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Stereocontrolled Synthesis of a C^n–C^{n+6} Building Block for the Unnatural Enantiomers of Important Polyol,Polyene Antibiotics from an Epoxy Alcohol by a Reduction/Conjugate Addition/Hydroxylation Sequence

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Epoxy alcohol *anti*-**10**, derived from a desymmetrizing Sharpless epoxidation (up to 97 % *ee*) of divinylcarbinol **9**, provided the unsaturated 1,3-diol *syn*-**11** upon treatment with RedAl®; *syn*-**11** was converted into the α,β-unsaturated esters (*E*)- or (*Z*)-**7b** in three steps. Cu-promoted 1,4-addition of vinylmagnesium halides to the (*E*)-ester proceeded with diastereoselectivities of up to 91 % and Cu-catalyzed 1,4-additions with diastereoselectivities of up to 82 %. The potassium enolate of the major vinylation product *syn*-**22b** was hydroxylated by the Davis oxaziridine with perfect but unprecedented diastereoselectivity. The resulting hydroxy ester, $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32**, furnished the "eastern moiety" building block **6** of the title compounds in three steps.

Introduction

The polyol,polyene macrolides are a family of several hundred secondary metabolites from bacterial pathogens of the genus *Streptomyces*.[1] Scheme 1 illustrates typical structural features of such polyol,polyene macrolides through a compilation of the unnatural enantiomers **1**–**5** of the aglycons of the antifungal agents amphotericin B[2] (aglycon = *ent*-**1**) and nystatin A_1[3] (aglycon = *ent*-**2**) as well as of candidin[4] (aglycon = *ent*-**3**), pimaricin,[5,6] (aglycon = *ent*-**4**), and rimocidin[7] (aglycon = *ent*-**5**). An accompanying paper[8] enumerates a few related macrolides,[9] which have the identical trisubstituted tetrahydropyrancarboxylic acid moiety (the "eastern moiety") as *ent*-**1**–**5**. That paper[8] also reviews our cumulative knowledge of structure–activity relationships, which has been derived from omissions or derivatizations of naturally occurring polyol,polyene macrolides. Moreover, the accompanying paper[8] explains why it could be interesting to include artificial polyol/polyenes in the mentioned structure–activity relationships. For example, such artifacts might resemble *ent*-**1**–**5** by being composed of an unmodified "eastern moiety" and of unprecedented polyol and/or polyene sections. Whether the resulting macrolides, or glycosides thereof, turn out to be antibiotics would be interesting to determine.

Given that motivation, we have developed synthetic routes to the "eastern moiety" both of the natural polyol, polyene macrolides **1**–**5**[10] and their unnatural counterparts *ent*-**1**–**5**.[11] The synthetic procedures used for the former are described in ref.[8] and those for the latter in the present publication (**6**; cf. Scheme 1) and an accompanying paper.[12]

Building block **6** for the "eastern moiety" of the unnatural enantiomers **1**–**5** of macrolides *ent*-**1**–**5** contains an oxirane at one end (C^n) and a latent OH group at the other (C^{n+6}). These functional groups should allow the "northern moiety", that is, polyol building block, to be attached (by nucleophilic attack on C^n) as well as the "southwestern moiety", that is, hydroxylated polyene building block (by olefination of a C^{n+6} aldehyde) of the respective target.

Results and Discussion

As Scheme 1 shows, the "eastern moiety" building block **6** can be traced back to the monoepoxide *anti*-**10**. The latter was obtained from divinylcarbinol **9** by a desymmetrizing Sharpless epoxidation, which had been developed in a systematic study[13,14] of that transformation.[15] It delivered the desired monoepoxide *anti*-**10** in an inseparable mixture with its diastereomer *syn*-**10** in a ratio of around 75:25. Separation from the undesired material was postponed until after the subsequent step, which involved reducing the desired monoepoxide *anti*-**10** to the 1,3-diol *syn*-**11** regioselectively. Red-Al® [$NaH_2Al(OCH_2CH_2OMe)_2$] brings about this transformation in many Sharpless epoxides.[16] The major constituent (*anti*-**10**) of our mixture of diastereomeric

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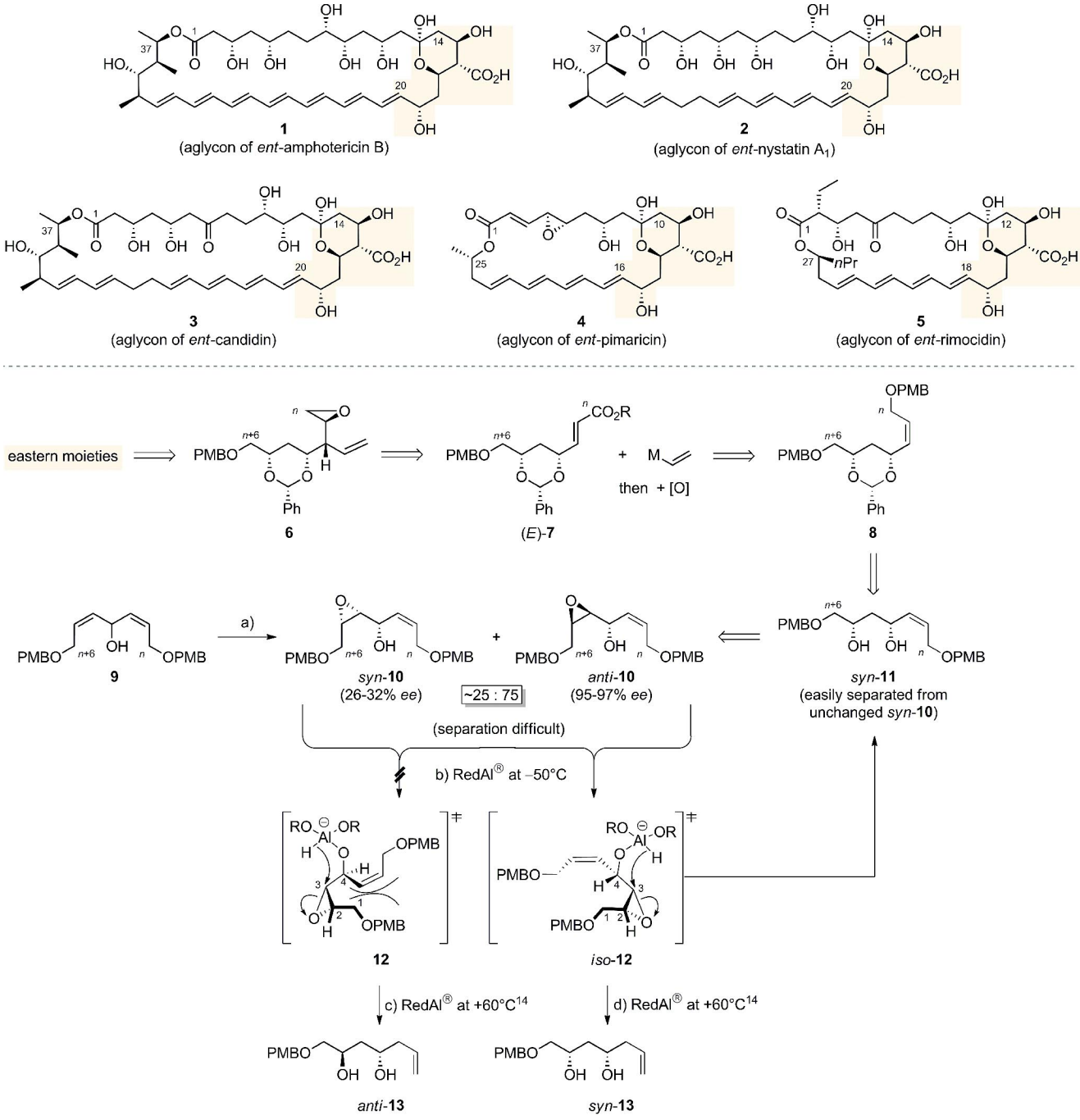


Scheme 1. Top: Unnatural enantiomers **1**–**5** of the naturally occurring polyol,polyene macrolides amphotericin B[2] (*ent*-**1**), nystatin A_1[3] (*ent*-**2**), candidin[4] (*ent*-**3**), pimaricin[5,6] (*ent*-**4**), and rimocidin[7] (*ent*-**5**). Compounds **1**–**5** have in common a tetrahydropyrancarboxylic acid ("eastern moiety") motif. Center: Simplifying the "eastern moiety" building block **6** retrosynthetically to the known[13] bis(*cis*-alkenyl)carbinol **8** as the starting material. Bottom: Chemo- and substrate-selective epoxy alcohol reductions. Reagents and conditions: a) sequential addition of 4 Å molecular sieves, $Ti(OiPr)_4$ (1.05 equiv.), and L-(+)-DiPT (1.1 equiv.), CH_2Cl_2, –20 °C, 30 min; *t*BuOOH (2.0 equiv.), 1 h; **9**, 72 h; *syn*-**10**:*anti*-**10** = 25:75 in the crude product and 16:84 after purification by flash chromatography on silica gel; 72%; *syn*-**10**: 27% *ee*, *anti*-**10**: 96% *ee*;[14] b) starting from a 16:84 *syn*-**10**/*anti*-**10** mixture: Red-Al® (10-fold molar amount relative to the fraction of *anti*-**10**), toluene, –50 °C, 16 h; *syn*-**11**: 97%; recovered *syn*-**10**: 90%; c) starting from epoxide *ent*-*syn*-**10** diol, *ent*-*anti*-**13** was accessed as follows: Red-Al® (10-fold molar amount), toluene, –30→ 60 °C, 4.5 h; $NaIO_4$ (1.0 equiv.), THF/H_2O (1:1), room temp., 2 h; 51%;[14] d) Red-Al® (4-fold molar amount), toluene, 60 °C, 2 h; 83%.[14] DiPT = diisopropyl tartrate; Red-Al® = $NaH_2Al(OCH_2CH_2OMe)_2$.

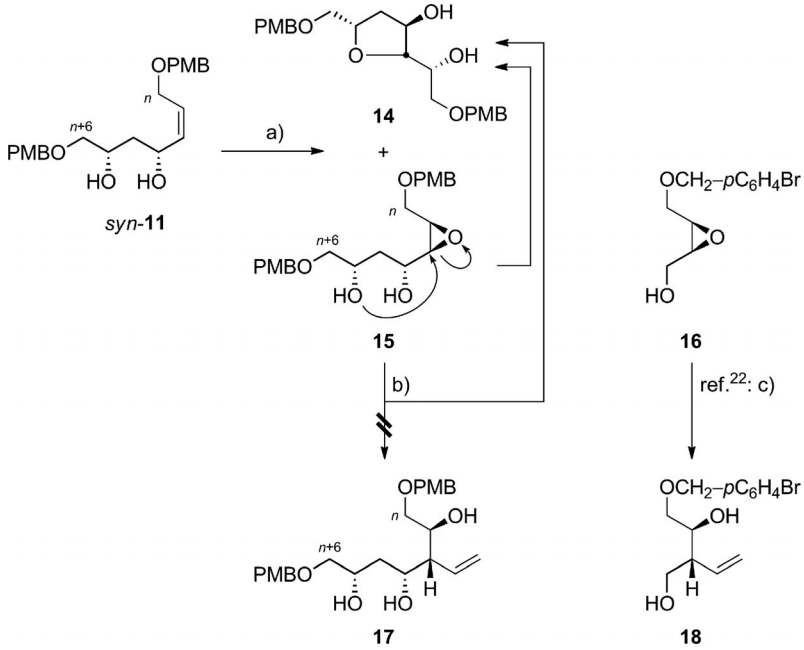
Sharpless epoxides could be reduced by this method, but not the minor component (*syn*-**10**). The first-mentioned epoxy alcohol *anti*-**10** reacted with Red-Al® at –50 °C to give the desired 1,3-diol *syn*-**11** in 97% yield. In contrast, the epoxy alcohol *syn*-**10** remained essentially untouched under these conditions. It was separated by flash chromatography

on silica gel[17] and recovered in 90% yield. As a result of this separation, we continued our synthesis with pure specimens of diol *syn*-**11**, as will be described below (Scheme 2).

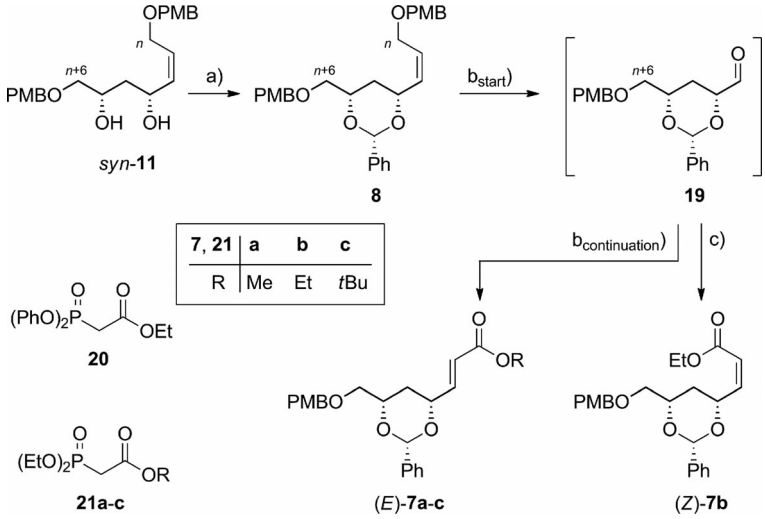
The fact that epoxy alcohol *anti*-**10** can be reduced by Red-Al® at –50 °C but epoxy alcohol *syn*-**10** cannot, can be rationalized by the absence versus presence of steric hindrance in the corresponding trialkoxyaluminates (**12** vs. *iso*-**12**, Scheme 1). These intermediates form from the reactants when 1 equiv. of H_2 is liberated and the initially produced epoxy-alkoxide binds to the initially resulting alane HAl-$(OCH_2CH_2OMe)_2$. It is assumed that the trialkoxyaluminate continues to react by intramolecular hydride addition to C^β, which induces epoxide ring-opening by regioselective scission of the C^β–O bond.[16] As the structures of the trialkoxyaluminates **12** and *iso*-**12** indicate (Scheme 1 bottom), the required collinearity of the Al–H and C^β–O bonds enforces a U-shaped (**12**) versus sickle-shaped conformation (*iso*-**12**) in the substrate moiety. The former is thus more hindered than the latter.[18-20]

First, we wished to epoxidize the 1,3-diol *syn*-**11** diastereoselectively[21] and ring-open the expected epoxydiol **15** by using a vinylcopper reagent[22] with the same regioselectively as reported for the ring-opening of **16** to **18** (Scheme 2).[22f] At –27 °C, the epoxidation of *syn*-**11** with 2.0 equiv. of MCPBA required 16 days to reach completion.[23] It delivered none of the desired epoxide **15** but 88% of a single diastereomer of a tetrahydrofuran.[23] We ascribe the stereostructure **14** to it based on the surmised 3D structure of the precursor epoxide **15** and an intramolecular epoxide ring-opening with an inversion of the configuration. We suspected that the ease of this follow-up reaction was due to proton catalysis by *m*-chlorobenzoic acid, which forms as a stoichiometric byproduct. Corroborating this interpretation, epoxidation at virtually the same temperature (–30 °C) with a total of 6.0 equiv. of MCPBA in the presence of a total of 12.0 equiv. of $NaHCO_3$[24] led to complete consumption of diol *syn*-**11** within a total of 60 h. The ^1H NMR spectrum (C_6D_6/C_6D_5H) of the crude product revealed no evidence of the tetrahydrofuran **14**, but showed exclusively resonances of the epoxide **15**. Those for its epoxide core were observed at $\delta_{5\text{-H}}$ = 2.85 ppm (dd, $J_{\text{exocyclic}}$ = 7.8, $J_{\text{endocyclic}}$ = 4.5 Hz) and $\delta_{6\text{-H}}$ = 3.08 ppm (ddd, $J_{\text{exocyclic,\#1}}$ = $J_{\text{exocyclic,\#2}}$ = 5.3, $J_{\text{endocyclic}}$ = 4.6 Hz). Attempts to purify the epoxide **15** by flash chromatography on silica gel,[17] silica gel deactivated with 5% NEt_3, neutral alumina, or basic alumina always led to some tetrahydrofuran formation. At best, we isolated 57% of an 87:13 mixture of the desired epoxide **15** and the tetrahydrofuran **14**. We gave up on the strategy shown in Scheme 2 when a reagent formed from 4 equiv. of vinylMgBr and 0.2 equiv. of CuI, which is known to effect the epoxide ring-opening **16**→**18** selectively,[22f] converted the crude epoxide **15** into the notorious tetrahydrofuran **14** again (64% yield) rather than into the desired alcohol **17**.

