Flexible molecules with defined shape. Part 5.[1] Conformational analysis of 2,4,6,*n*-polymethylated alkane derivatives

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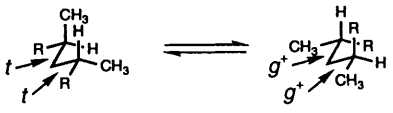
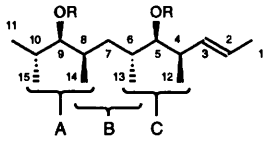
Poly-2,4,6,*n*-methylated undecene- (3–6) and pentadecene-derivatives (8–11) have been synthesized. In these compounds each backbone segment displays local bi-conformational behaviour. The effect of oxygen-substituents on the conformer population of the individual backbone segments has been studied by evaluating $^3J_{H,H}$ and $^3J_{C,C}$ coupling constants.

2,4-Dimethylpentane **1** populates two isoenergetic low energy conformations[2] and is therefore a prototype of a bi-conformational molecule. When a 2,4-dimethylpentane unit, *cf.* **2**, is part of a larger molecular skeleton, this subunit still maintains its bi-conformational behaviour. The two local conformers of **2** will be designated as *trans,trans* '*tt*' and *gauche, gauche* '*gg*' respectively.[3] In the case of **2**, the two local conformers will be populated to an unequal extent. With increasing conformational bias caused by substituents, a mono-conformational situation is approached.



1 R = CH_3
2 R = Alkyl

In the course of synthetic efforts aimed at a partial structure of venturicidine, we obtained the diol **3**.[4] The latter contains three 2,4-dimethylpentane subunits, A–C, each substituted in a different way. We undertook a conformational analysis of this diol and its derivatives **4**–**6** in order to learn more, on how substitution patterns affect the bi-conformational behaviour in each of the subsegments.



3 R = H
4 R = Ac
5 R = $SiMe_3$
6 R = Me

Results and discussion

Conformational analysis of the dioxytetramethylundecenes 3–6

As detailed elsewhere,[1] the conformers differ in the $^3J_{H,H}$ coupling constants along the chain. In a bi-conformational situation such as in **1** the weighted time average of the coupling constants of the two conformers results in apparent coupling constants of *ca.* 7 Hz. Any shift from local bi-conformational behaviour, *i.e.* two conformers populated in a *ca.* 1:1 ratio, to the predominance of one local conformation manifests itself in a divergence of $^3J_{H,H}$ coupling constants (one becoming >7 Hz, one becoming <7 Hz) along the chain segment. We embarked therefore on a detailed analysis of the vicinal coupling constants for the diacetate **4**. Coupling constants were taken from the 500 MHz NMR spectra in $CDCl_3$ as solvent and assigned with the aid of 2D phase-sensitive COSY experiments.[5]

In segment A there are two couplings of 6.1 Hz manifest on H-9. The fact, that the coupling constants are equal, signals a bi-conformational situation in this segment.

In segment B there are two sets of vicinal coupling constants, one referring to H-7a, the other to H-7b. The coupling constants differ within the two sets by less than 0.5 Hz. We take the average of the small ones, *i.e.* 3.0 and of the larger ones 10.8 Hz, as being representative for segment B. The strong divergence of the coupling constants indicates a substantial predominance of a single conformation.

Finally, monitoring H-5, the two coupling constants were found to be 3.8 and 8.7 Hz, again this divergence characterizes a conformational bias in the segment C.

The structures and relative energies of the various low energy conformers of **4** have been calculated with the MM3*-force field implemented in the MACROMODEL program.[6] MACROMODEL also has a routine, which predicts the individual $^3J_{H,H}$ coupling constants for each conformer based on modified Karplus equations.[7] Since the measured coupling constant is a weighted average over all local conformers, *i.e.* to a first approximation the two low energy conformers, these data allow an estimate of the position of the conformer equilibrium. Thus, for segment A the calculations indicate a *ca.* 1:1 local conformer ratio, for segment B *ca.* 9:1 and for segment C a *ca.* 4:1 *gg*:*tt* ratio.

While the MM3* calculations suggest the nature of the predominant local conformer to be *tt* for segment B, independent experimental evidence for this assignment was sought by studying NOE contacts between the individual hydrogens in **4**, *cf.* Table 1.

In segment A, nuclear Overhauser effect (NOE) contacts characteristic for both the *tt* and *gg*-local conformers were found. For segment B only one NOE contact, characteristic of the *tt*-conformation, was recorded, whereas for segment C the NOE contacts for the *gg*-conformer had a considerably higher intensity than that for the *tt*-conformer. While these results

Table 1 NOE contacts in the diacetate **4** for the *tt* and *gg* local conformations

	Expected *tt*-conformation between hydrogens	Found	Expected *gg*-conformation between hydrogens	Found
Segment A	8–9	+	7–10	
	10–14		9–10	+
Segment B	6–14		5–8	
	8–13		6–9	
	13–14	+	9–13	
Segment C	4–5	+	3–6	+
	4–13		4–7	+
	6–12		5–6	+

