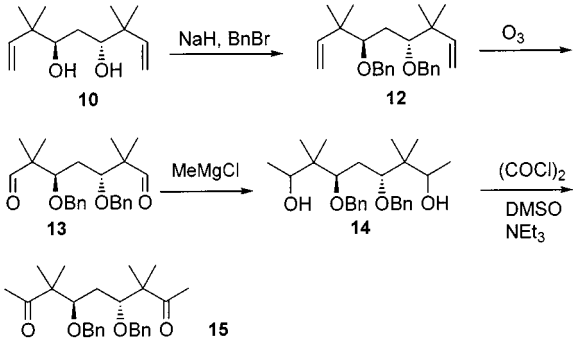

## Synthesis

The synthesis of the *oligo*-dioxanylmethanes has to take into account that all the target compounds are either $C_2$- or σ-symmetric (*meso*) compounds. A simplification of the syntheses might therefore be attained by use of a bidirectional strategy.[12,13] For *meso* compounds, however, this implies that stereogenic centres of opposite relative configuration would have to be created in a single reaction, a fact that would preclude any reagent-based asymmetric induction. The syntheses described below therefore had to rely only on substrate-based asymmetric induction to create the stereogenic centres (for a preliminary account see ref.[14]).

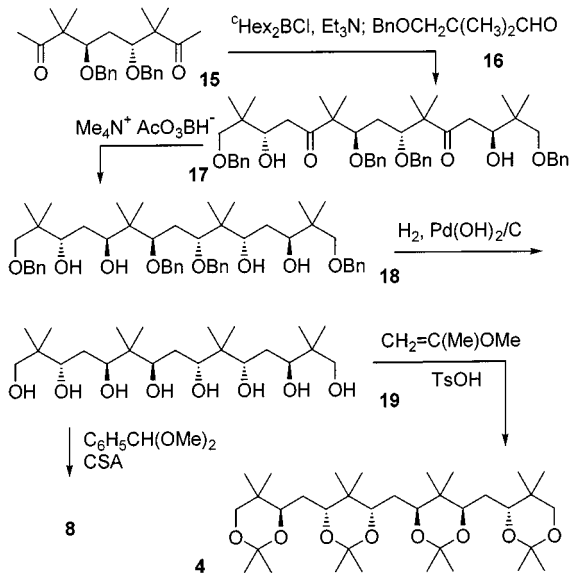
The synthesis of the prototype structure **1** started from malondialdehyde, which was diprenylated by Imai's method[15] to give a 4:1 mixture of the *rac*- and *meso*-diols **10** and **11**. The $C_2$-symmetric diol **10** could be obtained in 25% yield by crystallisation. Ozonolysis, followed by reductive workup and acetalisation, provided **1** in 75% yield. Transacetalisation with benzaldehyde dimethyl acetal furnished compound **2**.



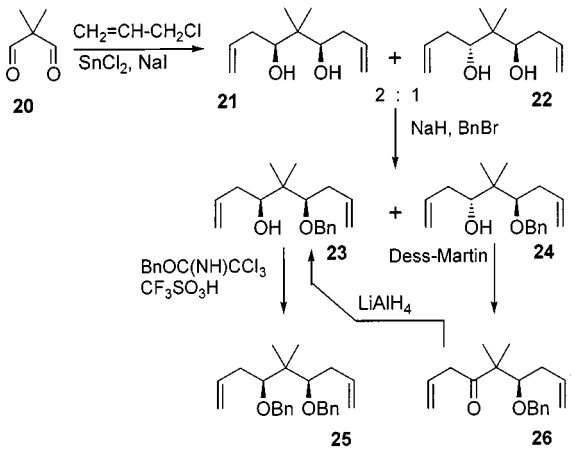

The same building block **10** can be used to enter into the synthesis of the tetrakis(dioxanyl)methanes **4** and **8**. The diol **10** was converted into the bis(benzyl ether) **12** (71%). We were unable to produce the diketone **15** by Wacker oxidation and so took a longer route by ozonolysis to afford the dialdehyde **13**, Grignard addition to give the diol **14** and oxidation to provide the desired diketone **15**.




For the next bidirectional chain extension we relied on the sizeable 1,5-asymmetric induction inherent in boron aldol additions.[16,17] Thus, the diketone was converted into the bis(dicyclohexylboron) enolate and allowed to react with the aldehyde **16**[18] at −90 °C. This resulted in 65% of a diastereomer mixture, in which the *anti*/*anti*/*anti* diastereomer **17** predominated over the *anti*/*anti*/*syn* diastereomer by 4:1. The symmetric nature of the *anti*/*anti*/*anti* diastereomer **17** was readily apparent from its $^{13}C$ NMR spectrum. The resulting diastereomer mixture was subjected to standard 1,3-*anti* reduction[19] with tris(acetoxy)borohydride to give the tetraol **18**, together with its diastereomer. The benzyl groups were removed by catalytic hydrogenation and the resulting octaol **19** (80%) was converted into the tetrakis(acetonide) **4** (65%) or the tetrakis(benzylidene acetal) **8** (62%) by standard acetalisation reactions. Flash chromatography in both cases furnished diastereomerically pure products.



The tris- and tetrakis(dioxanyl)methanes required the *meso* compound **25** as a starting material for a bidirectional synthesis. Its synthesis started with a double allylation of dimethylmalondialdehyde (**20**), which afforded a 2:1 mixture of **21** and **22**.

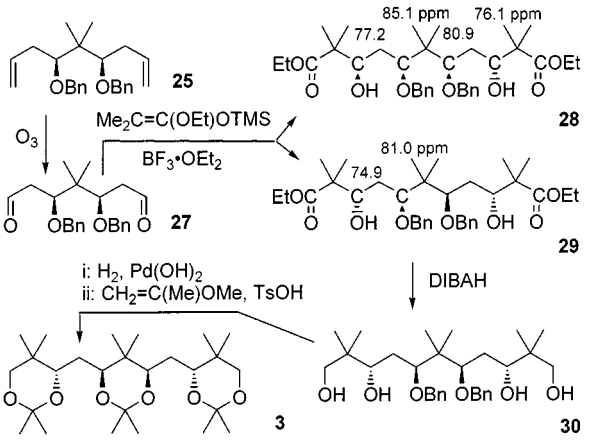



While the structures could easily be assigned through the number of the $^{13}C$ NMR signals, separation of **21** and **22** could not be achieved, nor that of their derived acetonides. This necessitated a somewhat lengthier route in order to reach the *meso*-bis(benzyl ether) **25**. The mixture of diols **21** and **22** was monobenzylated to give 85% of a 2:1 mixture of **23** and **24**. This latter mixture could be separated by flash chromatography. The desired major diastereomer **23** was then benzylated to give the symmetrical bis(benzyl ether) **25** (95%). The undesired diastereomer **24** may be converted into **23** through an oxidation-reduction sequence. High selectivities (16:1) in the reduction step were attained by use of $LiAlH_4$ in $Et_2O$/THF at −120 °C.[20]

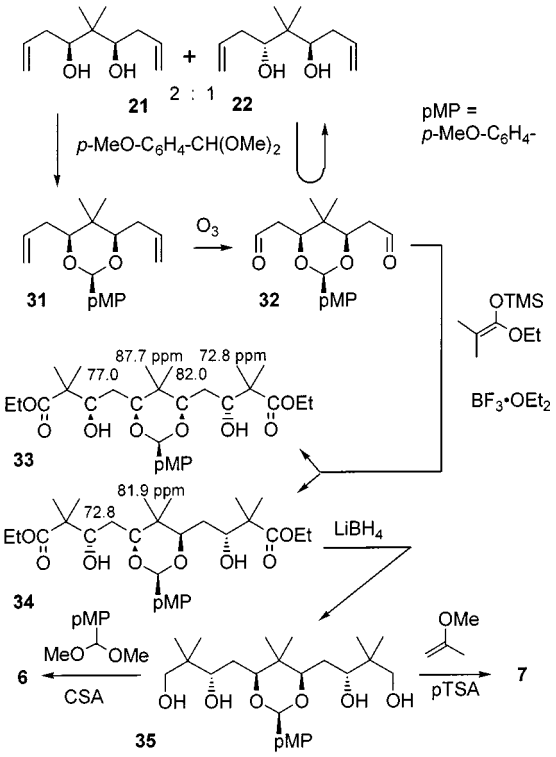
With the *meso* compound **25** in hand, ozonolysis of both double bonds furnished the dialdehyde **27** (88%). The subsequent chain-extension had to establish a 1,3-diol unit with 1,3-*anti* diastereoselectivity. By following a precedent from Evans' group,[21,22] this was achieved with the Mukaiyama aldol procedure and a nonchelating Lewis acid ($BF_3$·$OEt_2$). The *anti*/*anti* diastereomer **29** was obtained with a 6:1 preference over the *anti*/*syn* diastereomer **28**, structure assignment being based on the number of $^{13}C$ NMR signals. That the symmetrical isomer **29** was the *anti*/*anti* diastereomer (as indicated) and not the *syn*/*syn* one could be established by comparison of the signal positions of certain $^{13}C$ NMR signals, since a *syn*-β-hydroxy ether has the $^{13}C$ signals of its oxygen-bearing carbon atoms downfield from those of the corresponding *anti* diastereomer.[23]

The subsequent transformation of **29** into compound **3** proceeded uneventfully; reduction of **29** with DIBAH furnished the tetraol **30**, which was straightaway debenzylated [$H_2$/$Pd(OH)_2$] and converted into the tris(acetonide) **3** (80%).

When we attempted the synthesis of the mixed tris(dioxanyl) compounds **6** and **7**, we took account of the unsatisfactory diastereomer separation of **21** and **22**. We found



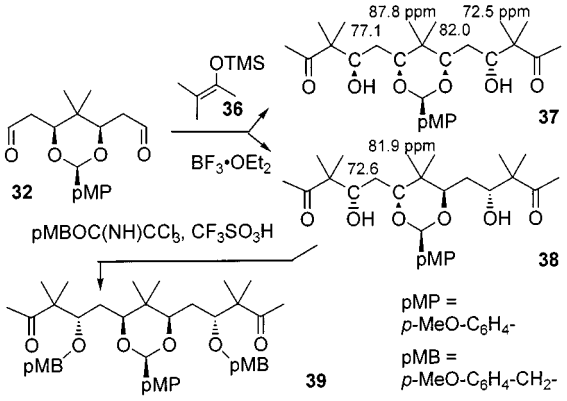

that treatment of the 2:1 mixture of **21** and **22** with *p*-methoxybenzaldehyde dimethyl acetal in the presence of camphorsulfonic acid readily converted **21** into the acetal **31**, but left **22** essentially unchanged. The polarity difference between **31** and **22** allowed for ready chromatographic separation.



