Functionalized Diorganozinc Compounds: Key Reagents for the Synthesis of Enantiomerically Pure 2,5-Disubstituted *cis*- and *trans*-Tetrahydrofurans

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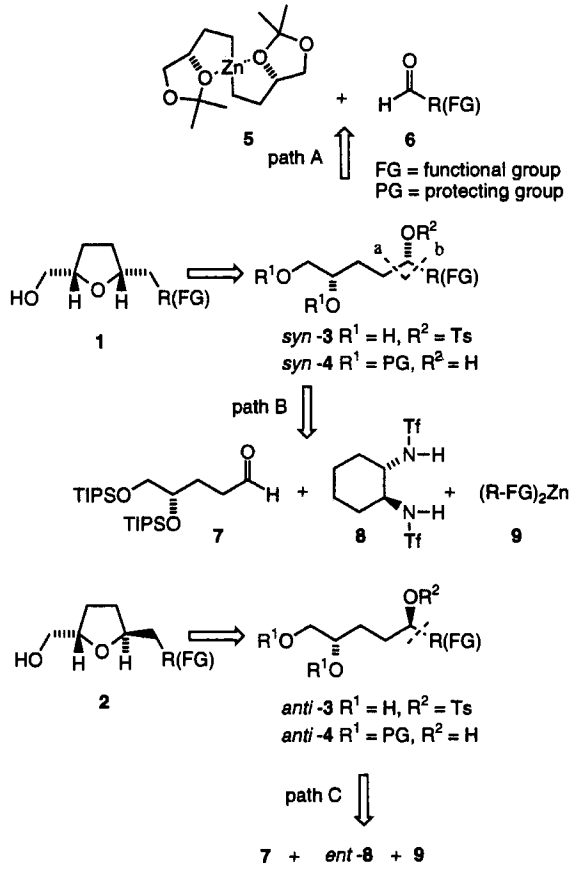
1,4-Diol derivatives **4a–i** were synthesized stereoselectively by either reagent- or catalyst-controlled routes using the addition of functionalized diorganozinc reagents to aldehydes. The stereoselectivities along the reagent-controlled synthetic path were in the range between 80:20 and 95:5. The stereoselectivities along the catalyst route exceeded 95:5. The 1,4-diol derivatives **4** thus obtained were transformed into enantiomerically pure *cis*- and *trans*-2,5-disubstituted tetrahydrofurans (**16–20**) by means of an intramolecular Williamson reaction.

2,5-Disubstituted tetrahydrofurans represent substructures of polyether antibiotics[1], *Annonaceae* acetogenins[2], and C-glycosides[3]. Considering the biological and pharmacological importance of these natural products, synthetic routes to enantiomerically pure 2,5-disubstituted tetrahydrofurans are of central interest[4]. Furthermore, such structures are building blocks for nonnatural oligo-THFs[5], which possess potential applications in the fields of THF podands[6] and artificial ion channels[7]. Most of the known synthetic routes to 2,5-disubstituted tetrahydrofurans yield either the *trans* or the *cis* isomer[4]. In this paper we report on a general solution to this problem by using functionalized diorganozinc reagents[8], which allow the synthesis of both stereoisomers starting from common building blocks.

Assuming that an intramolecular Williamson reaction will be used to close the THF ring, the following retrosynthetic scheme results (Scheme 1).

The *cis*-THF **1** could be obtained from the dihydroxy tosylate *syn*-**3**, while the *trans*-THF **2** could be generated from the dihydroxy tosylate *anti*-**3**. Compound *syn*-**3** should be available from the alcohol *syn*-**4**, which can either be obtained from the diorganozinc compound **5** and the aldehyde **6** (path A) or the diorganozinc compound **9** and the aldehyde **7** (path B). In path A a stereodirecting effect of the chiral center of the organozinc reagent **5** is used[9]. In contrast, path B makes use of the stereodirecting effect of a chiral catalyst **8**[10] after blocking of the chiral center in **7** with a sterically demanding silyl ether. By use of the other enantiomer of the catalyst, *ent*-**8**, the dihydroxy tosylate *anti*-**3** should be available via the alcohol *anti*-**4** from the building blocks **7** and **9** (path C).

Scheme 1. Retrosynthetic considerations on 2,5-disubstituted oligo-THFs: Reagent-controlled (path A) and catalyst-controlled (paths B and C) routes



Reagent Control: Path A

Previous studies had revealed that the organozinc iodide prepared from the enantiomerically pure acetonide iodide **10** showed a stereodirecting effect of the chiral center in the acetonide group in Lewis acid-catalyzed addition reactions with achiral and chiral aldehydes[9]. In this paper we report

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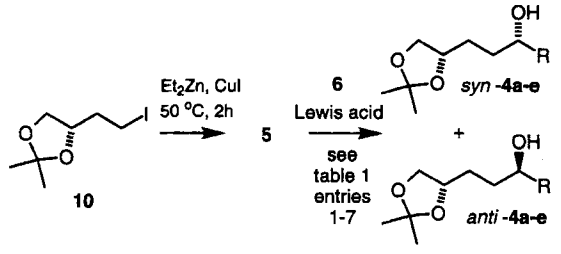
on the fact that this stereodirecting effect can be highly increased, if the diorganozinc compound **5**, which was prepared by an iodine-zinc exchange mediated by diethylzinc[8], is used instead of the corresponding organozinc iodide (Scheme 2).

Scheme 2



For example, the stereoselectivity in the reaction with benzaldehyde increases from 76:24 (organozinc iodide) to 95:5 (diorganozinc compound). Table 1 summarizes the results of reactions with various aldehydes (entries 1–7). Different Lewis acids were examined as catalysts for these reactions. $BF_3 \cdot OEt_2$ and $MeAlCl_2$ gave good selectivities (entries 1–6), while Me_2AlCl was found to be less suitable (entry 7). The new stereocenter in **4** was assigned by a comparison with data based on an X-ray structural analysis[9].

Table 1. Stereoselective addition of dialkylzinc reagents to aldehydes yielding the *syn* and *anti* alcohols **4**. With method A the following Lewis acids were used: a) $BF_3 \cdot OEt_2$, b) $MeAlCl_2$, c) Me_2AlCl

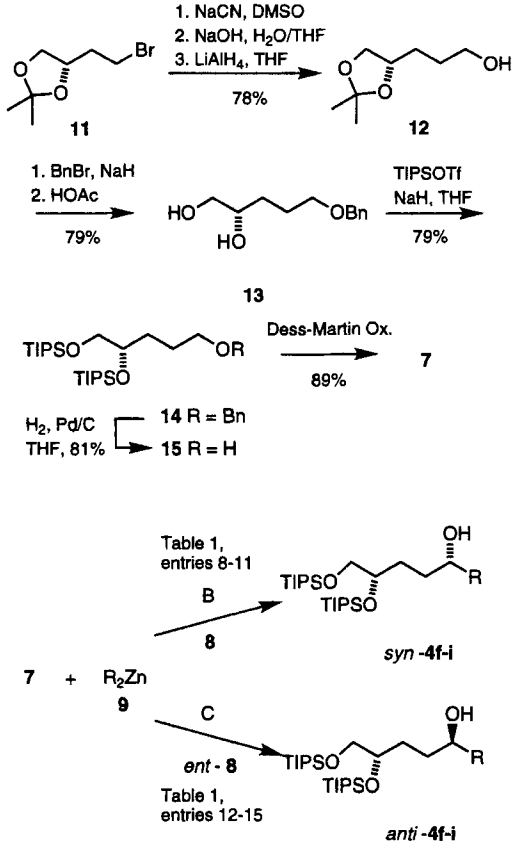
Entry	R	method	product	*syn/anti*	yield (%)
1	Ph	A [a]	**4a**	95 : 5	89
2	Et	A [a]	**4b**	91 : 9	65
3	C_5H_{11}	A [a]	**4c**	92:8	52
4	$(CH_2)_3OPiv$	A [a]	**4d**	87:13	76
5	$(CH_2)_5OPiv$	A [a]	**4e**	84 : 16	83
6	C_5H_{11}	A [b]	**4c**	83 : 17	87
7	C_5H_{11}	A [c]	**4c**	66 : 34	46
8	Et	B	**4f**	> 98 : 2	86
8	C_5H_{11}	B	**4g**	> 98 : 2	82
10	$(CH_2)_3OPiv$	B	**4h**	> 98 : 2	71
11	$(CH_2)_5OPiv$	B	**4i**	94 : 6	59
12	Et	C	**4f**	2 : > 98	88
13	C_5H_{11}	C	**4g**	2 : > 98	86
14	$(CH_2)_3OPiv$	C	**4h**	2 : > 98	77
15	$(CH_2)_5OPiv$	C	**4i**	5 : 95	61

It should be noted that the enantiomerically pure iodide **10** was used for the preparation of the diorganozinc compound. If one starts with the racemic iodide *rac*-**10**, three stereoisomers of the diorganozinc compound can be formed: the *SS*, the *SR*, and the *RR* dimer[11]. It will be interesting to investigate, whether there is a difference in reactivity and stereoselectivity of the homochiral dimers (*SS*, *RR*) and the heterochiral dimer (*SR*).

