Stereoselective Additions of Chiral, Functionalized Organozinc Reagents to Achiral and Chiral Aldehydes: a Matched-Mismatched Case in Organozinc Chemistry

Ulrich Koert*, Holger Wagner, and Ulrich Pidun

Fachbereich Chemie der Universität Marburg,
D-35032 Marburg/Lahn, Germany

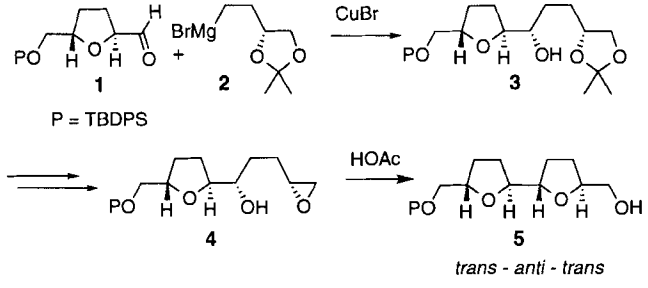
Received February 8, 1994

Key Words: Addition, stereoselective, nonchelation-controlled / Reagent, organozinc / Stereodifferentiation, double / Oligo(tetrahydrofuran)

The additions of the enantiomerically pure organozinc reagents **17** and **33** to the THF-aldehyde **1** in the presence of the monodentate Lewis acid boron trifluoride–ether give the nonchelation-controlled addition products **7** and **36**, respectively (stereoselectivity 95:5, 86:14). These results provide a route to oligo(tetrahydrofuran)s with the relative stereochemistry *trans-syn-cis*. A stereodirecting effect of the chiral center in the organozinc reagent **17** is found, leading to simple diastereoselectivies in the reaction with achiral aldehydes and to a matched-mismatched case in the reaction with the chiral aldehyde **1**.

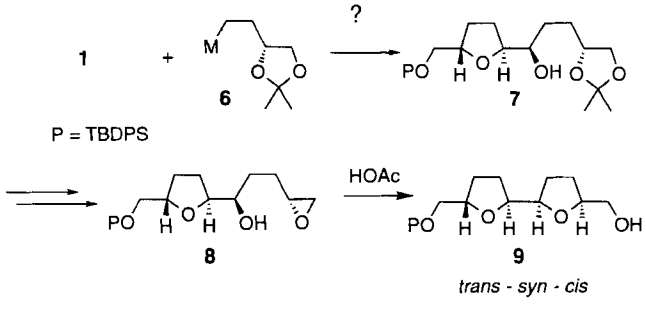
During our studies directed to the stereoselective synthesis of natural[1] and non-natural[2] oligo(tetrahydrofuran)s (oligo-THFs) we used a chelation-controlled Grignard reaction as a synthetic route to THF dimers and trimers with the relative configuration *trans-anti-trans*[3]. Cu(I)-catalyzed addition of the enantiomerically pure Grignard reagent **2** to the THF-aldehyde **1** gave the alcohol **3** with a stereoselectivity of 93:7. The acetonide functionality of **3** was stereoselectively transformed into the epoxide function of the alcohol **4**. An intramolecular epoxide opening was used to close the new THF ring, thus providing the THF dimer **5** (relative configuration: *trans-anti-trans*).

Scheme 1



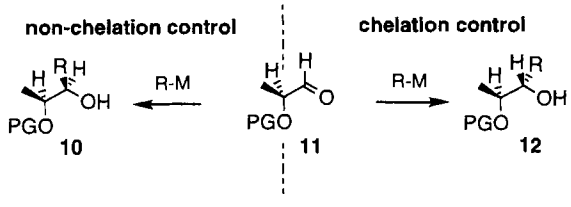
In order to realize a stereoselective synthesis of oligo-THFs with the relative configuration *trans-syn-cis*, it would be very efficient to use the same route as in Scheme 1, but a nonchelation-controlled addition step instead of the chelation-controlled one. This suggests the use of another organometallic reagent as the Grignard compound, i.e. we wanted to control the stereochemical outcome of the addition reaction by metal tuning. In this way the new organometallic reagent **6** should add to the THF-aldehyde **1** to give an acetonide alcohol **7**. Transformation of the acetonide into the epoxide **8** and intramolecular ring closure would provide access to a THF dimer **9** with the relative configuration *trans-syn-cis*.

Scheme 2



Which metal is the right one, to achieve nonchelation-control in this particular situation? In this paper we report on synthetic studies to answer this question. The choice of the metal has to be based on the knowledge[4] of stereoselective additions of organometallic reagents R–M to chiral α-alkoxy aldehydes of type **11**, leading to the *anti* product **12** via a chelation-controlled pathway and to the *syn* product **10** via a nonchelation-controlled pathway.

Scheme 3



Introduced by Cram[5], chelation control was a transition-state concept in its beginning. Nowadays, it is exper-

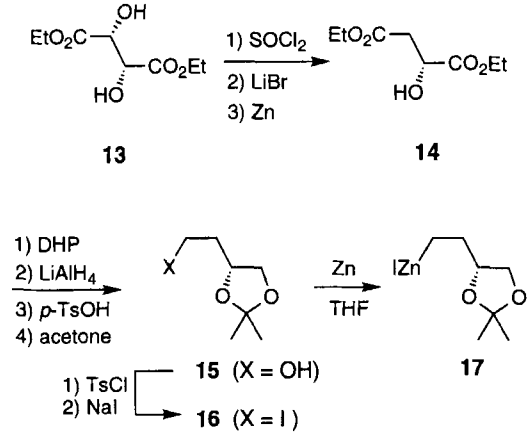
  0009–2940/94/0808–1447 $ 10.00+.25/0

imentally supported by kinetic[6a], NMR[6b], and X-ray data[6c]. Chelation control occurs if the metal M is a strong bidentate Lewis acid (Mg) or if a strong bidentate Lewis acid is additionally present (e.g. $TiCl_4$)[4]. These observations correspond to our results, whereby the use of the Grignard reagent resulted in chelation control as described in Scheme 1. Nonchelation-control has been reported to be achieved with weakly Lewis-acidic reagents [e.g. $R-Ti(OR)_3$][7]. In our case preliminary tests using organotitanium reagents were unsuccessfull. Looking for other organometallic reagents with a reactivity low enough to avoid bidentate Lewis acidic behavior, we focused on organozinc reagents. We hoped that in the organozinc case, the known[8] low reactivity of the organozinc compound might be overcome by the use of an additional monodentate Lewis acid, e.g. boron trifluoride–ether ($BF_3 \cdot OEt_2$), to activate the aldehyde. This idea was supported by the finding[9] that the addition of organozinc reagents to simple aliphatic aldehydes can be accelerated by $BF_3 \cdot OEt_2$[10]. For these reasons, the preparation of the enantiomerically pure organozinc reagent **17** was undertaken.

Preparation of the Enantiomerically Pure Organozinc Reagents 17 and *ent*-17

The enantiomerically pure organozinc reagents **17** and *ent*-**17** were prepared by starting from (+)-diethyl L-tartrate (**13**) and (−)-diethyl L-malate (*ent*-**14**), respectively.

Scheme 4



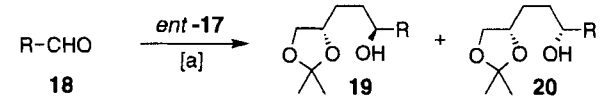
According to Gao's procedure[11], (+)-diethyl L-tartrate (**13**) was converted into (+)-diethyl D-malate (**14**) in an overall yield of 55%. Next, we focused on the conversion of **14** into the acetonide alcohol **15**. While direct reduction of **14** with $LiAlH_4$ gave a very low yield – obviously due to workup problems in connection with the very hydrophilic triol intermediate –, a four-step sequence including a protection/deprotection step was preferred. DHP protection[12a], $LiAlH_4$ reduction, THP deprotection, and acetonide formation[12b] succeeded in an overall yield of 69%. Tosylation of the alcohol **15** and subsequent treatment of the tosylate with NaI in acetone provided the acetonide iodide **16** (62%). The corresponding acetonide iodide *ent*-**16**[13] was synthesized by an analogous route starting from (−)-diethyl L-malate (*ent*-**14**).

The iodides **16** and *ent*-**16** were converted into the corresponding organozinc reagents **17** and *ent*-**17** by treatment with activated zinc powder in THF at 45–50°C. Activated zinc powder was prepared by Knochel's method[14] with 1,2-dibromoethane and chlorotrimethylsilane. The yields of the organozinc reagents were estimated by GC analysis[14] to be 80–85%. Compounds **17** and *ent*-**17** could be isolated as white solids and characterized by NMR spectroscopy [^1H NMR (500 MHz), [D$_6$]DMSO: δ = −0.29 to −0.24 (m, 2H, CH_2Zn); CD_2Cl_2: δ = 0.30 (bs, 1H, CH_2Zn), 0.60 (bs, 1H, CH_2Zn); ^{13}C NMR (125 MHz), [D$_6$]DMSO: δ = 5.33 (C–Zn); CD_2Cl_2: δ = 8.09 (C–Zn)]. The solid organozinc reagents were redissolved in CH_2Cl_2 for reactions with aldehydes.

Reaction of the Organozinc Reagents with Achiral Aldehydes

In order to evaluate the reactivity of the organozinc reagents **17** and *ent*-**17**, their reactions with achiral aldehydes were investigated first. For the reasons discussed above, $BF_3 \cdot OEt_2$ (2–3 equiv.) was added as a monodentate Lewis acid. CH_2Cl_2 was found to be the solvent of choice, while THF gave poorer results. Table 1 summarizes the results of the reactions of the organozinc reagent *ent*-**17** with different achiral aldehydes **18** to give the two epimeric alcohols **19** and **20**.

Table 1. Reactions of the organozinc reagent *ent*-**17** with achiral aldehydes



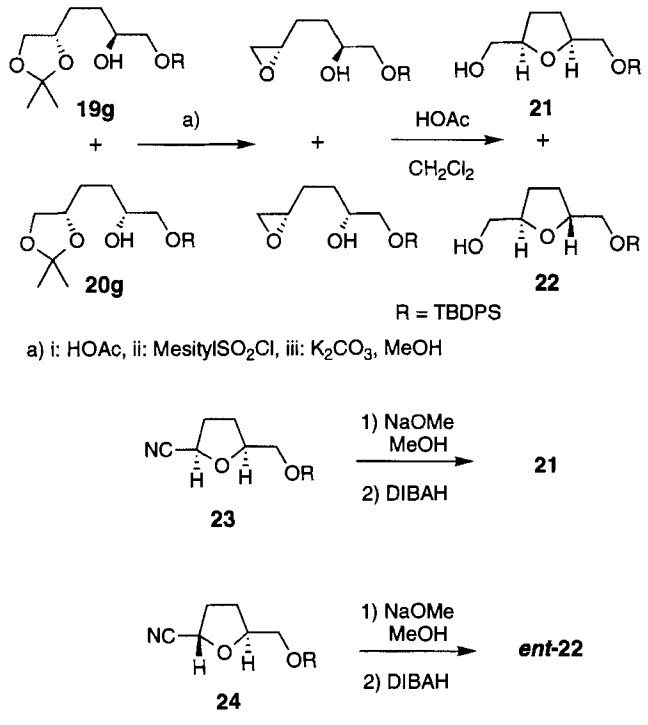
	R	yield (%)	19 : 20[b]
a	Ethyl	56	73 : 27
b	*n*-Propyl	76	69 : 31
c	Isopropyl	56	76 : 24
d	Phenyl	96	76 : 24
e	Thiophen-3-yl	92	77 : 23
f	Crotyl	51	71 : 29
g	$TBDPSOCH_2$	58	85 : 15

[a] $BF_3 \cdot OEt_2$, CH_2Cl_2, −30 to 0°C, 3 h, 0°C. – [b] Ratios determined by HPLC and NMR.