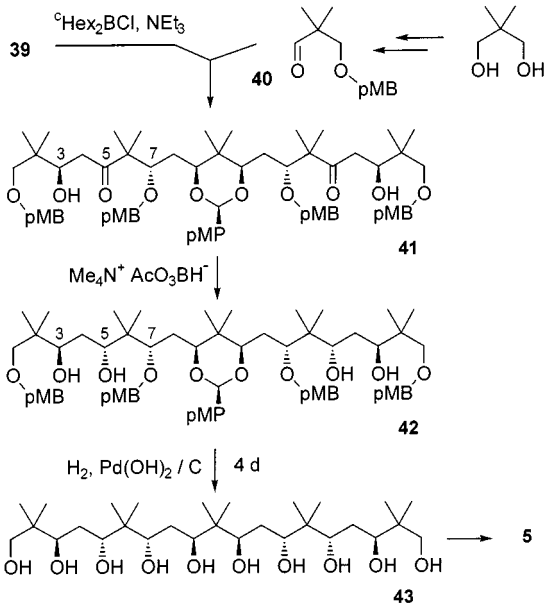

The further conversion of **31** into **6** and **7** followed the route developed above for **3**; ozonolysis of **31**, followed by Mukaiyama aldol addition, provided a 5:1 mixture of **34** and **33**. Their structure assignment was again based on $^{13}C$ NMR spectroscopic data, as outlined above for **28** and **29**. Chromatographic purification furnished pure **34**, which was reduced with $LiBH_4$ to give the tetraol **35** (90%). This could be converted without problem into the acetals **6** (67%) and **7** (55%).

Having gained experience in the generation of stereochemically defined skipped polyol sequences using bidirec-

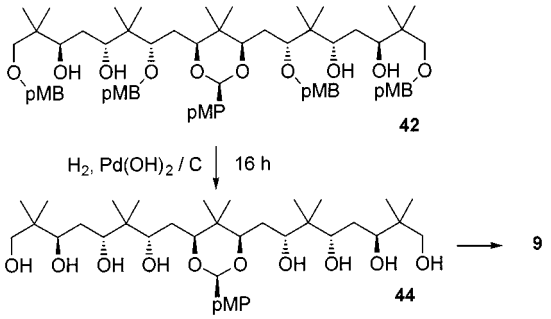
tional techniques, we had become confident that we could also master a synthesis of the pentakis(dioxanyl)methane compounds **5** and **9**. We used the dialdehyde **32** as a starting point for this endeavour. Chain extension by the Mukaiyama aldol technique involved the enol silyl ether **36**[24] and again the nonchelating Lewis acid $BF_3{\cdot}OEt_2$. This reaction afforded 73% of a 6:1 mixture of a symmetrical (**38**) and a nonsymmetrical (**37**) bis(aldol) adduct, which could be separated by chromatography. The structure assignment was based, as before, on the relative positions of the characteristic $^{13}C$ NMR signals.[23]




The free hydroxy groups in **38** were converted into *p*-methoxybenzyl ethers to give **39** in 69% yield. This set the stage for the next bidirectional chain extension using the 1,5-asymmetric induction inherent in the boron aldol methodology. The required aldehyde **40** was generated in two steps from 2,2-dimethylpropanol. Treatment of **40** with the bis(dicyclohexylboron) enolate of **39** afforded the full-length carbon skeleton (72%) with a 5:1 selectivity in favour of a symmetrical product, to which we assigned (see below) the desired structure **41**. This mixture was subjected to an 1,3-*anti*-specific reduction of the aldol units with tris(acetoxy)borohydride[19] to give 96% of the tetraol **42** admixed with its stereoisomer. To obtain definite proof of the stereostructure of **42**, all protecting groups were removed by hydrogenolysis and the resulting decaol **43** was converted into the pentakis(acetonide) **5**. The diagnostic $^{13}C$ NMR chemical shifts of the acetal carbon atoms all fell in the range of $\delta = 99.5-99.9$, showing that all acetonide rings were derived from *syn*-1,3-diol units.[25,26] Moreover, there is precedent to show that these characteristic $^{13}C$ NMR signal positions are also found in 5,5-disubstituted 1,3-dioxanes.[27] The fact that all the acetonides in **5** were based on *syn*-1,3-diol units would require that the aldol addition between **39** and **40** had given the anticipated 3,7-*anti*-diol relationship. Otherwise, the subsequent 3,5-*anti*-selective reduction of di-epi-**41** with tris(acetoxy)borohydride would have resulted in a 5,7-*anti* relationship at the stage of **42**. Hence, upon conversion into the pentakis(acetonide), two of the acetonide rings should then be derived from an *anti*-1,3-diol unit.




With the relative configurations at all stereocenters in **42** established, we attempted a selective deprotection of the *p*-methoxybenzyl ethers in the presence of the *p*-methoxybenzylidene acetal. After what was a short reaction time (16 h) for a hydrogenolysis, we were able to secure substantial amounts of the octaol **44**. Subsequent acetalisation with 2-methoxypropene furnished the differentially protected pentakis(dioxane) **9**.



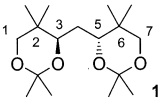

We have described here a sequence of transformations that allowed us to access skipped polyols with an *anti*/*syn*/*anti* pattern of stereocentres. In order to achieve a bidirectional approach we were restricted to the use only of substrate-based asymmetric induction. The key to success is the high 1,3-asymmetric induction in the Mukaiyama aldol reaction, the high 1,5-asymmetric induction in the Paterson/Evans enol borinate addition and in the reliable 1,3-*anti* reduction with tris(acetoxy)borohydride. This efficiency, in combination with a bidirectional approach, made it possible to access structures such as **5** or **9** in only eight steps from malondialdehydes.

## Force Field Calculations

Force field calculations were carried out with the MM3* force field implemented in the MACROMODEL pro-

gram[28] (versions 4.5 or 7.0) in order to estimate conformational preferences for the compounds synthesised. For compound **1**, the data shown in Table 1 were obtained by means of a Monte Carlo search,[29] with torsion allowed about the inter-ring and stereochemically indifferent intra-ring bonds. The structures generated were minimised to the nearest minimum, and of the resulting structures only those with energies lying $\leq 25$ kJ·mol$^{-1}$ higher than that of the lowest energy conformer were considered further. The conformer population was estimated by subjecting the ensemble of conformations generated in this fashion to a Boltzmann distribution for 25 °C, taking the statistical degeneracy of certain conformations into account. This is demonstrated for compound **1** in Table 1.

Table 1. Conformer energies of **1** calculated with the MM3* force field method



**1**

| Conformer | Dihedral angles [°] 1−4 | 2−5 | 3−6 | 4−7 | Energy [kJ/mol] | Population (%; 25 °C) |
|---|---|---|---|---|---|---|
| 1 | −176 | −177 | −175 | −176 | 0.00 | 94.09 |
| 2[a] | −157 | −174 | −175 | −176 | 11.37 | 2.88 |
| 3[a] | −176 | −175 | −174 | −157 | 11.37 | 2.88 |
| 4[a] | −156 | −171 | −172 | −156 | 18.34 | 0.06 |
| 5[a] | −74 | 178 | −177 | 176 | 20.70 | 0.02 |
| 6 | −176 | −177 | 178 | −74 | 20.70 | 0.02 |
| 7 | −178 | 93 | −165 | −175 | 21.34 | 0.02 |
| 8 | −175 | −165 | 93 | −178 | 21.34 | 0.02 |

[a] Conformers 2−5 have a twist-boat conformation.

The global minimum conformation was found to be **1a**, corresponding to a diamond lattice arrangement. Conformers 2 and 3 each have a twist-boat conformation in one of the dioxane rings, conformer 4 in both. Nevertheless, conformers 2−4 maintain the same arrangement as conformer 1 at the inter-ring bonds. Therefore, the predicted conformational preference at the inter-ring bonds of **1** amounted to 99.9% (i.e. > 99%) at 25 °C. Similarly, the preferences for compounds **3** (**4**) were predicted to > 99 (> 99) % including twist-boat conformers at either or both of the outer rings.[30]

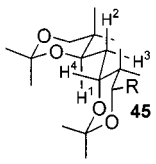
The calculations therefore suggested that the energy difference between the ground state conformation with an extended backbone and the higher energy conformations with distorted backbones was so high (> 20 kJ·mol$^{-1}$) for **1** and the related compounds **3**, **4**, and **5** that a conformational preference in excess of 99% should result irrespective of the number of modules involved.

The benzylidene acetal **2** appeared to fit nicely into this pattern, with a 99.0% predicted conformational preference for a conformation of the **1a** type at the inter-ring bonds. Of course, there was a multitude of conformers differing in the torsion of the aryl−acetal bond. However, compounds **6** and **8** showed a deviating pattern, as the calculated conformational preferences for the fully extended conformations fell to 92 and 89%. The difference in energy between the most stable conformation of **6** and the one with a distorted inter-ring bond decreased from 15.5 kJ·mol$^{-1}$ in **2** to merely 7.5 kJ·mol$^{-1}$. Clearly, we had no clue why this should be so. This was yet another reason to synthesise and study compounds **6** and **7**.

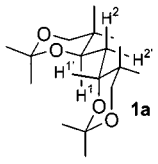
The calculations for the mixed acetal compound **7** predicted conformational behaviour close to that for the tris(acetonide) **3**, the energy difference between the most stable conformation and the one with a distorted inter-ring bond was calculated to be 17 kJ·mol$^{-1}$, corresponding to a conformational preference of > 99%. The same applied to the mixed acetal **9**, for which the lowest-energy non-diamond-lattice conformation involved a distortion next to a benzylidene acetal ring. We were curious at this point as to which of these features would stand the test of experimental conformational analysis.

## Conformational Analysis

Conformational analysis of the compounds of interest here was based on $^3J_{H,H}$ NMR coupling constants.[31] Compound **1** has only one spin system in which protons $H^1$ and $H^{1'}$ as well as $H^2$ and $H^{2'}$ are homotopic (cf. **1a**) due to the $C_2$ symmetry of the molecule. This results in a higher order spin system. The individual coupling constants were estimated to ±0.2 Hz by simulation of the coupling patterns. This indicated that the $H^1$,$H^2$ coupling constant at room temperature amounted to 10.4 and the $H^1$,$H^{2'}$ coupling to 1.7 Hz. The coupling constants in the corresponding benzylidene acetal were approximated to 11.1 and 1.8 Hz, respectively.



**45**



**1a**

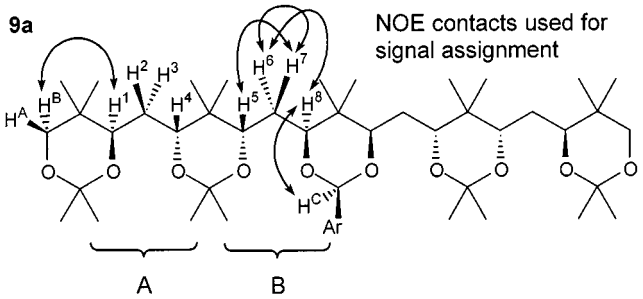
Compounds **3**−**9** each have more than one spin system. These spin systems are separated and can be analysed individually. They reflect the local conformational preferences in the individual segments. Within each of the tris(dioxanyl)methanes **3**, **6**, and **7** the two spin systems are identical, due to the σ symmetry of the molecules. Each spin system comprises four protons $H^1$ to $H^4$ (cf. **45**). As the coupling constants $H^1$,$H^2$; $H^3$,$H^4$ and $H^1$,$H^3$; $H^2$,$H^4$ turned out to be pairwise identical for compounds **3**, **6**, and **7**, there was no need for an individual assignment of the proton signals. The coupling constants found are listed in Table 2.