Scheme 3 shows how we modified the 1,3-diol *syn*-**11** so that the vinyl group, which had eluded introduction by nucleophilic substitution (Scheme 2), could be incorporated by a 1,4-addition reaction: By synthesizing the α,β-unsaturated esters (*E*)-**7a**–**c** or the isomeric α,β-unsaturated esters (*Z*)-**7b**. The modification of *syn*-**11** first involved the synthesis of the all-*trans*-substituted benzylidene acetal **8** in 95% yield. Ozonolysis of the olefinic C=C bond in CH_2Cl_2/

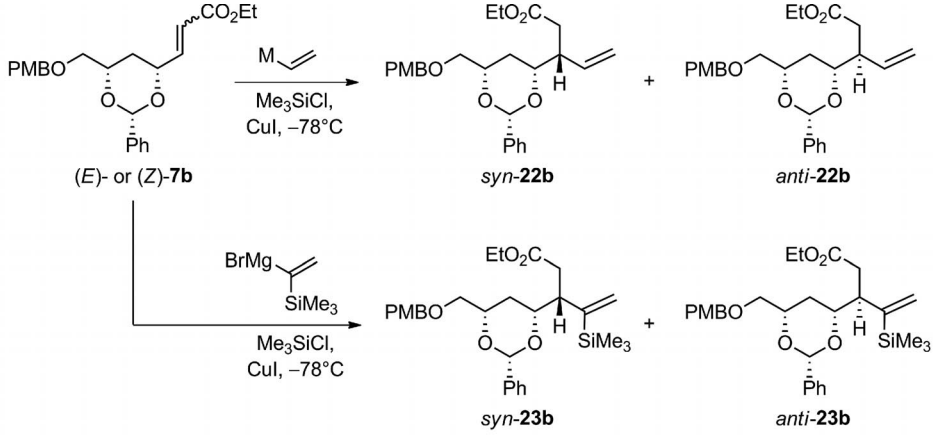


Scheme 2. Nonfeasibility of a short-cut to compound **17**, which exhibits the stereoarray of building block **6**. Reagents and conditions: a) Variant 1: MCPBA (2.0 equiv.), CH_2Cl_2, –27 °C, 16 d; 88% **14**;[23] variant 2: MCPBA (2.0 equiv.), $NaHCO_3$ (4.0 equiv.), CH_2Cl_2, –30 °C, 20 h; the same once more; the same a third time; 57% of 87:13 **15**/**14**; b) vinylMgBr (4.0 equiv.), CuI (0.2 equiv.), THF, –78 °C, 10 min; addition of **15** (as a crude product), 30 min; in the course of 12 h →room temp.; 64% **14** (contaminated). c) Same as (b) but –78 °C→room temp. overnight; 73%.[22] MCPBA = *m*-chloroperbenzoic acid.



Scheme 3. Syntheses of γ-chiral Michael acceptors **7**. Reagents and conditions: a) $PhCH(OMe)_2$ (3.0 equiv.), PPTS (2 mol-%), DMF, 60 °C, 3 h; 95%; b_{start}) stream of O_3, pyridine [1% (v/v)], CH_2Cl_2/MeOH (1:1), –78 °C; stream of N_2; Me_2S (5.6 or 9.2 equiv.), 30–90 min; in the course of 2 h → room temp.; **19** was used after removal of the solvent but without purification; $b_{continuation}$) NaH (2.1–2.5 equiv.), phosphonoacetate **21** (2.1–2.5 equiv.), THF, –10 or 0 °C; → room temp.; →–20 or –10 °C; addition of **19**, 15–60 min; **7a**: 75%; **7b**: 82%; **7c**: 62%; c) NaH (2.5 equiv.), phosphonoacetate **20** (2.2 equiv.), THF, –5 °C, 45 min; →–78 °C; addition of **19**; in the course of 100 min →–30 °C; 52%. PPTS = pyridinium *p*-toluenesulfonate.

Table 1. Conjugate addition of vinylmagnesium bromide or lithium divinylcuprate to the γ-chiral Michael acceptors (*E*)- and (*Z*)-**7b** in the presence of Me_3SiCl (over-stoichiometric) and Cu^I (over-stoichiometric).



Entry	Substrate	**7** [mmol]	Vinylmetallic M	[equiv.]	CuI [equiv.]	Me_3SiCl [equiv.]	Solvent	*T* [°C]	*t* [h]	Product	Yield [%]	*syn*/*anti*
1	(*E*)-**7b**	0.2	Li	8	4	5	Et_2O	–78	4	starting material	50 (recov.)	–
2	(*E*)-**7b**	0.2	Li	8	4	–	Et_2O	–35	4	unidentified mixture	–	–
3	(*E*)-**7b**	0.2	Li	8	4	5	THF	–78	4	starting material	95 (recov.)	–
4	(*E*)-**7b**	0.2	Li	8	4	–	THF	–35	4	unidentified mixture	–	–
5	(*E*)-**7b**	0.1	BrMg	16	8	17	Et_2O/THF (3:1)	–78	0.5	**22b**	64	91: 9[a]
6	(*E*)-**7b**	0.3	BrMg	16	8	17	Et_2O/THF (3:1)	–78	0.5	**22b**	62	87:13[a]
7	(*E*)-**7b**	0.6	BrMg	16	8	17	Et_2O/THF (3:1)	–78	0.5	**22b**	60	82:18[a]
8	(*E*)-**7b**	0.1	BrMg	16	8	17	THF	–78	0.75	**22b**	84	78:22[a]
9	(*E*)-**7b**	1.0	BrMg	16	8	17	THF	–78	0.75	**22b**	82	79:21[a]
10	(*E*)-**7b**	4.0	BrMg	12	6	13	THF	–78	0.75	**22b**	81	78:22[a]
11	(*E*)-**7b**	0.2	BrMg	12	6	–	THF	–78	2	**22b**	60	79:21[a]
12	(*E*)-**7b**	1.0	BrMg	8	4	9	THF	–78	1	**22b**	66	79:21[a]
13	(*E*)-**7b**	0.1	$BrMg_{\alpha\text{-SiMe3}}$	16	8	17	THF	–78	6	**23b**	64	74:26[b]
14	(*Z*)-**7b**	0.5	BrMg	10	5	11	THF	–78→20	14	**22b**	68	65:35[a]

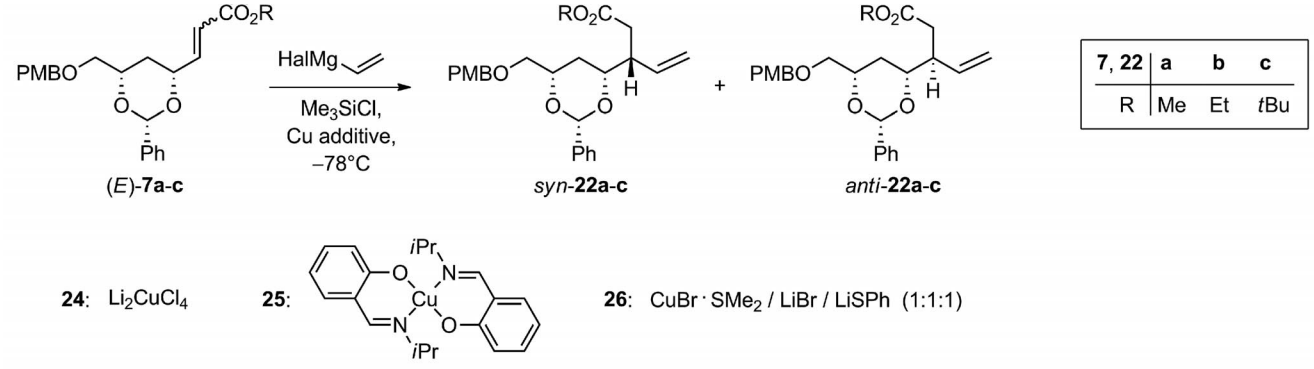
[a] Determined from the mean integral ratio of the following ^1H NMR resonances (400.1 MHz, $CDCl_3$/TMS): δ = 2.37 [dd, $^2J_{2\text{-H(A)},2\text{-H(B)}}$ = 16.3, $J_{2\text{-H(A)},3}$ = 9.9 Hz, 2-H^A (*syn*-**22b**)] vs. AB signal [δ_A = 2.46, δ_B = 2.66, J_{AB} = 15.5 Hz, in addition split by $J_{A,3}$ = 8.6 and $J_{B,3}$ = 6.0, 2-H_2 (*anti*-**22b**)] and δ = 3.72 [ddd, $J_{4',5'\text{-H(ax)}}$ = 10.8, $J_{4',3}$ = 7.9, $J_{4',5'\text{-H(eq)}}$ = 2.3 Hz, 4′-H (*syn*-**22b**)] vs. 3.91 ppm [ddd, $J_{4',5'\text{-H(ax)}}$ = 11.1, $J_{4',3}$ = $J_{4',5'\text{-H(eq)}}$ = 3.4 Hz, 4′-H (*anti*-**22b**)]. [b] Determined from the mean integral ratio of the following ^1H NMR resonances (400.1 MHz, $CDCl_3$/TMS): δ = 0.11 [s, $SiMe_3$ (*anti*-**23b**)] vs. δ = 0.13 ppm [s, $SiMe_3$ (*syn*-**23b**)]; δ = 1.12 [dd, 2′′′-H_2 ($^{\beta,\gamma}$*anti*-**23b**)] vs. δ = 1.21 ppm [dd, 2′′′-H_2 (*anti*-**23b**)]; δ = 2.97 [ddd, 3-H (*syn*-**23b**)] vs. δ = 3.14 ppm [ddd, 3-H (*anti*-**23b**)]; δ = 5.50 [s, 2′-H (*anti*-**23b**)] vs. δ = 5.52 ppm [s, 2′-H (*syn*-**23b**)].

MeOH, to which we added 1 vol-% pyridine[25] to protect the PMB group from being oxidized to the *p*-methoxybenzoate,[26] was then performed. This provided the desired aldehyde **19** and its byproduct 2-PMB-acetaldehyde. These compounds were not completely separable by flash chromatography on silica gel,[17] **19** eluting more slowly. Therefore we subjected mixtures of these aldehydes to *trans*-selective Horner–Wadsworth–Emmons reactions with the deprotonated (NaH) phosphonates **21a**–**c**[27] or to the *cis*-selective Ando variant with the deprotonated (NaH) phosphonate **20**.[28] The desired α,β-unsaturated esters (*E*)-**7a**–**c** and (*Z*)-**7b** were readily separable from the accompanying 4-[(*p*-methoxybenzyl)oxy]crotonates by flash chromatography on silica gel.[17]

The literature contains plenty of reports on diastereoselective 1,4-additions of copper-containing organometallics to α,β-unsaturated γ-alkoxy esters.[29] This statement is equally true for copper-containing vinylmetals.[30] 1,4-Additions of the latter reagents to *E*-configured α,β-unsaturated γ-alkoxy esters lead to a relative configuration of the newly created stereocenter (C^{β}) vs. the previously present stereocenter (C^{γ}), which we designate as *syn* in accordance with the nomenclature chosen in Table 1.[31] This is also true for 1,4-additions of large excesses of vinylMgBr/CuI/Me_3SiCl to *E*-configured α,β-unsaturated γ-alkoxy esters,[30f,30h] which are structurally very similar to ours. We are aware of two exceptions for the 1,4-addition of organocopper compounds: The addition of $(methallyl)_2CuLi$ to *E*-configured α,β-unsaturated γ-alkoxy esters displays an *anti* preference.[29a,32] 1,4-Additions of copper-containing organometallics to *Z*-configured α,β-unsaturated γ-alkoxy esters seem to exhibit a less reliable *syn* preference.[29] However, there are exceptions, which convinced us to include 1,4-additions to the α,β-unsaturated esters (*Z*)-**7b** in our investigation: $Vinyl_2CuLi$ added to the unsaturated ethyl esters derived from the benzyl ether of L-lactic acid by aldehyde formation and olefination with a 72:28 *syn*/*anti* bias when the ester was *E*-configured but with >99% *syn* selectivity when the ester was *Z*-configured.[29a]

In the 1,4-addition reactions in this study, 2–16 equiv. of vinylmagnesium bromide or vinylmagnesium chloride served as the standard vinyl source (Table 1 and Table 2) because vinyllithium failed to react properly (Table 1, entries 1–4). THF proved to be the solvent of choice rather than Et_2O (Table 1, entries 1–4 vs. 5–7 vs. 8–14; Table 2, entry 2 vs. 1). The presence of comparably large amounts of Me_3SiCl (3–17 equiv.) seemed to have the effect of increasing the yield (Table 2, entries 5 vs. 6), but we did not establish this unambiguously. The *E*-configured ethyl ester (*E*)-**7b** reacted much more quickly with vinylmagnesium bromide/CuI than isomer (*Z*)-**7b** (Table 1, entries 11,12 vs. 14). Addition of the CuI-modified α-(trimethylsilyl)vinylmagnesium bromide (Table 1, entry 13) instead of the unsubstituted vinylmagnesium bromide (Table 1, entry 8) negatively affected the reaction time, yield, and diastereocontrol. The largest *syn*/*anti* diastereoselectivity observed was

Table 2. Conjugate addition of vinylmagnesium halides to the γ-chiral Michael acceptors (*E*)-**7a**–**c** in the presence of Me_3SiCl (over-stoichiometric) and Cu^{I} (catalytic).



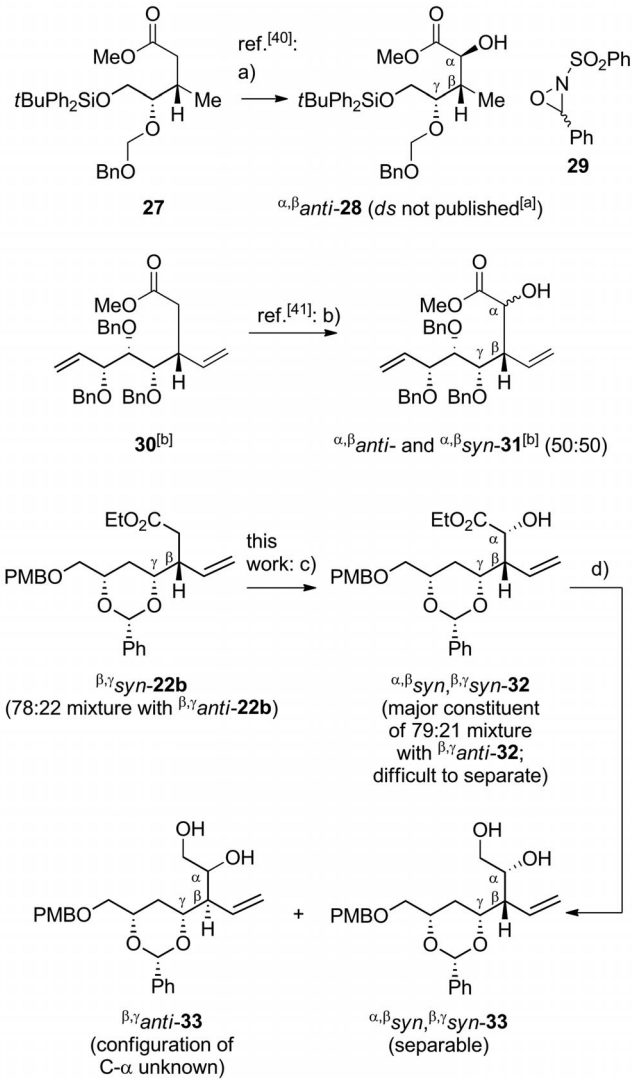
Entry	Substrate	Grignard reagent Hal	[equiv.]	Cu additive	[mol-%]	Me_3SiCl [equiv.]	Solvent	*T* [°C]	*t* [h]	Product	Yield [%]	*syn*/*anti*
1	(*E*)-**7b**	Cl	2.0	**24**	20	3	THF	–78	5	**22b**	70	77:23[a]
2	(*E*)-**7b**	Br	2.0	**25**	10	3	Et_2O	–78	4	**22b**	50	78:22[a]
3	(*E*)-**7b**	Br	2.0	**25**	10	3	THF	–78	6	**22b**	58	79:21[a]
4	(*E*)-**7b**	Br	2.0	**25**	20	3	THF	–78	4	**22b**	76	80:20[a]
5	(*E*)-**7b**	Cl	2.0	**26**	20	3	THF	–78	5	**22b**	84	82:18[a]
6	(*E*)-**7b**	Cl	2.0	**26**	20	–	THF	–78	5	**22b**	59	81:19[a]
7	(*E*)-**7a**	Cl	2.0	**26**	20	3	THF	–78	4	**22a**	83	85:15[b]
8	(*E*)-**7c**	Cl	2.0	**26**	20	3	THF	–78	6	**22c**	69	58:42[c]

[a] Cf. Table 1, footnote [a]. [b] Determined from the mean integral ratio of the following ^1H NMR resonances (499.9 MHz, $CDCl_3$/TMS): δ = 2.40 [dd, α-H^A (*syn*-**22a**)] vs. AB signal [δ_A = 2.48, δ_B = 2.68, α-H_2 (*anti*-**22a**)]; δ = 3.71 [ddd, 4′-H (*syn*-**22a**)] vs. 3.92 ppm [ddd, 4′-H (*anti*-**22a**)]; 5.507 [2 s, 2′-H (*syn*-**22a**)] vs. 5.515 ppm [2 s, 2′-H (*anti*-**22a**)]; and 5.69 [ddd, 4-H (*syn*-**22a**)] vs. 5.82 ppm [ddd, 4-H (*anti*-**22a**)]. [c] Determined from the mean integral ratio of the following ^1H NMR resonances (400.1 MHz, $CDCl_3$/TMS): δ = 3.71 [ddd, $J_{4',5'\text{-H(eq)}}$ = 2.5, $J_{4',3}$ = 8.1, $J_{4',5\text{-H(ax)}}$ = 11.1 Hz, 4′-H (*syn*-**22c**)] vs. 3.89 ppm [ddd, $J_{4',5'\text{-H(ax)}}$ = 10.6, $J_{4',5'\text{-H(eq)}} = J_{4',3}$ = 3.5 Hz, 4′-H (*anti*-**22c**)] and δ = 5.70 [ddd, $J_{4,5\text{-H}(Z)}$ = 17.2, $J_{4,5\text{-H}(E)}$ = 10.3, $J_{4,3}$ = 8.7 Hz, 4-H (*syn*-**22c**)] vs. 5.81 ppm [m_c, 4-H (*anti*-**22c**)].