Catalyst Control: Paths B and C

The aldehyde **7**, necessary for path B, was synthesized by starting from the enantiomerically pure bromide **11**[12] (Scheme 3). C1 homologization of **11** led to a nitrile, which after hydrolysis and reduction gave the alcohol **12**. After benzylation of the primary hydroxy function of **12**, the acetonide group was removed to yield the diol **13**. This was protected to yield the disilyl ether **14**. Hydrogenolysis of the benzyl ether (**14** → **15**) and subsequent Dess-Martin oxidation of the resulting alcohol gave the aldehyde **7**. The triisopropylsilyl (TIPS) protecting group was chosen to prevent any chelating effect of the chiral center in **7**[13,14]. This choice was based on earlier, related experiments with a benzyl protecting group, in which case only moderate selectivities could be achieved due to the interfering chelating properties of the benzyl ether function[14].

Scheme 3

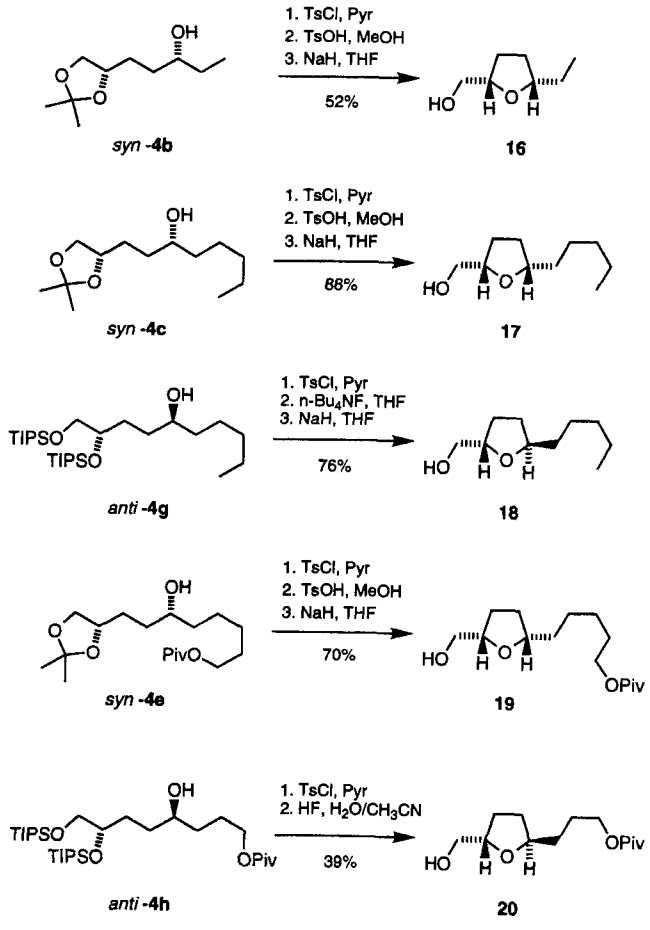


According to path B a number of functionalized diorganozinc reagents were allowed to react with the aldehyde **7** in the presence of the chiral catalyst **8** (8 mol-%) and $Ti(OiPr)_4$ (2 eq.). The resulting alcohols *syn*-**4f–i** were obtained with very high diastereoselectivities (Table 1, entries 8–11). Using the other enantiomer of the catalyst, *ent*-**8**, we prepared the corresponding alcohols *anti*-**4f–i** with very high diastereoselectivities, too (path C, Table 1, entries 12–15). Thus, blocking of the chiral center in **7** with a bulky silyl ether resulted in nearly complete reagent control by the catalyst.

Ring Closure to 2,5-Disubstituted Tetrahydrofurans

The ring-closure reaction sequence started with the tosylation of the alcohol *syn*-**4** or *anti*-**4**. The tosylates thus obtained were further treated to deprotect the 1,2-diol unit. *p*-TsOH/MeOH was used for the acetonide deprotection, while fluoride anion sources (nBu$_4$NF in THF, HF in aqueous CH_3CN) were suitable for the removal of the TIPS groups. The intramolecular Williamson reactions were carried out in THF by using NaH as a base (Scheme 4). In the case of the *trans*-THF **20**, ring closure occurred during deprotection with HF in acetonitrile. The resulting 2,5-disubstituted tetrahydrofurans **16**–**20** could be purified by chromatography.

Scheme 4



The relative configuration of the *cis*- and *trans*-tetrahydrofurans was proven by NOE studies for compounds **16**–**19** and by a comparison with data based on an X-ray structural analysis[9].

Conclusion

To summarize, a general stereoselective, synthetic route to *cis*- and *trans*-tetrahydrofurans was developed. Functionalized diorganozinc reagents were found to be key reagents for this purpose. Both reagent (path A) and catalyst control (paths B and C) was possible. The nearly complete catalyst control in the diastereoselective additions of the diorganozinc reagents to the chiral aldehyde **7** is remarkable.

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Experimental

All temperatures quoted are uncorrected. – Melting points: Tottoli apparatus (Büchi). – Elemental analyses: Analytik-Servicelabor Marburg, CHN-Rapid (Heraeus). – Thin-layer chromatography (TLC): Merck silica gel 60 on glass plates with fluorescence indicator F-254, TLC detection was carried out by UV irradiation and/or heatgun treatment with 5% phosphomolybdic acid in ethanol. – HPLC: Merck LiChroGraph L-6200, L-4200 UV/Vis detector (λ = 254 nm), D-2500 chromato-integrator, column: Merck Supersphere Si 60 (250-4). – Optical rotations: Polarimeter 241 (Perkin Elmer). – IR: Interferometer Bruker IFS 88. – NMR: Bruker AT 200, AC-300, WH 400, AMX-500. – MS: Varian MAT CH 7A. – Column chromatography (CC): Merck silica gel 60 (70–200 mesh ASTM). – Dry solvents [petroleum ether (PE), diethyl ether (Et_2O), ethyl acetate (AcOEt)]: All solvents used for the organozinc reactions were dried and handled under argon; THF was predried with KOH, distilled first from $LiAlH_4$ and then from sodium/benzophenone; Et_2O was predried with $CaCl_2$ and distilled from sodium/benzophenone; CH_2Cl_2 was distilled from CaH_2, MeOH from $Mg(OMe)_2$, acetone from P_4O_{10}, and toluene was distilled from sodium/benzophenone. – Boiling range of PE: 40–60°C.

1) *Bis[(3S)-3,4-(isopropylidenedioxy)butyl]zinc* (**5**): A 50-ml Schlenk flask was charged with 2.56 g (10.0 mmol) of the iodide **10** and 10 mg (0.052 mmol) of CuI. To the mixture was added 3.40 ml (20.0 mmol) of diethylzinc. The reaction mixture was heated at 50°C for 2 h. The flask was then connected to a vacuum line (0.1 Torr), and the resulting ethyl iodide and excess diethylzinc were distilled off. The remaining dialkylzinc reagent **5** was redissolved in toluene or CH_2Cl_2. The resulting solution was ready for use. – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.00–0.06 (m, 1H, 1-H), 0.27–0.32 (m, 1H, 1-H), 1.36, 1.41 (s, 6H, CH_3), 1.47–1.53 (m, 1H, 2-H), 1.98–2.03 (m, 1H, 2-H), 3.48 (t, J = 5.8 Hz, 1H, 4-H), 3.89–3.95 (m, 1H, 3-H), 4.03 (dd, J = 1.9/5.9 Hz, 1H, 4-H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 6.8 (C-1), 25.9, 27.2 (CH_3), 31.3 (C-2), 69.4 (C-4), 79.4 (C-3), 108.7 (acetonide).

2) *General Procedure for the Lewis Acid-Catalyzed Addition of the Organozinc Reagent* **5** *to Aldehydes (Path A):* The corresponding Lewis acid was added at −78°C to a solution of the aldehyde in 5 ml of toluene. After 15 min a solution of 5 mmol of the diorganozinc reagent **5** in 10 ml of toluene, prepared as described in 1), was added dropwise to the reaction mixture. After 3 h at −60°C, the reaction mixture was warmed to −30°C during 2 h. At that point 20 ml of a satd. aqueous NH_4Cl solution and 50 ml of *t*BuOMe were added. The aqueous layer was extracted twice with 50 ml of *t*BuOMe each. The combined organic layers were washed with 50 ml of a satd. aqueous NaCl solution and dried with $MgSO_4$. After evaporation of the solvent the remaining residue was purified by CC.