Noteworthy is the stereoselective outcome of these reactions. The chiral center of the organozinc reagent controls to some extent the relative configuration of the new chiral center. The selectivities observed were normally in the range of 75:25. Only in the case of the bulky aldehyde **18g** a higher selectivity of 85:15 was obtained. For the structural assignments of the two epimeric products **19** and **20**, the epimeric mixture of the two alcohols **19g** and **20g** was

transformed into the two epimeric tetrahydrofuran alcohols **21** and **22**.

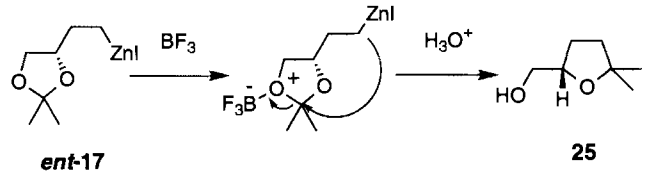
Scheme 5



The two tetrahydrofuran alcohols **21** and *ent*-**22** were synthesized independently from the two tetrahydrofurancarbonitriles **23** and **24**. Based on an X-ray structural analysis of the *cis* nitrile **23**[3], the relative configurations of the tetrahydrofuran alcohols **21** and **22** were assigned. By a comparison of NMR data, the major isomer from the organozinc route was shown to be the *cis* alcohol **21**.

While the yields for the reactions of aromatic aldehydes with the organozinc reagent *ent*-**17** were over 90%, the reactions of aliphatic aldehydes gave only yields of 50–60% of the corresponding products. Closer inspection of the reaction mixture led to the isolation and characterization of a side product, the tetrahydrofuran alcohol **25**. The formation of **25** can be rationalized by a Lewis acid-assisted, intramolecular attack of the organozinc functionality on the acetonide group.

Scheme 6

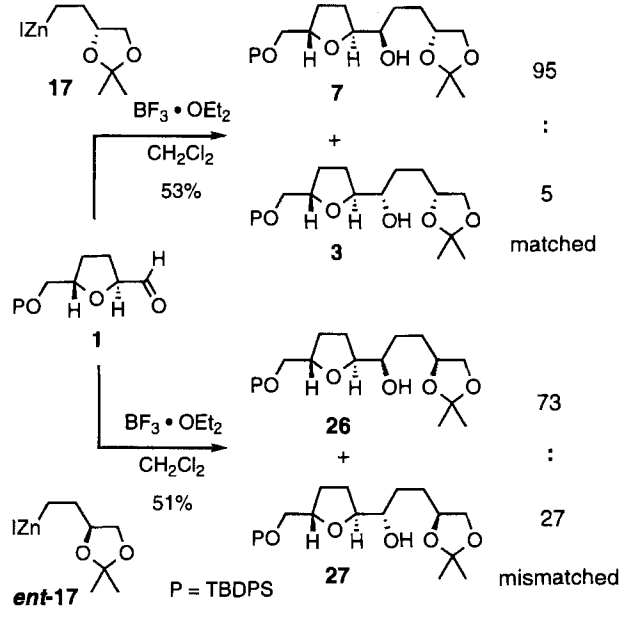


To support this mechanistic view, the organozinc reagent was allowed to react with $TiCl_4$ in the absence of any aldehyde. Under these conditions the tetrahydrofuran alcohol **25** was isolated in 55% yield.

Reaction of the Organozinc Reagents with the Chiral THF-Aldehyde 1

Having worked out experimental conditions for the addition of the organozinc reagents to achiral aldehydes, we focused our attention on the reaction with the chiral THF-aldehyde **1**. Reaction of **17** with the aldehyde **1** afforded the nonchelation product **7** with 95:5 stereoselectivity.

Scheme 7



In contrast, the same reaction with the enantiomeric reagent *ent*-**17** gave only a moderate selectivity (73:27) towards the nonchelation product **26**. This illustrates a case of double stereodifferentiation[15] in organozinc chemistry. Two directing effects determine the stereochemical outcome of this reaction: The stereocenter in the organozinc reagent and the stereocenter in the α-alkoxy aldehyde. In the reaction of the organozinc reagents **17** and *ent*-**17** with the THF-aldehyde **1** the influence of the aldehyde stereocenter dominates the influence of the organozinc stereocenter. The net result is a nonchelation-controlled addition. This example presents, to our knowledge, the first case of a matched-mismatched pair in organozinc chemistry.

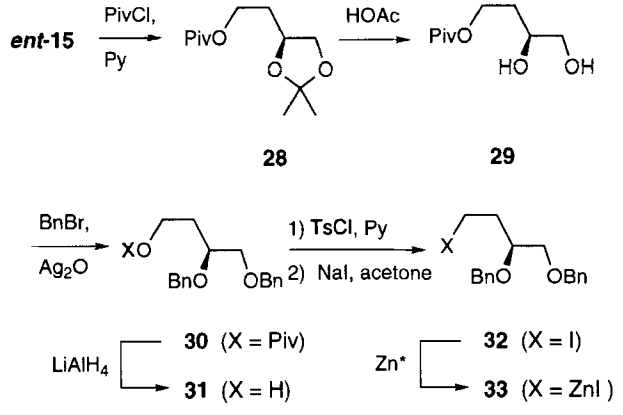
While the selectivities observed were quite satisfactory, the yields of the adducts were only in the range of 50%, while unreacted THF-aldehyde **1** could be recovered in 45% yield. This indicates that the organozinc reagent is partially consumed by the transformation to the tetrahydrofuran alcohol **25**. Indeed, compound **25** was always formed in these reactions as a byproduct.

Changing the Protective Group: How to Avoid the Intramolecular Side Reaction

The intramolecular attack of the organozinc functionality on the acetonide moiety (Scheme 6) gave rise to the formation of byproduct **25**. Thus, an only moderate yield in the additions to aliphatic aldehydes was the price to pay for the acetonide group. While the acetonide func-

tionality was only used as a diol-protecting group, we looked for a more suitable protecting group. The benzyl ether group seemed promising. Therefore, we synthesized the enantiomerically pure bis(benzyloxy) iodide **32** starting from the acetonide alcohol *ent*-**15**.

Scheme 8



Pivaloylation (80%) followed by acidic acetonide cleavage (73%) gave the diol **29**. Dibenzylation of **29** to **30** was successfully achieved by using the silver oxide modification (78%)[16]. The standard procedure with NaH as a base gave low yields due to the formation of side products resulting from transesterification reactions. Reductive ester cleavage (97%) of the bis(benzyloxy) pivalate **30** afforded the bis(benzyloxy) alcohol **31**, which was tosylated and transformed into the iodide **32** by reaction with NaI in acetone (74%). From **32**, the corresponding organozinc reagent **33** was prepared as described above by using activated zinc powder.

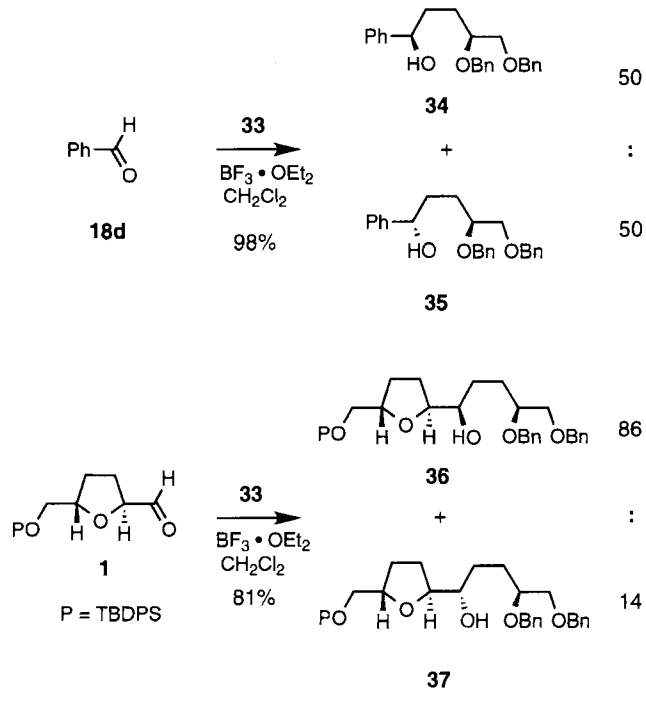
Reaction of the organozinc reagent **33** with benzaldehyde (**18d**) gave the two epimeric alcohols **34** and **35** as an epimeric mixture in 98% yield.

In this example no side product resulting from an intramolecular side reaction of the organozinc compound was observed. No stereodirecting effect of the organozinc reagent was found. The two alcohols **34** and **35** were formed in a 1:1 ratio.

Reaction of the organozinc reagent **33** with the THF-aldehyde **1** gave the two epimeric alcohols **36** and **37** in 81% yield. The stereoselectivity of the reaction was 86:14 in favor of the nonchelation product **36**. This 86:14 selectivity lies between the matched (95:5) and the mismatched (73:27) case, observed with the acetonide zinc reagents **17** and *ent*-**17**. Replacement of the acetonide zinc reagent **17** by the bis(benzyloxy)zinc reagent **33** led to disappearence of the stereodirecting effect. The existence of the cyclic acetonide function seems to be essential for the double stereodifferentiation.

In summary, a high degree of nonchelation control has been achieved in the $BF_3 \cdot OEt_2$-catalyzed additions of functionalized organozinc reagents **17** and **33** to the THF-aldehyde **1**. This provides a stereoselective route to oligo(tetrahydrofuran)s with the relative configuration *cis-syn-trans*. The non-chelation-controlled route via the organozinc reagent presented in this paper is complementary to the route via the Cu(I)-catalyzed Grignard reagent[3], which leads to the chelation-controlled product. Noteworthy is the stereodirecting effect of the acetonide organozinc reagents **17** and *ent*-**17** leading to moderate and simple diastereoselectivities in the addition to achiral aldehydes and to a matched-mismatched case in the addition to the chiral THF-aldehyde **1**.

Scheme 9



Financial support by the *Deutsche Forschungsgemeinschaft* (SFB 260) is gratefully acknowledged. We thank the *BASF AG* and the *Wacker AG* for gifts of chemicals.

Experimental

All temperatures quoted are not corrected. – 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 irridiation and/or heatgun treatment with 5% phosphomolybdic acid in ethanol. – Analytical gas chromatography (GC). Hewlett-Packard (5890, series II) with a 5 m × 0.53 mm quartz capillary column with methylpolysiloxane Hewlett-Packard 1, neat thickness: 2.65 mm, 13 kP He. – 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 Buker IFS 88. – NMR: Bruker AT 200, AC-300, WH 400, AMX-500. – Column chromatography (CC): Merck silica gel 60 (70–200 mesh ASTM). – Dry solvents: 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; diethyl ether 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 dis-

tilled from sodium/benzophenone. – Boiling range of petroleum ether: 40–60°C.