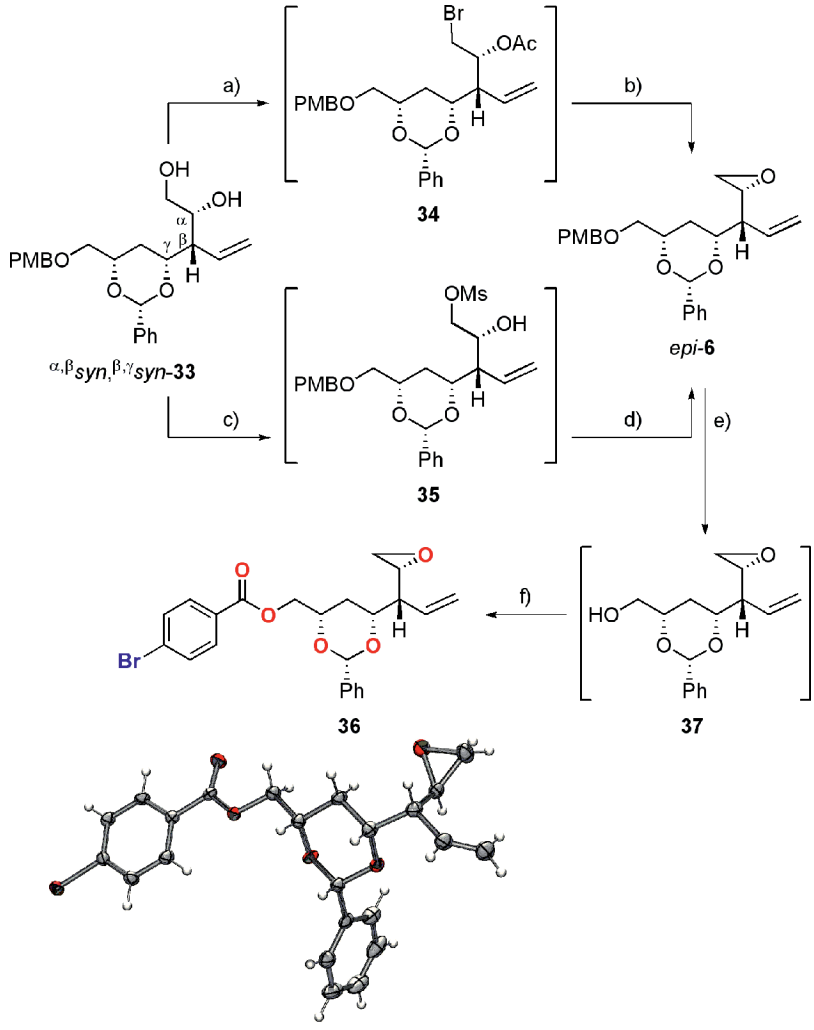
91:9[33] (Table 1, entry 5). Entries 6 and 7 illustrate the inability to maintain this level of diastereocontrol by increasing the amount of substrate **7** from 0.1 to 0.6 mmol. Given the need to carry out this reaction on a scale of several mmol at least, we accepted that the conditions of entry 10 (Table 1) represent the best compromise between investment of labor (4 mmol scale) and return in terms of yield (81%) and *syn*/*anti* diastereoselectivity (78:22).

The amounts of reagents required to realize the desired 1,4-addition under the conditions of entry 10 of Table 1 remained a concern: We used 12 equiv. of vinylMgBr, 6 equiv. of CuI, and 13 equiv. of Me_3SiCl, and lowering any of these excesses reduced the yield. Table 2 shows how we managed to make improvements in this regard. We varied the copper source to make the metal more (readily) available to the vinylmagnesium halide. By confining ourselves to 2.0 equiv. of vinylmagnesium halide in the experiments of Table 2 we found that 10–20 mol-% of the following Cu^I species sufficed to reach if not surpass both the yields and the *syn*/*anti* selectivities of the previous (cf. Table 1) addition reactions: Li_2CuCl_4 (**24**),[34] the Cu^{II}salen complex **25**,[35] and CuBr·SMe_2/LiBr/LiSPh (**26**).[36] In detail, in the presence of **26**, vinylmagnesium chloride added to the methyl ester (*E*)-**7a** to give a yield of 83% (→**22a**, *syn*/*anti* = 85:15; entry 7);[37] a yield of 84% was obtained with the ethyl ester (*E*)-**7b** (→**22b**, *syn*/*anti* = 82:18; entry 5) and of 69% with the *tert*-butyl ester (*E*)-**7c** (→**22c**, *ds* = 58:42; entry 8).[38] Such an effect of the ester group (Me/Et vs. *t*Bu) on the induced diastereoselectivity was not predicted by the pertinent transition-state models.[31]

We hydroxylated the *syn* isomer of the vinyl-containing ester **22b** at C-α by using the Davis oxaziridine *rac*-**29**[39] (Scheme 4). The desired hydroxy ester $^{\alpha,\beta}$*anti*,$^{\beta,\gamma}$*syn*-**32** needed to exhibit an *anti* orientation of the α-OH bond relative to the smaller substituent at C-β of substrate $^{\beta,\gamma}$*syn*-**22b**, that is, relative to the vinyl group. To the extent that the esters $^{\beta,\gamma}$*syn*-**27**[40] and $^{\beta,\gamma}$*syn*-**30**[41] modeled our substrate *syn*-**22b** in their oxidation reactions with *rac*-**29**[39] asymmetric induction of the required kind had been observed in some instances (→*anti*-**28**[40]) but in others not (→*anti*- and *syn*-**31**[41]). With the examples in hand (Scheme 4, upper half), asymmetric induction depended upon whether the smaller β substituent was methyl (→$^{\alpha,\beta}$*anti* induction) or vinyl (→no induction), or on whether the smaller γ substituent contains one oxygen atom (→no induction) or two oxygen atoms (→$^{\alpha,\beta}$*anti* induction).[42] Successive treatment of our approximate 80:20 mixture of β,γ-chiral esters $^{\beta,\gamma}$*syn*- and $^{\beta,\gamma}$*anti*-**22** with KHMDS[43] and excess oxaziridine **29**[39] provided >80% of a mixture of one major α-hydroxy ester, one minor α-hydroxy ester, and no additional isomer in a ratio of 79:21 (according to 300 or 400 MHz ^{1}H NMR spectroscopy in $CDCl_3$). This meant that, other than the α-hydroxylation of ester $^{\beta,\gamma}$*syn*-**30**,[41] the α-hydroxylation of ester $^{\beta,\gamma}$*syn*-**22b** had occurred with an asymmetric induction. A difficult separation by flash chromatography on silica gel[17] delivered the isomerically pure major α-hydroxy ester contained in the above-mentioned mixture in 59% yield. Neither its ^{1}H nor ^{13}C NMR spectroscopic data revealed the configuration at the newly formed stereocenter. The assignment of the stereostructure $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32** to this hydroxylation product stems from an X-ray crystal structure analysis of the final product **36** prepared from a series of follow-up transformations (Schemes 4 and 5).[44] Accordingly, the α-hydroxylation of ester $^{\beta,\gamma}$*syn*-**22** occurred with an asymmetric induction, which was opposite to the asymmetric induction observed in the α-hydroxylation of ester $^{\beta,\gamma}$*syn*-**27**[40].[45]



Scheme 4. Contrasting diastereoselectivities in the α-hydroxylation of the potassium enolates of the β-branched γ-alkoxy esters **27**, **30**, and *syn*-**22b** with the Davis oxazoridine (**29**[39]). Reagents and conditions: a) KHMDS (1.2 equiv.), THF, –78 °C, 30 min; addition of **29** (1.5 equiv.), 3 h; 80%;[40] b) KHMDS (1.4 equiv.), THF, –78 °C, 30 min; addition of **29** (2.7 equiv.), 3 h; 82%;[41] c) KHMDS (1.3 equiv.), THF, –78 °C, 1 h; addition of **29** (2.6 equiv.), 3 h; 83%; d) $LiAlH_4$ (4.0 equiv.), THF, –20 °C; in the course of 2 h→room temp.; pure $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**33**: 68% (= 82% relative to the fraction of *syn*-**22b** in the substrate) separated from a 40:60 $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**33**/$^{\beta,\gamma}$*anti*-**33**-mixture: 30% (= 98% total yield and *ds* ca. 80:20).
[a] Ref.[40] only states "enantiomerically pure after chromatography". [b] This reaction was performed[41] with the mirror-image of the stereoisomer, which is shown here for easier comparison.

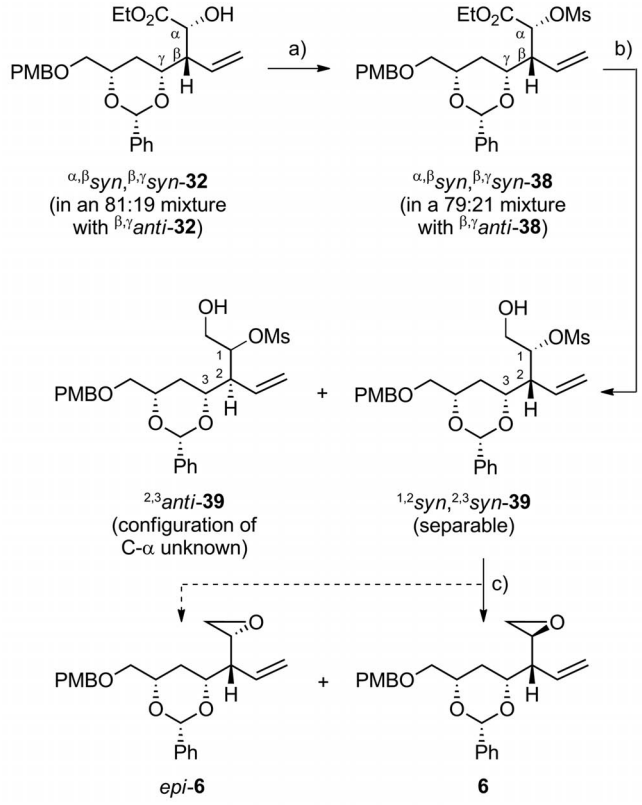


Scheme 5. Elucidation of the 3D structure of the hydroxy ester $^{\alpha,\beta}syn,^{\beta,\gamma}syn$-**32** (cf. Scheme 4) through the conversion of the derived (cf. Scheme 4) diol $^{\alpha,\beta}syn,^{\beta,\gamma}syn$-**33** into the *p*-bromobenzoate **36**. Reagents and conditions: a) (i) Trimethyl orthoacetate (1.2 equiv.), PPTS (2 mol-%), CH_2Cl_2, room temp., 60 min; evaporation of volatiles; (ii) acetyl bromide (1.1 equiv.), NEt_3 (10 mol-%), room temp., 2 h; evaporation of volatiles; b) K_2CO_3 (2.0 equiv.), MeOH, room temp., 2 h; 70% (*ds* ≥ 98:2); c) NEt_3 (3.0 equiv.), $MeSO_2Cl$ (1.1 equiv.), CH_2Cl_2, –10 °C, 1 h; the resulting mixture was used in the next step; d) addition of MeOH and K_2CO_3 (6.0 equiv.), → room temp., 3 h; 94% (*ds* ≥ 96:4); e) DDQ (1.3 equiv.), NaH_2PO_4/KH_2PO_4 buffer (pH = 7), CH_2Cl_2, 0 °C, 4 h; DDQ (0.65 equiv.), 0 °C, 2 h; the crude product was used in the next step without purification; f) *p*-$BrC_6H_4CO_2H$ (1.02 equiv.), DCC (1.02 equiv.), DMAP (10 mol-%), CH_2Cl_2, 0 °C, 4 h; 83% over the two steps. Bottom: ORTEP plot of the crystal structure of **36** (at 100 K).[50] PPTS = pyridinium *p*-toluenesulfonate; DDQ = 2,3-dichloro-4,5-dicyanobenzoquinone; DCC = dicyclohexylcarbodiimide; DMAP = 4-(dimethylamino)pyridine.

$LiAlH_4$ reduction of the 79:21 mixture of the α-hydroxy esters $^{\alpha,\beta}syn,^{\beta,\gamma}syn$-**32** and $^{\beta,\gamma}anti$-**32** gave an around 80:20 mixture of the corresponding diols $^{\alpha,\beta}syn,^{\beta,\gamma}syn$-**33** and $^{\beta,\gamma}anti$-**33**[44] in 98% yield (Scheme 4). Flash chromatography on silica gel[17] allowed the major diastereomer ($^{\alpha,\beta}syn,^{\beta,\gamma}syn$-**33**) to be isolated in 68% yield as a pure isomer. We tested two ways for converting this diol into the epoxide *epi*-**6** (Scheme 5). Firstly, we tried the one-pot procedure from Sharpless' asymmetric dihydroxylation chemistry.[46] It involves (i) transorthoesterification with trimethyl orthoacetate, (ii) orthoester cleavage with acetyl bromide (→ bromohydrin acetate **34**), and (iii) K_2CO_3-catalyzed methanolysis of the acetate followed by epoxide formation from the liberated bromohydrin. This protocol delivered the epoxide *epi*-**6** in 70% yield. Alternatively this epoxide could be synthesized from the diol $^{\alpha,\beta}syn,^{\beta,\gamma}syn$-**33** in 94% yield by forming the monomesylate **35** with methanesulfonyl chloride and NEt_3 and by subsequently adding K_2CO_3 and MeOH.[47] At –10 °C, this procedure delivered *epi*-**6** with less than 4% of the diastereomeric epoxide **6** as a contaminant.[48] However, the ^1H and ^{13}C NMR spectra did not reveal the configuration of epoxide *epi*-**6**. Therefore we removed the PMB group with DDQ and esterified the resulting alcohol **37** to the *p*-bromobenzoate **36**. This compound provided monocrystals that were studied by X-ray diffraction. This established the relative and absolute configurations (Bijvoet method[49]) of the stereocenters in ester **36**.[50]

Because the epoxide *epi*-**6** was obtained, it was deduced that the α-hydroxylation of ester $^{\beta,\gamma}syn$-**22** had furnished the

α-hydroxy ester $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32** rather than $^{\alpha,\beta}$*anti*,$^{\beta,\gamma}$*syn*-**32**. This is correctly depicted in Scheme 4, but came as a surprise (cf. above). Determined to obtain epoxide **6**, we returned to one of the ca. 80:20 mixtures of the α-hydroxy esters $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32** and $^{\beta,\gamma}$*anti*-**32** shown in Scheme 4 and converted it into a ca. 80:20 mixture of the corresponding monomesylates $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38** and $^{\alpha,\beta}$*anti*-**38**[44] (Scheme 6) in 98% yield. This mixture was reduced with $LiAlH_4$. Flash chromatography on silica gel[17] allowed the expected hydroxymesylates to be separated in yields of 78 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**39**) and 18% ($^{\alpha,\beta}$*anti*-**39**[44]). Epoxide formation (90% yield) upon treatment of the hydroxymesylate $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**39** with K_2CO_3 in MeOH furnished the desired epoxide **6**, which contained no more than trace amounts (≤2 mol-%) of the diastereomer *epi*-**6**. Epoxide **6** represents the desired building block for the "eastern moiety" of the unnatural enantiomers of the aglycons of the polyol,polyene antibiotics *ent*-**1**–**5**.