2.1) *(2S,5S)-1,2-O-Isopropylidene-5-phenylpentane-1,2,5-triol* (*syn*-**4a**): According to the general procedure 2), 5 mmol of **5**, 200 mg (1.88 mmol) of benzaldehyde, and 240 mg (1.60 mmol) of $BF_3 \cdot OEt_2$ were allowed to react to yield 395 mg (1.67 mmol, 89%) of the alcohol *syn*-**4a** as a colorless oil. Inspection of the ^{1}H- and

the (integrated) ^{13}C-NMR spectra revealed a ratio *syn/anti* of 95:5. – TLC (PE/Et_2O, 1:1): R_f = 0.67. – $[\alpha]_D^{20}$ = +4.3, $[\alpha]_{578}^{20}$ = +4.8, $[\alpha]_{546}^{20}$ = +5.8, $[\alpha]_{436}^{20}$ = +11.5, $[\alpha]_{365}^{20}$ = +21.1 (*c* = 1.62, $CHCl_3$). – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.28 and 1.34 (s, 6H, CH_3, acetonide), 1.25–1.80 (m, 4H, 3,4-H_2), 2.57 (s, 1H, OH), 3.20–3.30 (m, 1H, 1-H), 3.75–3.86 (m, 1H, 1-H), 3.80–3.95 (m, 1H, 2-H), 4.40–4.55 (m, 1H, 5-H), 7.00–7.20 (m, 5H, Ph). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.9, 27.1 (CH_3, acetonide), 30.2, 35.7 (C-3,4), 69.6 (C-1), 74.5, 76.2 (C-2,5), 109.2 (acetonide), 126.1, 127.7, 128.7, 144.9 (Ph). – $C_{14}H_{20}O_3$ (236.3): calcd. C 71.16, H 8.53; found C 70.91, H 8.60.

2.2) *(2S,5R)-1,2-O-Isopropylideneheptane-1,2,5-triol* (*syn*-**4b**): According to the general procedure 2), 5 mmol of **5**, 144 mg (2.48 mmol) of propionaldehyde, and 341 mg (2.40 mmol) of $BF_3 \cdot OEt_2$ were allowed to react to yield 304 mg (1.61 mmol, 65%) of the alcohol *syn*-**4b** as a colorless oil. Inspection of the ^1H- and the (integrated) ^{13}C-NMR spectra revealed a ratio *syn/anti* of 91:9. – TLC (PE/Et_2O, 1:1): R_f = 0.51. – $[\alpha]_D^{20}$ = +4.3, $[\alpha]_{578}^{20}$ = +4.9, $[\alpha]_{546}^{20}$ = +5.2, $[\alpha]_{436}^{20}$ = +11.5, $[\alpha]_{365}^{20}$ = +21.1 (*c* = 1.62, $CHCl_3$). – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.3 Hz, 3H, 7-H_3), 1.28 and 1.34 (s, 6H, CH_3, acetonide), 1.36–1.72 (m, 6H, 3,4,6-H_2), 2.76 (bs, 1H, OH), 3.43–3.48 (m, 2H, 1,5-H), 3.95–4.20 (m, 2H, 1,2-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.9 (C-7), 25.7, 26.9 (CH_3, acetonide), 30.0, 30.2, 33.2 (C-3,4,6), 69.4 (C-1), 72.9 (C-5), 76.2 (C-2), 108.9 (acetonide). – $C_{10}H_{20}O_3$ (188.3): calcd. C 63.79, H 10.71; found C 63.65, H 10.77.

2.3) *(2S,5R)-1,2-O-Isopropylidenedecane-1,2,5-triol* (*syn*-**4c**)

a) According to the general procedure 2), 5 mmol of **5**, 201 mg (2.00 mmol) of *n*-hexanal, and 240 mg (1.70 mmol) of $BF_3 \cdot OEt_2$ were allowed to react to yield 239 mg (1.04 mmol, 52%) of the alcohol *syn*-**4b** as a colorless oil. Inspection of the ^1H- and the (integrated) ^{13}C-NMR spectra revealed a ratio *syn/anti* of 92:8. – TLC (PE/Et_2O, 1:1): R_f = 0.44. – $[\alpha]_D^{18}$ = +9.6, $[\alpha]_{578}^{18}$ = +11.8, $[\alpha]_{546}^{18}$ = +12.0, $[\alpha]_{436}^{18}$ = +20.3, $[\alpha]_{365}^{18}$ = +38.5 (*c* = 0.374, $CHCl_3$). – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.3 Hz, 3H, 10-H_3), 1.28 and 1.32 (s, 6H, CH_3, acetonide), 1.13–1.80 (m, 12H, 3,4,6–9-H_2), 2.30 (bs, 1H, OH), 3.43 (t, *J* = 7.4 Hz, 1H, 1-H), 3.50–3.55 (m, 1H, 5-H), 3.98 (t, *J* = 7.4 Hz, 1H, 1-H), 4.04–4.08 (m, 1H, 2-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9 (C-10), 25.6, 26.8 (CH_3, acetonide), 22.5, 25.3, 30.0, 31.8, 33.7, 37.5 (C-3,4,6–9), 69.4 (C-1), 71.6 (C-5), 76.1 (C-2), 108.9 (acetonide). – $C_{13}H_{26}O_3$ (230.35): calcd. C 67.79, H 11.37; found C 67.73, H 11.41.

b) According to the general procedure 2), 5 mmol of **5**, 161 mg (1.61 mmol) of *n*-hexanal, and 2.2 ml (2.2 mmol) of a 1 M solution of $MeAlCl_2$ in *n*-hexane were allowed to react for 3 h at −40 °C to yield 319 mg (1.39 mmol, 87%) of *syn*-**4c** as a colorless oil. Inspection of the ^1H- and the (integrated) ^{13}C-NMR spectra revealed a ratio *syn/anti* of 83:17. The spectroscopic data of the product were in accordance with those of a).

c) According to the general procedure 2), 2.5 mmol of **5**, 137 mg (1.37 mmol) of *n*-hexanal, and 2.0 ml (2.0 mmol) of a 1 M solution of Me_2AlCl in *n*-hexane were allowed to react for 3 h at −30 °C to yield 146 mg (0.64 mmol, 46%) of *syn*-**4c** as a colorless oil. Inspection of the ^1H- and the (integrated) ^{13}C-NMR spectra revealed a ratio *syn/anti* of 66:34. The spectroscopic data of the product were in accordance with the data of a).

2.4) *(2S,5R)-1,2-O-Isopropylidene-8-O-pivaloyloctane-1,2,5,8-tetrol* (*syn*-**4d**): According to the general procedure 2), 5 mmol of **5**, 250 mg (1.45 mmol) of 4-(pivaloyloxy)butanal[8b], and 0.36 ml (3.00 mmol) of $BF_3 \cdot OEt_2$ were allowed to react for 6 h at −20 °C to yield 334 mg (1.10 mmol, 76%) of the alcohol *syn*-**4d** as a colorless oil. Inspection of the ^1H- and the (integrated) ^{13}C-NMR spectra revealed a ratio *syn/anti* of 87:13. – TLC (PE/*t*BuOMe, 1:1): R_f = 0.20. – $[\alpha]_D^{20}$ = +6.2, $[\alpha]_{578}^{20}$ = +7.0, $[\alpha]_{546}^{20}$ = +7.7, $[\alpha]_{436}^{20}$ = +14.0, $[\alpha]_{365}^{20}$ = +21.3 (*c* = 4.15, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3449 (OH), 2937, 2872, 1728 (C=O), 1481, 1459, 1160, 1061 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.12 [s, 9H, $(CH_3)_3C$], 1.27 and 1.35 (s, 6H, CH_3, acetonide), 1.39–1.78 (m, 8H, 3,4,6,7-H_2), 2.74 (bs, 1H, OH), 3.45 (t, *J* = 7.4 Hz, 1H, 1-H), 3.52–3.61 (m, 1H, 5-H), 3.94–4.10 (m, 4H, 1,2-H, 8-H_2). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.1, 27.0 (CH_3, acetonide), 27.5 [(CH_3)$_3$C], 25.8, 30.2, 33.8, 34.1 (C-3,4,6,7), 38.8 [$(CH_3)_3C$], 64.5 (C-8), 69.5 (C-1), 71.2 (C-5), 76.2 (C-2), 109.0 (acetonide), 178.7 (C=O). – $C_{16}H_{30}O_5$ (302.4): calcd. C 63.55, H 9.99; found C 63.71, H 9.72.