In the pentakis(dioxanyl)methane **5**, the signals of the four spin systems were completely superimposed. No resolution could be attained at 800 MHz by changing the solvent from $CDCl_3$ to $CD_3OD$, $CD_3COCD_3$, or $C_6D_6$. We therefore resorted to an analysis of the pentakis(dioxanyl)methane **9**, containing one benzylidene acetal. Because of the σ symmetry of the molecule, two of the four spin sys-

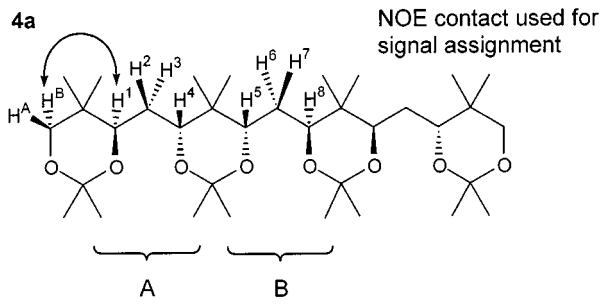
Table 2. Summary of the relevant $^3J$ coupling constants

| Compound | Solvent | $T$ [K] | Segment | $^3J$ [Hz] $H^1,H^2 = H^3,H^4$ | $H^1,H^3 = H^2,H^4$ |
|---|---|---|---|---|---|
| **1** | $C_6D_5CD_3$ | 298 | | 10.4 | 1.7 |
| **2** | $CDCl_3$ | 298 | | 11.1 | 1.8 |
| **3** | $CDCl_3$ | 298 | | 9.6 | 2.4 |
| **4** | $CDCl_3$ | 273 | A | 9.6; 9.9 | 2.3; 2.5 |
| **6** | $CDCl_3$ | 223 | | 9.6 | 2.2 |
| **7** | $C_6D_6$ | 298 | | 8.6 | 2.9 |
| | $CDCl_3$ | 298 | | 9.9 | 2.0 |
| | $CDCl_3$ | 223 | | 9.9 | 2.0 |
| **9** | $CDCl_3$ | 298 | A | 9.0 | 3.0 |
| | | | B | 9.9 | 1.1 |
| | $CDCl_3$ | 213 | A | 9.3 | 3.5 |
| | | | B | 10.0 | 0.5 |

tems are pairwise identical, and so only two spin systems have to be analysed. Assignment of the individual proton signals was based on NOE experiments, as shown in **9a**. The sequences of NOE contacts originated either at protons $H^A$ and $H^B$ in the terminal $CH_2-O$ group or at the acetal proton $H^C$ of the benzylidene acetal.




Conformational analysis of the tetrakis(dioxanyl)methane **4** was again hampered by signal overlap. There are two identical spin systems at the outer methylene bridges and one spin system in the centre of the molecule, which because of the $C_2$ symmetry should give a higher order multiplet. At 237 K the splitting pattern of two CH−O group protons could be recorded separately from the rest. None of these multiplets appeared as a higher order pattern similar to that recorded for − for instance − **1**. We therefore assigned both signals to spin system A. One signal could be clearly assigned to $H^1$, thanks to an NOE contact with $H^B$. The coupling constants to $H^1$ amounted to 9.6 and 2.5 Hz, the coupling constants to $H^4$ were recorded as 9.9 and 2.3 Hz. Thus, only limited information was available for compound **4**.




If the ensemble of the data obtained (cf. Table 2) is examined, some general features become evident. In the tetrakis(dioxanyl)methanes **3**, **6**, and **7**, and also in the pentakis(dioxanyl)methane **9**, there are only two coupling constants (instead of four) to characterise each spin system. This indicates that local $C_2$ symmetry in each of the modules is retained when several modules are combined. It is a moot point whether the four coupling constants found for the spin system in the tetrakis(dioxanyl)methane **4** are really different. The numerical values are pairwise so close to one another that they are not indicative of an absence of local $C_2$ symmetry. Moreover, the coupling constants in **1**, **3**, and **7** were found to be temperature-invariant over a temperature change of 75°C. This indicated that the local conformer preference was higher than 95% even at room temperature.[32]

One question to be addressed is whether the local conformer preference in each module remains the same when several modules are combined. The difference between the large and small coupling constants (i.e., the variation of the coupling constants) is a measure of the prevailing conformational preference.[31] This alteration decreases on going from **1** to **3** (or from **2** to **6**), but then stays constant on going to **4**. This reflects the statistical argument outlined in the introduction: the coupling constants in compounds **3** and **4** relate to the average over two modules, in **1** they are characteristic for a single module. The alteration of the coupling constants is, however, somewhat lower for the two outer modules (segment A) in **9** than for the inner ones (segment B). A lower overall conformational preference ($<$ 95%) for the two outer segments in **9** is also indicated by the change in the coupling constants observed on lowering the temperature by 85 °C.

Regarding segment B in **9**, the coupling constants of 9.9 and 1.1 Hz suggest a high local conformer preference. The increased alteration of the coupling constants on lowering the temperature by 85°C indicates that the conformer preference at room temperature does not exceed 95%. Actually, the conformational behaviour of segment B in **9** should be compared to **7**, as a model compound that also contains one central benzylidene acetal. The coupling constants are

essentially the same in **7** and **9**. These findings show that the conformational preference in a given module is by and large, but not completely, independent of the nature and number of the neighbouring modules.

We next wanted to learn whether there was any evidence for a lower conformational preference in modules incorporating benzylidene acetals versus those with acetonides, as suggested by the force field calculations. The coupling constants in the monobenzylidene acetal **7** were almost the same as those of the tris(acetonide) **3**. On going from the monobenzylidene acetal **7** to the tris(benzylidene acetal) **6**, there is indeed a decrease in the alteration of the coupling constants. It remains a moot point whether these changes reflect a decrease in the conformer preference in the benzylidene vs. the acetonide systems, as suggested by the force field calculations, or whether this is caused by slightly different torsional angles at the inter-ring bonds in the benzylidene and acetonide systems. The direction of such changes is not uniform (cf. the differences in the coupling constants between **2** and **3**). There are therefore at least grounds for scepticism regarding the validity of the force field calculations.

The aim of this study was to evaluate to what extent high overall conformational preferences could be attained by combining an increasing number of modules **1**. We report that on "combining" up to four bis(dioxanyl)methane units **1** (cf. compound **9**) a high local conformer preference still prevails, endowing compound **9** with a sizeable (ca. 90%) overall conformational preference over eight rotatable bonds.

## Experimental Section

**General Remarks:** All temperatures quoted are uncorrected. $^1$H NMR, $^{13}$C NMR: Bruker ARX 200, AC 300, WH 400, AM 400, AMX 500. Boiling range of petroleum ether: 40−60 °C. Flash chromatography: Silica gel SI 60, E. Merck KGaA, Darmstadt, 40−63 μm. Buffer (pH = 7): $NaH_2PO_4 \cdot 2H_2O$ (56.2 g) and $Na_2HPO_4 \cdot 4H_2O$ (213.6 g) made up to 1 L with water.

**1. (4*R**,4′*R**)-Bis(2,2,5,5-tetramethyl-1,3-dioxan-4-yl)methane [(4*R**,4′*R**)-2,2,2′,2′,5,5,5′,5′-Octamethyl-4,4′-methanediylbis(1,3-dioxane)] (1):** A stream of ozone was introduced at −78 °C to a solution of the diol **10**[33] (1.06 g, 5.00 mmol) in methanol (10 mL) until the blue colour persisted. Excess ozone was purged with nitrogen, and $NaBH_4$ (1.51 g, 40.0 mmol) was added. The mixture was allowed to reach room temperature over 15 h. Aqueous hydrochloric acid (1 M, 40 mL) was added, and the phases were separated. The aqueous phase was extracted with ethyl acetate (5 × 50 mL). The combined organic phases were washed with brine (50 mL), dried ($Na_2SO_4$), and concentrated. The residue was taken up in a mixture of acetone and 2,2-dimethoxypropane (10:1; 20 mL). *p*-Toluenesulfonic acid (ca. 10 mg) was added, and the mixture was stirred for 2 d at room temperature. Saturated aqueous $K_2CO_3$ solution (50 mL) was added, the phases were separated, and the aqueous phase was extracted with pentane (3 × 50 mL). The combined organic phases were dried ($MgSO_4$) and concentrated. Flash chromatography of the residue with *tert*-butyl methyl ether/pentane (1:10) furnished compound **1** (1.14 g, 75%) as a colourless oil. $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.67 (s, 6 H), 0.93 (s, 6 H), 1.27 (m, 2 H), 1.34 (s, 6 H), 1.35 (s, 6 H), 3.24 (d, *J* = 11.3 Hz, 2 H), 3.50 (d, *J* = 11.3 Hz, 2 H), 3.58 (m, 2 H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 18.0, 18.8, 21.6, 28.7, 30.0, 32.4, 72.0, 72.1, 98.4. $C_{17}H_{32}O_4$ (300.2): calcd. C 67.96, H 10.74; found C 67.91, H 10.96.

**2. (4*R**,4′*R**)-Bis(2-phenyl-5,5-dimethyl-1,3-dioxan-4-yl)methane (2):** Camphorsulfonic acid (ca. 10 mg) was added to a solution of compound **1** (0.19 g, 0.63 mmol) and benzaldehyde dimethyl acetal (241 mg, 1.58 mmol) in dichloromethane (5 mL). The mixture was heated to 40 °C at 25 mbar in a rotary evaporator for 3 h. Flash chromatography of the residue with *tert*-butyl methyl ether/pentane (1:10) furnished compound **2** (0.155 g, 62%) as a colourless oil. $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.79 (s, 6 H), 1.15 (s, 6 H), 1.60−1.63 (m, 2 H), 3.62 (d, *J* = 11.1 Hz, 2 H), 3.73 (d, *J* = 11.1 Hz, 2 H), 3.80−3.83 (m, 2 H), 5.50 (s, 2 H), 7.35−7.42 (m, 6 H), 7.51−7.53 (m, 4 H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 18.8, 21.6, 29.6, 32.8, 79.1, 80.9, 101.7, 126.2, 128.3, 128.8, 139.2. $C_{25}H_{32}O_4$ (396.2): calcd. C 75.73, H 8.13; found C 75.41, H 8.18.

**3. (4*S**,6*S**)-4,6-Bis(benzyloxy)-3,3,7,7-tetramethyl-1,8-nonadiene (12):** Sodium hydride (60% in white oil, 1.26 g, 31.5 mmol) was added to a solution of the diol **10**[33] (3.20 g, 15.0 mmol) in DMF (45 mL) at 0 °C. After this mixture had been stirred for 30 min at 0 °C, benzyl bromide (3.80 mL, 31.5 mmol) was added and stirring was continued for 1.5 h. Tetrabutylammonium iodide (ca. 20 mg) was added and stirring was continued for 15 h at room temperature. Water (50 mL) and saturated aqueous $NH_4Cl$ solution (50 mL) were added. The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (4 × 60 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (98:2) furnished the product **12** (4.20 g, 71%) as a slightly yellowish oil. $^1$H NMR (200 MHz, $CDCl_3$): δ = 0.91 (s, 12 H), 1.50 (m, 2 H), 3.14 (m, 2 H), 4.44 (m, 4 H), 4.87 (m, 4 H), 5.66 (m, 2 H), 7.19 (m, 10 H). $^{13}$C NMR (50 MHz, $CDCl_3$): δ = 25.9, 26.6, 37.1, 45.3, 77.6, 87.6, 114.6, 129.8, 129.9, 131.1, 142.1, 148.9. $C_{27}H_{36}O_2$ (392.6): calcd. C 82.61, H 9.24; found C 82.52, H 9.18.