Scheme 6. Completion of the synthesis of the "eastern building block" **6** from hydroxy ester $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32** (cf. Scheme 4). Reagents and conditions: a) NEt_3 (3.0 equiv.), methanesulfonyl chloride (1.3 equiv.), DMAP (0.1 equiv.), CH_2Cl_2, 0 °C, 3 h; 98% ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**/$^{\beta,\gamma}$*anti*-**38** = 79:21); b) $LiAlH_4$ (3.0 equiv.), THF, –20 °C, 30 min, ^{1,2}*syn*,^{2,3}*syn*-**39**: 78% (99% with respect to the fraction of ^{1,2}*syn*,^{2,3}*syn*-**38** in the substrate); ^{2,3}*anti*-**39**: 18% (88% with respect to the fraction of ^{2,3}*anti*-**38** in the substrate); c) K_2CO_3 (6.0 equiv.), MeOH; either room temp., 12 h (91%, **6**/*epi*-**6** ≥ 93:7) or –20 °C, 22 h (90%, **6**/*epi*-**6** ≥ 98:2).

Conclusions

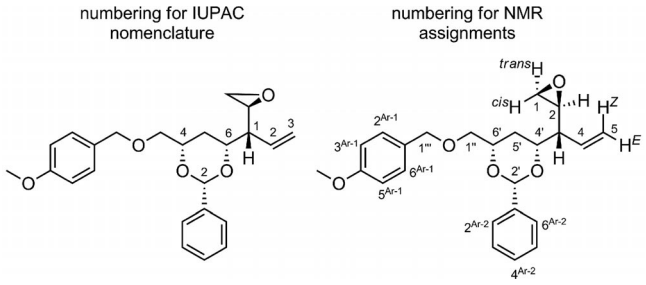
Starting from propargyl alcohol and ethyl formate we have synthesized the C^n–C^{n+6} fragment **6** common to the unnatural enantiomers **1**–**5** of the macrolides amphotericin (*ent*-**1**), candidin (*ent*-**2**), nystatin (*ent*-**3**), pimaricin (*ent*-**4**), and rimocidin (*ent*-**5**) in a 13-step sequence. The overall yield was 12%, the average 85% per step. Epoxy alcohol *anti*-**10** (95–97% *ee*) was obtained by a desymmetrizing Sharpless epoxidation of divinylcarbinol **9** (→ 75:25 *anti*/*syn* mixture), the latter being derived from propargyl alcohol and ethyl formate in two steps. The epoxy alcohol *anti*-**10** was transformed into the α,β-unsaturated ester (*E*)-**7b**, which was vinylated through a 1,4-addition reaction; the best results were obtained with vinylMgCl (2 equiv.), Me_3SiCl (3 equiv.), and 20 mol-% CuBr·SMe_2/LiBr/LiSPh (**26**). An inseparable 82:18 mixture of the esters *syn*- and *anti*-**22** resulted in a yield of 84%. The α-hydroxylation of the potassium enolate of the major ester (*syn*-**22**) with the Davis oxaziridine (**29**) succeeded with perfect diastereocontrol but nonetheless with the opposite asymmetric induction (→ $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32**) to the α-hydroxylation of ester *syn*-**27** (→ $^{\alpha,\beta}$*anti*,$^{\beta,\gamma}$*syn*-**32**). The resulting α-hydroxy ester $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32** was used to obtain epoxide **6** via mesylate $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38** and hydroxymesylate $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**39**.

Experimental Section

General: Reactions were performed in heat-gun- and vacuum-dried glassware under N_2. THF was freshly distilled from potassium. Products were purified by flash chromatography[17] on Merck silica gel 60 (0.040–0.063 mm), yields refer to analytically pure samples. ^{1}H NMR [TMS (δ = 0.00 ppm) as internal standard in $CDCl_3$; CHD_5 (δ = 7.16 ppm) as internal standard in C_6D_6]: Varian Mercury VX 300, Bruker AM 400, and Bruker DRX 500 spectrometers. ^{13}C NMR [$CDCl_3$ (δ = 77.10 ppm) as internal standard in $CDCl_3$; C_6D_6 (δ = 128.00 ppm) as internal standard in C_6D_6]: Bruker AM 400 and Bruker DRX 500 spectrometers. Assignments of ^{1}H and ^{13}C NMR resonances refer to the IUPAC nomenclature except within substituents (for which primed numbers are used) or where explicitly indicated otherwise. MS: Dr. J. Wörth, C. Warth, Institut für Organische Chemie, University of Freiburg. Combustion analyses: E. Hickl, F. Tönnies, and A. Siegel, Institut für Organische Chemie, University of Freiburg. IR spectra: Perkin–Elmer Paragon 1000 spectrometer. Optical rotations were measured with a Perkin–Elmer polarimeter 341 at 589 nm and 20 °C and were calculated by the Drude equation: $[a]_D = (100a_{exp})/(cd)$; rotational values are the average of five measurements of a_{exp} in a given solution of the corresponding sample. Melting points were measured with a Dr. Tottoli apparatus (Büchi). The *ee* values were determined by chiral HPLC with a Chiralpak AD-H column (0.46 × 25 cm, Daicel Chemical Ind. Ltd.) by G. Fehrenbach, Institut für Organische Chemie, University of Freiburg.

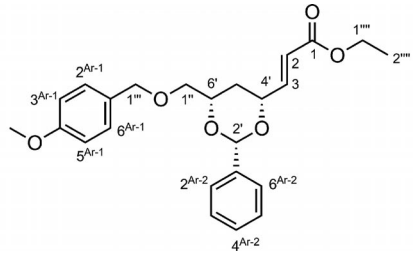
(2*S*,4*S*,6*R*)-4-{[(4-Methoxybenzyl)oxy]methyl}-6-{(1*S)-1-[(*S*)-oxiranyl]prop-2-enyl}-2-phenyl-1,3-dioxane (6):**

* We are not sure whether this stereodescriptor actually means the configuration represented in the formula drawing; the latter is correct.



Powdered K_2CO_3 (980 mg, 7.1 mmol, 6.0 equiv.) was added to a solution of the mesylate ^{1,2}*syn*,^{2,3}*syn*-**39** (581 mg, 1.18 mmol) in MeOH (40 mL) at –20 °C. The reaction mixture was stirred at –20 °C for 22 h and added to a mixture of CH_2Cl_2 and an aq. satd. NaCl solution (2:1, 300 mL) at room temp. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (4× 20 mL). The combined organic phases were dried with $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (4.0 cm, C_6H_{12}/EtOAc, 5:1) to yield **6**^{I} as a colorless liquid (fractions 12–23, 421 mg, 90%). The sample contained 2 mol-% *epi*-**6** as determined from the ratio of the integrals over thefollowing ^{1}HNMRsignals(400.1 MHz,$CDCl_3$/Me_4Si):δ=2.55[dd, $^2J_{1\text{-H}(cis),1\text{-H}(trans)}$ = 4.9, $J_{1\text{-H}(cis),2}$ = 2.8 Hz, 1-H^{cis} (*epi*-**6**)] versus δ = 2.62 [dd, $^2J_{1\text{-H}(cis),1\text{-H}(trans)}$ = 5.1, $J_{1\text{-H}(cis),2}$ = 2.8 Hz, 1-H^{cis} (**6**)] ppm. $[\alpha]_D^{20}$ = –15.1 (*c* = 1.315, $CHCl_3$). $[\alpha]_{365}^{20}$ = –39.07 (*c* = 1.315, $CHCl_3$). ^{1}H NMR (400.1 MHz, $CDCl_3$/Me_4Si): δ = 1.45 [ddd, $^2J_{5'\text{-H(ax)},5'\text{-H(eq)}}$ = 13.2, $J_{5'\text{-H(ax)},4'} = J_{5'\text{-H(ax)},6'}$ = 11.4 Hz ≡ 2×$J_{ax,ax}$, 5′-H^{ax}], 1.69 [ddd, $^2J_{5'\text{-H(eq)},5'\text{-H(ax)}}$ = 13.2, $J_{5'\text{-H(eq)},4'} = J_{5'\text{-H(eq)},6'}$ = 2.5 Hz ≡ 2×$J_{eq,eq}$, 5′-H^{eq}], 2.27 (ddd, $J_{3,4} = J_{3,4'}$ = 8.8, $J_{3,2}$ = 5.1 Hz, 3-H), 2.62 [dd, $^2J_{1\text{-H}(cis),1\text{-H}(trans)}$ = 5.1, $J_{1\text{-H}(cis),2}$ = 2.8 Hz, 1-H^{cis}], 2.79 [dd, $^2J_{1\text{-H}(trans),1\text{-H}(cis)}$ = 5.1, $J_{1\text{-H}(trans),2}$ = 4.0 Hz, 1-H^{anti}], 3.28 [ddd, $J_{2,3}$ = 5.1, $J_{2,1\text{-H}(trans)}$ = 4.0, $J_{2,1\text{-H}(cis)}$ = 2.7 Hz, 2-H], AB signal (δ_A = 3.49, δ_B = 3.63, J_{AB} = 10.2 Hz, A part additionally split by $J_{A,6'}$ = 4.7 Hz, B part additionally split by $J_{B,6'}$ = 5.9 Hz, 1′′-H$_2$), 3.80 (s, OMe), 3.97 [ddd, $J_{4',5'\text{-H(ax)}}$ = 11.2, $J_{4',3}$ = 8.7, $J_{4',5'\text{-H(eq)}}$ = 2.5 Hz, 4′-H], 4.07 [dddd, $J_{6',5'\text{-H(ax)}}$ = 11.2, $J_{6',1''\text{-H(B)}}$ = 6.0, $J_{6',1''\text{-H(A)}}$ = 4.9, $J_{6',5'\text{-H(eq)}}$ = 2.3 Hz, 6′-H], AB signal (δ_A = 4.50, δ_B = 4.54, J_{AB} = 11.7 Hz, 1′′′-H$_2$), 5.17–5.25 (m, 5-H$_2$), 5.62 [ddd, $J_{4,5\text{-H}(Z)}$ = 16.9, $J_{4,5\text{-H}(E)}$ = 10.6, $J_{4,3}$ = 9.0 Hz, 4-H] superimposed by 5.59 (s, 2-H), AA′BB′ signal centered at δ = 6.87 and 7.26 [2-H$^{Ar\text{-}1}$, 3-H$^{Ar\text{-}1}$, 5-H$^{Ar\text{-}1}$, 6-H$^{Ar\text{-}1}$; contains solvent peak at δ = 7.26 ($CHCl_3$)], 7.29–7.37 and 7.47–7.51 (2 m, 2-H$^{Ar\text{-}2}$, 3-H$^{Ar\text{-}2}$, 4-H$^{Ar\text{-}2}$, 5-H$^{Ar\text{-}2}$, 6-H$^{Ar\text{-}2}$) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$/$CDCl_3$): δ = 32.36 (C-5′)^A, 46.31 (C-1)^A, 51.55 (C-3)^A, 51.87 (C-2)^A, 55.33 (OCH_3)^A, 72.61 (C-1′′)^A, 73.26 (C-1′′′)^A, 76.20 (C-6′)^A, 76.78 (C-4′)^A, 100.58 (C-2), 113.87 (C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$)^I, 119.92 (C-5)^A, 126.13 and 128.18 (C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$), 128.71 (C-4$^{Ar\text{-}2}$; assignment and differentiation based on intensity, which is half as large as the intensities of the two preceding signals), 129.49 (C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$)^I, 130.27 (C-1$^{Ar\text{-}1}$; significantly lower intensity than the preceding signal)^{I,II}, 132.90 (C-4)^A, 138.51 (C-1$^{Ar\text{-}2}$)^{II}, 159.34 ppm (C-4$^{Ar\text{-}1}$)^I. ^{I}Assignment based on a comparison with chemical shifts resulting from a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 113.8 (C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$), 127.6 (C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$), 130.7 (C-1$^{Ar\text{-}1}$), 159.3 (C-4$^{Ar\text{-}1}$) ppm.[51] ^{II}Assignment and differentiation by comparison with a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 130.7 (C-1$^{Ar\text{-}1}$), 138.5 (C-1$^{Ar\text{-}2}$) ppm.[51] ^{A}The indicated nuclei, which are nonquaternary, were identified on the basis of an edHSQC analogy ("short-range C,H COSY spectrum"; 100.6/400.1 MHz, $CDCl_3$) by their cross-peaks with directly bonded protons (the latter had previously been assigned unequivocally) [δ_H(^{1}H) ↔ δ_C(^{13}C)]: δ_H = 1.45 (ddd, 5′-H^{ax}) ↔ δ_C = 32.36 (C-5), δ_H = 1.69 (ddd, 5′-H^{eq}) ↔ δ_C = 32.36 (C-5), δ_H = 2.62 (dd, 1-H^{cis}) ↔ δ_C = 46.31 (C-1), δ_H = 2.79 (dd, 1-H^{trans}) ↔ δ_C = 46.31 (C-1), δ_H = 2.27 (ddd, 3-H) ↔ δ_C = 51.55 (C-3), δ_H = 3.28 (ddd, 2-H) ↔ δ_C = 51.87 (C-2), δ_H = 3.80 (s, O-Me) ↔ δ_C = 55.33 (OCH_3), δ_H = AB signal (δ_A = 3.49, δ_B = 3.63, 1′′-H$_2$) ↔ δ_C = 72.61 (C-1′′), δ_H = AB signal (δ_A = 3.49, δ_B = 3.63, 1′′-H$_2$) ↔ δ_C = 73.26 (C-1′′′), δ_H = 4.07 (dddd, 6′-H) ↔ δ_C = 76.20 (C-6′), δ_H = 3.97 (ddd, 4′-H) ↔ δ_C = 76.78 (C-4′), δ_H = 5.59 (s, 2-H) ↔ δ_C = 100.58 (C-2), δ_H = 5.17–5.25 (m, 5-H$_2$) ↔ δ_C = 119.92 (C-5), δ_H = 5.62 (ddd, 4-H) ↔ δ_C = 132.90 (C-4), δ_H = 7.29–7.37 and δ_H = 7.47–7.51 (2-H$^{Ar\text{-}2}$, 3-H$^{Ar\text{-}2}$, 4-H$^{Ar\text{-}2}$, 5-H$^{Ar\text{-}2}$, 6-H$^{Ar\text{-}2}$) ↔ δ_C = 128.18 (C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$) and δ_C = 128.71 (C-4$^{Ar\text{-}2}$), δ_H = AA′BB′ signal centered at δ = 6.87 and δ_H = 7.26 (2-H$^{Ar\text{-}1}$, 3-H$^{Ar\text{-}1}$, 5-H$^{Ar\text{-}1}$, 6-H$^{Ar\text{-}1}$) ↔ δ_C = 113.87 (C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$) and δ_C = 129.49 (C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$). IR (film): $\tilde{\nu}$ = 3035, 2915, 2860, 1610, 1585, 1515, 1455, 1390, 1340, 1300, 1250, 1175, 1100, 1030, 925, 820, 760, 700 cm^{-1}. $C_{24}H_{28}O_5$ (396.48): calcd. C 72.71, H 7.12; found C 72.49, H 7.25.