2.5) *(2S,5R)-1,2-O-Isopropylidene-10-O-pivaloyldecane-1,2,5,10-tetrol* (*syn*-**4e**): According to the general procedure 2), 2.5 mmol of **5**, 180 mg (0.90 mmol) of 6-(pivaloyloxy)hexanal[8b], and 0.23 ml (1.80 mmol) of $BF_3 \cdot OEt_2$ were allowed to react for 4 h at −50 °C to yield 246 mg (0.75 mmol, 83%) of the alcohol *syn*-**4e** as a colorless oil. Inspection of the ^1H- and the (integrated) ^{13}C-NMR spectra revealed a ratio *syn/anti* of 84:16. – TLC (PE/AcOEt, 1:1): R_f = 0.31. – IR (neat): $\tilde{\nu}$ = 3451 (OH), 2935, 2869, 1728 (C=O), 1481, 1459, 1286, 1160, 1061 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.28 [s, 9H, $(CH_3)_3C$], 1.30 and 1.38 (s, 6H, CH_3, acetonide), 1.39–1.70 (m, 12H, 3,4,6–9-H_2), 2.37 (bs, 1H, OH), 3.46 (t, *J* = 7.3 Hz, 1H, 1-H), 3.48–3.60 (m, 1H, 5-H), 3.92–4.11 (m, 4H, 1,2-H, 10-H_2). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.3, 26.8 (CH_3, acetonide), 27.1 [(CH_3)$_3$C], 25.7, 25.9, 28.6, 30.1, 33.9, 37.4 (C-3,4,6–9), 38.7 [$(CH_3)_3C$], 64.2 (C-10), 69.4 (C-1), 71.5 (C-5), 76.2 (C-2), 108.9 (acetonide), 178.6 (C=O). – $C_{18}H_{34}O_5$ (330.5): calcd. C 65.42, H 10.37; found C 65.35, H 10.40.

3) *(2S)-1,2-O-Isopropylidenepentane-1,2,5-triol* (**12**): 4.81 g (98.2 mmol) of NaCN was added to a solution of 10.3 g (49.1 mmol) of the bromide **11**[12] in 80 ml of DMSO. The reaction mixture was heated at 90 °C for 2 h, then it was cooled to room temp. and partitioned between 200 ml of Et_2O and 200 ml of a half-satd. aqueous NH_4Cl solution. The aqueous layer was extracted twice with 100 ml of Et_2O. The combined organic layers were washed with 100 ml of a satd. aqueous NaCl solution and dried with $MgSO_4$. After evaporation of the solvent the remaining residue was distilled (110–130 °C, 12 Torr) to yield 6.50 g of the corresponding nitrile. The latter was added to a solution of 6.50 g (162.5 mmol) of NaOH in 160 ml of EtOH/20 ml of H_2O. The reaction mixture was refluxed for 3 h. It was cooled to 0 °C, while HCl was added dropwise until the pH reached 2. The mixture was partitioned between 200 ml of Et_2O and 50 ml of H_2O. The aqueous layer was extracted three times with 100 ml of Et_2O each, and the combined organic layers were dried with $MgSO_4$. After evaporation of the solvent 7.10 g (40.8 mmol) of the crude acid could be obtained. This was dissolved in 50 ml of THF, and the obtained solution was added dropwise to a suspension of 4.09 g (81.5 mmol) of $LiAlH_4$ in 100 ml of THF at 0 °C. The reaction mixture was refluxed for 1 h. After cooling to 0 °C, successively 4 ml of H_2O, 4 ml of 3 N NaOH, and 4 ml of H_2O were added dropwise with great caution. The reaction mixture was stirred for 30 min at room temp. and then filtered through a Celite pad. Evaporation of the solvent from the filtrate and distillation (85–88 °C, 0.5 Torr) of the residue gave 6.10 g (38.1 mmol, 78%) of the alcohol **12** as a colorless liquid. – TLC (PE/AcOEt, 4:1): R_f = 0.13. – $[\alpha]_D^{20}$ = +13.7, $[\alpha]_{578}^{20}$ = +14.4, $[\alpha]_{546}^{20}$ = +16.6, $[\alpha]_{436}^{20}$ = +30.2, $[\alpha]_{365}^{20}$ = +49.6 (*c* = 2.50, $CHCl_3$). – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.34 and 1.39 (s, 6H, CH_3, acetonide), 1.61–1.80 (m, 4H, 3,4-H_2), 2.50 (bs, 1H, OH), 3.51 (t, *J* = 7.3 Hz, 1H, 1-H), 3.60–3.68 (m, 2H, 5-H_2), 4.02 (t, *J* = 7.3 Hz, 1H, 1-H), 4.08–4.15 (m, 1H, 2-H). – ^{13}C NMR (75

MHz, $CDCl_3$): δ = 25.7, 26.9 (CH_3, acetonide), 30.3, 35.8 (C-3,4), 60.5 (C-5), 69.5 (C-1), 74.9 (C-2), 109.1 (acetonide). – $C_8H_{16}O_3$ (160.2): calcd. C 59.97, H 10.67; found C 59.69, H 10.51.

4) *(2S)-5-O-Benzylpentane-1,2,5-triol* (**13**): 3.27 g (109 mmol) of NaH (80% in mineral oil) was added at 0°C to a solution of 11.6 g (72.7 mmol) of the alcohol **12** in 100 ml of DMF. After 30 min a solution of 13.0 ml (109 mmol) of benzyl bromide in 50 ml of THF was added dropwise. The reaction mixture was stirred at room temp. for 10 h and then cooled to 0°C, while 50 ml of a satd. aqueous NH_4Cl solution was added. The aqueous layer was extracted twice with 100 ml of Et_2O each. The combined organic layers were washed with 200 ml of a satd. aqueous NaCl solution and dried with $MgSO_4$. After evaporation of the solvent the remaining residue was distilled (110–111°C, 0.5 Torr) to yield 15.1 g of the corresponding benzyl ether. The latter was mixed with 150 ml of 80% acetic acid at room temp. After 3 h of reaction, the acetic acid was distilled off, and the resulting product was purified by CC (150 g of silica gel, Et_2O) to yield 12.1 g (57.4 mmol, 79%) of the diol **13** as a colorless liquid. – TLC (Et_2O): R_f = 0.20. – $[\alpha]_D^{20}$ = –5.0 (*c* = 2.30, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3350 (OH), 3040, 2930, 2870, 1370, 1175 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.45–1.90 (m, 4H, 3,4-H_2), 2.06 (s, 1H, OH), 2.95 (s, 1H, OH), 3.53 (t, *J* = 6.1 Hz, 2H, 5-H_2), 3.39–3.70 (m, 3H, 2-H, 1-H_2), 4.47 (s, 2H, OCH_2Ph), 7.28–7.37 (m, 5H, Ph). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.1, 30.6 (C-3,4), 66.8 (C-1), 70.5 (C-5), 72.1 (C-2), 73.2 (OCH_2Ph), 127.8, 128.5, 138.2 (Ph). – MS (70 eV), *m/z* (%): 107 (38), 92 (29), 91 (100), 71 (19), 65 (18). – $C_{12}H_{18}O_3$ (210.3): calcd. C 68.55, H 8.63; found C 68.25, H 8.85.

5) *(2S)-5-O-Benzyl-1,2-bis-O-(triisopropylsilyl)pentane-1,2,5-triol* (**14**): 0.33 g (10.9 mmol) of NaH (80% in mineral oil) was added at 0°C to a solution of 0.92 g (4.37 mmol) of diol **13** in 3 ml of THF. After 30 min 0.90 g (2.90 mmol) of triisopropylsilyl triflate and 1.50 g (8.00 mmol) of chlorotriisopropylsilane were added to the reaction mixture, which was stirred at room temp. for 12 h. It was cooled to 0°C while 50 ml of a satd. aqueous NH_4Cl solution was added. The aqueous layer was extracted twice with 100 ml of Et_2O each. The combined organic layers were washed with 100 ml of a satd. aqueous NaCl solution and dried with $MgSO_4$. CC (100 g of silica gel, PE) afforded 1.82 g (3.48 mmol, 79%) of the disilyl ether **14** as a colorless liquid. – TLC (PE): R_f = 0.31. – $[\alpha]_D^{20}$ = –13.5 (*c* = 2.30, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 2940, 2870, 1460, 1110, 880, 675 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.94–1.06 [m, 42H, SiCH(CH_3)$_2$], 1.22–1.70 (m, 4H, 3,4-H_2), 3.42–3.46 (m, 3H, 2-H, 5-H_2), 3.60–3.69 (m, 2H, 1-H_2), 4.45 (s, 2H, OCH_2Ph), 7.20–7.29 (m, 5H, Ph). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.1, 12.7 [SiCH(CH_3)$_2$], 18.0, 18.2 [SiCH(CH_3)$_2$], 24.5, 30.9 (C-3,4), 66.9 (C-1), 71.0 (C-5), 72.7 (C-2), 72.8 (OCH_2Ph), 127.4, 128.3, 138.9 (Ph). – MS (70 eV), *m/z* (%): 115 (12), 107 (44), 92 (11), 91 (100), 85 (15), 59 (15). – $C_{30}H_{58}O_3Si_2$ (523.0): calcd. C 68.90, H 11.18; found C 68.75, H 11.26.