1) *(+)-Diethyl D-Malate* (**14**): A 500-ml three-necked flask was charged with 206 g (1.00 mol) of (+)-diethyl L-tartrate (**13**). To this was added with ice cooling and magnetic stirring 81.0 ml (132 g, 1.10 mol) of thionyl chloride. Then 1.0 ml (13 mmol) of dry DMF was added. The cooling bath was removed. Upon warming to room temp., vigorous HCl evolution started. The HCl was swept away by a steady stream of nitrogen. After 1 h the reaction mixture was warmed to 45–50°C. It was kept at this temp. for 2 h. At this stage, the gas evolution ceased indicating complete turnover of the starting material. The cyclic sulfite was purified by vacuum distillation (b.p. 130–135°C/0.5 Torr) to yield 250 g of a colourless liquid, which was dissolved in 700 ml of dry acetone. At 0°C 113 g (1.30 mol) of anhydrous lithium bromide was added. The reaction mixture was stirred for 12 h at 45–50°C. It was then cooled to 0°C, and 131 g (2.00 mol) of Zn (activated by washing zinc dust with 10% aqueous HCl and drying for 30 min at 0.5 Torr) was added. With great caution, 700 ml of water was added in 35-ml portions during 2 h. A vigorous exothermic reaction occurred. The reaction mixture was stirred for 3 h at 50°C to complete the reduction. It was then cooled to 0°C and filtered through Celite. The Celite plug was washed successively with 100 ml of water and 100 ml of ethyl acetate. The filtrate was acidified with conc. HCl to pH 2–3. It was concentrated in vacuo to remove most of the acetone. The remaining solution was extracted three times with 400 ml of ethyl acetate each. The combined organic layers were washed with satd. aqueous NaCl solution and dried with $MgSO_4$. Evaporation of the solvent and fractional distillation (b.p. 86°C/0.5 Torr) of the residue afforded 105 g (0.55 mol, 55%) of **14** as a colorless liquid. – TLC (petroleum ether/diethyl ether, 2:1):– R_f = 0.11. – $[\alpha]_D^{20}$ = +10.5 (*c* = 2.93, EtOH). – IR (neat): $\tilde{\nu}$ = 3437 (OH), 2966, 2929, 1444, 1034 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.15–1.24 (m, 6H, CH_3), 2.65–2.81 (m, 2H, 3-H_2), 3.36 (br. s, 1H, OH), 4.05–4.22 (m, 4H, OCH_2CH_3), 4.41 (t, *J* = 5.4 Hz, 1H, 2-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8, 13.9 (CH_3), 38.6 (C-3), 60.7, 61.7 (OCH_2), 67.2 (C-2), 170.3, 173.2 (C-1,4); cf. data in ref.[17].

2) *(2R)-1,2-O-Isopropylidenebutane-1,2,4-triol* (**15**): To a magnetically stirred solution of 80.0 g (421 mmol) of (+)-diethyl D-malate (**14**) in 500 ml of CH_2Cl_2 was added 70.0 ml (767 mmol) of dihydropyran. After addition of 300 mg (1.58 mmol) of *p*-toluenesulfonic acid an exothermic reaction started which was controlled by occasional ice cooling. The reaction mixture was stirred for 2 h at room temp. to complete the reaction. Then 1.12 g (10.0 mmol) of K_2CO_3 was added, and the reaction mixture was stirred for 30 min. The solvent was evaporated in vacuo. Two portions of 200 ml of toluene each were added to the residue, and the mixture was concentrated each time to remove excess dihydropyran. The remaining residue was dissolved in 120 ml of THF and the solution added dropwise during 2 h to an ice-cooled suspension of 35.0 g (922 mmol) of $LiAlH_4$ in 500 ml of THF. The reaction mixture was refluxed for 12 h. After cooling to 0°C, 40 ml of water was added dropwise with great caution. Subsequently, 50 ml of 3 N NaOH and 50 ml of water were added successively. The resulting mixture was refluxed for 2 h, whereupon a yellow solution with a white precipitate was formed. The mixture was filtered through a Celite plug. The plug was suspended in 300 ml of THF, refluxed for 10 min, and filtered off. This operation was repeated twice. The filtrates were combined, and the solvent was removed in vacuo. The remaining oil (78.0 g) was dissolved in 500 ml of MeOH. Then 5.00 g (26.3 mmol) of *p*-toluenesulfonic acid was added, and the reaction mixture was refluxed for 3 h. The volatile components were removed in a rotary evaporator. 200 ml of toluene was added twice, and the mixture was concentrated each time to remove residual methanol. To the residue were added 500 ml of acetone and 80.0 g (501 mmol) of anhydrous $CuSO_4$. The reaction mixture was stirred for 2 d at room temp. Then 5.00 g (44.6 mmol) of K_2CO_3 was added. After stirring for 1 h, the mixture was filtered through Celite. The Celite plug was washed three times with 100 ml of acetone each. The filtrates were combined, and the solvent was evaporated in vacuo. Vacuum distillation of the residue afforded 42.2 g (289 mmol 69%) of the acetonide alcohol **15** (b.p. 70–75°C/0.5 Torr) as a colorless liquid. – TLC (petroleum ether/diethyl ether, 2:1): R_f = 0.11. – $[\alpha]_D^{20}$ = –2.4 (*c* = 1.8, $CHCl_3$). – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.30 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.72–1.78 (m, 2H, 3-H_2), 2.43 (br. s, 1H, OH), 3.53 (t, *J* = 7.5 Hz, 1H, 1-H′), 3.72 (t, *J* = 5.9 Hz, 2H, 4-H_2), 4.02 (dd, *J* = 6.1/7.5 Hz, 1-H″), 4.20 (quint, *J* = 6.1 Hz, 1H, 2-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.6, 26.8 (CH_3), 35.7 (C-3), 60.3 (C-4), 69.4 (C-1), 74.9 (C-2), 109.0 (acetonide). – $C_7H_{14}O_3$ (146.2): calcd. C 57.51, H 9.65; found C 57.80, H 9.67.

3) *(2R)-4-Iodo-1,2-O-isopropylidenebutane-1,2-diol* (**16**): To a stirred solution of 10.0 g (68.0 mmol) of alcohol **15** were added at 0°C 39.0 ml (483 mmol) of pyridine and 15.7 g (82.1 mmol) of *p*-tosyl chloride. The reaction mixture was warmed to room temp. and stirred for 12 h. Then 200 ml of ice/water was added, and the resulting mixture was extracted twice with 75 ml of CH_2Cl_2 each. The combined organic phases were washed successively with 200 ml of 1 M HCl, twice with 100 ml of a satd. aqueous $NaHCO_3$ solution each, and two times with 100 ml of a satd. aqueous NaCl solution each. After drying with $MgSO_4$ the solvent was evaporated in vacuo. The residue was filtered over a short silica gel column (200 g of silica gel) with petroleum ether/diethyl ether (2:1) to yield 17.0 g (56.6 mmol) of the corresponding tosylate, which was used directly for the following step. It was dissolved in 300 ml of acetone and 16.8 g (112.4 mmol) of NaI and 779 mg (5.60 mmol) of K_2CO_3 were added. The reaction mixture was stirred for 3 d at room temp. It was partitioned between 400 ml of diethyl ether and 400 ml of water. The aqueous phase was extracted twice with 150 ml of diethyl ether each. The combined organic phases were washed twice with 200 ml of a satd. aqueous NaCl solution each and dried with $MgSO_4$. After evaporation of the solvent the residue was purified by bulb-to-bulb distillation (150°C bath temp./12 Torr) to afford 9.00 g (35.1 mmol, 62%) of the iodide **16** as a colorless liquid. – TLC (petroleum ether/diethyl ether, 2:1): R_f = 0.65. – $[\alpha]_D^{20}$ = +23.0, $[\alpha]_{578}^{20}$ = +23.6, $[\alpha]_{546}^{20}$ = +26.5, $[\alpha]_{436}^{20}$ = +42.2, $[\alpha]_{365}^{20}$ = +59.0 (*c* = 1.02 in $CHCl_3$). – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.28 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 1.95–2.02 (m, 2H, 3-H_2), 3.20–3.24 (m, 2H, 4-H_2), 3.48–3.51 (m, 1H, 1-H′), 4.03 (dd, *J* = 6.1/8.0 Hz, 1H, 1-H″), 4.06–4.14 (m, 1H, 2-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 1.0 (C-4), 25.4, 26.8 (CH_3), 37.8 (C-3), 68.5 (C-1), 75.5 (C-2), 108.9 (acetonide). – $C_7H_{13}IO_2$ (256.1): calcd. C 32.83, H 5.12; found C 32.99, H 5.09.

4) *(3R)-3,4-(Isopropylidenedioxy)butylzinc Iodide* (**17**)

4.1) *Preparation of the THF Solution of the Organozinc Reagent* **17**: A dry 100-ml three-necked round-bottomed flasked was equipped with a magnetic stirring bar, a rubber septum, an inert gas inlet, and a thermometer. The air in the flask was replaced by argon, and the flask was charged with 3.00 g (45.9 mmol) of zinc dust. Then 3 ml of THF and 100 µl (218 mg, 1.16 mmol) of 1,2-dibromoethane were successively injected into the flask. The reaction mixture was gently heated three times with a heat gun until ebullition of the solvent was observed. After cooling to room temp. 0.10 ml (86 mg, 0.79 mmol) of chlorotrimethylsilane was added, and the reaction mixture was heated for 15 min to 35°C. After

cooling to room temp. the rubber septum was exchanged for an addition funnel charged with 5.12 g (20.0 mmol) of the iodide **16** and 1.98 g (1.00 mmol) of *n*-tetradecane (as internal standard for GC analysis) dissolved in 20 ml of THF. GC analysis of the iodide THF solution [starting temp. 100°C, 1 min at 100°C, heating rate 50°C/min, final temperature 250°C, R_t (iodide) = 2.67 min, R_t (standard) = 3.23 min] yielded a ratio of iodide **16** to standard of 21.5:1. The iodide solution was added dropwise to the reaction mixture during 30 min. During addition of the iodide the temp. of the reaction mixture rose to 48°C. After the addition the reaction mixture was stirred for 3 h at 50°C. Stirring was stopped, and excess zinc dust was allowed to settle down during 1 h. The supernatant colorless slightly turbid THF solution of the zinc reagent **17** was transferred to a Schlenk flask by means of a stainless steel canula. GC analysis of a hydrolyzed aliquot (0.1 ml of the reaction mixture to 1 ml of a satd. aqueous NH_4Cl solution/1 ml diethyl ether) showed complete consumption of the starting iodide (R_t of the alkane resulting from the hydrolysis = 1.80 min). GC analysis of an iodinated aliquot (0.1 ml of the reaction mixture, relative to 100 mg of iodine in 1 ml of THF, addition of 1 ml of a satd. aqueous $Na_2S_2O_3$ solution) yielded a ratio of iodide **16** to standard of 17.5:1. Therefore, a yield of 81% of zinc reagent could be assumed on the basis of GC analysis.

4.2) *Spectroscopic Characterization of the Organozinc Reagent* **17**: The THF solution of **17** was concentrated in vacuo to give a white solid. ^{1}H- and ^{13}C-NMR spectra of the solid showed a 1:1 adduct of compound **17** and THF. – ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = −0.29 to −0.24 (m, 2H, 1-H$_2$), 1.18 (s, 3H, CH$_3$), 1.21 (s, 3H, CH$_3$), 1.44−1.48 (m, 1H, 2-H′), 1.64−1.69 (m, 1H, 2-H″), 1.71 (quint, J = 3.1 Hz, 4H, THF), 3.31 (t, J = 7.5 Hz, 1H, 4-H′), 3.35−3.56 (m, 4H, THF), 3.81−3.85 (m, 1H, 3-H), 3.90 (t, J= 7.5 Hz, 1H, 4-H″); ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 0.30 (br. s, 1H, 1-H′), 0.60 (bs, 1H, 1-H″), 1.44 (s, 3H, CH$_3$), 1.50 (s, 3H, CH$_3$), 1.99−2.10 (m, 6H, 2-H$_2$, THF), 3.52 (t, J = 8.0 Hz, 1H, 4-H′), 3.97−4.10 (m, 6H, 3-H, 4-H″, THF). – ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 5.3 (C-1), 25.1 (THF), 25.9 (CH$_3$), 27.1 (CH$_3$), 32.3 (C-2), 67.5 (THF), 69.0 (C-4), 79.9 (C-3), 107.4 (acetonide); ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 8.1 (C-1), 25.6 (THF), 26.2 (CH$_3$), 27.5 (CH$_3$), 31.5 (C-2), 69.6 (THF), 70.6 (C-4), 80.0 (C-3), 109.9 (acetonide).

4.3) *Preparation of a CH_2Cl_2 Solution of the Organozinc Reagent* **17**: To the neat organozinc reagent (16.2 mmol), prepared as described in 4.1), was added 40 ml of freshly distilled degassed CH_2Cl_2 to give a colorless slightly turbid solution of **17**, which was used directly for the following experiments. The solution was determined by GC analysis to be 0.4 molar as described in 4.1).