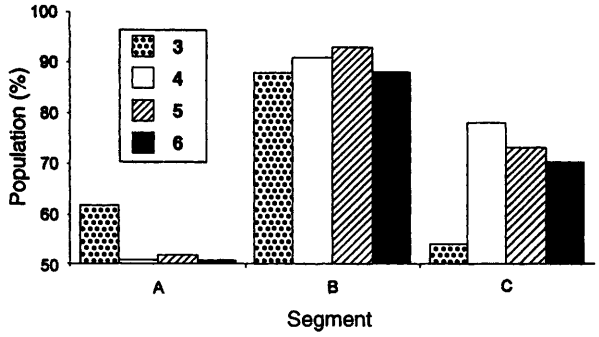
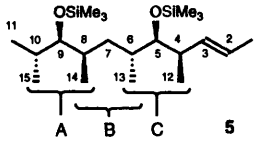


Fig. 1 Percent population of the major local conformer in **3–6** as judged from vicinal ^1H–^1H coupling constants

support the assignment of a *tt*-conformation in segment B, the absence of NOE contacts for the *gg*-local conformer in that segment cannot be considered as evidence for the latter not being significantly populated. Positive evidence for the nature of the major conformer was then sought by determining $^3J_{C,C}$ coupling constants. These experiments were carried out on the bis(trimethylsilyl) ether **5** using the newly developed gradient enhanced measurement of carbon–carbon coupling constants (GRECCO) technique.[8]



$^3J_{C,C}$ (Hz)

Segment A	Segment B	Segment C
7–10 = 2.3 Hz	5–8 = 3.4 Hz *trans*	3–6 = 2.3 Hz
8–11 = 2.0 Hz	6–9 = 4.0 Hz *trans*	4–7 = 1.4 Hz *gauche*
8–15 = 2.0 Hz	6–14 = 1.1 Hz *gauche*	6–12 = 1.1 Hz *gauche*
	8–13 = 1.2 Hz *gauche*	

The $^3J_{C,C}$ coupling constants are also a weighted average over the populated local conformers. Since a Karplus relationship exists for $^3J_{C,C}$ coupling constants,[9] the larger coupling constants, *e.g.* 3.4 to 4.0 Hz represent predominant *trans*-arrangements, the smaller coupling constants, *e.g.* 1.1 Hz, represent a *gauche* arrangement. The results listed therefore definitely establish the *tt*-conformation in segment B as being the predominant one. In segment C, the predominance of the *gg*-conformation is also supported by the low C-4/C-7 and C-6/C-12 couplings found. No conclusions are drawn from the C-3/C-6-coupling involving an sp^2-hybridized carbon, since we do not have sufficient reference values to judge the magnitude of this coupling constant. The 'average' values found for the $^3J_{C,C}$ couplings in segment A are again in accord with its bi-conformational nature.

From these results it is evident, that the substituent pattern present in the individual segments A, B and C of **4** or **5** affects the tendency to populate individual local conformation in a distinct manner.

The effect of oxygen substituents and of solvents

In order to see, whether the nature of the oxygen substituent has a significant effect on the population of the local conformers, we determined the vicinal H–H coupling constants for the alcohol **3**, the bis(trimethylsilyl) ether **5**, and the bis(methyl) ether **6** and assigned them by 2D phase-sensitive COSY experiments. With reference to the coupling constants for the individual local conformers calculated by the MACROMODEL package we can summarize the conformational preferences as shown in Fig. 1.

Among the four compounds studied, the diacetate **4**, the bis(trimethylsilyl) ether **5**, and the bis(methyl) ether **6** show only minor variations in the local conformer population. Some differences are noticeable with the diol **3**, mainly in the hydroxy-bearing segments A and C. In both segments the *tt*-conformation is populated to a larger extent than is the case for the OR compounds. This is possibly related to some sort of hydrogen-bonding interactions. For this reason we also determined the coupling constant for the compounds **3–6** in methanol as solvent (*cf.* Table 2).

Table 2 Vicinal ^1H–^1H coupling constants found for the compounds **3–6** in methanol as solvent

Segment	A		B		C	
3	5.0	6.6	2.8	11.0	3.7	8.3
4	5.0	7.2	3.1	10.6	4.2	8.3
5	4.3	6.5	2.5	11.4	3.7	7.7
6	4.9	6.7	3.1	10.8	3.9	7.7

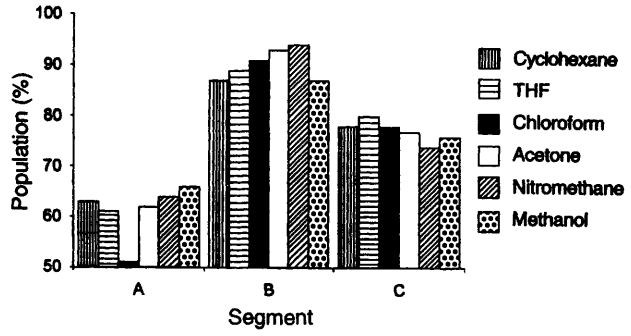


Fig. 2 Percent population of the major local conformer for the diacetate **4** in various solvents as judged from vicinal ^1H–^1H coupling constants

It becomes apparent that the coupling constants of the diol **3** no longer deviate in this hydrogen-bonding solvent from those of the other compounds. Finally, we checked briefly the coupling constants of the diacetate **4** in a broader set of solvents. The results are summarized in Fig. 2, indicating the absence of a significant solvent effect on the conformer population of **4**. The only deviation was found for $CDCl_3$ in segment A. This did not appear spectacular enough to warrant further scrutiny.