**4. (2*RS**,4*S**,6*S**,8*RS**)-4,6-Bis(benzyloxy)-3,3,7,7-tetramethylnonane-2,8-diol (14):** A stream of ozone was introduced at −78 °C to a solution of compound **12** (1.15 g, 2.90 mmol) in dichloromethane (10 mL) until the blue colour persisted. Excess ozone was purged with oxygen, and triphenylphosphane (4.60 g, 11.7 mmol) was added. The mixture was allowed to reach room temperature over 3 h. Silica gel (5 g) was added, and the suspension was concentrated. The remaining solid was placed on top of a chromatography column. Flash chromatography with pentane/*tert*-butyl methyl ether (9:1) furnished the bis(aldehyde) **13** (1.07 g, 85%) as a colourless oil. $^1$H NMR (200 MHz, $CDCl_3$): δ = 1.04 (s, 6 H), 1.10 (s, 6 H), 1.60 (m, 2 H), 3.99 (dd, *J* = 6.5, 4.2 Hz, 2 H), 4.43 (d, *J* = 11.3 Hz, 2 H), 4.57 (d, *J* = 11.3 Hz, 2 H), 7.38 (m, 10 H), 9.55 (s, 2 H). $^{13}$C NMR (50 MHz, $CDCl_3$): δ = 20.1, 43.1, 45.8, 73.0, 78.0, 127.7, 127.9, 128.4, 138.1, 201.2. A solution of methylmagnesium chloride (2.68 M in THF, 9.0 mL, 24 mmol) was added at −20 °C over 30 min to a solution of the bis(aldehyde) **13** (3.5 g, 8.9 mmol) in THF (18 mL). After stirring for 5 min, the mixture was allowed to reach room temperature and poured into saturated aqueous $NH_4Cl$ solution (50 mL). The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (5 × 30 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated to give the diol **14** (3.8 g, quantitative) as a 1.2:1 mixture of diastereomers. $^1$H NMR (200 MHz, $CDCl_3$): δ = 0.81 (m, 6 H), 0.98 (m, 3 H), 1.10 (m, 6 H), 1.25 (m, 3 H), 1.83 (m, 2 H), 3.74

(m, 2 H), 3.90 (m, 2 H), 4.60 (m, 4 H), 7.32 (m, 10 H). $C_{27}H_{40}O_4$ (428.6): calcd. C 75.66, H 9.41; found C 75.62, H 9.19.

**5. (4*S**,6*S**)-4,6-Bis(benzyloxy)-3,3,7,7-tetramethylnonane-2,8-dione (15):** A solution of dimethyl sulfoxide (3.70 mL, 51.8 mmol) in dichloromethane (6 mL) was added dropwise at −78 °C to a solution of oxalyl chloride (2.26 mL, 25.8 mmol) in dichloromethane (10 mL). After this mixture had been stirred for 45 min, a solution of the diol **14** (3.70 g, 8.60 mmol) in dichloromethane (21 mL) was added. After this in turn had been stirred for a further 70 min at −78 °C, triethylamine (8.30 mL, 60.2 mmol) was added dropwise, resulting in the formation of a precipitate. The mixture was stirred for 30 min at −78 °C and allowed to reach room temperature over 90 min. It was poured into saturated aqueous $NH_4Cl$ solution (150 mL). 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 aqueous hydrochloric acid (1 M, 100 mL) and brine (100 mL), dried with $Na_2SO_4$, and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (4:1 to 1.5:1) furnished the diketone **15** (3.17 g, 86%) as a yellowish oil. $^1$H NMR (200 MHz, $CDCl_3$): δ = 1.04 (m, 12 H), 1.21 (m, 6 H), 1.45 (m, 2 H), 3.85 (m, 2 H), 4.54 (m, 4 H), 7.38 (m, 10 H). $^{13}$C NMR (50 MHz, $CDCl_3$): δ = 20.7, 26.3, 34.3, 52.7, 74.4, 74.9, 81.7, 127.1, 127.2, 128.8, 138.4, 212.9. $C_{27}H_{36}O_4$ (424.6): calcd. C 76.38, H 8.55; found C 76.54, H 8.34.

**6. (3*R**,7*S**,9*S**,13*R**)-1,7,9,15-Tetrakis(benzyloxy)-3,13-dihydroxy-2,2,6,6,10,10,14,14-octamethylpentadecane-5,11-dione (17):** Triethylamine (230 μL, 2.00 mmol) was added at 0 °C to a solution of chlorodicyclohexylborane (320 μL, 1.50 mmol) in diethyl ether (2.5 mL). After addition of a solution of the diketone **15** (212 mg, 0.50 mmol) in diethyl ether (1 mL), a white precipitate formed. After stirring for 3 h at 0 °C, the mixture was cooled to −90 °C. A solution of 3-benzyloxy-2,2-dimethyl-1-propanal (**16**)[18] (384 mg, 2.00 mmol) in diethyl ether (1 mL) was added dropwise. After stirring for 3 d at −90 °C, the mixture was poured into a mixture of buffer (pH = 7; 5 mL), methanol (5 mL), and water (2 mL). Hydrogen peroxide (30% in water, 5 mL) was added at 0 °C and the mixture was stirred for 3 h. The phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (5 × 50 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography with pentane/*tert*-butyl methyl ether (9:1 to 1.5:1) provided the bis(aldol) **17** (263 mg, 65%) as a 4:1 diastereomer mixture. Major diastereomer: $^1$H NMR (400 MHz, $CDCl_3$): δ = 0.78 (s, 6 H), 0.84 (s, 6 H), 1.07 (m, 6 H), 1.22 (m, 6 H), 1.51 (m, 2 H), 1.71 (broad signal, 2 H), 1.72 (m, 2 H), 1.89 (m, 2 H), 2.70 (m, 2 H), 3.26 (m, 2 H), 3.60 (m, 2 H), 3.91 (m, 2 H), 4.43 (m, 4 H), 4.52 (m, 4 H), 7.28 (m, 20 H). $^{13}$C NMR (50 MHz, $CDCl_3$): δ = 19.9, 20.5, 21.2, 21.9, 34.3, 38.1, 40.7, 53.1, 72.7, 73.3, 74.6, 78.0, 81.9, 127.3, 127.4, 127.5, 128.2, 128.3, 138.4, 138.5, 216.1. $C_{51}H_{68}O_8$ (809.1): calcd. C 75.71, H 8.47; found C 75.36, H 8.23.

**7. (3*R**,4*R**,7*S**,9*S**,11*R**,13*R**)-1,7,9,15-Tetrakis(benzyloxy)-2,2,6,6,10,10,14,14-octamethylpentadecane-3,5,11,13-tetraol (18):** Acetic acid (3.20 mL, 54.8 mmol) was added to a suspension of tetramethylammonium tris(acetoxy)borohydride (7.21 g, 27.4 mmol) in 4 mL of acetone. The resulting clear solution was cooled to 0 °C, and a solution of the bis(aldol) **17** (263 mg, 0.325 mmol) in acetone (4 mL) was added. After this mixture had been stirred for 1 h at 0 °C and 24 h at room temperature, saturated aqueous sodium potassium tartrate solution (3 mL) was added, resulting in vigorous gas evolution. After stirring for 20 min, the mixture was poured into saturated aqueous $NaHCO_3$ solution (40 mL) and the phases were separated. The aqueous phase was extracted with dichloromethane (5 × 40 mL) and the combined organic phases were dried ($Na_2SO_4$). Cyclohexane (5 mL) was added, and the solution was concentrated. Flash chromatography with pentane/*tert*-butyl ether (1:1) furnished the tetraol **18** (213 mg, 80%) as a 4:1 diastereomer mixture and as a yellowish resin. $^1$H NMR (400 MHz, $CDCl_3$): δ = 0.82 (s, 6 H), 0.89 (s, 6 H), 0.90 (s, 6 H), 0.97 (s, 6 H), 1.50 (m, 4 H), 1.91 (m, 2 H), 3.33 (m, 6 H), 3.67 (m, 2 H), 3.89 (m, 2 H), 4.47 (m, 4 H), 4.65 (m, 4 H), 7.30 (m, 20 H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 19.1, 19.3, 19.6, 22.4, 32.8, 33.2, 38.0, 42.8, 72.2, 73.2, 74.4, 74.5, 79.2, 83.8, 127.1, 127.3, 128.0, 128.2, 137.7, 137.8, 138.6, 138.7. $C_{51}H_{72}O_8$ (813.1): calcd. C 75.33, H 8.93; found C 75.27, H 8.93.

**8. (4*R**,6S*)-2,2,5,5-Tetramethyl-4-[(4*R**)-2,2,5,5-tetramethyl-1,3-dioxan-4-ylmethyl]-6-{(4*S**,6*R**)-2,2,5,5-tetramethyl-6-[(4*R**)-2,2,5,5-tetramethyl-1,3-dioxan-4-ylmethyl]}-1,3-dioxan-4-ylmethyl]-1,3-dioxane (4):** Palladium hydroxide on carbon (ca. 30 mg) was added to a solution of the tetrabenzyl ether **18** (213 mg, 0.262 mmol) in THF (3 mL). The mixture was stirred under 1 bar of hydrogen for 1 d. Dichloromethane (10 mL) was added, and the mixture was filtered through kieselguhr. The filtrate was concentrated to give the octaol **19** (95 mg, 80%) as a yellow resin. $^1$H NMR (500 MHz, $CH_3OD$): δ = 0.74 (s, 6 H), 0.83 (s, 3 H), 0.85 (s, 3 H), 0.89 (s, 6 H), 1.50 (m, 6 H), 3.34 (d, *J* = 10.8 Hz, 2 H), 3.42 (d, *J* = 10.8 Hz, 2 H), 3.67 (dd, *J* = 10.6, 1.7 Hz, 2 H), 3.77 (m, 4 H). $^{13}$C NMR (50 MHz, $CH_3OD$): δ = 19.5, 20.1, 21.0, 21.7, 34.0, 34.1, 34.3, 41.4, 42.6, 71.0, 74.4, 74.5, 75.7. The octaol **19** (25 mg, 0.055 mmol) was taken up in DMF (0.5 mL), and 2-methoxypropene (80 mg, 1.1 mmol) and *p*-toluenesulfonic acid (ca. 10 mg) were added. After this mixture had been stirred for 15 h at room temperature, water (10 mL) was added. The phases were separated, and the aqueous phase was extracted with diethyl ether (5 × 10 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography with pentane/*tert*-butyl methyl ether (9:1) furnished compound **4** (22 mg, 65%), diastereomerically pure and as a colourless resin. $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 13.0, 18.1, 19.0, 19.4, 20.5, 21.7, 28.5, 28.6, 29.7, 30.3, 32.6, 35.1, 72.4, 72.6, 73.3, 73.7, 98.2, 98.5. For the other physical data see ref.[14]