5) *General Procedure for the Addition of the Organozinc Reagent ent-***17** *to Achiral Aldehydes* **18**: A solution of 20.0 ml (8.00 mmol) of *ent*-**17** in CH_2Cl_2, prepared as described in 4.1), was cooled to −30°C. To this solution were added successively 2.00 mmol of the corresponding aldehyde **18** and 500 µl (570 mg, 4.00 mmol) of $BF_3 \cdot OEt_2$. After stirring for 5 min the reaction mixture was warmed to 0°C during 3 h. Then 50 ml of a satd. aqueous NH_4Cl solution was added. The reaction mixture was extracted with 100 ml of diethyl ether. The organic phase was washed successively with 50 ml of a satd. aqueous Na_2CO_3 solution and 50 ml of a satd. aqueous NaCl solution. It was subsequently dried with $MgSO_4$ and concentrated. The residue was purified by CC (30 g of silica gel) with petroleum ether/diethyl ether (1:1), to give the addition product as an epimeric mixture of compounds **19** and **20**. The ratio of the two epimers was determined by NMR and/or HPLC analysis.

5.1) *(2S,5R)-1,2-O-Isopropylideneheptane-1,2,5-triol* (**19a**) *and (2S,5S)-1,2-O-Isopropylideneheptane-1,2,5-triol* (**20a**): According to the general procedure 5) 20.0 ml (8.00 mmol) of the organozinc reagent *ent*-**17**, 140 µl (116 mg, 2.00 mmol) of propionaldehyde (**18a**) and 500 µl (570 mg, 4.00 mmol) of $BF_3 \cdot OEt_2$ were allowed to react to yield 210 mg (1.11 mmol, 56%) of an epimeric mixture of alcohols **19a** and **20a** as a colorless liquid; epimeric ratio determined by ^{1}H-NMR analysis = 73:27. – TLC (petroleum ether/diethyl ether, 2:1): R_f = 0.14. – IR (neat): $\tilde{\nu}$ = 3441 (OH), 2956, 2935, 1060 cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, J = 7.3 Hz, 3H, 7-H$_3$), 1.28 (s, 3H, CH$_3$, acetonide), 1.34 (s, 3H, CH$_3$, acetonide), 1.37−1.72 (m, 6H, 3,4,6-H$_2$), 2.76 (s, 1H, OH), 3.43−3.48 (m, 2H, 1-H′, 5-H), 3.95−4.20 (m, 2H, 1-H″, 2-H). – ^{13}C NMR (75 MHz, $CDCl_3$): major diastereomer **19a**: δ = 10.0 (C-7), 25.7 (CH$_3$, acetonide), 26.9 (CH$_3$, acetonide), 30.0, 30.2, 33.1 (C-3,4,6), 69.4 (C-1), 72.9 (C-5), 76.2 (C-2), 108.9 (acetonide); additional signals of the minor diastereomer **20a**: δ = 29.7, 30.2, 33.0, 72.7, 76.3, 108.9. – $C_{10}H_{20}O_3$ (188.3): calcd. C 63.79, H 10.71; found C 63.64, H 10.58.

5.2) *(2S,5R)-1,2-O-Isopropylideneoctane-1,2,5-triol* (**19b**) *and (2S,5S)-1,2-O-Isopropylideneoctane-1,2,5-triol* (**20b**): According to the general procedure 5) 20.0 ml (8.00 mmol) of the organozinc reagent *ent*-**17**, 180 µl (144 mg, 2.00 mmol) of butyraldehyde (**18b**), and 500 µl (570 mg, 4.00 mmol) of $BF_3 \cdot OEt_2$ were allowed to react to yield 310 mg (1.53 mmol, 76%) of an epimeric mixture of alcohols **19b** and **20b** as a colorless liquid. – TLC (petroleum ether/diethyl ether, 1:1): R_f = 0.17. – Analytical HPLC: analyzed as TBDPS ethers, supersphere column, flow rate: 1.0 ml/min, eluent: *n*-hexane/ethyl acetate (15:1), major isomer: R_t = 1.3 min, minor isomer: R_t = 1.8 min, ratio **19b**/**20b** = 69:31. – IR (neat): $\tilde{\nu}$ = 3442 (OH), 2957, 2934, 1063 cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, J = 7.2 Hz, 3H, 8-H$_3$), 1.29 (s, 3H, CH$_3$, acetonide), 1.35 (s, 3H, CH$_3$, acetonide), 1.20−1.70 (m, 8H, 3,4,6,7-H$_2$), 2.23 (s, 1H, OH), 3.37−3.48 (m, 1H, 1-H′), 3.50−3.61 (m, 1H, 5-H), 3.95−4.20 (m, 2H, 1-H″, 2-H). – ^{13}C NMR (75 MHz, $CDCl_3$): major diastereomer **19b**: δ = 14.1 (C-8), 18.8 (C-7), 25.9 (CH$_3$, acetonide), 26.9 (CH$_3$, acetonide), 30.1, 33.8, 39.7 (C-3,4,6), 69.5 (C-1), 71.4 (C-5), 76.2 (C-2), 108.9 (acetonide); additional signals of the minor diastereomer **20b**: δ = 29.6, 33.6, 71.1, 108.9. – $C_{11}H_{22}O_3$ (202.3): calcd. C 65.31, H 10.96; found C 65.56, H 11.06.

5.3) *(2S,5S)-1,2-O-Isopropylidene-6-methylheptane-1,2,5-triol* (**19c**) *and (2S,5R)-1,2-O-Isopropylidene-6-methylheptane-1,2,5-triol* (**20c**): According to the general procedure 5) 20.0 ml (8.00 mmol) of the organozinc reagent *ent*-**17**, 200 µl (160 mg, 2.20 mmol) of isobutyraldehyde (**18c**), and 500 µl (570 mg, 4.00 mmol) of $BF_3 \cdot OEt_2$ were allowed to react to yield 250 mg (1.24 mmol, 56%) of an epimeric mixture of alcohols **19c** and **20c** as a colorless liquid; epimeric ratio determined by ^{1}H-NMR analysis = 76:24. – TLC (petroleum ether/diethyl ether, 1:1): R_f = 0.20. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (d, J = 6.8 Hz, 6H, 6,7-H$_3$), 1.29 (s, 3H, CH$_3$, acetonide), 1.35 (s, 3H, CH$_3$, acetonide), 1.38−1.75 (m, 5H, 3,4-H$_2$, 6-H), 2.25 (s, 1H, OH), 3.24−3.35 (m, 1H, 5-H), 3.42−3.50 (m, 1H, 1-H′), 3.96−4.11 (m, 2H, 1-H″, 2-H). – ^{13}C NMR (75 MHz, $CDCl_3$): major diastereomer **19c**: δ = 17.2, 18.7 (C-7, 6-CH$_3$), 25.6 (CH$_3$, acetonide), 26.8 (CH$_3$, acetonide), 30.3, 30.4, 33.6 (C-3,4,6), 69.4 (C-1), 76.1, 76.5 (C-2,5), 108.8 (acetonide); additional signals of the minor diastereomer **20c**: δ = 29.9, 76.2. – $C_{11}H_{22}O_3$ (202.3): calcd. C 65.31, H 10.96; found C 65.10, H 11.09.

5.4) *(2S,5S)-1,2-O-Isopropylidene-5-phenylpentane-1,2,5-triol* (**19d**) *and (2S,5R)-1,2-O-Isopropylidene-5-phenylpentane-1,2,5-triol* (**20d**): According to the general procedure 5) 20.0 ml (8.00 mmol) of the organozinc reagent *ent*-**17**, 200 µl (212 mg, 2.00 mmol) of benzaldehyde (**18d**), and 500 µl (570 mg, 4.00 mmol) of $BF_3 \cdot OEt_2$

were allowed to react to yield 453 mg (1.92 mmol, 96%) of an epimeric mixture of alcohols **19d** and **20d** as a colorless liquid. – Analytical HPLC: supersphere column, flow rate 1.0 ml/min, eluent *n*-hexane/ethyl acetate (4:1), major isomer **19d**: R_t = 8.0 min, minor isomer **20d**: R_t = 8.6 min, ratio **19d/20d** = 76:24. – TLC (petroleum ether/ether acetate, 2:1): R_f = 0.27. – IR (neat): $\tilde{\nu}$ = 3443 (OH), 2986, 2935, 1603, 1056, 702 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.12 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 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, phenyl). – ^{13}C NMR (50 MHz, $CDCl_3$): major diastereomer **19d**: δ = 25.9 (CH_3), 27.1 (CH_3), 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 (phenyl); additional signals of the minor diastereomer **20d**: δ = 29.8, 35.5, 74.2. – $C_{14}H_{20}O_3$ (236.3): calcd. C 71.16, H 8.53; found C 71.23, H 8.65.

5.5) *(2S,5S)-1,2-O-Isopropylidene-5-(thiophen-3-yl)pentane-1,2,5-triol* (**19e**) *and (2S,5R)-1,2-O-Isopropylidene-5-(thiophen-3-yl)pentane-1,2,5-triol* (**20e**): According to the general procedure 5) 20.0 ml (8.00 mmol) of the organozinc reagent *ent*-**17**, 200 µl (256 mg, 2.30 mmol) of thiophene-3-carbaldehyde (**18e**), and 500 µl (570 mg, 4.00 mmol) of $BF_3 \cdot OEt_2$ were allowed to react to yield 510 mg (2.10 mmol, 92%) of an epimeric mixture of alcohols **19e** and **20e** as a colorless liquid. – Analytical HPLC: supersphere column, flow rate 1.0 ml/min, eluent *n*-hexane/ethyl acetate (4:1), major isomer **19e**: R_t = 5.7 min, minor isomer **20e**: R_t = 6.4 min, epimeric ratio **19e/20e** = 77:23. – TLC (petroleum ether/ethyl acetate, 2:1): R_f = 0.18. – IR (neat): $\tilde{\nu}$ = 3437 (OH), 2984, 2935, 1057, 852, 789 cm^{-1}. – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.37 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.55–2.00 (m, 4H, 3,4-H_2), 2.87 (s, 1H, OH), 3.52 (t, *J* = 7.3 Hz, 1H, 1-H′), 4.05 (t, *J* = 7.3 Hz, 1H, 1-H″), 4.07–4.22 (m, 1H, 2-H), 4.78–4.85 (m, 1H, 5-H), 7.09 [dd, *J* = 5.5/1.1 Hz, 1H, 4-H (thiophene)], 7.21 [d, *J* = 1.1 Hz, 1H, 2-H (thiophene)], 7.32 [d, *J* = 5.5 Hz, 1H, 5-H (thiophene)]. – ^{13}C NMR (50 MHz, $CDCl_3$): major diastereomer **19e**: δ = 25.9 (CH_3), 27.1 (CH_3), 30.1, 35.1 (C-3,4), 69.6 (C-1), 70.6 (C-5), 76.2 (C-2), 109.2 (acetonide), 120.9, 125.9, 126.3, 146.3 (thiophene); additional signals of the minor diastereomer **20e**: δ = 29.7, 34.9, 70.4, 76.15. – $C_{12}H_{18}O_3S$ (242.3): calcd. C 59.48, H 7.49; found C 59.36, H 7.65.