The trioxypentadecene system

The conformational analysis of the dioxyundecenes **3–6** showed, that the central segment B has a high tendency to adopt a fully extended *tt*-conformation. This nourished the hope, that longer hydrocarbon chains with a similar substitution pattern, such as **8**, could show a significant preference for a fully extended conformation. We therefore synthesized the pentadecene derivative **8** starting from the undecene **5** using transformations already mapped out in the synthesis of **3**.[4]

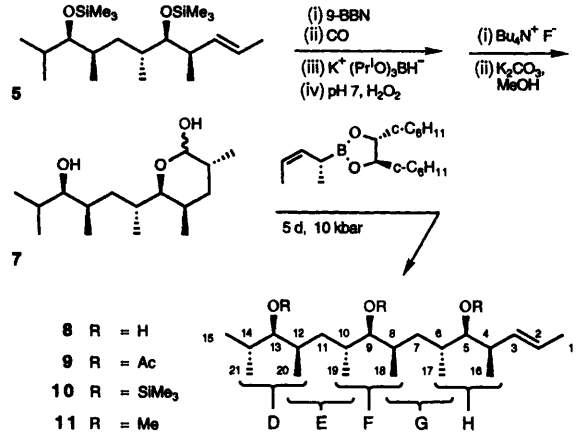


Table 3 Vicinal ^1H–^1H coupling constants for the compounds **3–6** and **8–11** in $CDCl_3$

	Segment	A (or D)		C (or H)		F	
R = H	**3**	4.7	6.6	5.8	5.8		
	8	4.6	6.6	5.7	5.7	4.9	6.6
R = Ac	**4**	6.1	6.1	3.8	8.7		
	9	5.3	6.9	3.5	9.0	5.4	6.9
R = $SiMe_3$	**5**	5.4	5.4	3.1	7.4		
	10	5.4	5.4	3.1	7.6	3.7	6.5
R = Me	**6**	5.3	5.3	4.1	7.5		
	11	4.9	6.4	4.0	7.2	5.4	5.4

The triol **8** was then converted into the acetate **9**, the silyl derivative **10**, and the methyl ether **11**. While the signal overlap in the 500 MHz ^1H NMR-spectra of **8–11** was considerable, practically all of the relevant vicinal coupling constants could be extracted and assigned by 2D phase-sensitive COSY experiments. The relevant coupling constants for the segments D, H and F are summarized in Table 3 and compared to those of **3–6**.

The conformational preferences in segment D of **8–11** resemble those of segment A in **3–6** as the similarity in coupling constants suggest. Thus, a bi-conformational situation prevails in segment D with occasionally a slight (2 : 1) preference for the *tt*-conformer. NOE contacts characteristic for both the *tt*- and *gg*-conformer in this segment have been found for each of the compounds **8–11**.

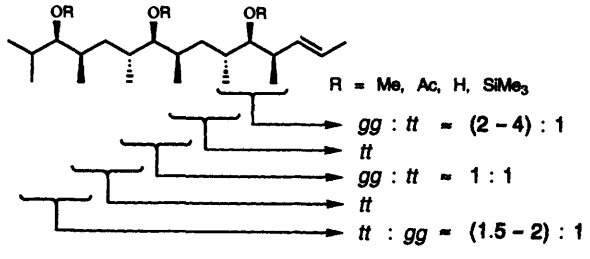
Likewise, the segment H of **8–11** should resemble in its conformational preference that of segment C in **3–6**. This was substantiated by the coupling constants, listed in Table 3.

The coupling constants for segments E and G in **8–11** (not listed in Table 3) varied between 2.0 and 3.5 Hz for the small ones and between 10.5 and 11.5 Hz for the large ones. This again indicates a substantial preference for a single conformation in each of the segments E and G. In analogy to the results found with **3–6**, we assume that this is the *tt*-conformation.

The only segment in **8–11**, which had no precedent in **3–6** is the central segment F. The coupling constants found differ only a little from an average value *ca.* 5.5–6.0 Hz. Thus, contrary to our expectation, this central segment remained bi-conformational, showing little tendency to favour the *tt*-conformation. In fact, a small preference for the *gg*-conformer was noted. In those cases, in which the individual coupling constants could be assigned to the individual sides of the segment F, NOE contacts between H-8 and H-9, characteristic for the *tt*-conformer and between H-9 and H-10, characteristic for the *gg*-conformer in segment F, were recorded for compounds **9**, **10** and **11**.

When considering the core region E, F, G of the structures **8–11** this adopts with almost equal preference a *tt*, *tt*, *tt* and a *tt*, *gg*, *tt* conformation. Since this core region in **8–11** has an obvious similarity to syndiotactic polypropylene, it is no surprise to find precedent for this behaviour there: syndiotactic polypropylene crystallizes in two modifications,[10] which therefore differ little in energy, one with a fully extended *tt tt tt* sequence and one with a *tt gg tt gg* sequence.