**9. (2*R**,4*R**,6*S**)-5,5-Dimethyl-4-[(2*S**,4*R**)-5,5-dimethyl-2-phenyl-1,3-dioxan-4-ylmethyl]-6-{(2*R**,4*S**,6*R**)-6-[(2*S**,4*R**)-5,5-dimethyl-2-phenyl-1,3-dioxan-4-ylmethyl]-5,5-dimethyl-2-phenyl-1,3-dioxan-4-ylmethyl}-2-phenyl-1,3-dioxane (8):** Benzaldehyde dimethyl acetal (42 mg, 0.28 mmol) and camphorsulfonic acid (ca. 10 mg) were added to a solution of the octaol **19** (60 mg, 0.074 mmol) in dichloromethane (1 mL). The mixture was heated to 40 °C at 25 mbar for 4 h in a rotary evaporator. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (9:1) furnished diastereomerically pure **8** (28 mg, 62%) as a yellowish oil. $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.79 (s, 6 H), 0.81 (s, 6 H), 0.98 (s, 6 H), 1.14 (s, 6 H), 1.65 (m, 2 H), 1.68 (m, 4 H), 3.63 (d, *J* = 11.2 Hz, 2 H), 3.73 (d, *J* = 11.2 Hz, 2 H), 3.77 (m, 4 H), 3.82 (m, 2 H), 5.51 (s, 2 H), 5.58 (s, 2 H), 7.36 (m, 12 H), 7.51 (m, 8 H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 14.0, 18.7, 20.8, 21.6, 25.3, 29.4, 32.7, 35.3, 79.0, 81.3, 81.4, 82.0, 100.7, 101.5, 126.0, 126.1, 128.0, 128.1, 128.4, 128.5, 139.0, 139.4. $C_{51}H_{64}O_8$ (exact mass, FAB): calcd. 804.4601; found 804.4619.

**10. (4*R**,6*S**)- and (4*R**,6*R**)-5,5-Dimethyl-1,8-nonadiene-4,6-diol (21, 22):** Dimethylmalondialdehyde (**20**) (9.00 g, 88.1 mmol) was added to a solution of allyl chloride (23.0 mL, 282 mmol), tin dichloride dihydrate (79.5 g, 352 mmol), and sodium iodide (58.1 g, 388 mmol) in DMF (440 mL). After stirring for 6 d, the mixture was poured into 10% aqueous $NH_4F$ solution (500 mL). The mix-

ture was extracted with *tert*-butyl methyl ether (5 × 100 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography with pentane/*tert*-butyl methyl ether (7:3) furnished a 2:1 mixture of **21** and **22** (11.1 g, 69%) as a colourless liquid. For analysis a sample was distilled at 104 °C/5 mbar. $C_{11}H_{20}O_2$ (184.3): calcd. C 71.70, H 10.94; found C 71.57, H 11.04. **21:** $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.79 (s, 3 H), 0.91 (s, 3 H), 1.97−2.45 (m, 4 H), 2.99 (broad s, 2 H), 3.51−3.62 (m, 2 H), 5.07−5.19 (m, 4 H), 5.75−5.97 (m, 4 H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 14.8, 20.9, 21.1, 36.6, 40.7, 78.1, 117.8, 136.1. The following signals of **22** could be recorded: δ = 21.1, 36.5, 40.1, 77.4, 117.6, 136.2.

**11. (4*R**,6*S**)- and (4*R**,6*R**)-6-Benzyloxy-5,5-dimethyl-1,8-nonadien-4-ol (23, 24):** Sodium hydride (80% in white oil, 0.100 g, 3.44 mmol) was added in small portions at 0 °C to a solution of **21** and **22** (2:1, 577 mg, 3.13 mmol) in DMF (0.73 mL) and THF (8 mL). After this mixture had been stirred for 30 min, benzyl bromide (0.39 mL, 3.3 mmol) was added dropwise. Tetrabutylammonium iodide (ca. 20 mg) was added, and the mixture was allowed to reach room temperature over 15 h. It was poured into saturated aqueous $NH_4Cl$ solution (20 mL). The phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (4 × 20 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (95:5) furnished **24** (0.24 g, 28%) and **23** (0.485 g, 57%) as colourless oils. **24:** $^1$H NMR (400 MHz, $CDCl_3$): δ = 0.80 (s, 3 H), 0.94 (s, 3 H), 1.96 (m, 1 H), 2.12 (m, 1 H), 2.36 (m, 2 H), 3.35 (dd, *J* = 7.6, 4.0 Hz, 1 H), 3.58 (d, *J* = 2.2 Hz, 1 H), 3.63 (dt, *J* = 10.2, 2.5 Hz, 1 H), 4.43 (d, *J* = 10.9 Hz, 1 H), 4.62 (d, *J* = 10.9 Hz, 1 H), 5.00 (m, 4 H), 5.87 (m, 2 H), 7.22 (m, 5 H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 20.1, 22.1, 35.3, 36.4, 41.6, 74.5, 75.1, 88.2, 116.4, 116.8, 127.5, 127.6, 127.7, 136.6, 136.8, 137.9. **25:** $^1$H NMR (200 MHz, $CDCl_3$): δ = 0.87 (s, 3 H), 1.01 (s, 3 H), 2.05 (m, 1 H), 2.33 (m, 2 H), 2.54 (m, 1 H), 2.67 (s, 1 H), 3.48 (dd, *J* = 7.4, 3.7 Hz, 1 H), 3.56 (dd, *J* = 10.2, 1.2 Hz, 1 H), 4.60 (d, *J* = 11.1 Hz, 1 H), 4.92 (d, *J* = 11.1 Hz, 1 H), 5.10 (m, 2 H), 5.14 (m, 2 H), 5.92 (m, 2 H), 7.33 (m, 5 H). $^{13}$C NMR (50 MHz, $CDCl_3$): δ = 17.4, 20.4, 35.5, 36.6, 42.7, 73.5, 76.0, 86.0. 116.3, 117.4, 127.5, 127.6, 128.3, 136.5, 137.1, 138.4. $C_{18}H_{26}O_3$ (274.4): calcd. C 78.79, H 9.55; found C 78.61, H 9.40.

**12. 6-Benzyloxy-5,5-dimethyl-1,8-nonadien-4-one (26):** Dess−Martin periodinane[34] (0.575 g, 1.36 mmol) was added to a solution of **24** (0.248 g, 0.904 mmol) and pyridine (0.219 mL, 2.71 mmol) in dichloromethane (4.5 mL). After stirring for 2 h at room temperature, the mixture was poured into a combination of saturated aqueous $NaHCO_3$ solution (10 mL), saturated aqueous $Na_2S_2O_3$ solution (10 mL) and *tert*-butyl methyl ether (20 mL). After the mixture had been stirred vigorously for 30 min, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 20 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (98:2) furnished the ketone **26** (0.236 g, 95%) as a colourless oil. $^1$H NMR (200 MHz, $C_6D_6$): δ = 1.00 (s, 3 H), 1.11 (s, 3 H), 2.20 (m, 2 H), 3.01 (dt, *J* = 6.7, 1.4 Hz, 2 H), 3.84 (dd, *J* = 7.1, 4.7 Hz, 1 H), 4.31 (d, *J* = 11.2 Hz, 1 H), 4.55 (d, *J* = 11.2 Hz, 1 H), 5.04 (m, 4 H), 5.85 (m, 1 H), 6.13 (m, 1 H), 7.24 (m, 5 H). $^{13}$C NMR (50 MHz, $C_6D_6$): δ = 20.6, 21.2, 36.0, 43.4, 52.5, 74.0, 84.2, 116.8, 117.9, 127.4, 127.5, 128.2, 131.5, 136.1, 138.5, 211.2. $C_{18}H_{24}O_2$ (272.4): calcd. C 79.37, H 8.88; found C 79.35, H 8.99.

**13. (4*R**,6*S**)-6-Benzyloxy-5,5-dimethyl-1,8-nonadien-4-ol (23):** A pre-cooled (−120 °C) solution of ketone **26** (0.230 g, 0.844 mmol) in diethyl ether/THF (9:1; 1 mL) was added dropwise by cannula at −120 °C to a solution of lithium aluminium hydride (0.096 g, 2.53 mmol) in diethyl ether/THF (9:1; 25 mL). After stirring for 6 h at −120 °C, the mixture was allowed to reach −60 °C over 18 h. Saturated aqueous $NH_4Cl$ solution (20 mL) was added, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (4 × 20 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl ether (20:1) gave **24** (0.032 g, 14%) and **23** (0.190 g, 82%) as colourless oils.

**14. (4*R**,6*S**)-4,6-Dibenzyloxy-5,8-dimethyl-1,8-nonadiene (25):** Benzyl trichloroacetimidate (0.90 mL, 3.8 mmol) was added dropwise to a solution of **23** (0.52 g, 1.9 mmol) in diethyl ether (2 mL). Trifluoromethanesulfonic acid (1 drop) was added, and the mixture was stirred for 15 h. The mixture was poured into water (10 mL) and the phases were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (4 × 10 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (98:2) furnished **25** (0.64 g, 92%) as a colourless oil. $^1$H NMR (200 MHz, $CDCl_3$): δ = 0.95 (s, 3 H), 1.10 (s, 3 H), 2.36 (m, 2 H), 2.43 (m, 2 H), 3.49 (dd, *J* = 8.1, 3.2 Hz, 2 H), 4.56 (d, *J* = 11.3 Hz, 2 H), 4.71 (d, *J* = 11.3 Hz, 2 H), 5.10 (m, 4 H), 5.98 (m, 2 H), 7.37 (m, 10 H). $^{13}$C NMR (50 MHz, $CDCl_3$): δ = 19.6, 20.0, 35.8, 44.2, 73.9, 84.0, 116.2, 127.3, 127.4, 128.2, 137.4, 139.0. $C_{25}H_{32}O_2$ (274.4): calcd. C 82.37, H 8.85; found C 82.47, H 8.81.

**15. (3*R**,5*S**)-3,5-Bis(benzyloxy)-4,4-dimethylheptane-1,7-dial (27):** The diene **25** (0.365 g, 1.00 mmol) was ozonised as described under 2. Flash chromatography of the crude product with pentane/*tert*-butyl methyl ether (7:3) furnished the product **27** (0.32 g, 88%) as a colourless oil, which was used as obtained. $^1$H NMR (200 MHz, $CDCl_3$): δ = 0.91 (s, 3 H), 1.04 (s, 3 H), 2.69 (m, 4 H), 3.99 (dd, *J* = 6.6, 4.2 Hz, 2 H), 4.43 (d, *J* = 11.3 Hz, 2 H), 4.57 (d, *J* = 11.3 Hz, 2 H), 7.31 (m, 10 H), 9.76 (t, *J* = 1.7 Hz, 2 H). $^{13}$C NMR (50 MHz, $CDCl_3$): δ = 20.1, 43.1, 45.8, 73.0, 78.0, 127.7, 127.9, 128.4, 138.0, 201.2.