5.6) *(2S,5S,6E)-1,2-O-Isopropylidene-6-octene-1,2,5-triol* (**19f**) *and (2S,5R,6E)-1,2-O-Isopropylidene-6-octene-1,2,5-triol* (**20f**): According to the general procedure 5) 20.0 ml (8.00 mmol) of the organozinc reagent *ent*-**17**, 160 µl (140 mg, 2.00 mmol) of crotonaldehyde (**18f**), and 500 µl (570 mg, 4.00 mmol) of $BF_3 \cdot OEt_2$ were allowed to react to yield 205 mg (1.02 mmol, 51%) of an epimeric mixture of alcohols **19f** and **20f** as a colorless liquid; epimeric ratio determined by ^1H-NMR analysis = 71:29. – TLC (petroleum ether/diethyl ether, 1:1): R_f = 0.17. – IR (neat): $\tilde{\nu}$ = 3401 (OH), 2986, 2935, 2870, 1710, 1450, 1375, 1058, 968 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.28 (s, 3H, CH_3, acetonide), 1.40 (s, 3H, CH_3, acetonide), 1.41–1.64 (m, 4H, 3,4-H_2), 1.63 (d, *J* = 6.5 Hz, 3H, 8-H_3), 1.97, 2.11 (s, 1H, OH), 3.46 (t, *J* = 7.4 Hz, 1H, 1-H′), 3.95–4.09 (m, 3H, 1-H″, 2,5-H), 5.41 (ddd, *J* = 1.5/6.9/15.4 Hz, 1H, 6-H), 5.60 (dq, *J* = 6.3/15.3 Hz, 1H, 7-H). – ^{13}C NMR (75 MHz, $CDCl_3$): major diastereomer **19f**: δ = 17.7 (C-8), 25.8 (CH_3, acetonide), 27.0 (CH_3, acetonide), 29.7, 33.6 (C-3,4), 69.5 (C-1), 72.7 (C-5), 76.0 (C-2), 108.9 (acetonide), 126.8, 130.1 (C=C); additional signals of the minor diastereomer **20f**: δ = 29.5, 33.5, 69.5, 72.6, 76.1. – $C_{11}H_{20}O_3$ (200.3): calcd. C 65.97, H 10.07; found C 65.91, H 10.06.

5.7) *(2S,5S)-6-(tert-Butyldiphenylsiloxy)-1,2-O-isopropylidene-hexane-1,2,5-triol* (**19g**) *and (2S,5R)-6-(tert-Butyldiphenylsiloxy)-1,2-O-isopropylidenehexane-1,2,5-triol* (**20g**): According to the general procedure 5) 20.0 ml (8.00 mmol) of the organozinc reagent *ent*-**17**, 500 mg (1.70 mmol) of aldehyde **18g**, and 500 µl (570 mg, 4.00 mmol) of $BF_3 \cdot OEt_2$ were allowed to react to yield 420 mg (0.98 mmol, 58%) of an epimeric mixture of alcohols **19g** and **20g** as a colorless liquid; epimeric ratio determined by ^1H-NMR analysis = 85:15. – TLC (petroleum ether/ethyl acetate, 2:1): R_f = 0.35. – IR (neat): $\tilde{\nu}$ = 3469 (OH), 2932, 2860, 1114, 703, 505 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.04 [s, 9H, $C(CH_3)_3$], 1.31 (s, 3H, CH_3, acetonide), 1.36 (s, 3H, CH_3, acetonide), 1.44–1.75 (m, 4H, 3,4-H_2), 2.70 (d, *J* = 3.5 Hz, 1H, OH), 3.42–3.54 (m, 2H, 6-H_2), 3.63 (dd, *J* = 3.8/10.0 Hz, 1H, 1-H′), 3.67–3.78 (m, 1H, 5-H), 3.99 (dd, *J* = 6.0/10.0 Hz, 1H, 1-H″), 4.00–4.12 (m, 1H, 2-H), 7.36–7.41 (m, 6H, phenyl), 7.62–7.66 (m, 4H, phenyl). – ^{13}C NMR (75 MHz, $CDCl_3$): major diastereomer **19g**: δ = 19.2 [*C*$(CH_3)_3$], 25.7 (CH_3, acetonide), 26.9 [C(*C*$H_3)_3$ and CH_3-acetonide], 28.9, 29.4 (C-3,4), 67.9 (C-6), 69.3 (C-1), 71.6 (C-5), 75.7 (C-2), 108.8 (acetonide), 127.8, 129.8, 133.2, 135.5 (phenyl); additional signals of the minor diastereomer **20g**: δ = 29.2, 29.6, 69.4, 71.8, 76.1. – $C_{25}H_{36}O_4Si$ (428.6): calcd. C 70.05, H 8.47; found C 69.96, H 8.57.

6) *(2R,5S)-5-[(tert-Butyldiphenylsiloxy)methyl]tetrahydrofuran-2-methanol* (**21**) *and (2R,5R)-5-[(tert-Butyldiphenylsiloxy)-methyl]tetrahydrofuran-2-methanol* (**22**)

6.1) *From the Organozinc Route:* A solution of 370 mg (0.86 mmol) of the acetonide alcohol **19g/20g** (epimeric ratio 85:15) in 5.00 ml of acetic acid and 0.50 ml of water was stirred at room temp. for 14 h. The solvent was evaporated. Then 10 ml of toluene was added to the residue, and the solvent was again evaporated. The residue was dissolved in 5.0 ml of CH_2Cl_2. At 0°C 2.0 ml of pyridine and 223 mg (1.02 mmol) of mesitylenesulfonyl chloride were added. The reaction mixture was stirred at 0°C for 4 h. After addition of 0.50 ml of water the solvent was evaporated. The residue was partitioned between 50 ml of diethyl ether and 10 ml of water. The organic layer was washed successively with 10 ml of 1 M HCl, 30 ml of a satd. aqueous $NaHCO_3$ solution, and with 20 ml of a satd. aqueous NaCl solution. After drying with $MgSO_4$ the solvent was evaporated. The residue was dissolved in dry MeOH, and 400 mg (2.90 mmol) of K_2CO_3 was added to the solution. The reaction mixture was stirred for 1 h at room temp. The solvent was evaporated in vacuo. The residue was dissolved in 20 ml of CH_2Cl_2, and 5 ml of HOAc was added to the solution. After stirring for 3 h at room temp. the solvent was evaporated. The residue was partitioned between 100 ml of diethyl ether and 40 ml of water. The organic layer was washed successively with 50 ml of a satd. aqueous $NaHCO_3$ solution and with 50 ml of a satd. aqueous NaCl solution. After drying with $MgSO_4$ the solvent was evaporated. The residue was purified by CC (30 g of silica gel) with petroleum ether/diethyl ether (1:1) to give 150 mg (48%) of a 85:15 mixture of **21** and **22** as a colorless liquid. – TLC (petroleum ether/ethyl acetate, 4:1): R_f = 0.22. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.01 [s, 9H, $C(CH_3)_3$], 1.75–2.00 (m, 4H, 3,4-H_2), 2.20 (d, *J* = 5.2 Hz, 1H, OH), 3.35–3.75 (m, 4H, α,α′-H_2), 4.01–4.05 (m, 2H, 2,5-H), 7.32–7.36 (m, 6H, phenyl), 7.60–7.64 (m, 4H, phenyl). – ^{13}C NMR (75 MHz, $CDCl_3$): major diastereomer (*cis*) **21**: δ = 19.2 [*C*$(CH_3)_3$], 26.9 [C(*C*$H_3)_3$], 27.5, 27.8 (C-3,4), 65.6, 66.1 (C-α,α′), 79.9, 80.1 (C-2,5), 127.8, 129.8, 133.5, 135.7 (phenyl); additional signals of the minor diastereomer (*trans*) **22**: δ = 29.2, 29.6, 65.1, 66.6, 79.7. – $C_{22}H_{30}O_3Si$ (370.6): calcd. C 71.31, H 8.04; found C 71.31, H 8.16.

6.2) *From the Nitrile Route:* **21** (*cis* alcohol): A solution of NaOMe in MeOH was prepared from 190 mg (8.26 mmol) of sodium in 20 ml of dry MeOH. To this was added 2.00 g (5.47 mmol) of

the *cis* nitrile **23**. The reaction mixture was stirred for 1 h at room temp. After cooling to 0°C 6.0 ml of ice-cooled 2 M HCl was added. The reaction mixture was partitioned between 50 ml of a satd. aqueous NH_4Cl solution and 100 ml of diethyl ether. The organic layer was separated and washed with 50 ml of a satd. aqueous NaCl solution. After drying with $MgSO_4$ the solvent was evaporated. The residue was dissolved in 50 ml of THF. After cooling to −30°C 300 mg (8.11 mmol) of $LiAlH_4$ was added. The stirred reaction mixture was warmed to 0°C during 30 min. Then 0.50 ml of water was added with caution followed by 0.50 ml of 3 M NaOH and 1 ml of water. The reaction mixture was stirred for 30 min at room temp. It was subsequently filtered through Celite. The Celite plug was washed with 50 ml of THF. The combined filtrates were dried with $MgSO_4$. After evaporation of the solvent the residue was purified by CC (50 g of silica gel) to yield 1.23 g (3.54 mmol, 65%) of the *cis* alcohol **21** as a colorless liquid. − TLC (petroleum ether/ethyl acetate, 4:1): R_f = 0.22. − $[\alpha]_D^{20}$ = −1.9 (*c* = 1.18, $CHCl_3$). − IR (neat): $\tilde{\nu}$ = 3449 (OH), 3071, 3048, 2932, 2858, 1429, 1112, 1084, 824, 741, 703, 505 cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.05 [s, 9H, $C(CH_3)_3$], 1.73−2.01 (m, 4H, 3,4-H_2), 2.37 (dd, *J* = 5.4/7.3 Hz, 1H, OH), 3.44−3.51 (m, 1H, α-H′), 3.62 (dd, *J* = 10.8/3.9 Hz, 1H, α′-H′), 3.73 (ddd, *J* = 11.5/5.3/3.2 Hz, 1H, α-H″), 3.77 (dd, *J* = 10.8/3.8 Hz, 1H, α′-H″), 4.03−4.12 (m, 2H, 2,5-H), 7.34−7.43 (m, 6H, phenyl), 7.65−7.72 (m, 4H, phenyl). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.2 [$C(CH_3)_3$], 26.8 [$C(CH_3)_3$], 27.3, 27.7 (C-3,4), 65.4, 66.0 (C-α,α′), 79.8, 80.0 (C-2,5), 127.7, 129.7, 133.4, 135.5 (phenyl). − $C_{22}H_{30}O_3Si$ (370.6): calcd. C 71.31, H 8.04; found C 71.31, H 8.16.

ent-**22** (*trans* alcohol): A solution of NaOMe in MeOH was prepared from 190 mg (8.26 mmol) of sodium in 20 ml of dry MeOH. To this was added 2.00 g (5.47 mmol) of the *trans* nitrile **24**. According to the procedure described for the methanolysis and the $LiAlH_4$ reduction of the *cis* nitrile **23**, 1.17 g (3.16 mmol, 58%) of the *trans*-alcohol *ent*-**22** was isolated as a colorless liquid. − TLC (petroleum ether/ethyl acetate, 4:1): R_f = 0.22. − $[\alpha]_D^{20}$ = +5.9 (*c* = 1.7, $CHCl_3$). − IR (neat): $\tilde{\nu}$ = 3442 (OH), 3070, 3049, 2956, 2932, 1429, 1111, 1081, 823, 742, 705, 507 cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.06 [s, 9H, $C(CH_3)_3$], 1.62−2.04 (m, 4H, 3,4-H_2), 2.26 (t, *J* = 6.2 Hz, 1H, OH), 3.40−3.48 (m, 1H, α-H′), 3.60−3.68 (m, 3H, α-H″, α′-H_2), 4.04−4.18 (m, 2H, 2,5-H), 7.34−7.46 (m, 6H, phenyl), 7.64−7.72 (m, 4H, phenyl). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.2 [$C(CH_3)_3$], 26.8 [$C(CH_3)_3$], 27.4, 28.1 (C-3,4), 64.9, 66.4 (C-α,α′), 79.6, 79.7 (C-2,5), 127.6, 129.5, 133.6, 135.6 (phenyl). − $C_{22}H_{30}O_3Si$ (370.6): calcd. C 71.31, H 8.04; found C 71.39, H 8.10.