Ethyl (*E*)-3-{(2*S*,4*R*,6*S*)-6-[(4-Methoxybenzyloxy)methyl]-2-phenyl-1,3-dioxan-4-yl}prop-2-enoate [(*E*)-7b]



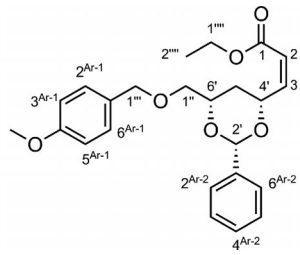
Ozonolysis: At –78 °C, a stream of ozone was bubbled through a solution of the benzylidene acetal **8** (3.0 g, 6.1 mmol) and pyridine (1.6 mL) in CH_2Cl_2/MeOH [1:1 (v/v), 160 mL] until a slightly blue color persisted (ca. 15 min.). Excess ozone was removed by bubbling a stream of N_2 through the solution for 15 min followed by the addition of Me_2S (2.5 mL, 2.1 g, 34 mmol, 5.6 equiv.). The resulting mixture was stirred for 30 min before raising the temperature to room temp. over 2 h. The solvents were removed in vacuo and the crude product (**19**) was used in the next step without further purification.

Horner–Wadsworth–Emmons Reaction: At –10 °C, the phosphonate **21b** (2.60 mL, 2.91 g, 13 mmol, 2.13 equiv.) was added to a suspension of NaH (312 mg, 13.0 mmol, 2.13 equiv.) in THF (130 mL). After complete addition the temperature was raised to room temp. and the mixture was stirred until it became clear and colorless (ca. 10 min). The crude ozonolysis product was dissolved in THF (30 mL) and slowly added to the phosphonate solution at –10 °C over 30 min. TLC control indicated complete conversion of the intermediate (**19**) after 15 min. An aq. satd. NH_4Cl solution (25 mL) followed by water (75 mL) were added and the mixture was warmed to room temp. At room temp., the phases were separated and the aqueous phase was extracted with *t*BuOMe (3× 50 mL). The combined organic phases were washed with an aq. satd. NaCl solution (100 mL), dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography (5.0 cm, C_6H_{12}/EtOAc, 9:1, from fraction 30, 6:1). Fractions 20–36 contained a 95:5^I mixture (1.45 g, 94%) of (*E*)- and (*Z*)-**7b**. Fractions 38–51 contained pure (*E*)-**7b** (2.06 g, 82%) as a colorless oil. ^{I}Determined from the ratio of the integrals over the following ^{1}H NMR signals: δ = 5.81 [dd, $J_{2,3}$ = 11.8, $^4J_{2,4'}$ = 1.4 Hz, 2-H (*Z* isomer)] versus 6.11 [dt, $J_{2,3}$ = 14.9, $^4J_{2,3}$ = 1.8 Hz, 2-H (*E* isomer)] ppm. $[\alpha]_D^{20}$ = –3.35 (*c* = 1.05, $CHCl_3$). $[\alpha]_{20}^{365}$ = –12.74 (*c* = 1.05, $CHCl_3$). ^{1}H NMR

(400.1 MHz, $CDCl_3$/Me_4Si): δ = 1.28 (t, $J_{2'''',1''''}$ = 7.2 Hz, 2′′′′-H_3), AB signal (δ_A = 1.57, δ_B = 1.81, J_{AB} = 13.2 Hz, A part additionally split by $J_{A,4'} = J_{A,6'}$ = 11.4 Hz ≡ 2 × $J_{ax,ax}$, B part additionally split by $J_{B,4'} = J_{B,6'}$ = 2.6 Hz ≡ 2 × $J_{eq,eq}$, A: 5′-H^{ax}, B: 5′-H^{eq}), AB signal (δ_A = 3.50, δ_B = 3.64, J_{AB} = 10.2 Hz, A part additionally split by $J_{A,6'}$ = 5.1 Hz, B part additionally split by $J_{B,6'}$ = 5.7 Hz, 1′′-H_2), 3.79 (s, OCH_3), 4.13 [dddd, $J_{6',5'\text{-H(äx)}}$ = 11.1, $J_{6',1''\text{-H(A)}} = J_{6',1''\text{-H(B)}}$ = 5.4, $J_{6',5'\text{-H(eq)}}$ = 2.3 Hz, 6′-H], 4.19 (q, $J_{1'''',2''''}$ = 7.1 Hz, 1′′′′-H_2), AB signal (δ_A = 4.50, δ_B = 4.53, J_{AB} = 11.7 Hz, 1′′′-H_2), B part superimposed by 4.51–4.56 (m, 4′-H), 5.62 (s, 2′-H), 6.13 (dd, $J_{2,3}$ = 15.7, $^4J_{2,4'}$ = 1.8 Hz, 2-H), 6.94 (dd, $J_{3,2}$ = 15.8, $J_{3,4'}$ = 4.1 Hz, 3-H), AA′BB′ signal centered at 6.87 and 7.26 (2-$H^{Ar\text{-}1}$, 3-$H^{Ar\text{-}1}$, 5-$H^{Ar\text{-}1}$, 6-$H^{Ar\text{-}1}$; contained solvent peak at δ = 7.26 ppm), 7.32–7.39 and 7.51–7.54 (2 m, 2-$H^{Ar\text{-}2}$, 3-$H^{Ar\text{-}2}$, 4-$H^{Ar\text{-}2}$, 5-$H^{Ar\text{-}2}$, 6-$H^{Ar\text{-}2}$) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$/$CDCl_3$): δ = 14.28 (C-2′′′′)^A, 33.23 (C-5′)^A, 55.33 (OCH_3)^A, 60.54 (C-1′′′′)^A, 72.33 (C-1′′)^A, 73.28 (C-1′′′)^A, 74.98 (C-4′)^A, 75.98 (C-6′)^A, 100.76 (C-2′), 113.89 (C-$3^{Ar\text{-}1}$, C-$5^{Ar\text{-}1}$)^I, 120.90 (C-2)^A, 126.33 and 128.26 (C-$2^{Ar\text{-}2}$, C-$3^{Ar\text{-}2}$, C-$5^{Ar\text{-}2}$, C-$6^{Ar\text{-}2}$), 128.96 (C-$4^{Ar\text{-}2}$; assignment and differentiation based on intensity, which is half as large as the intensities of the two preceding signals), 129.46 (C-$2^{Ar\text{-}1}$, C-$6^{Ar\text{-}1}$)^I, 130.16 (C-$1^{Ar\text{-}1}$; significantly lower intensity compared with the preceding signal)^{I,II}, 138.10 (C-$1^{Ar\text{-}2}$)^{II}, 145.87 (C-3)^A, 159.36 (C-$4^{Ar\text{-}1}$)*, 166.41 (C-1) ppm. ^{I}Assignment based on a comparison with the chemical shifts resulting from a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 113.8 (C-$3^{Ar\text{-}1}$, C-$5^{Ar\text{-}1}$), 128.0 (±1.4) (C-$2^{Ar\text{-}1}$, C-$6^{Ar\text{-}1}$), 130.7 (C-$1^{Ar\text{-}1}$), 159.3 (C-$4^{Ar\text{-}1}$) ppm.[51] ^{II}Assignment and differentiation by comparison with a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ= 130.7 (C-$1^{Ar\text{-}1}$), 138.5 (±1.5) (C-$1^{Ar\text{-}2}$) ppm.[51] ^{A}The indicated nuclei, which are non-quaternary, were identified on the basis of an edHSQC analysis (“short-range C,H COSY spectrum”; 125.7/499.9 MHz, $CDCl_3$) by their cross-peaks with directly bonded protons (the latter had previously been assigned unequivocally) [$\delta_H(^1H) \leftrightarrow \delta_C(^{13}C)$]: δ_H = 1.28 (t, 2′′′′-H_3) ↔ δ_C = 14.28 (C-2′′′′), δ_H = AB signal (δ_A = 1.57, δ_B = 1.81, 5′-H_2) ↔ δ_C = 33.23 (C-5′), δ_H = 3.79 (s, OCH_3) ↔ δ_C = 55.33 (OCH_3), δ_H = 4.19 (q, 1′′′′-H_2) ↔ δ_C = 60.54 (C-1′′′′), δ_H = AB signal (δ_A = 3.50, δ_B = 3.64, 1′′-H_2) ↔ δ_C = 72.33 (C-1′′), δ_H = AB signal (δ_A = 4.50, δ_B = 4.53, 1′′′-H_2) ↔ δ_C = 73.28 (C-1′′′), δ_H = 4.51–4.56 (m, 4′-H) ↔ δ_C = 74.98 (C-4′), δ_H = 4.13 (dddd, 6′-H) ↔ δ_C = 75.98 (C-6′), δ_H = 6.13 (dd, 2-H) ↔ δ_C = 120.90 (C-2), δ_H = 6.94 (dd, 3-H) ↔ δ_C = 145.87 (C-3), δ_H = AA′BB′ signal centered at 6.87 and 7.26 (2-$H^{Ar\text{-}1}$, 3-$H^{Ar\text{-}1}$, 5-$H^{Ar\text{-}1}$, 6-$H^{Ar\text{-}1}$) ↔ δ_C = 113.89 (C-$3^{Ar\text{-}1}$, C-$5^{Ar\text{-}1}$) and 129.46 (C-$2^{Ar\text{-}1}$, C-$6^{Ar\text{-}1}$), δ_H = 7.39 and 7.51–7.54 (2 m, 2-$H^{Ar\text{-}2}$, 3-$H^{Ar\text{-}2}$, 4-$H^{Ar\text{-}2}$, 5-$H^{Ar\text{-}2}$, 6-$H^{Ar\text{-}2}$) ↔ δ_C = 126.33, 128.26, and 128.96 (C-$2^{Ar\text{-}2}$, C-$3^{Ar\text{-}2}$, C-$4^{Ar\text{-}2}$, C-$5^{Ar\text{-}2}$, C-$6^{Ar\text{-}2}$) ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 2960, 2940, 2865, 2840, 1715, 1665, 1610, 1515, 1455, 1395, 1370, 1305, 1280, 1250, 1210, 1180, 1150, 1140, 1095, 1030, 980, 935, 880 cm^{-1}. $C_{24}H_{28}O_6$ (412.48): calcd. C 69.88, H 6.84; found C 69.82, H 6.59.

Ethyl (*Z*)-3-{(2*S*,4*R*,6*S*)-6-[(4-Methoxybenzyloxy)methyl]-2-phenyl-1,3-dioxan-4-yl}prop-2-enoate [(*Z*)-7b]:

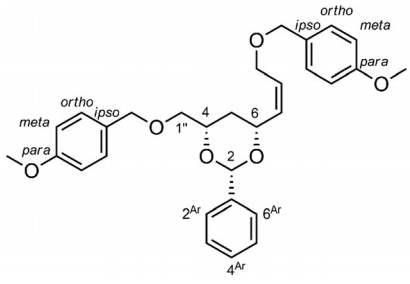
Ozonolysis: At –78 °C, a stream of ozone was bubbled through a solution of the benzylidene acetal **8** (493 mg, 1.0 mmol) and pyridine (0.26 mL) in CH_2Cl_2/MeOH [1:1 (v/v), 26 mL] until a slightly blue color persisted (ca. 10 min.). Excess ozone was removed by bubbling a stream of N_2 through the solution for 15 min followed by the addition of Me_2S (0.42 mL, 0.35 g, 5.7 mmol, 5.6 equiv.). The resulting mixture was stirred for 45 min at –78 °C, before raising the temperature to room temp. within 2 h. The solvents were removed in vacuo. The crude product (**19**) was used in the next step without further purification.



Horner–Wadsworth–Emmons Reaction: At –5 °C, a solution of the phosphonate **20** (670 mg, 2.2 mmol, 2.2 equiv.) in THF (5 mL) was added to a suspension of NaH (61 mg, 2.54 mmol, 2.5 equiv.) in THF (5 mL). The mixture was stirred for 45 min and then cooled to –78 °C. The crude ozonolysis product (**19**) dissolved in THF (5 mL) was added slowly to the phosphonate solution. The temperature was raised to –30 °C over 100 min followed by the addition of an aq. satd. NH_4Cl solution (12 mL). The mixture was warmed to room temp., the phases were separated, and the aqueous phase was extracted with *t*BuOMe (3 × 30 mL). The combined organic phases were washed with an aq. satd. NaCl solution (2 × 25 mL), dried with $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (4.0 cm, C_6H_{12}/EtOAc, 20:1, from fraction 20 17:1, from fraction 40 14:1) to yield (*Z*)-**7b** (fractions 57–74, 216 mg, 52%) as a colorless oil. $[\alpha]_D^{20}$ = +11.9 (*c* = 0.54, $CHCl_3$). $[\alpha]_{20}^{365}$ = +14.5 (*c* = 0.54, $CHCl_3$). ^{1}H NMR (400.1 MHz, $CDCl_3$/Me_4Si): δ = 1.30 (t, $J_{2'''',1''''}$ = 7.3 Hz, 2′′′′-H_3), AB signal (δ_A = 1.57, δ_B = 1.88, J_{AB} = 13.0 Hz, A part additionally split by $J_{A,4'} = J_{A,6'}$ = 11.3 Hz ≡ 2 × $J_{ax,ax}$, B part additionally split by $J_{B,4'} = J_{B,6'}$ = 2.5 Hz ≡ 2 × $J_{eq,eq}$, A: 5′-H^{ax}, B: 5′-H^{eq}), AB signal (δ_A = 3.52, δ_B = 3.62, J_{AB} = 10.5 Hz, A part additionally split by $J_{A,6'}$ = 4.2 Hz, B part additionally split by $J_{B,6'}$ = 5.9 Hz, 1′′-H_2), 3.80 (s, OCH_3), 4.18 (q, $J_{1'''',2''''}$ = 7.1 Hz, 1′′′′-H_2) superimposed by 4.21 [dddd, $J_{6',5'\text{-H(ax)}}$ = 11.2, $J_{6',1''\text{-H(B)}}$ = 6.3, $J_{6',1''\text{-H(A)}}$ = 4.2, $J_{6',5'\text{-H(eq)}}$ = 2.2 Hz, 6′-H], AB signal (δ_A = 4.50, δ_B = 4.55, J_{AB} = 11.8 Hz, 1′′′-H_2), 5.52 [dddd, $J_{4',5'\text{-H(ax)}}$ = 11.1, $J_{4',3}$ = 7.2, $J_{4',5'\text{-H(eq)}}$ = 2.6, $^4J_{4',2}$ = 1.5 Hz, 4′-H], 5.64 (s, 2′-H), 5.81 (dd, $J_{2,3}$ = 11.7, $^4J_{2,4'}$ = 1.5 Hz, 2-H), 6.32 (dd, $J_{3,2}$ = 11.7, $J_{3,4'}$ = 7.2 Hz, 3-H), AA′BB′ signal centered at 6.87 and 7.26 (2-$H^{Ar\text{-}1}$, 3-$H^{Ar\text{-}1}$, 5-$H^{Ar\text{-}1}$, 6-$H^{Ar\text{-}1}$; contained solvent peak at δ = 7.26 ppm), 7.31–7.38 and 7.50–7.54 ppm (2 m, 2-$H^{Ar\text{-}2}$, 3-$H^{Ar\text{-}2}$, 4-$H^{Ar\text{-}2}$, 5-$H^{Ar\text{-}2}$, 6-$H^{Ar\text{-}2}$) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$/$CDCl_3$): δ = 14.28 (C-2′′′′)^A, 31.76 (C-5′)^A, 55.35 (OCH_3)^A, 60.44 (C-1′′′′)^A, 72.50 (C-1′′)^A, 73.18 (C-1′′′)^A, 74.25 (C-4′)^A, 75.94 (C-6′)^A, 100.53 (C-2′), 113.86 (C-$3^{Ar\text{-}1}$, C-$5^{Ar\text{-}1}$)^I, 119.53 (C-2)^A, 126.35 and 128.27 (C-$2^{Ar\text{-}2}$, C-$3^{Ar\text{-}2}$, C-$5^{Ar\text{-}2}$, C-$6^{Ar\text{-}2}$), 128.87 (C-$4^{Ar\text{-}2}$; assignment and differentiation based on intensity, which is half as large as the intensities of the two preceding signals), 129.43 (C-$2^{Ar\text{-}1}$, C-$6^{Ar\text{-}1}$)^I, 130.37 (C-$1^{Ar\text{-}1}$; significantly lower intensity compared with the preceding signal)^{I,II}, 138.38 (C-$1^{Ar\text{-}2}$)^{II}, 148.60 (C-3)^A, 159.30 (C-$4^{Ar\text{-}1}$)^I, 165.72 ppm (C-1) ppm. ^{I}Assignment based on comparison with chemical shifts resulting from a simulation of the ^{13}C NMR spectrum with the program ACD CNMR-Predictor, which provided δ = 113.8 (C-$3^{Ar\text{-}1}$, C-$5^{Ar\text{-}1}$), 128.0 (C-$2^{Ar\text{-}1}$, C-$6^{Ar\text{-}1}$), 130.7 (C-$1^{Ar\text{-}1}$), 159.3 (C-$4^{Ar\text{-}1}$) ppm.[18] ^{II}Assignment and differentiation by comparison with a simulation of the ^{13}C NMR spectrum with the program ACD CNMR-Predictor, which provided δ = 130.7 (C-$1^{Ar\text{-}1}$), 138.5 (C-$1^{Ar\text{-}2}$) ppm.[51] ^{A}The indicated nuclei, which are non-quaternary, were identified on the basis of an edHSQC analysis (“short-range C,H COSY spectrum”; 100.6/400.1 MHz, $CDCl_3$) by their cross-peaks with directly