6) *(2S)-1,2-Bis-O-(triisopropylsilyl)pentane-1,2,5-triol* (**15**): 1.80 g (3.44 mmol) of the benzyl ether **14** was dissolved in 8 ml of MeOH and 100 mg of 10% palladium hydroxide on carbon was added to the obtained solution. Then the flask was evacuated and filled with hydrogen gas (a balloon was fixed to the apparatus to maintain a hydrogen atmosphere). The reaction mixture was stirred for 10 h. The Pd(OH)/C was removed by filtering the reaction mixture through a pad of Celite. The Celite pad was washed with 100 ml of Et_2O. After evaporation of the solvent from the filtrate CC (100 g of silica gel, PE/Et_2O, 1:1) of the residue afforded 1.20 g (2.77 mmol, 81%) of the alcohol **15** as a colorless oil. – TLC (PE/Et_2O, 1:1): R_f = 0.34. – $[\alpha]_D^{20}$ = –17.7 (*c* = 1.19, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3450 (OH), 2940, 2860, 1460, 1390 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.95–1.07 [m, 42H, SiCH(CH_3)$_2$], 1.61–1.65 (m, 4H, 3,4-H_2), 3.47–3.58 (m, 4H, 1,2,5-H, OH), 3.60–3.69 (m, 3H, 2-H, 1-H_2). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9, 12.5 [SiCH(CH_3)$_2$], 17.9, 18.0 [SiCH(CH_3)$_2$], 27.3, 30.7 (C-3,4), 63.4 (C-5), 66.1 (C-1), 72.4 (C-2). – MS (70 eV), *m/z* (%): 215 (80), 157 (67), 115 (99), 87 (75), 85 (78), 59 (100). – $C_{23}H_{52}O_3Si_2$ (432.8): calcd. C 63.82, H 12.11; found C 63.66, H 12.51.

7) *(4S)-4,5-Bis(triisopropylsilyloxy)pentanal* (**7**): To a solution of 1.10 g (2.54 mmol) of the alcohol **15** in 5 ml of CH_2Cl_2 was added 1.29 g (3.05 mmol) of the Dess Martin reagent. After 30 min at room temp. 5 ml of 1.3 N NaOH and 20 ml of Et_2O were added. The aqueous layer was extracted twice with 50 ml of Et_2O each. The combined organic layers were washed with 100 ml of a satd. aqueous NaCl solution and dried with $MgSO_4$. CC (60 g of silica gel, PE/Et_2O, 4:1) afforded 0.97 g (2.25 mmol, 89%) of the aldehyde **7** as a colorless liquid. – TLC (PE/Et_2O, 4:1): R_f = 0.42. – $[\alpha]_D^{20}$ = –18.0 (*c* = 1.00, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 2940, 2860, 1710 (C=O), 1460, 1100, 880 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.94–1.05 [m, 42H, SiCH(CH_3)$_2$], 1.85–1.97 (m, 2H, 3-H_2), 2.45–2.53 (m, 2H, 2-H_2), 3.37–3.43 (m, 1H, 5-H), 3.68 (dd, *J* = 4.7/9.7 Hz, 1H, 5-H), 3.70–3.91 (m, 1H, 4-H), 9.74 (t, *J* = 2.8 Hz, 1H, CHO). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.8, 12.1 [SiCH(CH_3)$_2$], 17.8, 17.9 [SiCH(CH_3)$_2$], 26.4 (C-3), 38.5 (C-2), 66.9 (C-5), 71.4 (C-4), 202.6 (C=O). – MS (70 eV), *m/z* (%): 213 (100), 187 (64), 157 (46), 115 (40), 87 (33), 59 (63). – $C_{23}H_{50}O_3Si_2$ (430.8): calcd. C 64.12, H 11.69; found C 64.15, H 11.50.

8) *General Procedure for the Preparation of Dialkylzinc Reagents* **9** *and the Subsequent Addition of Reagents* **9** *to the Aldehyde* **7** *Catalyzed by the Chiral Lewis Acid Prepared from Ti(iPrO)$_4$ and* **8** *or ent-***8**

8a) *Preparation of the Dialkylzinc Reagents* **9**: A 50-ml Schlenk flask equipped with an argon inlet, a septum, and a stirring bar was charged with 5 mmol of the corresponding iodide, 2.4 mg (0.3 mol-%) of CuI, and 7.5 mmol of diethylzinc. The reaction mixture was warmed to 50°C and stirred for 12 h. The flask was then connected to the vacuum line (0.1 Torr), and ethyl iodide and excess diethylzinc were distilled off (40°C, 4 h). The resulting dialkylzinc reagent (2.5 mmol) was dissolved in 1.5 ml of toluene. This solution was ready for use.

8b) *Preparation of the Catalyst for 1 mmol of Aldehyde* **7**: A 50-ml Schlenk flask equipped with an argon inlet, a septum and a stirring bar was charged with 30 mg (0.08 mmol, 8 mol%) of (1*R*,2*R*)-1,2-bis(trifluoromethanesulfonamido)cyclohexane[10], 0.5 ml of toluene, and 0.6 ml (2 mmol, 2 equiv) of titanium(IV) isopropoxide. The resulting solution was heated at 50°C for 0.5 h.

8c) *Addition of the Dialkylzinc Reagent* **9** *to the Aldehyde* **7** *with Formation of the Alcohols syn-***4** *and anti-***4**: To the catalyst solution prepared as described in 8b) was added at –40°C the solution of **9** (2.5 mmol) prepared as described in 8a). After 5 min a solution of the aldehyde (1 mmol) in 1 ml of toluene was added. The resulting solution was stirred for 12 h at –25°C. The reaction was quenched by careful addition of 2 ml of H_2O. 10% aqueous HCl was added till the pH reached 3–4. The reaction mixture was extracted three times with 50 ml of Et_2O each. The combined organic layers were washed with 100 ml of a satd. aqueous NaCl solution and dried with $MgSO_4$. CC afforded the corresponding alcohols *syn*-**4** and *anti*-**4**, respectively.

8d) *(2S,5R)-1,2-Bis-O-(triisopropylsilyl)heptane-1,2,5-triol* (*syn*-**4f**): Diethylzinc (0.60 mmol) was allowed to react according to pro-

cedure 8c) with 100 mg (0.23 mmol) of the aldehyde **7** and the chiral Lewis acid obtained from **8**. CC (PE/Et_2O, 4:1) of the crude product gave 91 mg (0.20 mmol, 86%) of the alcohol *syn*-**4f** as a colorless liquid. Only one single diastereomer (diastereoselectivity >98:2) was formed according to the NMR spectra. – TLC (PE/Et_2O, 4:1): R_f = 0.23. – $[\alpha]_D^{20}$ = −20.0 (*c* = 1.35, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3390, 2940, 2870, 1460, 880 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 6.1 Hz, 3H, 7-H_3), 0.96−1.05 [m, 42H, $SiCH(CH_3)_2$], 1.39−1.66 (m, 7H, OH, 3,4,6-H_2), 3.44−3.49 (m, 2H, 1,5-H), 3.66 (dd, *J* = 4.8/9.5 Hz, 1H, 1-H), 3.83−3.88 (m, 1H, 2-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.8 (C-7), 11.9, 12.5 [$SiCH(CH_3)_2$], 17.9, 18.2 [$SiCH(CH_3)_2$], 30.0, 30.5, 31.1 (C-3,4,6), 66.5 (C-1), 72.6, 73.5 (C-2,5). – MS (70 eV), *m/z* (%): 243 (38), 149 (100), 113 (46), 95 (45), 59 (29). – $C_{25}H_{56}O_3Si_2$ (460.9): calcd. C 65.15, H 12.25; found C 65.15, H 12.26.