7) *(2S)-Tetrahydro-5,5-dimethylfuran-2-methanol* (**25**): 7.50 ml (3.00 mmol) of a solution of the organozinc reagent *ent*-**17** in CH_2Cl_2, prepared as described in 4.1), was cooled to −78°C. Then 3.00 ml (3.00 mmol) of a 1 M solution of $TiCl_4$ in CH_2Cl_2 was added. The reaction mixture was warmed to room temp. during 3 h. Subsequently 10 ml of a satd. aqueous NH_4Cl solution was added. The aqueous phase was extracted twice with 10 ml of CH_2Cl_2 each. The combined organic phases were washed twice with 10 ml of a satd. aqueous NaCl solution each and dried with $MgSO_4$. Evaporation of the solvent yielded an oily residue. This was purified by CC (50 g of silica gel) with petroleum ether/diethyl ether (1:1) to give 192 mg (55%) of alcohol **25** as a colorless liquid. − TLC (petroleum ether/diethyl ether, 2:1): R_f = 0.11. − $[\alpha]_D^{20}$ = −9.7, $[\alpha]_{578}^{20}$ = −9.7, $[\alpha]_{546}^{20}$ = −11.4, $[\alpha]_{436}^{20}$ = −17.1, $[\alpha]_{365}^{20}$ = −22.3 (*c* = 1.75, $CHCl_3$). − IR (neat): $\tilde{\nu}$ = 3437 (OH), 2966, 2929, 1444, 1034 cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.18 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.65−1.96 (m, 4H, 3,4-H_2), 2.49 (s, 1H, OH), 3.42 (dd, *J* = 11.5/5.6 Hz, 1H, α-H′), 3.59 (dd, *J* = 11.5/3.5 Hz, 1H, α-H″), 3.99−4.07 (m, 1H, 2-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.5 (C-3), 27.6 (CH_3), 28.7 (CH_3), 38.3 (C-4), 65.1 (C-α), 78.7 (C-2), 81.3 (C-5). − $C_7H_{14}O_2$ (130.2): calcd. C 64.58, H 10.84; found C 64.27, H 10.72.

8) *(2R,5R,2′S,5′S)-5-{5′-[(tert-Butyldiphenylsiloxy)methyl]tetrahydro-2′-furyl}-1,2-O-isopropylidenepentane-1,2,5-triol* (**7**) *and (2R,5S,2′S,5′S)-5-{5′-[(tert-Butyldiphenylsiloxy)methyl]tetrahydro-2′-furyl}-1,2-O-isopropylidenepentane-1,2,5-triol* (**3**): A solution of 15.0 ml (6.00 mmol) of the organozinc reagent **17** in CH_2Cl_2 was cooled to −30°C. To this solution were added successively 737 mg (2.00 mmol) of THF-aldehyde **1** dissolved in 3.0 ml of CH_2Cl_2 and 370 μl (426 mg, 3.00 mmol) of $BF_3 \cdot OEt_2$. After stirring for 5 min the reaction mixture was warmed to 0°C during 3 h. Then 50 ml of a satd. aqueous NH_4Cl solution was added. The reaction mixture was extracted with 100 ml of diethyl ether. The organic phase was washed with 50 ml of a satd. aqueous Na_2CO_3 solution and 50 ml of a satd. aqueous NaCl solution, then dried with $MgSO_4$ and concentrated. The residue was purified by CC (70 g silica gel) with petroleum ether/*tert*-butyl methyl ether (2:1) to give 536 mg (1.07 mmol, 53%) of a 95:5 mixture (determined by ^1H-NMR analysis) of **7** and **3** as a colorless liquid. In addition, 317 mg (43%) of the aldehyde **1** was recovered. For analytical purposes the mixture of **7** and **3** was separated by CC (100 g of silica gel) with petroleum ether/diethyl ether (1:1) to give 478 mg of **7** and 30 mg of **3**.

7: TLC (petroleum ether/ethyl acetate, 4:1): R_f = 0.22. − $[\alpha]_D^{20}$ = −2.5, $[\alpha]_{578}^{20}$ = −2.7, $[\alpha]_{546}^{20}$ = −3.3, $[\alpha]_{436}^{20}$ = −7.9, $[\alpha]_{365}^{20}$ = −15.0 (*c* = 2.4, $CHCl_3$). − IR (neat): $\tilde{\nu}$ = 3466 (OH), 2982, 2932, 2858, 1472, 1462, 1429, 1378, 1369, 1309, 1254, 1114, 1066, 824, 741, 703, 615, 505 cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 [s, 9H, $C(CH_3)_3$], 1.32 (s, 3H, CH_3, acetonide), 1.38 (s, 3H, CH_3, acetonide), 1.22−2.00 (m, 8H, 3,4,3′,4′-H_2), 2.77 (s, 1H, OH), 3.47−3.56 (m, 1H, 1-H′), 3.62 (d, *J* = 4.7 Hz, 2H, 1″-H′), 3.66−3.85 (m, 2H, 2′,5-H), 3.99−4.26 (m, 3H, 1-H″, 2,5′-H), 7.30−7.40 (m, 6H, phenyl), 7.64−7.68 (m, 4H, phenyl). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.2 [$C(CH_3)_3$], 25.7 (CH_3, acetonide), 26.8 [$C(CH_3)_3$ and CH_3-acetonide], 26.9, 28.3, 29.2, 30.1 (C-3,4,3′,4′), 66.5 (C-1″), 69.3 (C-1), 72.1 (C-5), 75.9 (C-2), 79.8, 82.3 (C-5′,2′), 108.8 (acetonide), 127.6, 129.6, 133.6, 135.6 (phenyl). − $C_{29}H_{42}O_5Si$ (498.7): calcd. C 69.84, H 8.49; found C 69.86, H 8.26.

3: TLC (petroleum ether/ethyl acetate, 4:1): R_f = 0.27. − $[\alpha]_D^{20}$ = −7.9, $[\alpha]_{578}^{20}$ = −8.4, $[\alpha]_{546}^{20}$ = −9.7, $[\alpha]_{436}^{20}$ = −18.3, $[\alpha]_{365}^{20}$ = −31.2 (*c* = 1.06, $CHCl_3$). − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.07 [s, 9H, $C(CH_3)_3$], 1.37 (s, 3H, CH_3, acetonide), 1.43 (s, 3H, CH_3, acetonide), 1.51−2.06 (m, 8H, 3,4,3′,4′-H_2), 2.51 (d, *J* = 3.7 Hz, 1H, OH), 3.37−3.44 (m, 1H, 1-H′), 3.46−3.58 (m, 1H, 5-H), 3.68 (d, *J* = 4.7 Hz, 2H, 1″-H_2), 3.79−3.87 (m, 1H, 2-H), 4.02−4.18 (m, 3H, 1-H″, 2′,5′-H), 7.36−7.48 (m, 6H, phenyl), 7.66−7.75 (m, 4H, phenyl). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.1 [$C(CH_3)_3$], 25.6 (CH_3, acetonide), 26.7 [$C(CH_3)_3$], 26.9 (CH_3, acetonide), 28.2, 28.3, 29.8, 30.1 (C-3,4,3′,4′), 66.3 (C-1″), 69.4 (C-1), 73.8 (C-5), 76.2 (C-2), 79.5, 82.6 (C-2′,5′), 108.7 (acetonide), 127.5, 129.5, 133.5, 133.6, 135.5 (phenyl). − $C_{29}H_{42}O_5Si$ (498.7): calcd. C 69.84, H 8.49; found C 69.51, H 8.33.

9) *(2S,5R,2′S,5′S)-5-{5′-[(tert-Butyldiphenylsiloxy)methyl]tetrahydro-2′-furyl}-1,2-O-isopropylidenepentane-1,2,5-triol* (**26**) *and (2S,5S,2′S,5′S)-5-{5′-[(tert-Butyldiphenylsiloxy)methyl]tetrahydro-2′-furyl}-1,2-O-isopropylidenepentane-1,2,5-triol* (**27**): A solution of 20.0 ml (8.10 mmol) of the organozinc reagent *ent*-**17** in CH_2Cl_2 was cooled to −30°C. To this solution were added successively 1.10 g (3.00 mmol) of the aldehyde **1** dissolved in 3.0 ml of CH_2Cl_2 and 500 μl (570 mg, 4.00 mmol) of $BF_3 \cdot OEt_2$. After stirring for 5 min

the reaction mixture was warmed to 0°C during 3 h. Then 50 ml of a satd. aqueous NH_4Cl solution was added. The reaction mixture was extracted with 100 ml of diethyl ether. The organic phase was washed successively with 50 ml of a satd. aqueous Na_2CO_3 solution and 50 ml of a satd. aqueous NaCl solution, then dried with $MgSO_4$ and concentrated. The residue was purified by CC (50 g of silica gel) with petroleum ether/diethyl ether (1:1) to give 758 mg (1.52 mmol, 51%) of a 73:27 mixture (determined by ^{1}H-NMR analysis) of **26** and **27** as a colorless liquid. In addition, 508 mg (45%) of aldehyde **1** was recovered. For analytical studies the mixture of **26** and **27** was separated by CC (100 g of silica gel) with petroleum ether/diethyl ether (1:1) to give 331 mg of **26** and 107 mg of **27**.

26: TLC (petroleum ether/diethyl ether, 1:1): R_f = 0.23. – $[\alpha]_D^{20}$ = +1.3, $[\alpha]_{578}^{20}$ = +1.7, $[\alpha]_{546}^{20}$ = +1.7, $[\alpha]_{436}^{20}$ = +3.5, $[\alpha]_{365}^{20}$ = +4.3 (*c* = 2.3, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3468 (OH), 3070, 3050, 2932, 2858, 1472, 1429, 1369, 1255, 1114, 1066, 851, 824, 795, 742, 703, 615, 505 cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00 [s, 9H, $C(CH_3)_3$], 1.30 (s, 3H, CH_3, acetonide), 1.35 (s, 3H, CH_3, acetonide), 1.49–1.98 (m, 8H, 3,4,4′,4′-H_2), 2.26 (d, *J* = 2.8 Hz, 1H, OH), 3.47 (t, *J* = 7.5 Hz, 1H, 1-H′), 3.60 (d, *J* = 4.8 Hz, 2H, 1″-H_2), 3.67–3.85 (m, 2H, 5,2′-H), 3.97–4.11 (m, 3H, 1-H″, 2,5′-H), 7.29–7.37 (m, 6H, phenyl), 7.61–7.65 (m, 4H, phenyl). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.3 [$C(CH_3)_3$], 25.5 (CH_3, acetonide), 25.8 (CH_3, acetonide), 26.9 [$C(CH_3)_3$], 27.0, 28.2, 29.4, 30.2 (C-3,4,3′,4′), 66.6 (C-1″), 69.6 (C-1), 72.0 (C-5), 76.4 (C-2), 80.0, 82.3 (C-2′,5′), 109.0 (acetonide), 127.7, 129.7, 133.6, 135.7 (phenyl). – $C_{29}H_{42}O_5Si$ (498.7): calcd. C 69.84, H 8.49; found C 69.63, H 8.66.

27: TLC (petroleum ether/diethyl ether, 1:1): R_f = 0.30. – $[\alpha]_D^{20}$ = +0.5, $[\alpha]_{578}^{20}$ = +0.5, $[\alpha]_{546}^{20}$ = +0.9, $[\alpha]_{436}^{20}$ = +1.2, $[\alpha]_{365}^{20}$ = +1.5 (*c* = 0.74, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3465 (OH), 3071, 3050, 2932, 2862, 1466, 1428, 1372, 1254, 1111, 1069, 852, 824, 742, 705, 613, 508 cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.07 [s, 9H, $C(CH_3)_3$], 1.36 (s, 3H, CH_3, acetonide), 1.42 (s, 3H, CH_3, acetonide), 1.48–2.08 (m, 8H, 3,4,3′,4′-H_2), 2.46 (br. s, 1H, OH), 3.38–3.48 (m, 1H, 5-H), 3.54 (t, *J* = 7.5 Hz, 1H, 1-H′), 3.67 (d, *J* = 4.8 Hz, 2H, 1″-H_2), 3.80–3.88 (m, 1H, 2-H), 4.01–4.20 (m, 3H, 1-H″, 2′,5′-H), 7.35–7.48 (m, 6H, phenyl), 7.64–7.75 (m, 4H, phenyl). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.3 [$C(CH_3)_3$], 25.8 (CH_3, acetonide), 26.9 [$C(CH_3)_3$], 27.0 (CH_3, acetonide), 28.3, 28.4, 29.6, 29.7 (C-3,4,3′,4′), 66.4 (C-1″), 69.4 (C-1), 73.6 (C-5), 75.8 (C-2), 79.6, 82.6 (C-2′,5′), 108.8 (acetonide), 127.6, 129.6, 133.7, 135.6, 135.7 (phenyl). – $C_{29}H_{42}O_5Si$ (498.7): calcd. C 69.84, H 8.49; found C 69.68, H 8.44.