We may summarize the conformational behaviour of the trioxypentadecenes **8–11** as follows. This picture is probably the complex result of several effects: the placement of the oxygen containing functionalities along the chain, the relative configuration of the stereogenic centres, and the presence of the alkenyl end group. In order to interpret these results in a consistent manner, and to learn more about the underlying conformation determining factors, we carried out model studies on smaller compounds containing the segments A, B or C.[11] These studies will be reported in due course.



Experimental

All temperatures quoted are not corrected. Reactions were carried out under an atmosphere of dry nitrogen or argon. *J* values are given in Hz. Boiling range of light petroleum: 40–60 °C. ^1H,^{13}C NMR: Bruker AC-300 and AMX-500. All NOESY-contacts were determined with a mixing time of 2 s. pH 7 buffer: 56.2 g of $NaH_2PO_4 \cdot 2\ H_2O$ and 213.2 g of $Na_2HPO_4 \cdot 2\ H_2O$ in 1.0 l of water. Column chromatography: silica gel Si 60 (63–200 μm), E. Merck, Darmstadt. Flash chromatography: silica gel Si 60 (40–63 μm) E. Merck Darmstadt. MPLC: 30 × 2 cm column with silica gel Si 60 (15–25 μm), E. Merck, Darmstadt, 10 bar, detection by differential refractometry (Knaur).

(2*E*,4*R*,5*R*,6*R*,8*R*,9*R*)-5,9-Diacetoxy-4,6,8,10-tetramethylundec-2-ene 4

To a solution of (2*E*,4*R*,5*R*,6*R*,8*R*,9*R*)-5,9-dihydroxy-4,6,8,10-tetramethylundec-2-ene **3** (40 mg, 0.17 mmol) in acetic anhydride (10 ml) was added a solution of 4-dimethylaminopyridine (10 mg) in pyridine (15 ml) at 0 °C. Upon dropwise addition of acetyl chloride (1.0 ml) a colourless precipitate was formed. The mixture was allowed to reach room temp. over 2 h and was hydrolysed by addition of ice (30 g). The phases were separated and the aqueous phase was extracted with diethyl ether (3 × 20 ml). The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with light petroleum–diethyl ether = 10 : 1 furnished **4** (47 mg, 87%) as a colourless oil. $\delta_H(CDCl_3)$ 0.73 (d, *J* 6.7, 3 H, 14-CH_3), 0.80 (d, *J* 6.7, 3 H, 13-CH_3), 0.83 (d, *J* 6.8, 3 H, 11-CH_3), 0.85 (d, *J* 7.0, 3 H, 15-CH_3), 0.89 (d, *J* 6.8, 3 H, 12-CH_3), 1.05 (ddd, *J* 14.0, 11.0 and 3.5, 1 H, H-7), 1.18 (ddd, *J* 13.7, 11.2 and 3.2, 1 H, H-7), 1.60 (dd, *J* 6.4 and 1.5, 3 H, 1-CH_3), 1.70 (m, 1 H, H-8), 1.75 (m, 1 H, H-6), 1.88 (m, 1 H, H-10), 2.03 (s, 3 H), 2.07 (s, 3 H), 2.35 (m, 1 H, H-4), 4.58 (dd, *J* 6.5 and 5.8, 1 H, H-9), 4.67 (dd, *J* 8.6 and 3.8, 1 H, H-5), 5.17 (ddd, *J* 15.2, 8.6 and 1.5, 1 H, H-3), 5.38 (dq, *J* 15.0 and 6.2, 1 H, H-2). $\delta_C(CDCl_3)$ 13.1, 16.4, 16.9, 17.4, 17.9, 19.5, 20.9, 29.2, 31.4, 31.8, 33.4, 38.7, 81.0, 82.5, 125.6, 132.8, 171.0 (2C). $[\alpha]_{589}^{20}$ +30.7 (*c* 2.25, $CHCl_3$). $C_{19}H_{34}O_4$ (326.5): calc. C, 69.90; H, 10.50; found: C, 69.74; H, 10.31%.

(2*E*,4*R*,5*R*,6*R*,8*R*,9*R*)-4,6,8,10-Tetramethyl-5,9-bis(trimethylsilyloxy)undec-2-ene 5

Trimethylsilylimidazole (5.8 ml, 40 mmol) was added dropwise to a solution of **3** (1.58 g, 40 mmol) in anhydrous dimethylformamide (10 ml). After 15 h at room temp. water (20 ml) was added, the phases were separated and the aqueous phase was extracted with light petroleum (6 × 20 ml). The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with light petroleum–diethyl ether = 50 : 1 furnished **5** (2.45 g, 97%) as a colourless oil. $\delta_H(CDCl_3)$ 0.09 (s, 9 H), 0.12 (s, 9 H), 0.75 (d, *J* 6.6, 3 H), 0.83 (d, *J* 6.0, 3 H), 0.84 (d, *J* 6.7, 3 H), 0.86 (d, *J* 6.4, 3 H), 0.93 (d, *J* 6.7, 3 H), 1.01 (ddd, *J* 13.5, 10.9 and 2.6, 1 H), 1.23 (ddd, *J* 13.4, 10.2 and 3.2, 1 H), 1.62 (d, *J* 6.2, 3 H), 1.45–1.86 (m, 3 H), 2.24 (sextet, *J* 7.2, 1 H), 3.12 (dd, *J* 5.4 and 5.4, 1 H), 3.21 (dd, *J* 7.5 and 3.3, 1 H), 5.22 (ddq, *J* 15.4, 8.4 and 1.7, 1 H), 5.39 (dq, *J* 15.3 and 6.2, 1 H). $\delta_C(CDCl_3)$ 0.9 (3C), 1.0 (3C), 14.0 (C-14), 17.4 (C-13), 17.5 (C-12), 17.9 (C-11), 18.0 (C-1), 20.5 (C-15), 31.0 (C-10), 33.5 (C-8), 33.9 (C-6), 35.4 (C-7), 40.8 (C-4), 82.5