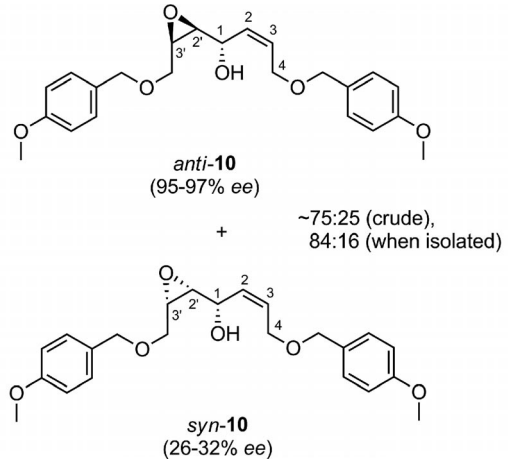
bonded protons (the latter had previously been assigned unequivocally) [$\delta_H(^1H) \leftrightarrow \delta_C(^{13}C)$]: δ_H = 1.30 (t, 2′′′′-H_3) $\leftrightarrow \delta_C$ = 14.28 (C-2′′′′), δ_H = AB signal (δ_A = 1.57, δ_B = 1.88, 5′-H_2) $\leftrightarrow \delta_C$ = 31.76 (C-5′), δ_H = 3.80 (s, OCH_3) $\leftrightarrow \delta_C$ = 55.35 (OCH_3), δ_H = 4.18 (q, 1′′′′-H_2) $\leftrightarrow \delta_C$ = 60.44 (C-1′′′′), δ_H = AB signal (δ_A = 3.52, δ_B = 3.62, 1′′-H_2) $\leftrightarrow \delta_C$ = 72.50 (C-1′′), δ_H = AB signal (δ_A = 4.50, δ_B = 4.55, 1′′′-H_2) $\leftrightarrow \delta_C$ = 73.18 (C-1′′′), δ_H = 5.52 (dddd, 4′-H) $\leftrightarrow \delta_C$ = 74.25 (C-4′), δ_H = 4.21 (dddd, 6′-H) $\leftrightarrow \delta_C$ = 75.94 (C-6′), δ_H = 5.81 (dd, 2-H) $\leftrightarrow \delta_C$ = 119.53 (C-2), δ_H = 6.32 (dd, 3-H) $\leftrightarrow \delta_C$ = 148.60 (C-3), δ_H = AA′BB′ centered at δ = 6.87 and δ = 7.26 (2-$H^{Ar\text{-}1}$, 3-$H^{Ar\text{-}1}$, 5-$H^{Ar\text{-}1}$, 6-$H^{Ar\text{-}1}$) $\leftrightarrow \delta_C$ = 113.86 (C-$3^{Ar\text{-}1}$, C-$5^{Ar\text{-}1}$) and 129.43 (C-$2^{Ar\text{-}1}$, C-$6^{Ar\text{-}1}$), δ_H = 7.31–7.38 and 7.50–7.54 (2 m, 2-$H^{Ar\text{-}2}$, 3-$H^{Ar\text{-}2}$, 4-$H^{Ar\text{-}2}$, 5-$H^{Ar\text{-}2}$, 6-$H^{Ar\text{-}2}$) $\leftrightarrow \delta_C$ = 126.35, 128.27, and 128.87 (C-$2^{Ar\text{-}2}$, C-$3^{Ar\text{-}2}$, C-$4^{Ar\text{-}2}$, C-$5^{Ar\text{-}2}$, C-$6^{Ar\text{-}2}$) ppm. IR (film): $\tilde{\nu}$ = 3035, 2960, 2910, 2860, 1715, 1650, 1615, 1585, 1515, 1455, 1420, 1385, 1335, 1300, 1250, 1195, 1125, 1095, 1030, 820 cm^{-1}. $C_{24}H_{28}O_6$ (412.48): calcd. C 69.88, H 6.84; found C 69.60, H 6.86.

(4*S*,6*R*)-{4-[(4-Methoxybenzyl)oxy]}methyl-6-{(*Z*)-3-[(4-methoxybenzyl)oxy]prop-1-enyl}-2-phenyl-1,3-dioxane (8):



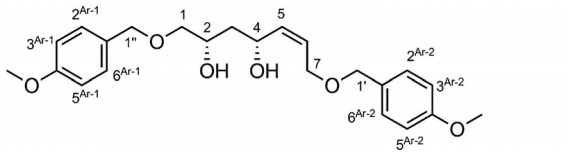
At room temp., pyridinium *p*-toluenesulfonate (25 mg, 0.1 mmol, 0.02 equiv.) was added to a solution of the diol *syn*-**11** (1.95 g, 4.84 mmol) and benzaldehyde dimethyl acetal (2.2 mL, 2.2 g, 14.5 mmol, 3.0 equiv.) in DMF (30.0 mL). The mixture was heated to 60 °C and stirred at constant temperature for 3 h. After consumption of the diol *syn*-**11** (TLC control), the mixture was cooled to room temp. and poured into a mixture of H_2O (75 mL) and *t*BuOMe (75 mL). After phase separation the aqueous phase was extracted with *t*BuOMe (3 × 30 mL) and the combined organic phases were dried with Na_2SO_4. After concentrating the organic phase under reduced pressure the residue was purified by flash chromatography (3.0 cm, C_6H_{12}/EtOAc, 4:1) to yield the title compound **8** (fractions 12–27, 2.25 g, 95%) as a colorless liquid. $[\alpha]_D^{20}$ = –32.8 (*c* = 1.20, $CHCl_3$). $[\alpha]_{20}^{365}$ = –145.6 (*c* = 1.20, $CHCl_3$). ^1H NMR (499.9 MHz, $CDCl_3$/Me_4Si): δ = 1.57–1.62 (m, 5-H_2), AB signal (δ_A = 3.47, δ_B = 3.62, J_{AB} = 10.2 Hz, A part additionally split by $J_{A,4}$ = 4.8 Hz, B part additionally split by $J_{B,4}$ = 5.9 Hz, 1′′-H_2)^A, 3.777 and 3.785 (2 s, 2 OCH_3), 4.06 (m_c, 4-H)^A, 4.11 (m_c, 3′-H_2)^A, AB Signal (δ_A = 4.43, δ_B = 4.46, J_{AB} = 11.4 Hz, first benzyl-CH_2), AB signal (δ_A = 4.50, δ_B = 4.53, J_{AB} = 11.7 Hz, second benzyl-CH_2), 4.61 [m_c, presumably interpretable as ddd, $J_{6,1''} \approx J_{6,5(A)} \approx J_{6,5(B)} \approx$ 7 Hz, 6-H], 5.54 (s, 2-H)^A, AB signal (δ_A = 5.66, δ_B = 5.71, J_{AB} = 11.3 Hz, A part additionally split by $J_{A,6}$ = 7.2, $^4J_{A,3''}$ = 1.3 Hz, B part additionally split by $J_{B,3''}$ = 5.9 Hz, downfield part shows additional not fully resolved allylic coupling, A: 1′-H, B: 2′-H), two superimposing AA′BB′ signals centered at δ = 6.856 or 6.865 or δ = 7.253 or 7.257, respectively (2 × C_6H_4; contained solvent peak at δ = 7.26 ppm), 7.29–7.36 and 7.46–7.51 (2 m, 2 × 2^{Ar}-H, 2 × 3-^{Ar}-H, 4^{Ar}-H) ppm. ^{A}The indicated protons were distinguished by means of a DQF COSY analysis ["H,H COSY spectrum" (499.9 MHz, $CDCl_3$)] by their cross-peaks with protons that had been assigned unequivocally [$\delta_H(^1H) \leftrightarrow \delta_H(^1H)$]: δ = 5.66 (A part of AB signal with ddd, 1′-H) $\leftrightarrow \delta$ = 4.61 (m_c, 6-H), δ = 1.57–1.62 (m, 5-H_2) $\leftrightarrow \delta$ = 4.61 (m_c, 6-H), δ_B = 5.71 (B part of AB signal with dd, 2′-H) $\leftrightarrow \delta$ = 4.11 (m_c, 3′-H_2), δ = 1.57–1.62 (m, 5-H_2) $\leftrightarrow \delta$ = 4.06 (m_c, 4-H), δ = 1.57–1.62 (m, 5-H_2) $\leftrightarrow$ AB signal (δ_A = 3.47, δ_B = 3.62, 1′′-H_2) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$/$CDCl_3$): δ = 33.83 (C-5)^A, 55.31 (2 × OCH_3)^A, 65.61 (C-3′)^A, 71.92 and 73.23 (2 × Benzyl-C)^A, 72.55 (C-1′′)^A, 73.31 (C-6)^A, 75.89 (C-4)^A, 100.71 (C-2), 113.86 (2 × C_{meta})^I, 126.30, 128.21 and 128.79 (2 × C-2^{Ar}, 2 × C-3^{Ar}, C-4^{Ar}), 128.88 (C-2′)^A, 129.44 and 129.50 (2 × C_{ortho})*, 130.21 and 130.25 (2 × C_{ipso})^{I,II}, 132.39 (C-1′)^A, 138.42 (C-1^{Ar})**, 159.32 (2 × C_{para})^I ppm. ^{I}Assignment based on a comparison with chemical shifts resulting from a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ_{meta} = 113.8, δ_{ortho} = 128.0, δ_{ipso} = 130.8, and δ_{para} = 159.3 ppm.[51] ^{II}Assignment and differentiation by comparison with a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 130.8 (C_{ipso}), δ = 138.5 (C-1^{Ar}) ppm.[51] ^{A}The indicated nuclei, which are nonquaternary, were identified on the basis of an edHSQC analysis ("short-range C,H COSY spectrum"; 125.7/499.9 MHz, $CDCl_3$) by their cross-peaks with directly bonded protons (the latter had previously been assigned unequivocally) [$\delta_H(^1H) \leftrightarrow \delta_C(^{13}C)$]: δ_H = 3.777 and 3.785 (2 s, 2 × OCH_3) $\leftrightarrow \delta_C$ = 55.31 (2 × OCH_3), δ_H = 4.11 (m_c, 3′-H_2) $\leftrightarrow \delta_C$ = 65.61 (C-3′), δ_H = AB signal (δ_A = 4.43, δ_B = 4.46, benzyl-CH_2) and AB signal (δ_A = 4.50, δ_B = 4.53, benzyl-CH_2) $\leftrightarrow \delta_C$ = 71.92 and 73.23 (2 × Benzyl-C), δ_H = AB signal (δ_A = 3.47, δ_B = 3.62, 1′′-H_2) $\leftrightarrow \delta_C$ = 72.55 (C-1′′), δ_H = 4.61 (m_c, 6-H) $\leftrightarrow \delta_C$ = 73.31 (C-6), δ_H = 4.06 (m_c, 4-H) $\leftrightarrow \delta_C$ = 75.89 (C-4), δ_H = B part of the AB signals (δ_A = 5.66, δ_B = 5.71, A: 1′-H, B: 2′-H) $\leftrightarrow \delta_C$ = 128.88 (C-2′), δ_H = A part of the AB signals (δ_A = 5.66, δ_B = 5.71, A: 1′-H, B: 2′-H) $\leftrightarrow \delta_C$ = 132.39 (C-1′), δ_H = 7.29–7.36 and 7.46–7.51 (2 m, 2 × 2^{Ar}-H, 2 × 3-^{Ar}-H, 4^{Ar}-H) $\leftrightarrow \delta_C$ = 126.30, 128.21 and 128.79 (2 × C-2^{Ar}, 2 × C-3^{Ar}, C-4^{Ar}) ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 2980, 2935, 2875, 2810, 1615, 1585, 1515, 1490, 1455, 1445, 1385, 1350, 1300, 1250, 1180, 1150, 1115, 1075, 1035, 935 cm^{-1}. $C_{30}H_{34}O_6$ (490.59): calcd. C 73.45, H 6.99; found C 73.39, H 7.19.

(*Z*,*S*)-4-(4-Methoxybenzyl)oxy-1-[(2*S*,3*R*)-3-{[(4-methoxybenzyl)oxy]methyl}oxiran-2-yl]but-2-en-1-ol (*anti*-10) in Approximately 75:25 (Crude) and 84:16 (Isolated) Mixtures with (*Z*,*S*)-4-(4-Methoxybenzyl)oxy-1-[(2*R*,3*S*)-3-{[(4-methoxybenzyl)oxy]methyl}-oxiran-2-yl]but-2-en-1-ol (*syn*-10):



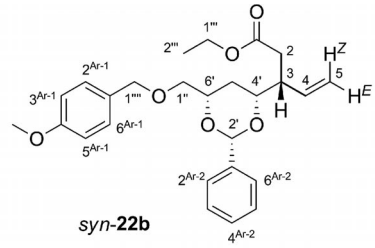
See ref.[14] for the mixture and ref.[13] for a characterization of pure *anti*-**10**. Under the optimum conditions, *anti*-**10** was formed with 97.3% *ee* (HPLC).