**16. Diethyl (3*R**,5*R**,7*S**,9*S**)-5,7-Bis(benzyloxy)-3,9-dihydroxy-2,2,6,6,10,10-hexamethylundecanedioate (29):** $BF_3{\cdot}OEt_2$ (62 μL, 0.49 mmol) was added dropwise at −90 °C over 15 min to a solution of the dialdehyde **27** (90 mg, 0.24 mmol) and 1-ethoxy-2-methyl-1-(trimethylsilyloxy)propene[35] in 1 mL of dichloromethane. After this had been stirred for 20 h at −90 °C, saturated aqueous $NaHCO_3$ solution (10 mL) was added, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (5 × 10 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography with pentane/*tert*-butyl methyl ether (7:3) furnished the bis(aldol) products **29** and **28** as a 6:1 mixture. $C_{35}H_{52}O_8$ (600.8): calcd. C 69.97, H 8.72; found C 70.15, H 8.92. **29:** $^1$H NMR (400 MHz, $CDCl_3$): δ = 0.92 (s, 3 H), 1.07 (s, 3 H), 1.13 (s, 6 H), 1.17 (s, 6 H), 1.23 (t, *J* = 7.0 Hz, 6 H), 1.57 (m, 2 H), 1.65 (m, 2 H), 2.67 (d, *J* = 7.0 Hz, 2 H), 3.78 (m, 4 H), 5.13 (q, *J* = 7.0 Hz, 4 H), 4.70 (s, 4 H), 7.35 (m, 10 H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 14.1, 19.8, 20.3, 21.5, 22.8, 33.3, 44.7, 46.8, 60.7, 73.7, 74.9, 81.0, 127.2, 127.6, 128.2, 139.4, 178.0.

**17. (3*R**,5*R**,7*S**,9*S**)-5,7-Bis(benzyloxy)-2,2,6,6,10,10-hexamethylundecane-1,3,9,11-tetraol (30):** A solution of diisobutylaluminium hydride (1 M in petroleum ether, 1.5 mL, 1.5 mmol) was added dropwise at −78 °C to a solution of the diesters **28** and **29** (90 mg, 0.15 mmol) in dichloromethane (1.5 mL). After stirring for 20 h at −78 °C, the mixture was kept for 20 h at room temperature.

Hydrochloric acid (1 M, 10 mL) was added, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (5 × 10 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography of the residue with ethyl acetate furnished the tetraol **30** (53 mg, 69%) as a colourless oil, which was used as obtained. $^1$H NMR (200 MHz, $CDCl_3$): δ = 0.83 (s, 6 H), 0.85 (s, 6 H), 0.99 (s, 3 H), 1.11 (s, 3 H), 1.68 (m, 4 H), 3.40 (d, *J* = 10.7 Hz, 2 H), 3.52 (d, *J* = 10.7 Hz, 2 H), 3.66 (m, 2 H), 3.74 (dd, *J* = 8.8, 1.8 Hz, 2 H), 4.69 (s, 4 H), 7.35 (m, 10 H). $^{13}$C NMR (50 MHz, $CDCl_3$): δ = 19.1, 20.1, 21.8, 22.4, 33.1, 38.4, 44.2, 72.3, 74.7, 76.4, 81.4, 127.5, 127.6, 128.3, 139.2.

**18. (4*R**,5*S**)-2,2,5,5-Tetramethyl-4-[(4*R**)-2,2,5,5-tetramethyl-1,3-dioxan-4-ylmethyl]-6-[(4*S**)-2,2,5,5-tetramethyl-1,3-dioxan-4-ylmethyl]-1,3-dioxane (3):** Palladium hydroxide on carbon (ca. 30 mg) was added to a solution of the tetraol **30** (40 mg, 0.074 mmol) in THF (1 mL). The mixture was stirred under 1 bar hydrogen for 35 h. Dichloromethane (10 mL) was added, and the mixture was filtered through kieselguhr. Concentration of the filtrate resulted in a crystalline solid (the hexaol). The residue was taken up in DMF (0.5 mL), and 2-methoxypropene (48 mg, 0.67 mmol) was added, followed by *p*-toluenesulfonic acid (ca. 10 mg). The mixture was stirred for 4 h at room temperature. Buffer solution (pH = 7; 10 mL) was added. The phases were separated, and the aqueous phase was extracted with dichloromethane (5 × 10 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (9:1) furnished diastereomerically pure **3** (28 mg, 80%) as a colourless resin. For the spectroscopic and physical data, see ref.[14]

**19. (2*s**,4*R**,6*S**)-4,6-Diallyl-2-(4-methoxyphenyl)-5,5-dimethyl-1,3-dioxane (31):** Camphorsulfonic acid (ca. 20 mg) was added to a solution of the diols **21** and **22** (ca. 2:1, 2.97 g, 16.1 mmol) and *p*-methoxybenzaldehyde diethyl acetal (3.23 g, 15.4 mmol) in dichloromethane (5 mL). The mixture was heated to 40 °C at 25 mbar in a rotary evaporator. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (98:2) furnished compound **31** (3.29 g, quantitative relative to **21**) as a yellowish oil. $^1$H NMR (200 MHz, $CDCl_3$): δ = 0.83 (s, 3 H), 0.98 (s, 3 H), 2.27 (m, 4 H), 3.45 (dd, *J* = 6.7, 5.5 Hz, 2 H), 3.78 (s, 3 H), 5.06 (m, 4 H), 5.50 (s, 1 H), 5.96 (m, 2 H), 6.87 (m, 2 H), 7.42 (m, 2 H). $^{13}$C NMR (50 MHz, $CDCl_3$): δ = 13.8, 20.7, 33.7, 35.7, 55.2, 85.7, 100.8, 113.4, 116.0, 127.2, 131.5, 136.3, 159.5. $C_{19}H_{26}O_3$ (302.4): Cald. C 75.46, H 8.67; found C 75.48, H 8.44.

**20. Ethyl (3*R**)-4-{(2*s**,4*R**,6*S**)-6-[(2*S**)-3-Ethoxycarbonyl-2-hydroxy-3-methylbutyl]-2-(4-methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-yl}-3-hydroxy-2,2-dimethylbutanoate (34):** The diene **31** (0.85 g, 2.8 mmol) was ozonised as described under 2. Flash chromatography with pentane/*tert*-butyl methyl ether (9:1 to 3:7) furnished the dialdehyde **32** (0.79 g, 92%) as a colourless oil, which was used as obtained. $^1$H NMR (200 MHz, $CDCl_3$): δ = 0.78 (s, 3 H), 1.00 (s, 3 H), 2.48 (m, 2 H), 2.65 (ddd, *J* = 16.6, 9.5, and 1.9 Hz, 2 H), 3.76 (s, 3 H), 4.17 (dd, *J* = 9.4, 2.7 Hz, 2 H), 5.62 (s, 1 H), 6.85 (m, 2 H), 7.35 (m, 2 H), 9.79 (broad s, 2 H). $^{13}$C NMR (50 MHz, $CDCl_3$): δ = 14.0, 20.3, 34.6, 43.2, 55.1, 80.1, 101.1, 113.4, 127.2, 130.2, 159.9, 200.6. The aldehyde obtained above and 1-ethoxy-2-methyl-1-trimethylsilyloxypropene[35] (1.07 g, 5.70 mmol) were taken up in dichloromethane (5 mL). $BF_3{\cdot}OEt_2$ (0.656 mL, 0.518 mmol) was added dropwise at −78 °C over 15 min. After this had been stirred for 2 d at −78 °C, buffer (pH = 7; 20 mL) was added, the phases were separated, and the aqueous phase was extracted with dichloromethane (5 × 10 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated to give a 5:1 mixture of the diesters **33** and **34** (1.09 g, 78%). Flash chromatography with *tert*-butyl methyl ether/pentane (7:3) furnished diastereomerically pure **34** (0.90 g, 65%) as a colourless oil. $^1$H NMR (400 MHz, $CDCl_3$): δ = 0.78 (s, 3 H), 0.90 (s, 3), 1.16 (s, 6 H), 1.21 (s, 6 H), 1.24 (t, *J* = 7.1 Hz, 6 H), 1.47 (ddd, *J* = 13.9, 10.1, and 1.5 Hz, 2 H), 1.58 (ddd, *J* = 13.9, 10.1, and 1.5 Hz, 2 H), 3.79 (s, 3 H), 3.81 (dd, *J* = 10.1, 1.5 Hz, 2 H), 3.87 (m, 2 H), 4.15 (q, *J* = 7.1 Hz, 4 H), 5.56 (s, 1 H), 6.86 (m, 2 H), 7.40 (m, 2 H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 14.0, 14.1, 20.5, 22.5, 31.5, 35.0, 46.7, 55.2, 60.6, 72.8, 81.9, 100.6, 113.3, 127.2, 131.9, 159.5, 177.7. $C_{29}H_{46}O_9$ (600.8): calcd. C 64.66, H 8.61; found C 64.49, H 8.70.

**21. (2*s**,4*R**,6*S**)-2-(4-Methoxyphenyl)-4-[(4*R**)-2-(4-methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-ylmethyl]-6-[(4*S**)-2-(4-methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-ylmethyl]-5,5-dimethyl-1,3-dioxane (6):** Lithium borohydride (58 mg, 2.67 mmol) was added at room temperature to a solution of the diester **34** (240 mg, 0.446 mmol) in dichloromethane (2.2 mL). After this had been stirred for 18 h, saturated aqueous $NH_4Cl$ solution (10 mL) was added. The phases were separated and the aqueous phase was extracted with ethyl acetate (6 × 10 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography with ethyl acetate/methanol (98:2) furnished the tetraol **35** (182 mg, 90%) as a colourless oil, which was used as obtained. $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.83 (s, 6 H), 0.84 (s, 6 H), 0.92 (s, 3 H), 0.97 (s, 3 H), 1.57 (s, 4 H), 3.46 (d, *J* = 10.8 Hz, 2 H), 3.55 (d, *J* = 10.8 Hz, 2 H), 3.70 (m, 2 H), 3.78 (s, 3 H), 3.89 (m, 2 H), 5.55 (s, 1 H), 6.88 (m, 2 H), 7.39 (m, 2 H). $^{13}$C NMR (50 MHz, $CH_3OD$): δ = 19.9, 20.9, 21.8, 22.3, 32.3, 36.2, 40.0, 55.7, 70.8, 74.9, 83.7, 102.6, 115.3, 128.7, 133.0, 161.3. The obtained tetraol **35** and *p*-methoxybenzaldehyde diethyl acetal (279 mg, 1.33 mmol) were taken up in dichloromethane (5 mL). After addition of camphorsulfonic acid (ca. 20 mg), the mixture was heated to 40 °C at 25 mbar in a rotary evaporator for 4 h. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (9:1) furnished **6** (184 mg, 67%) as a yellowish oil. $^1$H NMR (500 MHz, $C_6D_6$): δ = 0.50 (s, 6 H), 0.68 (s, 3 H), 1.06 (s, 3 H), 1.15 (s, 6 H), 1.69 (m, 4 H), 3.35 (s, 6 H), 3.36 (s, 3 H), 3.33 (d, *J* = 11.1 Hz, 2 H), 3.54 (d, *J* = 11.1 Hz, 2 H), 3.84 (m, 2 H), 3.89 (m, 2 H), 5.47 (s, 2 H), 5.65 (s, 1 H), 6.79 (m, 4 H), 6.89 (m, 2 H), 7.61 (m, 4 H), 7.66 (m, 2 H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 13.9, 18.6, 20.5, 21.5, 29.5, 32.6, 35.2, 55.3, 78.9, 81.1, 81.2, 100.5, 101.5, 113.5, 113.6, 127.2, 127.3, 131.5, 132.0, 159.7, 159.8. $C_{41}H_{54}O_9$ (690.4): calcd. C 71.28, H 7.88; found C 71.43, H 8.11.