(C-5), 83.7 (C-9), 124.2 (C-2), 135.2 (C-3). $[\alpha]_D^{20}$ +31.7 (*c* 0.60, $CHCl_3$). $C_{21}H_{46}Si_2O_2$ (386.8): calc. C, 65.21; H, 11.99; found: C, 64.90; H, 11.56%.

(2*E*,4*R*,5*R*,6*R*,8*R*,9*R*)-5,9-Dimethoxy-4,6,8,10-tetramethylundec-2-ene 6

To a suspension of sodium hydride (80% in white oil; 361 mg, 12 mmol) in tetrahydrofuran (THF) (10 ml) was added at 0 °C a solution of **3** (60 mg, 0.25 mmol) in THF (5 ml). After stirring for 1 h at room temp. the mixture was cooled to 0 °C and dimethyl sulfate (1.0 ml) was added. After 1 h pH 7 buffer (10 ml) and diethyl ether (5 ml) were added, the phases were separated and the aqueous phase was extracted with diethyl ether (3 × 5 ml). The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with petroleum ether–diethyl ether = 30 : 1 to 5 : 1 furnished **6** (42 mg, 63%) as a colourless oil. $\delta_H(CDCl_3)$ 0.79 (d, *J* 6.6, 3 H, 13-CH_3), 0.87 (d, *J* 6.8, 3 H, 11-CH_3), 0.90 (d, *J* 6.9, 3 H, 14-CH_3), 0.92 (d, *J* 6.6, 3 H, 15-CH_3), 1.01 (d, *J* 6.7, 3 H, 12-CH_3), 1.15 (m, 1 H, H-7), 1.35 (ddd, *J* 13.6, 11.0 and 2.9, 1 H, H-7), 1.62 (dd, *J* 6.2 and 1.4, 3 H, 1-CH_3), 1.62 (m, 1 H, H-8), 1.73 (m, 1 H, H-6), 1.77 (m, 1 H, H-10), 2.31 (m, 1 H, H-4), 2.68 (dd, *J* 7.5 and 4.0, 1 H, H-5), 3.00 (t, *J* 5.3, 1 H, H-9), 3.43 (s, 3 H), 3.95 (s, 3 H), 5.27 (ddd, *J* 15.2, 8.2 and 1.4, 1 H, H-3), 5.41 (dq, *J* 15.1 and 6.2, 1 H, H-2). $\delta_C(CDCl_3)$ 12.6, 16.9, 17.3, 17.6, 17.9, 19.7, 30.5, 32.7, 33.0, 34.8, 40.1, 58.5, 61.5, 81.8, 91.4, 124.3, 134.8. $[\alpha]_D^{20}$ +29.2 (*c* 1.40, $CHCl_3$). $C_{17}H_{34}O_2$ (270.5): calc. C, 75.50; H, 12.67; found: C, 75.66; H, 12.94%.

(2*RS*,4*R*,5*R*,6*R*,8*R*,9*R*)-5,9-Bis(trimethylsilyloxy)-2,4,6,8,10-pentamethylundecanal

To a solution of **5** (2.44 g, 6.3 mmol) in anhydrous THF (30 ml) was added at 0 °C a 0.5 M solution of 9-borabicyclo-[3.3.1]nonane (9-BBN) in diethyl ether (20 ml, 10 mmol). The mixture was held for 1 h at 0 °C, 1 h at room temp., and finally for 16 h under reflux. After cooling to 0 °C a 1.2 M solution of potassium triisopropoxyborohydride in THF (0.53 ml, 6.3 mmol) was added without stirring. A stream of 2–3 bubbles per second of dry carbon monoxide was passed into the solution and it was stirred for 2 h at room temp. After TLC indicated complete reaction the mixture was cooled to 0 °C and argon was introduced instead of carbon monoxide. pH 7 buffer (25 ml) was carefully added at 0 °C followed by aqueous H_2O_2 (5 ml, 30%). The mixture was stirred for 30 min at 0 °C and 30 min at room temp. After addition of potassium carbonate (20 g) the phases were separated and the aqueous phase was extracted with diethyl ether (4 × 20 ml). The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with light petroleum–diethyl ether = 100 : 1 to 10 : 1 furnished the aldehyde (2.26 g, 86%) as a 52 : 48 mixture of the C-2-epimers. $C_{22}H_{48}Si_2O_3$ (416.8): calc. C, 63.40; H, 11.61; found: C, 63.52; H, 11.76%.