(*Z*,2*S*,4*R*)-1,7-Bis[(4-methoxybenzyl)oxy]hept-5-ene-2,4-diol (*syn*-11):



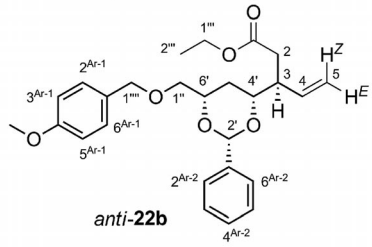
At –50 °C Red-Al (3.4 M in toluene, 18 mL, 61.2 mmol, 10.1-fold molar amount relative to the fraction of 6.05 mmol of pure *anti*-**10**) was added to a solution of an 84:16 mixture (2.88 g, 7.19 mmol) of *anti*- and *syn*-**10** in toluene (30 mL) over 90 min. The resulting mixture was stirred for 16 h. The reaction was then quenched by adding an aq. half-satd. solution of potassium sodium tartrate (100 mL). The mixture was warmed to room temp., stirring vigorously until both phases had become clear (ca. 1 h). After phase separation the aqueous phase was extracted with *t*BuOMe (3 × 50 mL). The combined organic phases were dried with Na_2SO_4. All volatile materials were removed under reduced pressure. The residue was purified by flash chromatography (5 cm, C_6H_{12}/EtOAc, 7:3) to furnish the title compound *syn*-**1** (fractions 46–83, 2.36 g, 97% relative to the fraction of pure *anti*-**10**) as a colorless oil. $[\alpha]_D^{20}$ = +17.8 (*c* = 1.03, $CHCl_3$) [ref.[52] +14.8, (*c* = 0.78, $CHCl_3$)]. ^{1}H NMR (499.9 MHz, $CDCl_3$/Me_4Si): AB signal (δ_A = 1.55, δ_B = 1.70, J_{AB} = 14.2 Hz, A part additionally split by $J_{A,4}$ = 4.3, $J_{A,2}$ = 2.6 Hz ≡ 2 × $J_{eq,eq}$, B part additionally split by $J_{B,2}$ = 10.0, $J_{B,4}$ = 8.9 Hz ≡ 2 × $J_{ax,ax}$, A: 3-H^{eq}, B: 3-H ^{ax}), δ = 3.10 (br. s, 2 × OH), AB signal (δ_A = 3.35, δ_B = 3.39, J_{AB} = 9.4 Hz, A part additionally split by $J_{A,2}$ = 6.9 Hz, B part additionally split by $J_{B,2}$ = 4.1 Hz, 1-H_2), 3.79 and 3.80 (2 s, 2 × OMe), 3.96 [dddd, $J_{2,3\text{-H(eq)}}$ = 2.6, $J_{2,1\text{-H(B)}}$ = 4.0, $J_{2,1\text{-H(A)}}$ = 7.0, $J_{2,3\text{-H(ax)}}$ = 9.6 Hz, 2-H], extreme AB signal (δ_A = 4.06, δ_B = 4.09, J_{AB} = 12.3 Hz, A part additionally split by $J_{A,6}$ = 6.0, $^4J_{A,5}$ = 1.2 Hz, B part additionally split by $J_{B,6}$ = 6.3, $^4J_{B,5}$ = 1.2 Hz, 7-H_2), extreme AB signal (δ_A = 4.43, δ_B = 4.45, J_{AB} = 11.4 Hz, 1′-H_2)^I, 4.47 (s, 1′′-H_2)^I, 4.66 [ddd, $J_{4,3\text{-H(ax)}}$ = $J_{4,5}$ = 8.5, $J_{4,3\text{-H(eq)}}$ = 4.3 Hz, 4-H], AB signal [δ_A = 5.60, δ_B = 5.67, J_{AB} = 11.2 Hz, A part additionally split by $J_{A,4}$ = 8.1 Hz, B part additionally split by $J_{B,7\text{-H(A)}}$ = $J_{B,7\text{-H(B)}}$ = 6.0 Hz, A: 5-H, B: 6-H], two overlapping AA′BB′ signals centered at δ = 6.86 or 6.88, respectively and 7.244 or 7.248, respectively ($2^{Ar\text{-}1}$-H, $3^{Ar\text{-}1}$-H, $5^{Ar\text{-}1}$-H, $6^{Ar\text{-}1}$-H, $2^{Ar\text{-}2}$-H, $3^{Ar\text{-}2}$-H, $5^{Ar\text{-}2}$-H, $6^{Ar\text{-}2}$-H; contained solvent peak at δ = 7.26 ppm). ^{I}Assignment interchangeable. ^{13}C NMR (125.7 MHz, $CDCl_3$/$CDCl_3$): δ = 39.83 (C-3)^A, 55.34 (2 × OCH_3)^A, 65.62 (C-7)^A, 67.67 (C-4)^A, 70.26 (C-2)^A, 72.27 (C-1′′)^{I,A}, 73.13 (C-1′)^{I,A}, 74.11 (C-1)^A, 113.93 (C-$3^{Ar\text{-}1}$, C-$5^{Ar\text{-}1}$, C-$3^{Ar\text{-}2}$, C-$5^{Ar\text{-}2}$)^{II}, 127.74 (C-6)^A, 129.48 and 129.58 (C-$2^{Ar\text{-}1}$, C-$6^{Ar\text{-}1}$,C-$2^{Ar\text{-}2}$, C-$6^{Ar\text{-}2}$)^{II}, 130.02 and 130.06 (C-$1^{Ar\text{-}1}$, C-$1^{Ar\text{-}2}$; both signals have a significantly lower intensity than the two preceding signals)^{II}, 135.81 (C-5)^A, 159.40 (C-$4^{Ar\text{-}1}$, C-$4^{Ar\text{-}2}$)^{II} ppm. ^{I}Assignment interchangeable. ^{II}Assignment based on a comparison with chemical shifts resulting from a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 113.8 (C-$3^{Ar\text{-}1}$, C-$5^{Ar\text{-}1}$ or C-$3^{Ar\text{-}2}$, C-$5^{Ar\text{-}2}$), , δ = 128.9 (C-$2^{Ar\text{-}1}$, C-$6^{Ar\text{-}1}$ or C-$2^{Ar\text{-}2}$, C-$6^{Ar\text{-}2}$), δ = 130.8 (C-$1^{Ar\text{-}1}$ or C-$1^{Ar\text{-}2}$), 159.3 (C-$4^{Ar\text{-}1}$ or C-$4^{Ar\text{-}2}$) ppm.[51] ^{A}The indicated nuclei, which are non-quaternary, were identified on the basis of an edHSQC analysis ("short-range C,H COSY spectrum"; 125.7/499.9 MHz, $CDCl_3$) by their cross-peaks with directly bonded protons (the latter had previously been assigned unequivocally) [δ_H(^{1}H) ↔ δ_C(^{13}C)]: δ_H = AB signal (δ_A = 1.55, δ_B = 1.70, A: 3-H^{eq}, B: 3-H ^{ax}) ↔ δ_C = 39.83 (C-3), δ_H = 3.79 and 3.80 (2 s, 2 × OMe) ↔ δ_C = 55.34 (2 × OCH_3), δ_H = AB signal (δ_A = 4.06, δ_B = 4.09, 7-H_2) ↔ δ_C = 65.62 (C-7), δ_H = 4.66 (ddd, 4-H) ↔ δ_C = 67.67 (C-4), δ_H = 3.96 (dddd, 2-H) ↔ δ_C = 70.26 (C-2), δ_H = AB signal (δ_A = 4.43, δ_B = 4.45, 1′-H_2) and δ_H = 4.47 (s, 1′′-H_2) ↔ δ_C = 72.27 (C-1′′) and δ_C = 73.13 (C-1′), δ_H = AB signal (δ_A = 3.35, δ_B = 3.39, 1-H_2) ↔ δ_C = 74.11 (C-1), δ_H = B part of AB signal (δ_A = 5.60, δ_B = 5.67, A: 5-H, B: 6-H) ↔ δ_C = 127.74 (C-6), δ_H = A part of AB signal (δ_A = 5.60, δ_B = 5.67, A: 5-H, B: 6-H) ↔ δ_C = 135.81 (C-5) ppm. $C_{23}H_{30}O_6$ (402.48): calcd. C 68.64, H 7.51; found C 68.38, H 7.64.

Ethyl (3*R*)-3-[(2*S*,4*R*,6*S*)-6-{[(4-Methoxybenzyl)oxy]methyl}-2-phenyl-1,3-dioxan-4-yl]pent-4-enoate (*syn*-22b) in a 78:22 or an 82:18 Mixture with Ethyl (3*S*)-3-[(2*S*,4*R*,6*S*)-6-{[(4-Methoxybenzyl)oxy]methyl}-2-phenyl-1,3-dioxan-4-yl]pent-4-enoate (*anti*-22b)



syn-**22b**

+



anti-**22b**

78:22 (by method A)
82:18 (by method B)

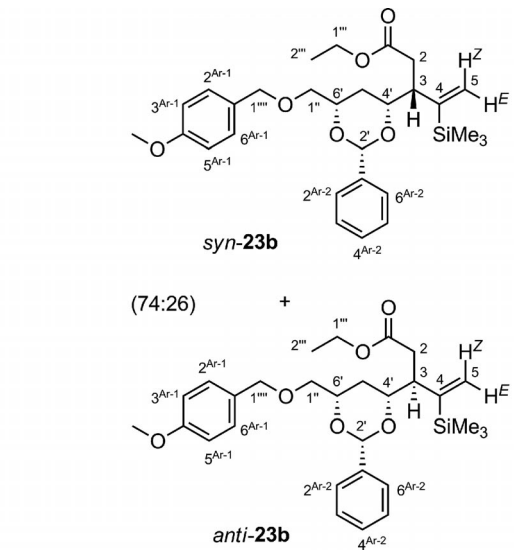
Method A: At –35 °C, vinylMgBr (1.0 M in THF, 48 mL, 48 mmol, 12 equiv.) was added during 1 h to a stirred suspension of CuI (4.57 g, 24 mmol, 6 equiv.) in THF (20 mL). After cooling to –78 °C, Me_3SiCl (6.6 mL, 5.6 g, 54 mmol, 13 equiv.) was added followed by a solution of the unsaturated ester (*E*)-**7b** (1.65 g, 4 mmol) in THF (50 mL), which was added during 45 min. The resulting mixture was stirred for 1 h and quenched by adding a mixture [2:1 (v/v), 150 mL] of aq. satd. NH_4Cl and aq. NH_3 (conc.). At room temp., the phases were separated and the aqueous phase was extracted with *t*BuOMe (3 × 100mL). The combined organic phases were washed with aq. satd. NaCl (100 mL), dried with $MgSO_4$, and filtered. All volatile material was removed under reduced pressure. The residue was purified by flash chromatography (5.0 cm, C_6H_{12}/EtOAc, 10:1) to yield a 78:22 mixture^I (fractions 18–31, 1.42 g, 81%) of *syn*- and *anti*-**22b** as a slightly yellow oil. ^{I}The isomeric composition of this mixture was determined from the average of the ratios of the integrals over the following ^{1}H NMR signals: δ = 2.37 [dd, $^2J_{2\text{-H(A)},2\text{-H(B)}}$ = 16.3, $J_{2\text{-H(A)},3}$ = 9.9 Hz, 2-H^A (*syn*-**22b**)] versus AB signal [δ_A = 2.46, δ_B = 2.66, J_{AB} = 15.5 Hz, A part additionally split by $J_{A,3}$ = 8.6 Hz, B part additionally split by $J_{B,3}$ = 6.0 Hz, 2-H_2 (*anti*-**22b**)], δ = 3.72 [ddd, $J_{4',5'\text{-H(ax)}}$ = 10.8, $J_{4',3}$ = 7.9, $J_{4',5'\text{-H(eq)}}$ = 2.3 Hz, 4′-H (*syn*-**22b**)] versus 3.91 [ddd, $J_{4',5'\text{-H(ax)}}$ = 11.1, $J_{4',3}$ = $J_{4',5'\text{-H(eq)}}$ = 3.4 Hz, 4′-H (*anti*-**22b**)] ppm.

Method B: At –78 °C, a freshly prepared solution of CuBr·SMe_2/LiBr/LiSPh (**26**; 0.1 M in THF, 1.0 mL, 0.1 mmol, 0.2 equiv.) was added to a solution of the unsaturated ester (*E*)-**7b** (207 mg, 0.5 mmol) in THF (3 mL). Thereafter Me_3SiCl (189 µL, 163 mg, 1.5 mmol, 3.0 equiv.) and subsequently vinylMgCl (1.2 M in THF,