8e) *(2S,5S)-1,2-Bis-O-(triisopropylsilyl)heptane-1,2,5-triol* (*anti*-**4f**): Diethylzinc (0.27 ml, 2.07 mmol) was allowed to react according to procedure 8c) with 300 mg (0.69 mmol) of the aldehyde **7** and the chiral Lewis acid obtained from *ent*-**8**. CC (PE/Et_2O, 4:1) of the crude product gave 280 mg (0.61 mmol, 88%) of the alcohol *anti*-**4f** as a colorless liquid. Only one single diastereomer (diastereoselectivity >98:2) was formed according to the NMR spectra. – TLC (PE/Et_2O, 4:1): R_f = 0.23. – $[\alpha]_D^{20}$ = −18.0 (*c* = 1.00, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3400 (OH), 2950, 2870, 1470, 880 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.4 Hz, 3H, 7-H_3), 1.00−1.06 [m, 42H, $SiCH(CH_3)_2$], 1.40−1.71 (m, 7H, OH, 3,4,6-H_2), 3.41−3.46 (m, 2H, 1,5-H), 3.67 (dd, *J* = 4.9/9.5 Hz, 1H, 1-H), 3.83−3.90 (m, 1H, 2-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.0 (C-7), 12.0, 12.6 [$SiCH(CH_3)_2$], 18.1, 18.2 [$SiCH(CH_3)_2$], 30.2, 30.6, 31.4 (C-3,4,6), 66.2 (C-1), 72.8, 73.8 (C-2,5). – $C_{25}H_{56}O_3Si_2$ (460.9): calcd. C 65.15, H 12.25; found C 65.00, H 12.20.

8f) *(2S,5R)-1,2-Bis-O-(triisopropylsilyl)decane-1,2,5-triol* (*syn*-**4g**): 0.28 ml (1.4 mmol) of dipentylzinc[15] was allowed to react according to procedure 8c) with 0.30 g (0.70 mmol) of the aldehyde **7** and the chiral Lewis acid obtained from **8**. CC (PE/Et_2O, 4:1) of the crude product gave 0.29 g (0.57 mmol, 82%) of the alcohol *syn*-**4g** as a colorless liquid. Only one single diastereomer (diastereoselectivity >98:2) was formed according to the NMR spectra. – TLC (PE/Et_2O, 4:1): R_f = 0.25. – $[\alpha]_D^{20}$ = −12.8 (*c* = 1.45, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3385, 2940, 2870, 1455, 890 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, *J* = 6.7 Hz, 3H, 10-H_3), 0.94−1.04 [m, 42H, $SiCH(CH_3)_2$], 1.19−1.67 (m, 13H, OH, 3,4,6,7,8,9-H_2), 3.46 (dd, *J* = 8.1/9.5 Hz, 1H, 1-H), 3.53−3.57 (m, 1H, 5-H), 3.66 (dd, *J* = 4.8/9.5 Hz, 1H, 1-H), 3.83−3.88 (m, 1H, 2-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.1, 12.7 [$SiCH(CH_3)_2$], 14.9 (C-10), 18.1, 18.2 [$SiCH(CH_3)_2$], 22.7, 25.4, 30.2, 31.7, 32.0, 37.4 (C-3,4,6,7,8,9), 66.5 (C-1), 72.3, 72.8 (C-2,5). – MS (70 eV), *m/z* (%): 285 (95), 155 (100), 137 (70), 115 (52), 59 (42). – $C_{28}H_{62}O_3Si_2$ (503.0): calcd. C 66.80, H 12.42; found C 66.95, H 12.30.

8g) *(2S,5S)-1,2-Bis-O-(triisopropylsilyl)decane-1,2,5-triol* (*anti*-**4g**): 0.09 ml (0.45 mmol) of dipentylzinc[15] was allowed to react according to procedure 8c) with 80 mg (0.19 mmol) of the aldehyde **7** and the chiral Lewis acid obtained from *ent*-**8**. CC (PE/Et_2O, 4:1) of the crude product gave 82 mg (0.16 mmol, 86%) of the alcohol *anti*-**4g** as a colorless liquid. Only one single diastereomer (diastereoselectivity > 98:2) was formed according to the NMR spectra. – TLC (PE/Et_2O, 4:1): R_f = 0.25. – $[\alpha]_D^{20}$ = −15.7 (*c* = 2.36, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3380 (OH), 2940, 2870, 1460, 1125, 890 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, *J* = 6.8 Hz, 3H, 10-H_3), 0.94−1.02 (m, 42H, $[SiCH(CH_3)_2]$], 1.20−1.78 (m, 12H, 3,4,6,7,8,9-H_2), 2.29 (s, 1H, OH), 3.49−3.58 (m, 2H, 1,5-H), 3.65 (dd, *J* = 5.0/9.5 Hz, 1H, 1-H), 3.86−3.90 (m, 1H, 2-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.4, 12.4 [$SiCH(CH_3)_2$], 13.8 (C-10), 17.8, 18.0 [$SiCH(CH_3)_2$], 22.5, 25.2, 30.3, 31.6, 31.8, 37.2 (C-3,4,6,7,8,9), 65.9 (C-1), 72.2, 72.5 (C-2,5). – MS (70 eV), *m/z* (%): 285 (80), 157 (90), 155 (100), 137 (76), 113 (92), 59 (85). – $C_{28}H_{62}O_3Si_2$ (503.0): calcd. C 66.80, H 12.42; found C 66.93, H 12.60.

8h) *(2S,5R)-1,2-Bis-O-(triisopropylsilyl)-8-(pivaloyloxy)octane-1,2,5-triol* (*syn*-**4h**): According to procedure 8a), the dialkylzinc compound was obtained from 1.46 g (5.40 mmol) of 3-iodopropyl pivalate[16], 3.1 mg (0.3 mol%) of CuI, and 0.81 ml (8.10 mmol) of diethylzinc. The dialkylzinc compound thus obtained was allowed to react according to procedure 8c) with 0.30 g (0.69 mmol) of the aldehyde **7** and the chiral Lewis acid obtained from **8**. CC (PE/Et_2O, 4:1) of the crude product gave 0.28 g (0.49 mmol, 71%) of the alcohol *syn*-**4h** as a colorless liquid. Only one single diastereomer (diastereoselectivity > 98:2) was formed according to the NMR spectra. – TLC (PE/Et_2O, 4:1): R_f = 0.21. – $[\alpha]_D^{20}$ = −14.0 (*c* = 1.86, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3450, 2950, 2870, 1730 (C=O), 1460, 1150, 880 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.91−1.05 [m, 42H, $SiCH(CH_3)_2$], 1.12 [s, 9H, $C(CH_3)_3$], 1.41−1.69 (m, 9H, OH, 3,4,6,7-H_2), 3.45 (dd, *J* = 8.4/9.4 Hz, 1H, 1-H), 3.54−3.58 (m, 1H, 5-H), 3.66 (dd, *J* = 4.7/9.5 Hz, 1H, 1-H), 3.82−3.87 (m, 1H, 2-H), 4.00 (t, *J* = 6.5 Hz, 2H, 8-H_2). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0, 12.6 [$SiCH(CH_3)_2$], 18.0, 18.1 [$SiCH(CH_3)_2$], 27.2 [$C(CH_3)_3$], 25.1, 30.1, 31.8, 33.7 (C-3,4,6,7), 38.6 [$C(CH_3)_3$], 64.5 (C-8), 66.5 (C-1), 71.7, 72.6 (C-2,5), 178.6 (C=O). – MS (70 eV), *m/z* (%): 287 (32), 215 (51), 130 (100), 87 (43), 57 (94). – $C_{31}H_{66}O_5Si_2$ (575.04): calcd. C 64.75, H 11.69; found C 64.50, H 11.68.

8i) *(2S,5S)-1,2-Bis-O-(triisopropylsilyl)-8-(pivaloyloxy)octane-1,2,5-triol* (*anti*-**4h**): According to procedure 8a), the dialkylzinc compound was obtained from 1.46 g (5.40 mmol) of 3-iodopropyl pivalate[16], 3.1 mg (0.3 mol%) of CuI, and 0.81 ml (8.10 mmol) of diethylzinc. The dialkylzinc compound thus obtained was allowed to react according to procedure 8c) with 0.30 g (0.69 mmol) of the aldehyde **7** and the chiral Lewis acid formed from *ent*-**8**. CC (PE/Et_2O, 4:1) of the crude product gave 0.30 g (0.52 mmol, 77%) of the alcohol *anti*-**4h** as a colorless liquid. Only one single diastereomer (diastereoselectivity > 98:2) was formed according to the NMR spectra. – TLC (PE/Et_2O, 4:1): R_f = 0.21. – $[\alpha]_D^{20}$ = −10.5 (*c* = 2.09, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3420, 2940, 2860, 1725 (C=O), 1475, 1150, 880 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.01−1.17 [m, 42H, $SiCH(CH_3)_2$], 1.17 [s, 9H, $C(CH_3)_3$], 1.44−1.81 (m, 9H, OH, 3,4,6,7-H_2), 3.50−3.56 (m, 2H, 1,5-H), 3.69 (dd, *J* = 4.8/9.5 Hz, 1H, 1-H), 3.86−3.92 (m, 1H, 2-H), 4.03 (t, *J* = 6.5 Hz, 2H, 8-H_2). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.0, 12.5 [$SiCH(CH_3)_2$], 18.0, 18.1 [$SiCH(CH_3)_2$], 27.2 [$C(CH_3)_3$], 25.0, 30.5, 31.9, 33.7 (C-3,4,6,7), 38.6 [$C(CH_3)_3$], 64.5 (C-8), 65.9 (C-1), 71.8, 72.5 (C-2,5), 178.6 (C=O). – $C_{31}H_{66}O_5Si_2$ (575.0): calcd. C 64.75, H 11.69; found C 64.70, H 11.53.