Major epimer: $\delta_H(CDCl_3)$ 0.09 (s, 18 H), 0.78 (d, *J* 6.2, 3 H), 0.80–0.87 (m, 12 H), 1.07 (d, *J* 6.8, 3 H), 1.13–1.30 (m, 1 H), 1.48–1.90 (m, 7 H), 2.39 (m, 1 H), 3.10 (t, *J* 5.3, 1 H), 3.22 (dd, *J* 8.7 and 4.2, 1 H), 10.00 (d, *J* 1.8, 1 H). $\delta_C(CDCl_3)$ 1.0 (6C), 14.3, 14.4, 14.6, 17.0, 18.1, 20.5, 30.7, 33.3, 33.6, 34.1, 36.3, 36.8, 44.3, 81.3, 83.5, 204.8.

Minor epimer: $\delta_H(CDCl_3)$ 1.09 (d, *J* 6.9, 3 H), 3.11 (m, 1 H), 9.56 (d, *J* 2.6, 1 H). $\delta_C(CDCl_3)$ 0.9 (6C), 13.1, 14.4, 14.5, 16.8, 17.9, 20.5, 30.9, 30.9, 33.8, 34.4, 35.2, 37.1, 44.1, 81.8, 83.4, 204.8.

(2*RS*,3*R*,5*R*,6*R*)-2-Hydroxy-6-[(1′*R*,3′*R*,4′*R*)-4′-hydroxy-1′,3′,5′-trimethylhexyl]-3,5-dimethyltetrahydropyran 7

A 1.0 M solution of tetrabutylammonium fluoride (15.0 ml, 15 mmol) in THF was added under nitrogen to a solution of the aldehyde described in the preceding paragraph (2.26 g, 5.4 mmol) in THF (50 ml). After TLC indicated complete reaction, the mixture was filtered over a bed of 5 cm of silica gel which was washed with diethyl ether (800 ml). The combined filtrates were dried with $MgSO_4$ and concentrated. The residue was taken up under nitrogen in anhydrous methanol (50 ml). Potassium carbonate (500 mg) was added and the solution was held for 5 h under reflux. Water (50 ml) and NaCl (2 g) were added, the phases were separated and the aqueous phase was extracted with diethyl ether (3 × 30 ml). The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with light petroleum–diethyl ether = 5 : 1 furnished **7** (1.38 g, 94%) as very fine, colourless needles, melting range 126–129 °C. $C_{16}H_{32}O_3$ (272.4): calc. C, 70.54; H, 11.84; found: C, 70.64; H, 11.62%.

Major anomer: $\delta_H(CDCl_3)$ 0.76 (d, *J* 6.7, 3 H), 0.83 (d, *J* 6.7, 3 H), 0.89 (d, *J* 6.7, 3 H), 0.89 (d, *J* 6.8, 3 H), 0.91 (d, *J* 6.6, 6 H), 1.20–1.40 (m, 3 H), 1.58–1.91 (m, 7 H), 3.02 (m, 2 H), 3.23 (s, 1 H), 4.19 (d, *J* 8.1, 1 H). $\delta_C(CDCl_3)$ 12.1, 12.6, 14.6, 16.7, 17.9, 19.6, 29.1, 30.6, 31.9, 32.3, 32.4, 38.0, 39.2, 81.9, 83.5, 102.3.

Minor anomer: $\delta_H(CDCl_3)$ 0.77 (d, *J* 6.7, 3 H), 0.82 (d, *J* 7.1, 3 H), 0.92 (d, *J* 7.0, 3 H), 3.57 (dd, *J* 10.0 and 2.3, 1 H), 5.02 (d, *J* 3.4, 1 H). $\delta_C(CDCl_3)$ 11.4, 12.6, 14.6, 16.8, 18.2, 19.5, 28.7, 28.9, 30.7, 31.8, 32.4, 33.8, 37.9, 74.1, 81.1, 95.0.

(2*E*,4*R*,5*R*,6*R*,8*R*,9*R*,10*R*,12*R*)-5,9,13-Trihydroxy-4,6,8,10,12,14-hexamethylpentadec-2-ene 8