10) *(3S)-3,4-(Isopropylidenedioxy)butyl Pivalate* (**28**): To a stirred solution of 21.0 g (143 mmol) of alcohol *ent*-**15** in 100 ml of CH_2Cl_2 were added at 0°C 26.5 ml (26.0 g, 216 mmol) of pivaloyl chloride and 23.2 ml (288 mmol) of pyridine. The reaction mixture was warmed to room temp. and stirred for 48 h. It was subsequently partitioned between 200 ml of CH_2Cl_2 and 200 ml of water. The aqueous layer was extracted twice with 100 ml of CH_2Cl_2 each. The combined organic phases were washed with 100 ml of water. After drying with $MgSO_4$ the solvent was evaporated in vacuo. The residue was purified by fractional vacuum distillation. The fraction obtained at 90–95°C/0.5 Torr gave 26.5 g (115 mmol, 80%) of pivalate **28** as a colorless liquid. – TLC (petroleum ether/diethyl ether, 1:1): R_f = 0.77. – $[\alpha]_D^{20}$ = –3.4, $[\alpha]_{578}^{20}$ = –3.6, $[\alpha]_{546}^{20}$ = –4.0, $[\alpha]_{436}^{20}$ = –5.5, $[\alpha]_{365}^{20}$ = –5.8 (*c* = 1.03, $CHCl_3$). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 [s, 9H, $C(CH_3)_3$], 1.28 (s, 3H, CH_3, acetonide), 1.34 (s, 3H, CH_3, acetonide), 1.76–1.92 (m, 2H, 2-H_2), 3.52 (dd, *J* = 7.9/7.1 Hz, 1H, 4-H′), 3.99–4.20 (m, 4H, 4-H″, 3-H, 1-H_2). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.7, 26.5, 26.9 (CH_3, acetonide, C-2), 27.2 [$C(CH_3)_3$], 32.8 [$C(CH_3)_3$], 61.3 (C-1), 69.4 (C-4), 73.4 (C-3), 108.9 (acetonide), 178.4 (C=O). – $C_{12}H_{22}O_4$ (230.3): calcd. C 62.58, H 9.63; found C 62.59, H 9.83.

11) *(3S)-3,4-Dihydroxybutyl Pivalate* (**29**): To a stirred solution of 5.00 g (21.7 mmol) of the pivalate **28** in 100 ml of MeOH was added 100 mg (0.53 mmol) of *p*-toluenesulfonic acid monohydrate. The reaction mixture was stirred for 4 h at room temp. Then 100 ml of a satd. aqueous $NaHCO_3$ solution was added, and most of the methanol was evaporated in vacuo. The residue was extracted three times with 100 ml of *tert*-butyl methyl ether each. The combined organic phases were dried with $MgSO_4$. The solvent was evaporated in vacuo and the residue purified by CC (50 g of silica gel) with diethyl ether to give 3.00 g (15.8 mmol, 73%) of the diol **29** as a colorless liquid. – TLC (diethyl ether): R_f = 0.32. – $[\alpha]_D^{20}$ = –11.5, $[\alpha]_{578}^{20}$ = –11.9, $[\alpha]_{546}^{20}$ = –13.5, $[\alpha]_{436}^{20}$ = –22.0, $[\alpha]_{365}^{20}$ = –32.4 (*c* = 2.91, $CHCl_3$). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 [s, 9H, $C(CH_3)_3$], 1.76–1.92 (m, 2H, 2-H_2), 3.47–3.74 (m, 5H, 4-H′, 1-H_2, 2 OH), 4.16–4.28 (m, 2H, 4-H″, 3-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.6 (C-2), 26.8 [$C(CH_3)_3$], 32.0 [$C(CH_3)_3$], 60.9 (C-1), 66.2 (C-4), 68.7 (C-3), 178.8 (C=O). – $C_3H_{18}O_4$ (190.2): calcd. C 56.82, H 9.54; found C 57.18, H 9.56.

12) *(3S)-3,4-Bis(benzyloxy)butyl Pivalate* (**30**): 11.5 g (60.4 mmol) of the diol **29** was dissolved in 500 ml of diethyl ether in the dark. To the obtained solution were subsequently added 28.7 ml (41.3 g, 242 mmol) of benzyl bromide and 84.0 g (363 mmol) of Ag_2O. The reaction mixture was refluxed for 6 h and stirred for ca. 12 h at room temp. It was then filtered through Celite. The Celite plug was washed with diethyl ether. Evaporation of the solvent from the combined filtrates and purification of the residue by CC (300 g of silica gel) with petroleum ether/diethyl ether (10:1) gave 17.5 g (47.2 mmol, 78%) of the dibenzylated compound **30** as a colorless oil. – TLC (petroleum ether/diethyl ether, 10:1): R_f = 0.32. – $[\alpha]_D^{20}$ = –33.3, $[\alpha]_{578}^{20}$ = –34.4, $[\alpha]_{546}^{20}$ = –38.8, $[\alpha]_{436}^{20}$ = –65.2, $[\alpha]_{365}^{20}$ = –98.2 (*c* = 1.19, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3088, 3064, 3030, 2970, 2933, 2870, 1727 (C=O), 1496, 1480, 1454, 1397, 1365, 1284, 1161, 1101, 737, 698 cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 [s, 9H, $C(CH_3)_3$], 1.82–2.02 (m, 2H, 2-H_2), 3.59 (d, *J* = 4.8 Hz, 2H, 1-H_2), 3.71–3.78 (m, 1H, 3-H), 4.20 (dd, *J* = 5.9/7.0 Hz, 2H, 4-H_2), 4.57 (d, *J* = 11.4 Hz, 1H, PhC*H*H-O-3), 4.58 (s, 2H, $PhCH_2O$-4), 4.74 (d, *J* = 11.5 Hz, 1H, PhCH*H*-O-3), 7.29–7.37 (m, 10H, phenyl). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.1 [$C(CH_3)_3$], 31.3 (C-2), 32.0 [$C(CH_3)_3$], 61.0 (C-1), 72.2, 72.6, 73.4, 74.9 (C-3,4, $PhCH_2O$-3,4), 127.5, 127.7, 128.3, 138.2, 138.5 (phenyl), 178.4 (C=O). – $C_{23}H_{30}O_4$ (370.5): calcd. C 74.56, H 8.16; found C 74.30, H 8.30.

13) *(3S)-3,4-Bis(benzyloxy)butan-1-ol* (**31**): To a stirred suspension of 8.00 g (211 mmol) of $LiAlH_4$ in 200 ml of THF was added dropwise at 0°C 24.4 g (65.7 mmol) of the benzylated pivalate **30** dissolved in 80 ml of THF. The reaction mixture was refluxed for 3 h and then cooled to 0°C. With great caution 8 ml of water was added dropwise. After 30 min 8 ml of 3 N NaOH and 8 ml of water were added successively. The resulting mixture was stirred for 1 h at room temp. It was then filtered trough Celite. The Celite plug was suspended in 200 ml of THF. The suspension was filtered. This operation was repeated once. The filtrates were combined, and the solvent was evaporated in vacuo. The residue was purified by CC (300 g of silica gel) to yield 18.3 g (63.9 mmol, 97%) of the alcohol **31** as a colorless liquid. – TLC (petroleum ether/diethyl ether, 1:1): R_f = 0.24. – $[\alpha]_D^{20}$ = –32.0, $[\alpha]_{578}^{20}$ = –34.0, $[\alpha]_{546}^{20}$ = –38.0, $[\alpha]_{436}^{20}$ = –65.0, $[\alpha]_{365}^{20}$ = –97.0 (*c* = 2.00, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3433 (OH), 3089, 3064, 3030, 2926, 2866, 1496, 1454, 1399, 1364, 1310,

1206, 1093, 1057, 738, 698 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.84–1.90 (m, 2H, 2-H_2), 2.45 (br. s, 1H, OH), 3.58–3.69 (m, 2H, 1-H_2), 3.74–3.80 (m, 2H, 4-H_2), 3.83–3.91 (m, 1H, 3-H), 4.60 (s, 2H, PhCH_2O-4), 4.61 (d, J = 11.2 Hz, 1H, PhC*H*HO-3), 4.77 (d, J = 11.2 Hz, 1H, PhCH*H*O-3), 7.30–7.42 (m, 10H, phenyl). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.6 (C-2), 60.1 (C-1), 72.0 (C-4), 72.4, 73.3 (*C*H_2Ph), 76.8 (C-3), 127.5, 127.6, 127.8, 128.2, 128.3, 137.9, 138.3 (phenyl). – $C_{18}H_{22}O_3$ (286.4): calcd. C 75.50, H 7.74; found C 75.54, H 7.94.

14) *(2S)-1,2-Bis(benzyloxy)-4-iodobutane* (**32**): To a stirred solution of 13.0 g (45.4 mmol) of the alcohol **31** in 100 ml of CH_2Cl_2 were added at 0°C 22.0 ml (272.6 mmol) of pyridine and 17.5 g (91.8 mmol) of *p*-tosyl chloride. The reaction mixture was warmed to room temp. and stirred for 12 h and subsequently cooled to 0°C. Then 20 ml of water was added. After stirring for 10 min the mixture was acidified by the addition of 1 N HCl until pH 3. The phases were separated. The aqueous phase was extracted twice with 250 ml of *tert*-butyl methyl ether each. The combined organic phases were washed successively with 200 ml of a satd. aqueous $NaHCO_3$ solution and with 200 ml of a satd. aqueous NaCl solution. After drying with $MgSO_4$ the solvent was evaporated in vacuo. The crude tosylate was used without further purification for the next step. It was dissolved in 150 ml of acetone, and 13.6 g (90.7 mmol) of NaI was added. The reaction mixture was refluxed for 2 h. After cooling to room temp. it was partitioned between 300 ml of *tert*-butyl methyl ether and 300 ml of water. The aqueous phase was extracted twice with 150 ml of *tert*-butyl methyl ether each. The combined organic phases were washed twice with 100 ml of a satd. aqueous NaCl solution and dried with $MgSO_4$. After evaporation of the solvent the residue was purified by CC (200 g of silica gel) with petroleum ether/*tert*-butyl methyl ether (2:1) to afford 13.3 g (33.5 mmol, 74%) of the iodide **32** as a colorless liquid. – TLC (petroleum ether/diethyl ether, 20:1): R_f = 0.67. – $[\alpha]_D^{20}$ = –39.3, $[\alpha]_{578}^{20}$ = –41.3, $[\alpha]_{436}^{20}$ = –79.4, $[\alpha]_{365}^{20}$ = –120.9 (c = 1.08, $CHCl_3$). – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.88–1.92 (m, 2H, 3-H_2), 3.26 (dd, J = 6.4/7.5 Hz, 2H, 4-H_2), 3.54 (dd, J = 2.6/4.8 Hz, 2H, 1-H_2), 3.68–3.76 (m, 1H, 2-H), 4.54 (s, 2H, PhCH_2O-1), 4.56 (d, J = 11.5 Hz, 1H, PhC*H*HO-2), 4.72 (d, J = 11.5 Hz, 1H, PhCH*H*O-2), 7.24–7.38 (m, 10H, phenyl). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 2.7 (C-4), 36.3 (C-3), 70.8 (C-1), 72.5, 73.4 (*C*H_2Ph), 77.8 (C-2), 127.5, 127.6, 127.9, 128.4, 128.5, 138.1, 138.4 (phenyl). – $C_{18}H_{21}IO_2$ (396.3): calcd. C 54.56, H 5.34; found C 54.73, H 5.39.