8j) *(2S,5R)-1,2-Bis-O-(triisopropylsilyl)-10-(pivaloyloxy)decan-1,2,5-triol* (*syn*-**4i**): According to procedure 8a) the dialkylzinc compound was obtained from 1.46 g (5.40 mmol) of 3-iodopentyl pivalate[17], 3.1 mg (0.3 mol%) of CuI, and 0.81 ml (8.10 mmol) of diethylzinc. The dialkylzinc compound thus obtained was allowed to react according to procedure 8c) with 100 mg (0.23 mmol) of the aldehyde **7** and the chiral Lewis acid generated from **8**. CC (PE/Et_2O, 4:1) of the crude product gave 83 mg (0.14 mmol, 59%) of the alcohol *syn*-**4i** as a colorless liquid. According to the NMR spectra the ratio of *syn*-**4i**/*anti*-**4i** was 94:6. – TLC (PE/Et_2O, 4:1): R_f = 0.27. – $[\alpha]_D^{20}$ = −13.5 (*c* = 1.35, $CHCl_3$). – IR (neat): $\tilde{\nu}$ =

3440, 2940, 2870, 1725 (C=O), 1460, 1290, 880 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.98–1.00 [m, 42H, $SiCH(CH_3)_2$], 1.19 [s, 9H, $C(CH_3)_3$], 1.34–1.66 (m, 12H, OH, 3,4,6,7,8,9-H_2), 1.70 (s, 1H, OH), 3.42–3.54 (m, 2H, 1,5-H), 3.65 (dd, *J* = 4.8/9.5 Hz, 1H, 1-H), 3.82–3.86 (m, 1H, 2-H), 3.98 (t, *J* = 6.6 Hz, 2H, 10-H_2). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.9, 12.6 [$SiCH(CH_3)_2$], 18.0, 18.1 [$SiCH(CH_3)_2$], 27.2 [$C(CH_3)_3$], 25.4, 26.0, 28.6, 30.0, 31.7, 37.3, 38.8 [C-3,4,6,7,8,9, $C(CH_3)_3$], 64.4 (C-10), 66.5 (C-1), 72.2, 72.7 (C-2,5), 178.5 (C=O). – MS (70 eV), *m/z* (%): 215 (42), 135 (100), 115 (48), 85 (42), 59 (41), 57 (56). – $C_{33}H_{70}O_5Si_2$ (603.1): calcd. C 65.73, H 11.70; found C 65.62, H 11.90.

8k) *(2S,5S)-1,2-Bis-O-(triisopropylsilyl)-10-(pivaloyloxy)decan-1,2,5-triol* (*anti*-**4i**): According to procedure 8a) the dialkylzinc compound was prepared from 1.23 g (4.14 mmol) of 5-iodopentyl pivalate[17], 2.4 mg (0.3 mol%) of CuI, and 0.62 ml (6.21 mmol) of diethylzinc. The dialkylzinc compound thus obtained was allowed to react according to procedure 8c) with 300 mg (0.69 mmol) of the aldehyde **7** and the chiral Lewis acid generated from *ent*-**8**. CC (PE/Et_2O, 4:1) of the crude product gave 250 mg (0.41 mmol, 61%) of the alcohol *anti*-**4i** as a colorless liquid. According to the NMR spectra the ratio (*anti*-**4i**/*syn*-**4i**) was 95:5. – TLC (PE/Et_2O, 4:1): R_f = 0.27. – $[\alpha]_D^{20}$ = –17.1 (*c* = 2.45, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3480 (OH), 2940, 2870, 1730 (C=O), 1570, 1280, 880 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.97–1.07 [m, 42H, $SiCH(CH_3)_2$], 1.19 [s, 9H, $C(CH_3)_3$], 1.30–1.69 (m, 12H, 3,4,6,7,8,9-H_2), 2.36 (s, 1H, OH), 3.48–3.54 (m, 2H, 1,5-H), 3.65 (dd, *J* = 4.9/9.9 Hz, 1H, 1-H), 3.88–3.89 (m, 1H, 2-H), 3.98 (t, *J* = 6.6 Hz, 2H, 10-H_2). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.8, 12.2 [$SiCH(CH_3)_2$], 17.8, 18.0 [$SiCH(CH_3)_2$], 27.2 [$C(CH_3)_2$], 25.3, 25.9, 28.5, 30.4, 31.8, 33.2, 38.6 [C-3,4,6,7,8,9 $C(CH_3)_2$], 64.2 (C-10), 65.8 (C-1), 71.9, 72.4 (C-2,5), 178.5 (C=O). – MS (70 eV), *m/z* (%): 215 (54), 135 (100), 115 (52), 85 (52), 59 (47), 57 (75). – $C_{33}H_{70}O_5Si_2$ (603.1): calcd. C 65.73, H 11.70; found C 65.81, H 11.67.

9) *(2'S,5'S)-(5-Ethyltetrahydrofuran-2-yl)methanol* (**16**): 1.25 g (6.59 mmol) of *p*-tosyl chloride was added at 0°C to a solution of 162 mg (0.870 mmol) of the alcohol *syn*-**4b** in 10 ml of pyridine. After 48 h at 0°C the solvent was evaporated and the remaining residue purified by CC (PE/*t*BuOMe, 10:1 → 1:1) to afford 252 mg of the corresponding tosylate, which was redissolved in 20 ml of MeOH. 20 mg (0.1 mmol) of *p*-toluenesulfonic acid was added to the obtained solution. After 3 h at room temp. the solvent was evaporated and the remaining residue redissolved in 20 ml of THF. 127 mg (4.23 mmol) of NaH (80% in mineral oil) was added to the resulting solution. The reaction mixture was stirred at room temp. for 3 h. Then 20 ml of a satd. aqueous NH_4Cl solution was added. The aqueous layer was extracted three times with 30 ml of *t*BuOMe each, and the combined organic layers were dried with $MgSO_4$. CC (20 g of silica gel, PE/*t*BuOMe, 1:1) afforded 59 mg (0.452 mmol, 52%) of the *cis*-tetrahydrofuran alcohol **16** as a colorless liquid. – TLC (PE/AcOEt, 1:1): R_f = 0.48. – $[\alpha]_D^{20}$ = +3.4 (*c* = 1.64, $CHCl_3$). – ^1H NMR (500 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.5 Hz, 3H, 2''-H_3), 1.40–1.51 (m, 2H), 1.55–1.67 (m, 2H) and 1.82–1.96 (m, 2H, 3',4',1''-H_2), 2.05 (s, 1H, OH), 3.43 (dd, *J* = 5.7/11.5 Hz, 1H, 1-H), 3.65 (dd, *J* = 3.3/11.5 Hz, 1H, 1-H), 3.75–3.80 (m, 1H, 5'-H), 3.94–4.00 (m, 1H, 2'-H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 10.3 (C-2''), 27.6, 28.6, 30.9 (C-3',4',1''), 65.3 (C-1), 79.2 (C-2'), 81.4 (C-5'). – $C_7H_{14}O_2$ (130.2): calcd. C 64.58, H 10.84; found C 64.42, H 10.92.