7 (572 mg, 2.10 mmol), (4*R*,5*R*)-4,5-dicyclohexyl-2-[(1*R*,2*Z*)-1-methylbut-2-enyl]-1,3,2-dioxaborolane (4.50 g, 14.8 mmol) and 2-hydroxypyridine (38 mg, 0.4 mmol) were dissolved in anhydrous methanol (6 ml). The solution was placed into a Teflon tube and was pressurized for 10 days to 10 kbar. Triethanolamine (1.0 ml, 7.0 mmol) was added and the mixture was stirred for 1 h. The mixture was filtered and the filtrate was concentrated *in vacuo*. A first purification was effected by column chromatography of the residue using gradients from pure light petroleum to pure diethyl ether. The combined eluates were purified by MPLC, eluting with light petroleum–ethyl acetate 1 : 1 to give unreacted pentenyl boronate (3.21 g), unreacted **7** (20.1 mg) and **8** (690 mg, 96%) as a colourless solid. Mp 93 °C. $\delta_H(CDCl_3)$ 0.81 (d, *J* 6.6, 3 H), 0.84 (d, *J* 6.6, 3 H), 0.85 (d, *J* 6.8, 3 H), 0.87 (d, *J* 6.9, 3 H), 0.88 (d, *J* 6.9, 3 H), 0.92 (d, *J* 6.6, 3 H), 0.97 (d, *J* 6.8, 3 H), 1.02–1.09 (broad t, *J* 10.5, 2 H), 1.57 (ddd, *J* 13.3, 10.7 and 2.7, 2 H), 1.66 (d, *J* 6.4, 3 H), 1.60–1.81 (m, 8 H), 2.33 (sextet, *J* 6.7, 1 H), 3.07 (dd, *J* 6.9 and 4.4, 1 H), 3.10 (dd, *J* 6.8 and 4.6, 1 H), 3.19 (dd, *J* 5.8 and 5.8, 1 H), 5.34 (ddq, *J* 15.4, 7.3 and 1.4, 1 H), 5.47 (dqd, *J* 15.4, 6.2 and 0.6, 1 H). $\delta_C(CDCl_3)$ 11.8, 11.8, 14.3, 15.7, 16.5, 17.9, 18.8, 19.4, 31.0, 32.0 (2C), 33.2, 33.3, 36.3, 37.2, 39.4, 79.8, 81.2, 82.1, 124.5, 135.1. $[\alpha]_D^{20}$ 53.5 (*c* 1.1, $CHCl_3$). $C_{21}H_{42}O_3$ (342.6): calc. C, 73.63; H, 12.36; found: C, 73.49; H, 12.24%.

(2*E*,4*R*,5*R*,6*R*,8*R*,9*R*,10*R*,12*R*,13*R*)-5,9,13-Triacetoxy-4,6,8,10,12,14-hexamethylpentadec-2-ene 9

The triol **8** (40.0 mg, 0.12 mmol) was acetylated as described in paragraph 2 of the Experimental section to give the triacetate **9** (398 mg, 71%) as a colourless oil. $\delta_H(CDCl_3)$ 0.71 (d, *J* 6.6, 3 H, 18-CH_3), 0.79 (d, *J* 6.9, 3 H, 17-CH_3), 0.80 (d, *J* 6.6, 3 H, 20-CH_3), 0.82 (d, *J* 6.8, 3 H, 19-CH_3), 0.83 (d, *J* 6.7, 3 H, 15-CH_3), 0.86 (d, *J* 6.8, 3 H, 21-CH_3), 0.88 (d, *J* 6.7, 3 H, 16-CH_3), 1.06 (m, 1 H, H-11), 1.07 (m, 1 H, H-7), 1.09 (m, 1 H, H-11), 1.15 (m, 1 H, H-7), 1.61 (dd, *J* 6.4 and 1.6, 3 H, 1-CH_3), 1.73 (m, 1 H, H-8), 1.75 (m, 1 H, H-12), 1.80 (m, 1 H, H-6), 1.83 (m, 1 H, H-10), 1.88 (m, 1 H, H-14), 2.02 (s, 3 H), 2.02 (s, 3 H), 2.03 (s, 3 H), 2.36 (m, 1 H, H-4), 4.58 (dd, *J* 6.9 and 5.3, 1 H, H-13), 4.63 (dd, *J* 6.8 and 5.4, 1 H, H-9), 4.68 (dd, *J* 8.9 and 3.6, 1 H, H-5), 5.18 (ddq, *J* 15.3, 8.7 and 1.6, 1 H, H-3), 5.43 (dq, *J* 15.2 and 6.4, 1 H, H-2). $\delta_C(CDCl_3)$ 13.1 (C-20), 13.7 (C-18), 16.2 (C-19), 16.5 (C-17), 17.1 (C-16), 17.6 (C-15), 17.9 (C-1), 19.4 (C-21), 20.8 (3C), 29.2, 31.1, 31.2, 31.3, 31.6, 32.6, 34.2, 38.8, 81.0 (C-9), 82.2 (C-13), 82.4 (C-5), 125.8 (C-2), 132.6 (C-3), 171.0 (2C), 171.1. $[\alpha]_D^{20}$ +31.7 (*c* 1.75, $CHCl_3$). $C_{27}H_{48}O_6$ (468.7): calc. C, 69.20; H, 10.32; found: C, 69.04; H, 10.40%.