**22. (2*s**,4*R**,6*S**)-2-(4-Methoxyphenyl)-5,5-dimethyl-4-[(4*R**)-2,2,5,5-tetramethyl-1,3-dioxan-4-ylmethyl]-6-[(4*S**)-2,2,5,5-tetramethyl-1,3-dioxan-4-ylmethyl]-1,3-dioxane (7):** 2-Methoxypropene (48 mg, 0.66 mmol) and *p*-toluenesulfonic acid (ca 5 mg) were added at 0 °C to a solution of the tetraol **35** (60 mg, 0.13 mmol) in DMF (1 mL). After this had been stirred for 8 h, buffer (pH = 7) solution (10 mL) was added. The phases were separated, and the aqueous phase was extracted with dichloromethane (5 × 10 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (9:1) furnished **7** (39 mg, 55%) as a colourless oil. $^1$H NMR (500 MHz, $C_6D_6$): δ = 0.51 (s, 6 H), 0.73 (s, 3 H), 1.06 (s, 3 H), 1.09 (s, 6 H), 1.38 (s, 6 H), 1.53 (s, 6 H), 1.61 (ddd, *J* = 13.9, 9.7, and 2.2 Hz, 2 H), 1.63 (ddd, *J* = 13.9, 9.7, and 2.2 Hz, 2 H), 3.22 (d, *J* = 11.3 Hz, 2 H), 3.26 (s, 3 H), 3.46 (d, *J* = 11.3 Hz, 2 H), 3.89 (dd, *J* = 9.7, 2.2 Hz, 2 H), 3.97 (dd, *J* = 9.7, 2.2 Hz, 2 H), 5.80 (s, 1 H), 6.87 (m, 2 H), 7.68 (m, 2 H). $^{13}$C NMR (50 MHz, $C_6D_6$): δ = 14.2, 18.3, 19.2, 20.5, 21.6, 29.6, 30.1, 32.7, 35.3, 54.7, 72.2, 73.2, 82.0, 98.8, 102.0, 113.9, 128.5, 131.8, 160.4. $C_{31}H_{50}O_7$ (exact mass, FAB): calcd. 534.3557; found 534.3566.

**23. (4*R**)-4-Hydroxy-5-{(2*s**,4*R**,6*S**)-6-[(2*S**)-2-hydroxy-3,3-dimethyl-4-oxopentyl]-2-(4-methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-yl}-3,3-dimethylpentanone (37, 38):** $BF_3{\cdot}OEt_2$ (1.76 mL, 13.9 mmol) was added dropwise at −78 °C to a solution of the bis(aldehyde) **32** (2.13 g, 6.96 mmol) and 3-methyl-2-trimethylsilyloxy-2-butene[24] (3.13 g, 15.3 mmol). After this had been stirred for 12 h at −78 °C, buffer (pH = 7) solution (50 mL) was added, the phases were separated, and the aqueous phase was extracted with diethyl ether (5 × 20 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated to give a 6:1 mixture of compound **38** and **37** according to the $^{13}C$ NMR spectrum. Flash chromatography with pentane/*tert*-butyl methyl ether (6:4) furnished compound **38** (2.12 g, 63%) and compound **37** (0.30 g, 10%) as colourless oils. **38:** $^1H$ NMR (500 MHz, $CDCl_3$): δ = 0.79 (s, 3 H), 0.89 (s, 3 H), 1.13 (s, 6 H), 1.58 (s, 6 H), 1.49 (m, 4 H), 2.15 (s, 6 H), 2.85 (d, *J* = 6.4 Hz, 2 H), 3.79 (m, 2 H), 3.80 (s, 3 H), 3.95 (m, 2 H), 5.56 (s, 1 H), 6.87 (m, 2 H), 7.38 (m, 2 H). $^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 14.0, 19.8, 20.5, 21.7, 26.2, 31.4, 35.1, 51.8, 55.2, 72.6, 81.9, 100.7, 113.3, 127.2, 131.7, 159.6, 215.5. $C_{27}H_{42}O_7$ (478.6): calcd. C 67.76, H 8.84; found C 67.74, H 8.85.

**24. (4*R**)-4-(4-Methoxybenzyloxy)-5-{(2*s**,4*R**,6*S**)-6-[(2*S**)-2-(4-methoxybenzyloxy)-3,3-dimethyl-4-oxopentyl]-2-(4-methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-yl}-3,3-dimethylpentane-2-one (39):** A solution of 4-methoxybenzyl trichloroacetimidate (0.500 g, 0.175 mmol) in diethyl ether (1 mL) was added at −20 °C to a solution of **38** (0.837 g, 1.75 mmol) in diethyl ether (7 mL). One drop of dilute trifluoromethanesulfonic acid in diethyl ether was added, and the mixture was stirred for 2 h at −20 °C. After it had reached room temperature, the addition of 4-methoxybenzyl trichloroacetimidate and of a trace of trifluoromethanesulfonic acid was repeated four times. Buffer solution (pH = 7; 10 mL) was added, the phases were separated and the aqueous phase was extracted with dichloromethane (4 × 10 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. By addition of cold dichloromethane, the trichloroacetamide was brought to crystallisation and filtered. Silica gel (2 g) was added to the mother liquor and the suspension was concentrated. The residue was placed on top of a flash chromatography column, which was eluted with pentane/*tert*-butyl methyl ether (9:1 to 6:4) to give compound **39** (0.86 g, 69%) as a yellowish oil. $^1H$ NMR (200 MHz, [D$_6$]acetone): δ = 0.76 (s, 3 H), 0.87 (s, 3 H), 1.06 (s, 6 H), 1.18 (s, 6 H), 1.43 (ddd, *J* = 14.3, 10.2, and 1.9 Hz, 2 H), 1.62 (ddd, *J* = 14.3, 9.7, and 1.6 Hz, 2 H), 2.13 (s, 6 H), 3.59 (dd, *J* = 10.2, 1.6 Hz, 2 H), 3.73 (s, 6 H), 3.81 (s, 3 H), 3.97 (dd, *J* = 9.7, 1.9 Hz, 2 H), 4.57 (m, 4 H), 5.35 (s, 1 H), 6.89 (m, 4 H), 6.96 (m, 2 H), 7.31 (m, 4 H), 7.48 (m, 2 H). $^{13}C$ NMR (50 MHz, [D$_6$]acetone): δ = 13.9, 15.6, 20.8, 21.7, 26.9, 32.3, 36.0, 55.4, 55.5, 66.1, 75.4, 81.0, 82.9, 101.5, 114.1, 114.5, 128.2, 130.2, 132.0, 132.7, 160.2, 160.7, 212.4. $C_{43}H_{58}O_9$ (exact mass, FAB): calcd. 718.4081; found 718.4089.

**25. 3-(4-Methoxybenzyloxy)-2,2-dimethyl-1-propanal (40):** Sodium hydride (60% in white oil, 5.00 g, 130 mmol) was added to a solution of 2,2-dimethyl-1,3-propanediol (13.6 g, 130 mmol) in THF (100 mL) at 0 °C. After this had been stirred for 30 min, 4-methoxybenzyl bromide (26.1 g, 130 mmol) was added at 0 °C. Tetrabutylammonium iodide (ca. 20 mg) was added, and the mixture was stirred for 18 h. Saturated aqueous $NH_4Cl$ solution (100 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 dried ($MgSO_4$) and concentrated. Bulb-to-bulb distillation furnished 20.4 g (70%) of 3-(4-methoxybenzyloxy)-2,2-dimethyl-1-propanol, which was used as obtained. $^1H$ NMR (200 MHz, $CDCl_3$): δ = 0.71 (s, 6 H), 2.83 (s, 1 H), 3.07 (s, 2 H), 3.26 (s, 2 H), 3.62 (s, 3 H), 4.25 (s, 2 H), 6.66 (m, 2 H), 7.05 (m, 2 H). Dimethyl sulfoxide (13.6 mL, 162 mmol) was added dropwise at −78 °C to a solution of oxalyl chloride (10.5 mL, 83.0 mmol) in dichloromethane (150 mL). After this had been stirred for 15 min at −78 °C, a solution of the alcohol obtained above (12.3 g, 54.0 mmol) in dichloromethane (20 mL) was added. After this mixture had in turn been stirred for 45 min at −78 °C, triethylamine (38.1 mL, 367 mmol) was added dropwise, resulting in the formation of a precipitate. After stirring for 30 min at −78 °C, the mixture was allowed to reach room temperature. Saturated aqueous $NH_4Cl$ solution (100 mL) was added, the phases were separated, and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with aqueous hydrochloric acid (1 M, 100 mL) and brine (100 mL). The solution was dried ($Na_2SO_4$) and concentrated. Bulb-to-bulb distillation furnished the aldehyde **40** (9.72 g, 81%) as a colourless liquid. $^1H$ NMR (200 MHz, $CDCl_3$): δ = 1.04 (s, 6 H), 3.40 (s, 2 H), 3.74 (s, 3 H), 4.41 (s, 2 H), 6.87 (m, 2 H), 7.20 (m, 2 H), 9.36 (s, 1 H). $^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 21.6, 49.6, 57.8, 75.6, 77.3, 116.3, 129.0, 131.9, 161.8, 207.9. $C_{13}H_{18}O_3$ (222.3): calcd. C 70.24, H 8.16; found C 70.19, H 8.33.