10) *(2'S,5'S)-(5-Pentyltetrahydrofuran-2-yl)methanol* (**17**): 1.26 g (6.59 mmol) of *p*-tosyl chloride was added at 0°C to a solution of 152 mg (0.659 mmol) of the alcohol *syn*-**4c** in 10 ml of pyridine. After 48 h at 0°C the solvent was evaporated and the remaining residue purified by CC (PE/*t*BuOMe, 10:1 → 1:1) to furnish 238 mg of the corresponding tosylate, which was redissolved in 10 ml of MeOH. 20 mg (0.1 mmol) of *p*-toluenesulfonic acid was added to the obtained solution. After 2 h at room temp. the solvent was evaporated and the remaining residue redissolved in 10 ml of THF. 102 mg (3.50 mmol) of NaH (80% in mineral oil) was added to the resulting solution. The reaction mixture was stirred at room temp. for 5 h. Then 40 ml of a satd. aqueous NH_4Cl solution was added. The aqueous layer was extracted three times with 30 ml of *t*BuOMe each, and the combined organic layers were dried with $MgSO_4$. CC (30 g of silica gel, PE/*t*BuOMe, 1:1) afforded 100 mg (0.580 mmol, 88%) of the *cis*-tetrahydrofuran alcohol **17** as a colorless liquid. – TLC (PE/AcOEt, 1:1): R_f = 0.33. – $[\alpha]_D^{20}$ = +6.2 (*c* = 0.435, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3433 (OH), 2929, 2860, 1462, 1378, 1044, 949, 883 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, *J* = 7.0 Hz, 3H, 5''-H_3), 1.20–1.98 (m, 12H, 1'',2'',3'',4'',3',4'-H_2), 2.20 (s, 1H, OH), 3.44 (dd, *J* = 5.4/11.2 Hz, 1H, 1-H), 3.64 (dd, *J* = 2.8/11.2 Hz, 1H, 1-H), 3.78–3.83 (m, 1H, 5'-H), 3.92–3.95 (m, 1H, 2'-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (C-5''), 22.6 (C-4''), 25.9, 27.0, 31.3, 31.9, 35.8 (C-3',4',1'',2'',3''), 65.2 (C-1), 78.9 (C-2'), 79.5 (C-5'). – $C_{10}H_{20}O_2$ (172.3): calcd. C 69.73, H 11.70; found C 69.46, H 11.96.

11) *(2'S,5'R)-(5-Pentyltetrahydrofuran-2-yl)methanol* (**18**): 1.14 g (6.00 mmol) of *p*-tosyl chloride was added at 0°C to a solution of 280 mg (0.557 mmol) of the alcohol *anti*-**4g** in 10 ml of pyridine. After 48 h at 0°C the solvent was evaporated and the remaining residue purified by CC (PE/*t*BuOMe, 20:1) to furnish 342 mg of the corresponding tosylate, which was redissolved in 5 ml of THF. 2.0 ml of a 1 M nBu_4NF solution in THF was added to the obtained solution. After 4 h at room temp. 100 mg (3.34 mmol) of NaH (80% in mineral oil) was added to the reaction mixture, which was stirred for 5 h. 40 ml of a satd. aqueous NH_4Cl solution was added. The aqueous layer was extracted three times with 30 ml of CH_2Cl_2 each, and the combined organic layers were dried with $MgSO_4$. CC (40 g of silica gel, Et_2O) afforded 73 mg (0.423 mmol, 76%) of the *trans*-tetrahydrofuran alcohol **18** as a colorless liquid. – TLC (PE/AcOEt, 1:1): R_f = 0.46. – $[\alpha]_D^{20}$ = +15.0 (*c* = 1.00, $CHCl_3$). – ^1H NMR (500 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.5 Hz, 3H, 5''-H_3), 1.23–2.03 (m, 12H, 3',4',1'',2'',3'',4''-H_2), 2.05 (s, 1H, OH), 3.47 (dd, *J* = 6.3/11.5 Hz, 1H, 1-H), 3.60 (dd, *J* = 3.3/11.5 Hz, 1H, 1-H), 3.90–3.94 (m, 1H, 5'-H), 4.08–4.10 (m, 1H, 2'-H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0 (C-5''), 22.6 (C-4''), 25.9, 27.5, 31.9, 32.0, 35.7 (C-3',4',1'',2'',3''), 65.1 (C-1), 78.8 (C-2'), 79.5 (C-5'). – $C_{10}H_{20}O_2$ (172.3): calcd. C 69.73, H 11.70; found C 69.56, H 11.61.

12) *(2'S,5'S)-5-[5-(Hydroxymethyl)tetrahydrofuran-2-yl]pentyl Pivalate* (**19**): 644 mg (3.38 mmol) of *p*-tosyl chloride was added at 0°C to a solution of 112 mg (0.338 mmol) of the alcohol *syn*-**4e** in 5 ml of pyridine. After 12 h at room temp. the solvent was evaporated and the remaining residue purified by CC (PE/*t*BuOMe, 10:1 → 1:1) to afford 130 mg of the corresponding tosylate, which was redissolved in 20 ml of MeOH. 20 mg (0.1 mmol) of *p*-toluenesulfonic acid was added to the obtained solution. After 3 h at room temp. the solvent was evaporated, the remaining residue was redissolved in 50 ml of PE/*t*BuOMe (1:1) and the solution filtered through a silica gel pad (10 g). The filtrate was concentrated in vacuo to yield the corresponding dihydroxy tosylate. This was dissolved in 20 ml of THF, and 21 mg (0.70 mmol) of NaH (80% in mineral oil) was added to the obtained solution. The reaction mixture was warmed to 35°C for 3 h. Then 20 ml of a satd. aqueous

NH_4Cl solution was added. The aqueous layer was extracted twice with 30 ml of CH_2Cl_2 each, and the combined organic layers were dried with $MgSO_4$. CC (30 g of silica gel, PE/*t*BuOMe, 1:1) afforded 65 mg (0.237 mmol, 70%) of the *cis*-tetrahydrofuran alcohol **19** as a colorless liquid. – TLC (PE/AcOEt, 1:1): R_f = 0.60. – $[\alpha]_D^{20}$ = +8.1 (c = 0.89, $CHCl_3$). – ^1H NMR (500 MHz, $CDCl_3$): δ = 1.16 [s, 9H, $C(CH_3)_3$], 1.19–1.80 (m, 10H) and 1.82–2.04 (m, 3H, OH, 2,3,4,5,3′,4′-H_2), 3.44 (dd, J = 5.6/11.4 Hz, 1H, 1″-H), 3.66 (dd, J = 3.3/11.4 Hz, 1H, 1″-H), 3.82–3.84 (m, 1H, 2′-H), 3.95–3.97 (m, 1H, 5′-H), 4.01 (t, J = 6.6 Hz, 2H, 1-H_2). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 25.8, 25.9, 27.0, 28.6, 31.4, 35.7 (C-2,3,4,5,3′,4′), 27.2 [$C(CH_3)_3$], 38.3 [$C(CH_3)_3$], 64.3 (C-1), 65.1 (C-1″), 79.2 (C-5′), 80.0 (C-2′). – $C_{15}H_{28}O_4$ (272.4): calcd. C 66.15, H 10.36; found C 66.25, H 10.33.

13) *(2′R,5′S)-5-[5-(Hydroxymethyl)tetrahydrofuran-2-yl)propyl Pivalate* (**20**): 500 mg (2.62 mmol) of *p*-tosyl chloride was added at 0 °C to a solution of 207 mg (0.36 mmol) of the alcohol *anti*-**4h** in 5 ml of pyridine. After 12 h at room temp. the solvent was evaporated and the remaining residue purified by CC (PE/*t*BuOMe, 10:1 → 1:1) yielding 107 mg of the corresponding tosylate, which was redissolved in 10 ml of a 5% aqueous HF solution in CH_3CN. After 12 h at room temp. the reaction mixture was partitioned between 50 ml of a satd. aqueous $NaHCO_3$ solution and 100 ml of *t*BuOMe. The aqueous layer was extracted twice with 30 ml of *t*BuOMe each, and the combined organic layers were dried with $MgSO_4$. CC (10 g of silica gel, *t*BuOMe) afforded 34 mg (0.140 mmol, 39%) of the *trans*-tetrahydrofuran alcohol **20** as a colorless oil. – TLC (PE/*t*BuOMe, 1:1): R_f = 0.60. – $[\alpha]_D^{20}$ = +6.1 (c = 0.62, $CHCl_3$). – ^1H NMR (400 MHz, $CDCl_3$): δ = 1.17 [s, 9H, $C(CH_3)_3$], 1.45–2.04 (m, 9H, OH, 2,3,3′,4′-H_2), 3.48 (dd, J = 6.3/11.5 Hz, 1H, 1″-H), 3.60 (dd, J = 3.2/11.5 Hz, 1H, 1″-H), 3.93–3.95 (m, 1H, 2′-H), 4.04–4.13 (m, 1H, 5′-H), 4.06 (t, J = 6.5 Hz, 2H, 1-H_2). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 25.5, 27.5, 32.0, 32.1 (C-2,3,3′,4′), 27.2 [$C(CH_3)_3$], 38.7 [$C(CH_3)_3$], 64.2 (C-1), 65.0 (C-1″), 78.8, 78.9 (C-2′,5′). – $C_{13}H_{24}O_4$ (244.3): calcd. C 63.90, H 9.90; found C 63.62, H 10.04.

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