(2*E*,4*R*,5*R*,6*R*,8*R*,9*R*,10*R*,12*R*,13*R*)-5,9,13-Tris(trimethylsilyloxy)-4,6,8,10,12,14-hexamethylpentadec-2-ene 10

The triol **8** (348 mg, 1.0 mmol) was silylated as described in paragraph 3 of the Experimental. Flash chromatography with light petroleum–diethyl ether = 3 : 1 furnished **10** (562 mg, 98%) as a colourless oil. $\delta_H(CDCl_3)$ 0.10 (s, 9 H), 0.11 (s, 9 H), 0.12 (s, 9 H), 0.75 (d, *J* 6.6, 3 H), 0.80 (d, *J* 6.6, 3 H), 0.82 (d, *J* 6.6, 3 H), 0.83 (d, *J* 6.8, 3 H), 0.85 (d, *J* 6.6, 3 H), 0.87 (d, *J* 6.6, 3 H), 0.90 (d, *J* 6.6, 3 H), 1.03 (ddd, *J* 13.2, 11.0 and 2.2, 2 H), 1.17 (ddd, *J* 13.2, 10.7 and 2.5, 1 H), 1.21 (m, 1 H), 1.45–1.73 (m, 4 H), 1.62 (dd, *J* 6.3 and 1.5, 3 H), 1.76 (septet, *J* 6.6, 1 H), 2.24 (sextet, *J* 7.3, 1 H), 3.11 (dd, *J* 5.2 and 5.2, 1 H), 3.15 (dd, *J* 6.6 and 3.7, 1 H), 3.21 (dd, *J* 7.7 and 3.3, 1 H), 5.22 (ddq, *J* 15.5, 8.5 and 1.5, 1 H), 5.39 (dq, *J* 15.4 and 6.3, 1 H). $\delta_C(CDCl_3)$ 0.9 (3C), 1.0 (6C), 14.4, 15.0, 17.5, 17.5 (2C), 17.9, 18.0, 20.5, 30.9, 33.2, 33.5 (2C), 33.6, 34.8, 35.9, 40.7, 82.6, 83.6 (2C), 124.3, 135.1. $[\alpha]_D^{20}$ 40.1 (*c* 6.21, $CHCl_3$). $C_{30}H_{66}O_3Si_3$ (559.1): calc. C, 64.45; H, 11.90; found: C, 64.31; H, 11.85%.

(2*E*,4*R*,5*R*,6*R*,8*R*,9*R*,10*R*,12*R*,13*R*)-5,9,13-Trimethoxy-4,6,8,10,12,14-hexamethylpentadec-2-ene 11

To a suspension of potassium hydride (850 mg, 21 mmol) in THF (20 ml) was added at 0 °C sequentially methyl iodide (5.0 g, 80 mmol) and a solution of the triol **8** (187 mg, 0.55 mmol) in THF (10 ml). After stirring for 30 min at 0 °C, propan-2-ol (5 ml) and saturated aqueous NH_4Cl solution (30 ml) were slowly added. The phases were separated and the aqueous phase was extracted with diethyl ether (3 × 10 ml). The combined organic phases were dried with $MgSO_4$ and concentrated. Flash chromatography of the residue with light petroleum–diethyl ether = 10 : 3 furnished **11** (181 mg, 86%) as a colourless oil. $\delta_H(CDCl_3)$ 0.82 (d, *J* 6.6, 3 H, 18-CH_3), 0.84 (d, *J* 6.6, 3 H, 20-CH_3), 0.87 (d, *J* 6.8, 3 H, 19-CH_3), 0.89 (d, overlaid, 3 H, 15-CH_3), 0.89 (d, overlaid, 3 H, 17-CH_3), 0.90 (d, *J* 6.4, 3 H, 21-CH_3), 1.00 (d, *J* 6.7, 3 H, 16-CH_3), 1.08 (ddd, *J* 13.5, 10.6 and 2.9, 1 H, H-11), partially overlaid with 1.10 (ddd, *J* 13.6, 10.8 and 2.8, 1 H, 7-H), 1.33 (ddd, *J* 13.5, 11.2 and 2.3, 1 H, H-7), 1.44 (ddd, *J* 13.5, 10.9 and 2.6, 1 H, H-11), 1.62 (d, *J* 6.4, 3 H, 1-CH_3), 1.68 (m, 1 H, H-12), 1.71 (m, 1 H, H-8), 1.73 (m, 1 H, H-6), 1.75 (m, 1 H, H-10), 1.79 (m, 1 H, H-14), 2.32 (m, 1 H, H-4), 2.56 (dd, *J* 6.1 and 5.0, 1 H, H-13), 2.62 (t, *J* 5.5, 1 H, H-9), 2.68 (dd, *J* 7.6 and 3.9, 1 H, H-5), 3.41 (s, 3 H), 3.42 (s, 3 H), 3.43 (s, 3 H), 5.27 (ddq, *J* 15.3, 8.5 and 1.4, 1 H, H-3), 5.41 (dq, *J* 15.2 and 6.2, 1 H, H-2). $\delta_C(CDCl_3)$ 13.3 (C-20), 13.8 (C-18), 16.6 (C-19), 16.9 (C-16), 17.1 (C-17), 17.9 (C-1), 18.0 (C-21), 20.2 (C-15), 29.7 (C-12), 30.8 (C-14), 32.8 (C-10), 32.9 (C-8), 32.9 (C-6), 34.9 (C-7), 35.8 (C-11), 40.4 (C-4), 61.3, 61.4, 61.5, 91.4 (C-5), 92.5 (C-13), 92.6 (C-9), 124.2 (C-3), 134.7 (C-2). $[\alpha]_D^{20}$ +26.1 (*c* 2.65, $CHCl_3$). $C_{24}H_{48}O_3$ (384.6): calcd. C, 74.94; H, 12.58; found: C, 74.94; H, 12.72.

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