**26. (2*R**,6*S**)-6-Hydroxy-1-{(2*s**,4*R**,6*S**)-6-[(2*S**,6*R**)-6-hydroxy-2,8-bis(4-methoxybenzyloxy)-3,3,7,7-tetramethyl-4-oxooctyl]-2-(4-methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-yl}-2,8-bis(4-methoxybenzyloxy)-3,3,7,7-tetramethyloctan-4-one (41):** Triethylamine (0.56 mL, 4.0 mmol) was added at 0 °C to a solution of chlorodicyclohexylborane (0.657 mL, 3.0 mmol) in diethyl ether (10 mL). After this had been stirred for 5 min, a solution of the diketone **39** (0.723 g, 1.01 mmol) in diethyl ether (1 mL) was added, resulting in the formation of a white precipitate. After stirring for 3 h at 0 °C, the mixture was cooled to −90 °C. A solution of the aldehyde **40** (0.778 g, 3.0 mmol) in diethyl ether (3 mL) was added dropwise at −90 °C. After stirring for 5 d at this temperature, the mixture was poured into a combination of buffer (pH = 7; 10 mL), methanol (20 mL), and water (10 mL). Hydrogen peroxide (30% in water, 10 mL) was added at 0 °C, and the mixture was stirred for 3 h. The phases were separated and the aqueous phase was extracted with dichloromethane (4 × 30 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography with pentane/*tert*-butyl methyl ether (1:1) furnished a 5:1 mixture of aldol (0.85 g, 72%), in which product **41** predominated. $^1H$ NMR (500 MHz, $CDCl_3$): δ = 0.74 (s, 3 H), 1.00 (s, 6 H), 1.03 (s, 3 H), 1.09 (s, 6 H), 1.23 (s, 6 H), 1.30 (s, 6 H), 1.73 (m, 2 H), 1.85 (m, 2 H), 2.74 (m, 2 H), 2.99 (m, 2 H), 3.33 (d, *J* = 14.0 Hz, 2 H), 3.34 (d, *J* = 14.0 Hz, 2 H), 3.39 (s, 6 H), 3.40 (m, 2 H), 3.41 (s, 6 H), 3.32 (s, 3 H), 3.76 (m, 2 H), 4.24 (m, 2 H), 4.37 (m, 4 H), 4.71 (m, 4 H), 5.51 (s, 1 H), 6.92 (m, 4 H), 6.88 (m, 4 H), 6.98 (m, 2 H), 7.42 (m, 8 H), 7.77 (m, 2 H). $^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 13.7, 15.2, 19.8, 20.5, 21.2, 22.0, 31.3, 35.3, 38.0, 40.6, 53.1, 55.1, 55.2, 55.3, 72.9, 73.0, 74.9, 77.9, 80.2, 82.0, 100.6, 113.5, 113.6, 113.7, 127.2, 129.0, 129.2, 130.1, 130.4, 131.6, 159.0, 159.2, 159.7, 215.9. $C_{69}H_{94}O_{15}$ (exact mass, FAB): calcd. for M + $Na^+$: 1185.6490; found 1185.6482.

**27. (3*S**,5*S**,7*R**)-8-{(2*s**,4*R**,6*S**)-6-[(2*S**,4*R**,6*R**)-4,6-Dihydroxy-2,8-bis(4-methoxybenzyloxy)-3,3,7,7-tetramethyloctyl]-2-(4-methoxyphenyl)-5,5-dimethyl-1,3-dioxan-4-yl}-1,7-bis(4-methoxybenzyloxy)-2,2,6,6-tetramethyloctane-3,5-diol (42):** Acetic acid (2.23 mL, 39.0 mmol) was added to a suspension of tetramethylammonium tris(acetoxy)borohydride (5.09 g, 19.3 mmol) in acetone (4.5 mL). After this had been stirred for 30 min, a clear solution resulted, and this was cooled to 0 °C. A solution of the aldol **41** (0.45 g, 0.39 mmol) in acetone (2.5 mL) was added, and the mixture

was stirred for 1 d at 0 °C and 5 d at room temperature. Saturated aqueous sodium potassium tartrate solution (6 mL) was added, resulting in vigorous evolution of gas. The mixture was stirred for 20 min and poured into saturated aqueous $NaHCO_3$ solution (50 mL). The phases were separated, and the aqueous phase was extracted with dichloromethane (5 × 50 mL). The combined organic phases were dried ($Na_2SO_4$). Cyclohexane (5 mL) was added and the solution was concentrated in vacuum. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (3:7) furnished the tetraol **42** as a 5:1 diastereomeric mixture (0.44 g, 96%) as a yellowish resin. $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.77 (s, 3 H), 0.80 (s, 6 H), 0.87 (s, 6 H), 0.89 (s, 6 H), 0.93 (s, 3 H), 0.95 (s, 6 H), 1.41 (m, 4 H), 1.71 (m, 4 H), 3.29 (m, 4 H), 3.47 (m, 2 H), 3.72 (s, 3 H), 3.73 (s, 6 H), 3.74 (m, 4 H), 3.67 (s, 6 H), 3.83 (m, 2 H), 4.50 (m, 8 H), 5.27 (s, 1 H), 6.84 (m, 10 H), 7.29 (m, 10 H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 13.8, 18.2, 19.6, 20.1, 20.6, 22.8, 30.9, 33.2, 38.0, 41.0, 42.5, 55.1, 72.7, 73.1, 74.3, 75.0, 79.5, 82.2, 83.4, 100.7, 113.5, 113.6, 113.7, 127.1, 129.1, 129.2, 129.7, 129.8, 131.0, 159.0, 159.1, 159.8. $C_{69}H_{98}O_{15}$ (1167.5): calcd. C 70.98, H 8.46; found C 70.70, H 8.57.

**28. (4*S**,6*R**)-2,2,5,5-Tetramethyl-4-[(4*R**,6*S**)-2,2,5,5-tetramethyl-6-{(4*S**,6*R**)-2,2,5,5-tetramethyl-6-[(4*R**)-2,2,5,5-tetramethyl-1,3-dioxan-4-ylmethyl]-1,3-dioxan-4-ylmethyl}-1,3-dioxan-4-ylmethyl]-6-[(4*S**)-2,2,5,5-tetramethyl-1,3-dioxan-4-ylmethyl]-1,3-dioxane (5):** Palladium hydroxide on carbon (ca. 10 mg) was added to a solution of compound **42** (70 mg, 0.060 mmol) in methanol (3 mL). After this had been stirred under 1 bar of hydrogen for 4 d, dichloromethane (10 mL) was added and the mixture was filtered through kieselguhr. The filtrate was concentrated to give the decaol **43** (31 mg, 90%) as a yellow resin, which was used as obtained. $^1$H NMR (500 MHz, $CD_3OD$): δ = 0.77 (s, 6 H), 0.87 (s, 6 H), 0.88 (s, 6 H), 0.89 (s, 3 H), 0.90 (s, 3 H), 0.93 (s, 6 H), 1.52 (m, 6 H), 3.38 (d, *J* = 11.0 Hz, 2 H), 3.46 (d, *J* = 11.0 Hz, 2 H), 3.38 (dd, *J* = 10.2, 1.2 Hz, 2 H), 3.80 (m, 6 H). $^{13}$C NMR (125 MHz, $CD_3OD$): δ = 18.8, 19.4, 19.5, 20.1, 21.8, 34.0, 34.1, 40.1, 41.4, 42.7, 71.0, 74.4, 74.5, 74.6, 74.7. 2-Methoxypropene (80 mg, 1.1 mmol) and *p*-toluenesulfonic acid (ca. 5 mg) were added to a solution of the decaol **43** (20 mg, 0.11 mmol) in DMF (0.5 mL). After this had been stirred for 18 h, water (10 mL) was added, the phases were separated, and the aqueous phase was extracted with diethyl ether (5 × 10 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (95:5) furnished compound **5** (21 mg, 52%) as a colourless oil. For the spectroscopic and analytical data see ref.[14]

**29. (2*s**,4*S**,6*R**)-2-(4-Methoxyphenyl)-5,5-dimethyl-4-[(4*S**,6*R**)-2,2,5,5-tetramethyl-6-{(4*S**,6*R**)-2,2,5,5-tetramethyl-6-[(4*R**)-2,2,5,5-tetramethyl-1,3-dioxan-4-ylmethyl]-1,3-dioxan-4-ylmethyl}-1,3-dioxan-4-ylmethyl]-6-[(4*S**)-2,2,5,5-tetramethyl-1,3-dioxan-4-ylmethyl]-1,3-dioxane (9):** Hydrogenolysis of compound **42** (0.26 g, 0.26 mmol) was carried out as described under 28. for 16 h. Flash chromatography of the crude product with dichloromethane/methanol (9:1) containing 1% of concd. aq. $NH_3$ furnished diastereomerically pure octaol **44** (37 mg, 48%) as a yellow resin, which was used as obtained. $^1$H NMR (500 MHz, $CD_3OD$): δ = 0.83 (s, 6 H), 0.88 (s, 9 H), 0.90 (s, 6 H), 0.98 (s, 6 H), 1.00 (s, 3 H), 1.49 (m, 2 H), 1.57 (m, 4 H), 1.77 (m, 2 H), 3.40 (d, *J* = 10.8 Hz, 2 H), 3.47 (d, *J* = 10.6 Hz, 2 H), 3.71 (m, 2 H), 3.81 (s, 3 H), 3.85 (m, 6 H), 3.62 (s, 1 H), 6.91 (m, 2 H), 7.45 (m, 2 H). $^{13}$C NMR (125 MHz, $CD_3OD$): δ = 13.9, 17.7, 18.9, 19.3, 20.2, 21.0, 31.5, 33.5, 35.7, 39.4, 41.9, 55.0, 70.3, 73.1, 73.8, 74.0, 83.2, 101.7, 113.7, 127.7, 131.7, 159.9. The octaol obtained was taken up in DMF (1 mL). 2-Methoxypropene (93 mg, 1.3 mmol) and *p*-toluenesulfonic acid (5 mg) were added at 0 °C. After this had been stirred at room temperature for 4 h, buffer (pH = 7) solution (10 mL) was added, the phases were separated, and the aqueous phase was extracted with dichloromethane (5 × 10 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated. Flash chromatography of the residue with pentane/*tert*-butyl methyl ether (85:15) furnished compound **9** (81 mg, 90%) as a colourless oil. $^1$H NMR (500 MHz, $CDCl_3$): δ = 0.71 (s, 12 H), 0.77 (s, 3 H), 0.83 (s, 6 H), 0.91 (s, 3 H), 0.99 (s, 6 H), 1.34 (m, 4 H), 1.36 (s, 6 H), 1.36 (s, 6 H), 1.37 (s, 6 H), 1.38 (s, 6 H), 1.45 (ddd, *J* = 13.8, 9.9, and 1.1 Hz, 2 H), 1.54 (ddd, *J* = 13.8, 9.9, and 1.1 Hz, 2 H), 3.27 (d, *J* = 11.3 Hz, 2 H), 3.58 (dd, *J* = 9.9, 1.1 Hz, 2 H), 3.59 (d, *J* = 11.3 Hz, 2 H), 3.62 (dd, *J* = 9.0, 3.0 Hz, 2 H), 3.69 (dd, *J* = 9.0, 3.0 Hz, 2 H), 3.73 (dd, *J* = 9.9, 1.1 Hz, 2 H), 3.82 (s, 3 H), 5.43 (s, 1 H), 6.91 (m, 2 H), 7.41 (m, 2 H). $^{13}$C NMR (125 MHz, $CDCl_3$): δ = 13.0, 14.0, 18.1, 18.9, 19.6, 20.5, 21.7, 28.6, 29.0, 29.7, 30.3, 32.6, 35.1, 35.2, 55.3, 72.3, 72.6, 73.2, 74.0, 81.9, 98.2, 98.5, 100.8, 113.4, 127.2, 132.3, 159.6. $C_{49}H_{82}O_{11}$ (exact mass, FAB): calcd. 846.5857; found 846.5826.

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