15) *Preparation of (3S)-3,4-Bis(benzyloxy)butylzinc Iodide* (**33**): A 100-ml three-necked round-bottomed flasked was equipped with a magnetic stirring bar, a rubber septum, an inert gas inlet, and a thermometer. The air in the flask was replaced by argon, and the flask was charged with 1.96 g (30.0 mmol) of zinc dust. Then 2 ml of THF and 100 µl (218 mg, 1.16 mmol) of dibromoethane were successively injected into the flask. The reaction mixture was gently heated three times with a heat gun until ebullition of the solvent was observed. After cooling to room temp., 10 µl (86 mg, 0.79 mmol) of chlorotrimethylsilane was added, and the reaction mixture was heated for 15 min to 35°C. After cooling to room temp., the rubber septum was replaced by an addition funnel charged with 3.96 g (10.0 mmol) of the iodide **32** dissolved in 20 ml of THF. The iodide solution was added dropwise to the reaction mixture over a period of 30 min, during which time the temp. of the reaction mixture rose to 32°C. The reaction mixture was subsequently stirred for 4 h at 45°C. After addition of 10 ml of THF stirring was stopped, and excess zinc dust was allowed to settle down overnight. The supernatant colorless, slightly turbid THF solution of the organozinc reagent **33** was transferred to a Schlenk flask by a stainless steel canula. The solvent was evaporated in vacuo. To the neat zinc reagent was added 40 ml of freshly distilled degassed CH_2Cl_2 to give a colorless, slightly turbid solution of **33**, which was used directly for the following experiments.

16) *(1R,4S)-4,5-Bis(benzyloxy)-1-phenylpentan-1-ol* (**34**) *and (1S,4S)-4,5-Bis(benzyloxy)-1-phenylpentan-1-ol* (**35**): 10.0 ml (4.00 mmol) of a CH_2Cl_2 solution of the organozinc reagent **33** was cooled to –30°C. To this stirred solution were added successively 200 µl (212 mg, 2.00 mmol) of benzaldehyde (**18d**) and 500 µl (570 mg, 4.00 mmol) of $BF_3 \cdot OEt_2$. The reaction mixture was warmed to room temp. during 3 h and stirred at this temp. for 16 h. Then 30 ml of a satd. aqueous NH_4Cl solution was added. The reaction mixture was extracted twice with 20 ml of *tert*-butyl methyl ether each. The combined organic phases were washed with 30 ml of a satd. aqueous NaCl solution, dried with $MgSO_4$, and concentrated. The residue was purified by CC (30 g of silica gel) with petroleum ether/*tert*-butyl methyl ether (1:1) to give 737 mg (1.96 mmol, 98%) of an epimeric mixture of the alcohols **34** and **35** as a colorless liquid. ^1H-NMR analysis revealed an epimeric ratio of 1:1. – TLC (petroleum ether/diethyl ether, 1:1): R_f = 0.39. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.58–1.95 (m, 4H, 2,3-H_2), 2.37, 2.42 (br. s, 1H, OH), 3.51–3.72 (m, 3H, 5-H_2, 4-H), 4.55–4.74 (m, 5H, 1-H, PhCH_2O-4,5), 7.26–7.40 (m, 15H, phenyl). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.2, 34.9, 71.9, 72.0, 72.1, 72.7, 73.4, 74.4, 77.8, 78.0, 79.5, 125.9, 127.4, 127.6, 127.7, 127.8, 127.9, 128.3, 128.4, 128.5, 138.3, 138.6. – $C_{25}H_{28}O_3$ (376.5): calcd. C 79.75, H 7.50; found C 79.33, H 7.35.

17) *(1R,4S,2'S,5'S)-1-{5'-[(tert-Butyldiphenylsiloxy)methyl]-tetrahydro-2'-furyl}-4,5-bis(benzyloxy)pentan-1-ol* (**36**) *and (1S,4S,2'S,5'S)-1-{5'-[(tert-Butyldiphenylsiloxy)methyl]tetrahydro-2'-furyl}-4,5-bisbenzyloxy)pentane-1-ol* (**37**): A solution of 737 mg (2.00 mmol) of the THF-aldehyde **1** in 20 ml of CH_2Cl_2 was cooled to –55°C. To this solution was added 500 µl (570 mg, 4.00 mmol) of $BF_3 \cdot OEt_2$. After stirring for 5 min 10.0 ml (4.00 mmol) of the solution of the organozinc reagent **33** in CH_2Cl_2 was added dropwise. The mixture was warmed to room temp. during 3 h and stirred at this temp. for 16 h. Then 30 ml of a satd. aqueous NH_4Cl solution was added. The reaction mixture was extracted two times with 100 ml of *tert*-butyl methyl ether each. The combined organic phases were washed with 30 ml of a satd. aqueous NaCl solution, dried with $MgSO_4$ and concentrated. The residue was purified by CC (40 g of silica gel) with petroleum ether/*tert*-butyl methyl ether (1:1) to give 1.03 g (1.61 mmol, 81%) of a 86:14 epimeric mixture (determined by ^1H-NMR analysis) of **36** and **37** as a colorless liquid. – TLC (petroleum ether/diethyl ether, 1:1): R_f = 0.38. – $[\alpha]_D^{20}$ = –7.5, $[\alpha]_{578}^{20}$ = –8.6, $[\alpha]_{546}^{20}$ = –9.8, $[\alpha]_{436}^{20}$ = –16.1, $[\alpha]_{365}^{20}$ = –25.3 (c = 1.74, $CHCl_3$). – IR (neat): $\tilde{\nu}$ = 3456 (OH), 3069, 3031, 2930, 2858, 1472, 1454, 1429, 1390, 1362, 1112, 1029, 1007, 824, 739, 701, 613, 505 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.09 [s, 9H, C(CH_3)$_3$], 1.48–2.07 (m, 8H, 2,3,3',4'-H_2), 2.36 (d, J = 2.5 Hz, 1H, OH), 3.56–3.59 (m, 2H, 5-H', 1-H), 3.62–3.73 (m, 2H, 5-H'', 4-H), 3.68 (d, J = 4.7 Hz, 2H, 1''-H_2), 3.83–3.91 (m, 1H, 2'-H), 4.11–4.20 (m, 1H, 5'-H), 4.57 (s, 2H, PhCH_2O-5), 4.60 (d, J = 11.8 Hz, 1H, PhC*H*HO-4), 4.74 (d, J = 11.8 Hz, 1H, PhCH*H*O-4), 7.37–7.49 (m, 16H, phenyl), 7.69–7.74 (m, 4H, phenyl). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.2 [*C*(CH_3)$_3$], 26.8 [C(*C*H_3)$_3$], 27.0, 28.2, 28.5, 28.7 (C-2,3,3',4'), 66.6 (C-1''), 72.0, 72.2 (C-1,5), 72.8, 73.3 (PhCH_2O-4,5), 78.2 (C-4), 79.9, 82.2 (C-2',5'), 127.5, 127.6, 127.7, 127.8, 128.2, 128.3, 129.6, 133.7, 135.6, 138.3, 138.7 (phenyl). – $C_{40}H_{50}O_5Si$ (638.9): calcd. C 75.19, H 7.89; found C 75.04, H 7.91.

[1] [1a] U. Koert, *Tetrahedron Lett.*, **1994**, *35*, 2517–2520. – [1b] J. K. Rupprecht, Y.-H. Hui, J. L. McLaughlin, *J. Nat. Prod.* **1990**, *53*, 237–278. – [1c] T. R. Hoye, P. Hanson, *Tetrahedron Lett.* **1993**, *34*, 5043–5046. – [1d] S. C. Sinha, E. Keinan, *J. Am. Chem. Soc.* **1993**, *115*, 4891–4892. – [1e] B. Figadere, J.-C. Harmange, L. X. Hai, A. Cave, *Tetrahedron Lett.* **1992**, *33*, 5189–5192. – [1f] J.-C. Harmange, B. Figadere, *Tetrahedron: Asymmetry* **1993**, *4*, 1711–1754.

[2] U. Koert, M. Stein, K. Harms, *Angew. Chem.* **1994**, *106*, 1238–1240; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1180–1182.

[3] U. Koert, M. Stein, K. Harms, *Tetrahedron Lett.* **1993**, *34*, 2229–2302.

[4] M. T. Reetz, *Angew. Chem.* **1984**, *96*, 542–555; *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 556–569.

[5] D. J. Cram, K. R. Kopecky, *J. Am. Chem. Soc.* **1959**, *81*, 2748–2755.

[6] [6a] X. Chen, E. R. Hortelano, E. L. Eliel, S. V. Frye, *J. Am. Chem. Soc.* **1992**, *114*, 1778–1784. – [6b] M. T. Reetz, M. Hüllmann, T. Seitz, *Angew. Chem.* **1987**, *99*, 478–480; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 477–479. – [6c] S. Shambayati, W. E. Crowe, S. L. Schreiber, *Angew. Chem.* **1990**, *102*, 273–290; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 256–273.

[7] [7a] M. T. Reetz, *Pure Appl. Chem.* **1985**, *57*, 1781–1788. – [7b] M. T. Reetz, K. Kesseler, *J. Chem. Soc., Chem. Commun.* **1984**, 1079–1080. – [7c] G. E. Keck, E. P. Boden, *Tetrahedron Lett.* **1984**, *25*, 265–269.

[8] P. Knochel, R. D. Singer, *Chem. Rev.* **1993**, *93*, 2117–2188.

[9] M. C. P. Yeh, P. Knochel, L. E. Santa, *Tetrahedron Lett.* **1988**, *29*, 3887–3890.

[10] Y. Nishigaichi, A. Takuwa, Y. Naruta, K. Maruyama, *Tetrahedron* **1993**, *49*, 7395–7426.

[11] Y. Gao, C. M. Zepp, *Tetrahedron Lett.* **1991**, *21*, 3155–3158.

[12] [12a] B. Seuring, D. Seebach, *Helv. Chim. Acta* **1977**, *60*, 1175–1181. – [12b] P. J. Kociensky, C. Yeates, S. D. A. Street, S. F. Campbell, *J. Chem. Soc., Perkin Trans. 1*, **1987**, 2183–2187.

[13] [13a] D. Seebach in *Modern Synthetic Methods* (Ed.: R. Scheffold), Salle & Sauerländer, Frankfurt am Main, **1980**, vol. 2, p. 93–162. – [13b] P. De Clercq, R. Mijnhgeer, *Bull. Soc. Chim. Belg.* **1978**, *87*, 495–496.

[14] [14a] P. Knochel, M. C. P. Yeh, S. C. Berk, J. Talbert, *J. Org. Chem.* **1988**, *53*, 2390–2392. – [14b] M. C. P. Yeh, H. G. Chen, P. Knochel, *Org. Synth.* **1991**, *70*, 195–203.

[15] S. Masamune, W. Choy, J. S. Petersen, L. R. Sita, *Angew. Chem.* **1985**, *97*, 1–31; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 1–31.

[16] R. D. Walkup, R. T. Cunningham, *Tetrahedron Lett.* **1987**, *28*, 4019–4022.

[17] D. Seebach, H.-O. Kalinowski, B. Bastani, G. Crass, H. Daum, H. Dörr, N. P. DuPreez, V. Ehrig, W. Langer, C. Nüssler, H.-A. Oei, M. Schmidt, *Helv. Chim. Acta* **1977**, *60*, 301–325.

[54/94]