0.83 mL, 1.0 mmol, 2.0 equiv.) were added. The reaction mixture was stirred for 5 h at –78 °C until ester (*E*)-**7b** was completely consumed (TLC). Aq. satd. NH_4Cl (10 mL) was added and the mixture was allowed to warm to room temp. The phases were separated and the aqueous phase was extracted with *t*BuOMe (3 × 20 mL). The combined organic phases were washed with aq. satd. NaCl (20 mL), dried with $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by flash chromatography (3.0 cm, C_6H_{12}/EtOAc, 8:1) to yield an 82:18 mixture[I] (fractions 23–39, 184 mg, 84%) of the diastereomeric esters *syn*- and *anti*-**22b** as a colorless oil. [I]The isomeric composition of this mixture was determined from the averaged ratios of the integrals over the following ^{1}H NMR signals: δ = 2.37 [dd, $^2J_{2\text{-H(A)},2\text{-H(B)}}$ = 16.4, $J_{2\text{-H(A)},3}$ = 9.9 Hz, 2-H^A (*syn*-**22b**)] versus AB signal [δ_A = 2.46, δ_B = 2.66, J_{AB} = 15.4 Hz, A part additionally split by $J_{A,3}$ = 8.5 Hz, B part additionally split by $J_{B,3}$ = 6.0 Hz, 2-H$_2$ (*anti*-**22b**)], δ = 3.72 [ddd, $J_{4',5'\text{-H(ax)}}$ = 11.0, $J_{4',3}$ = 8.2, $J_{4',5'\text{-H(eq)}}$ = 2.6 Hz, 4′-H (*syn*-**22b**)] versus 3.91 [ddd, $J_{4',5'\text{-H(ax)}}$ = 11.1, $J_{4',3}$ = $J_{4',5'\text{-H(eq)}}$ = 3.2 Hz, 4′-H (*syn*-**22b**)] ppm. ^{1}H NMR (499.9 MHz, $CDCl_3$/Me_4Si)*: δ = 1.18 [dd, $J_{2''',1'''\text{-H(A)}}$ = $J_{2''',1'''\text{-H(B)}}$ = 7.2 Hz, 2′′′-H$_2$ (*syn*-**22b**)**], 1.22 [dd, $J_{2''',1'''\text{-H(A)}}$ = $J_{2''',1'''\text{-H(B)}}$ = 7.2 Hz, 2′′′-H$_2$ (*anti*-**22b**)**], AB signal [δ_A = 1.41, δ_B = 1.70, J_{AB} = 13.2 Hz, A part additionally split by $J_{A,4'}$ = $J_{A,6'}$ = 11.3 Hz ≡ $J_{ax,ax}$, B part additionally split by $J_{B,4'}$ = $J_{B,6'}$ = 2.4 Hz ≡ $J_{eq,eq}$, A: 5′-H^{ax}, B: 5′-H^{eq} (*syn*-**22b**)**], AB signal [δ_A = 1.51, δ_B = 1.57, J_{AB} = 13.1 Hz, A part additionally split by $J_{A,4'}$ = $J_{A,6'}$ = 2.9 Hz ≡ $J_{eq,eq}$, B part additionally split by $J_{B,4'}$ = $J_{B,6'}$ = 11.1 Hz ≡ $J_{ax,ax}$, A: 5′-H^{eq}, B: 5′-H^{ax} (*anti*-**22b**)**], 2.37 [dd, $^2J_{2\text{-H(A)},2\text{-H(B)}}$ = 16.4, $J_{2\text{-H(A)},3}$ = 9.9 Hz, 2-H^A (*syn*-**22b**)**], AB signal [δ_A = 2.46, δ_B = 2.66, J_{AB} = 15.4 Hz, A part additionally split by $J_{A,3}$ = 8.5 Hz, A part additionally split by $J_{B,3}$ = 6.0 Hz, 2-H$_2$ (*anti*-**22b**)**], 2.76 [dd, $^2J_{2\text{-H(B)},2\text{-H(A)}}$ = 16.3, $J_{2\text{-H(B)},3}$ = 4.9 Hz, 2-H^B (*syn*-**22b**)**] overlapped by 2.72–2.80 [m, 3-H (*syn*-**22b**) and (*anti*-**22b**)]^A, AB signal [δ_A = 3.48, δ_B = 3.61, J_{AB} = 10.3 Hz, A part additionally split by $J_{A,6'}$ = 4.8 Hz, B part additionally split by $J_{B,6'}$ = 6.0 Hz, 1′′-H$_2$ (*syn*-**22b**)]^A, both parts of the AB signal are superimposed by another not completely resolved AB signal [δ_A = 3.45–3.51, δ_B = 3.62, J_{AB} = 10.3 Hz, B part additionally split by $J_{B,6'}$ = 6.0 Hz, 1′′-H$_2$ (*anti*-**22b**)], 3.72 [ddd, $J_{4',5'\text{-H(ax)}}$ = 11.0, $J_{4',3}$ = 8.2, $J_{4',5'\text{-H(eq)}}$ = 2.6 Hz, 4′-H (*syn*-**22b**)**]^A, 3.80 [s, OMe (*syn*-**22b**) and (*anti*-**22b**)], 3.91 [ddd, $J_{4',5'\text{-H(ax)}}$ = 11.1, $J_{4',3}$ = $J_{4',5'\text{-H(eq)}}$ = 3.2 Hz, 4′-H (*anti*-**22b**)**], 4.00–4.13 [m, 1′′′-H$_2$ (*syn*-**22b**) and (*anti*-**22b**), 6′-H (*syn*-**22b**) and (*anti*-**22b**)]^A, extreme AB signal [δ_A = 4.49, δ_B = 4.54, J_{AB} = 11.7 Hz, 1′′′′-H$_2$ (*syn*-**22b**), overlaps with another not fully resolved AB signal: 1′′′′′-H$_2$ (*anti*-**22b**)], 5.12 [dd, $J_{5\text{-H}(E),4}$ = 10.2, $^2J_{5\text{-H}(E),5\text{-H}(Z)}$ = 1.6 Hz, 5-H^E (*syn*-**22b**)], 5.16 [dd, $J_{5\text{-H}(Z),4}$ = 16.8, $^2J_{5\text{-H}(Z),5\text{-H}(E)}$ = 1.2, $^4J_{5\text{-H}(Z),3}$ = 0.6 Hz, 5-H^Z (*syn*-**22b**)] superimposed by 5.10–5.16 [m, 5-H$_2$, (*anti*-**22b**)], 5.509 and 5.515 [2 s, 2′-H (*syn*-**22b**) and (*anti*-**22b**)], 5.70 [ddd, $J_{4,5\text{-H}(Z)}$ = 17.2, $J_{4,5\text{-H}(E)}$ = 10.3, $J_{4,3}$ = 8.5 Hz, 4-H (*syn*-**22b**)**]^A, 5.82 [ddd, $J_{4,5\text{-H}(Z)}$ = 16.5, $J_{4,5\text{-H}(E)}$ = 11.0, $J_{4,3}$ = 8.9 Hz, 4-H (*anti*-**22b**)**], two overlapping AA′BB′ signals centered at δ = 6.87 and 7.26 [2-H$^{Ar\text{-}1}$, 3-H$^{Ar\text{-}1}$, 5-H$^{Ar\text{-}1}$, 6-H$^{Ar\text{-}1}$, (*syn*-**22b**) and (*anti*-**22b**); signal contained solvent peak at δ = 7.26 ppm], 7.29–7.37 and 7.47–7.50 [2 m, 2-H$^{Ar\text{-}2}$, 3-H$^{Ar\text{-}2}$, 4-H$^{Ar\text{-}2}$, 5-H$^{Ar\text{-}2}$, 6-H$^{Ar\text{-}2}$, (*syn*-**22b**) and (*anti*-**22b**)] ppm. *Interpretation was made by using a mixture of both diastereomers *syn*- and *anti*-**22b** in a ratio of 82:18. **Assignment within a pair of signals to the corresponding diastereomer based on a comparison of integrals. The signal with the lower integral was assigned to the minor diastereomer *anti*-**22b** and vice versa. [A]The indicated protons were distinguished by means of a DQF COSY analysis ["H,H COSY spectrum" (499.9 MHz, $CDCl_3$)] by their cross-peaks with protons, which had been assigned unequivocally) [δ_H(^{1}H) ↔ δ_H(^{1}H)]: δ = 5.12 [dd, 5-H^E (*syn*-**22b**)] ↔ 5.70 [ddd, 4-H (*syn*-**22b**)], δ = 5.16 [dd, 5-H^Z (*syn*-**22b**)] ↔ 5.70 [ddd, 4-H (*syn*-**22b**)], 5.70 [ddd, 4-H (*syn*-**22b**)] ↔ 2.72–2.80 [m, 3-H (*syn*-**22b**)], 2.72–2.80 [m, 3-H (*syn*-**22b**)] ↔ 3.72 [ddd, 4′-H (*syn*-**22b**)], AB signal [δ_A = 1.41, δ_B = 1.70, A: 5′-H^{ax}, B: 5′-H^{eq} (*syn*-**22b**)] ↔ 3.72 [ddd, 4′-H (*syn*-**22b**)], AB signal [δ_A = 1.41, δ_B = 1.70, A: 5′-H^{ax}, B: 5′-H^{eq} (*syn*-**22b**)] ↔ 4.00–4.13 [m, 1′′′-H$_2$ (*syn*-**22b**), 6′-H (*syn*-**22b**)], δ = 1.18 [dd, 2′′′-H$_3$ (*syn*-**22b**)] ↔ 4.00–4.13 [m, 1′′′-H$_2$ (*syn*-**22b**), 6′-H (*syn*-**22b**)], 4.00–4.13 [m, 1′′′-H$_2$ (*syn*-**22b**), 6′-H (*syn*-**22b**)] ↔ AB signal [δ_A = 3.48, δ_B = 3.61, 1′′-H$_2$ (*syn*-**22b**)] ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$/$CDCl_3$)*: δ = 14.27 [C-2′′′ (*syn*-**22b**)*]^A, 14.31 [C-2′′′ (*anti*-**22b**)*]^A, 30.77 [C-5′ (*anti*-**22b**)*]^A, 32.08 [C-5′ (*syn*-**22b**)*]^A, 36.01 [C-2 (*anti*-**22b**)*]^A, 36.05 [C-2 (*syn*-**22b**)*]^A, 45.20 [C-3 (*anti*-**22b**)*]^A, 46.19 [C-3 (*syn*-**22b**)*]^A, 55.35 [*O*-CH$_3$ (*syn*-**22b**) and (*anti*-**22b**)]^A, 60.28 [C-1′′′ (*syn*-**22b**)*]^A, 60.40 [C-1′′′ (*anti*-**22b**)*]^A, 72.68 [C-1′′ (*syn*-**22b**)*]^A, 72.71 [C-1′′ (*anti*-**22b**)*]^A, 73.26 [C-1′′′′ (*syn*-**22b**)*]^A, 76.07 [C-1′′′′ (*anti*-**22b**)*]^A, 76.17 [C-6′ (*syn*-**22b**) and (*anti*-**22b**)]^A, 77.89 [C-4′ (*anti*-**22b**)*]^A, 78.14 [C-4′ (*syn*-**22b**)*]^A, 100.71 [C-2′ (*anti*-**22b**)*], 100.79 [C-2′ (*syn*-**22b**)*], 113.88 [C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$ (*syn*-**22b**) and (*anti*-**22b**)]**, 117.78 [C-5 (*anti*-**22b**)*], 117.96 [C-5 (*syn*-**22b**)*]^A, 126.27 and 128.71 [C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$ (*anti*-**22b**)*], 126.29 and 128.15 [C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$ (*syn*-**22b**)*], 128.74 [C-4$^{Ar\text{-}2}$ (*syn*-**22b**) and (*anti*-**22b**); assignment and differentiation based on intensity, which is half as large as the intensities of the two preceding signals and the following signal], 129.51 [C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$ (*syn*-**22b**) and (*anti*-**22b**)]***, 130.30 [C-1$^{Ar\text{-}1}$ (*syn*-**22b**) and (*anti*-**22b**); significantly lower intensity than the preceding signal]***, 136.53 [C-4 (*anti*-**22b**)*]^A, 136.62 [C-4 (*syn*-**22b**)*]^A, 138.56 [C-1$^{Ar\text{-}2}$ (*syn*-**22b**) and (*anti*-**22b**)]***, 159.34 [C-4$^{Ar\text{-}1}$ (*syn*-**22b**) and (*anti*-**22b**)]**, 172.51 [C-1 (*syn*-**22b**) and (*anti*-**22b**)] ppm. *Assignment within a pair of signals to the corresponding diastereomer based on a comparison of integrals. The signal with the lower integral was assigned to the minor diastereomer *anti*-**22b** and vice versa. **Assignment based on a comparison with chemical shifts resulting from a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 113.8 (C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$), 127.6 (C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$), 159.3 (C-4$^{Ar\text{-}1}$) ppm.[51] ***Assignment and differentiation by comparison with a simulation of the ^{13}C NMR spectrum with the program ACD CNMR-Predictor, which provided δ = 130.7 (C-1$^{Ar\text{-}1}$), = 138.3 (±1.5) (C-1$^{Ar\text{-}2}$) ppm.[51] [A]The indicated nuclei, which are nonquaternary, were identified on the basis of an edHSQC analysis ("short-range C,H COSY spectrum"; 100.6/400.1 MHz, $CDCl_3$) by their cross-peaks with directly bonded protons (the latter had previously been assigned unequivocally) [δ_H(^{1}H) ↔ δ_C(^{13}C)]: δ_H = 1.18 [dd, 2′′′-H$_2$ (*syn*-**22b**)] ↔ δ_C = 14.27 [C-2′′′ (*syn*-**22b**)], δ_H = AB signal [δ_A = 1.41, δ_B = 1.70, A: 5′-H^{ax}, B: 5′-H^{eq} (*syn*-**22b**)] ↔ δ_C = 32.08 [C-5′ (*syn*-**22b**)], δ_H = 2.37 [dd, 2-H^A (*syn*-**22b**)] and δ_H = 2.76 [dd, 2-H^B (*syn*-**22b**)] ↔ δ_C = 36.05 [C-2 (*syn*-**22b**)], δ_H = 2.72–2.80 [m, 3-H (*syn*-**22b**) and (*anti*-**22b**)] ↔ δ_C = 46.19 [C-3 (*syn*-**22b**)] and 45.20 [C-3 (*anti*-**22b**)], δ_H = 55.35 [OCH$_3$ (*syn*-**22b**) and (*anti*-**22b**)] ↔ δ_C = 3.80 [s, OMe (*syn*-**22b**) and (*anti*-**22b**)], δ_H = 4.00–4.13 [m, 1′′′-H$_2$ (*syn*-**22b**) and (*anti*-**22b**), 6′-H (*syn*-**22b**) and (*anti*-**22b**)] ↔ δ_C = 60.28 [C-1′′′ (*syn*-**22b**)] and 76.17 [C-6′ (*syn*-**22b**) and (*anti*-**22b**)], δ_H = AB signal [δ_A = 3.48, δ_B = 3.61, 1′′-H$_2$ (*syn*-**22b**)] ↔ δ_C = 72.68 [C-1′′ (*syn*-**22b**)], δ_H = AB signal [δ_A = 4.49, δ_B = 4.54, 1′′′′-H$_2$ (*syn*-**22b**)] ↔ δ_C = 73.26 [C-1′′′′ (*syn*-**22b**)], δ_H = 3.72 [ddd, 4′-H (*syn*-**22b**)] ↔ δ_C = 78.14 [C-4′ (*syn*-**22b**)], δ_H = 5.10–5.18 {m, 5.12 [dd, 5-H^E (*syn*-**22b**)], 5.16 [dd, $J_{5\text{-H}(Z),4}$ = 16.8, $^2J_{5\text{-H}(Z),5\text{-H}(E)}$ = 1.2, $^4J_{5\text{-H}(Z),3}$ = 0.6 Hz (*syn*-**22b**)] superimposed by 5.10–5.16 [m, 5-H$_2$, (*anti*-**22b**)], 5-H$_2$, (*syn*-**22b**) and (*anti*-**22b**)]} ↔ δ_C = 117.78 and 117.96 [C-5 (*syn*-**22b**) and (*anti*-**22b**)], δ_H = 5.70 [ddd, 4-H (*syn*-**22b**)] ↔ δ_C = 136.62 [C-4 (*syn*-**22b**)], δ_H = AA′BB′ signal centered at δ = 6.87 and 7.26 [2-H$^{Ar\text{-}1}$, 3-H$^{Ar\text{-}1}$, 5-H$^{Ar\text{-}1}$, 6-H$^{Ar\text{-}1}$, (*syn*-**22b**) and (*anti*-**22b**)] ↔ δ_C = 113.88 and 129.51 [C-2$^{Ar\text{-}1}$, C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$ (*syn*-**22b**) and (*anti*-**22b**)], δ_H = 7.29–7.37 and 7.47–7.50 [2 m, 2-H$^{Ar\text{-}2}$, 3-H$^{Ar\text{-}2}$, 4-H$^{Ar\text{-}2}$, 5-H$^{Ar\text{-}2}$, 6-H$^{Ar\text{-}2}$, (*syn*-**22b**) and (*anti*-**22b**)] ↔ δ_C = 126.27, 126.29, 128.15, 128.71 and 128.74 [C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-4$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$ (*syn*-**22b**) and (*anti*-**22b**)] ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 3070, 3040, 2985, 2960, 2935, 2915, 2865, 2840, 1725, 1615, 1515, 1465, 1455, 1445, 1420, 1395, 1375, 1340, 1300, 1290, 1250, 1210, 1175, 1125, 1095, 1030, 940 cm^{-1}. $C_{26}H_{32}O_6$ (440.53): calcd. C 70.89, H 7.32; found C 71.02, H 7.38.

Ethyl (3*S*)-3-[(2*S*,4*R*,6*S*)-6-{[(4-Methoxybenzyl)oxy]methyl}-2-phenyl-1,3-dioxan-4-yl]-4-(trimethylsilyl)pent-4-enoate (*syn*-23b) in a

74:26 Mixture with Diastereomer (3*R*)-3-[(2*S*,4*R*,6*S*)-6-{[(4-Methoxybenzyl)oxy]methyl}-2-phenyl-1,3-dioxan-4-yl]-4-(trimethylsilyl)pent-4-enoate (*anti*-23b)



Preparation of the Grignard Reagent: At room temp., a few drops of 1-bromo-1-(trimethylsilyl)ethylene and some granules of iodine were added to a suspension of Mg (850 mg, 35 mmol, 1.4 equiv.) in THF (10.0 mL). Formation of the Grignard reagent was initiated by careful heating. Then a solution of 1-bromo-1(trimethylsilyl)ethylene (total: 4.3 g, 24 mmol) in THF (11 mL) was added dropwise such that the reaction mixture kept boiling slightly throughout the addition. After the addition was completed the reaction mixture was stirred for 1 h at reflux. It was cooled to room temp. and excess Mg was separated by transferring the supernatant through a needle into a different reaction flask. Titration of this Grignard reagent by using salicylaldehyde *N*-phenylhydrazone as an indicator[53] revealed a concentration of 0.85 M.

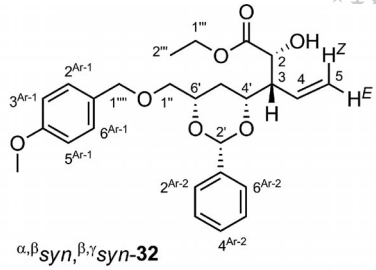
1,4-Addition: At –35 °C, a freshly prepared solution of vinylMgBr (0.85 M in THF, 1.9 mL, 1.6 mmol, 16 equiv.) was added over the course of 1 h to a well-stirred suspension of CuI (153 mg, 0.8 mmol, 8 equiv.) in THF (4.0 mL). The resulting mixture was cooled to –78 °C before adding successively Me_3SiCl (216 μL, 185 mg, 1.7 mmol, 17 equiv.) and a solution of the unsaturated ester (*E*)-**7b** (41.2 mg, 0.1 mmol) in THF (1.0 mL). The mixture was stirred for 6 h at –78 °C. The reaction was quenched by the addition of a mixture [2:1 (v/v), 15 mL] of aq. satd. NH_4Cl and aq. NH_3 (conc.). The resulting mixture was warmed to room temp. before separating the phases and extracting the aqueous phase with *t*BuOMe (3 × 10 mL). The combined organic phases were washed with aq. satd. NaCl (10 mL), dried with $MgSO_4$, and concentrated in vacuo. The resulting residue was purified by flash chromatography (1.5 cm, C_6H_{12}/EtOAc, 8:1) to yield a 74:26 mixture[I] (fractions 27–33, 33 mg, 64%) of the esters *syn*- and *anti*-**23b** as a slightly yellow oil. [I]The isomeric composition of this mixture was determined from the averaged ratios of the integrals over the following ^{1}H NMR signals: δ = 0.11 [s, $SiMe_3$ (*anti*-**23b**)] versus δ = 0.13 [s, $SiMe_3$ (*syn*-**23b**)], δ = 1.12 [dd, 2‴-H_2 (*syn*-**23b**)] versus δ = 1.21 [dd, 2‴-H_2 (*anti*-**23b**)], δ = 2.97 [ddd, 3-H (*syn*-**23b**)] versus δ = 3.14 [ddd, 3-H (*anti*-**23b**)], δ = 5.50 [s, 2′-H (*anti*-**23b**)] versus δ = 5.52 [s, 2′-H (*syn*-**23b**)] ppm.

^{1}H NMR (499.9 MHz, $CDCl_3$/Me_4Si): δ = 0.11 [s, $SiMe_3$ (*anti*-**23b**)]*, 0.13 [s, $SiMe_3$ (*syn*-**23b**)]*, 1.12 [dd, $J_{2‴,1‴\text{-H(A)}} = J_{2‴,1‴\text{-H(B)}}$ = 7.2 Hz, 2‴-H_2 (*syn*-**23b**)]*, 1.21 [dd, $J_{2‴,1‴\text{-H(A)}} = J_{2‴,1‴\text{-H(B)}}$ = 7.2 Hz, 2‴-H_2 (*anti*-**23b**)], 1.35 [ddd, $^2J_{5′\text{-H(ax)},5′\text{-H(eq)}}$ = 13.2, $J_{5′\text{-H(ax)},4′} = J_{5′\text{-H(ax)},6′}$ = 11.3 Hz ≡ $J_{ax,ax}$, 5′-H^{ax} (*syn*-**23b**)], AB signal [δ_A = 1.46, δ_B = 1.52, J_{AB} = 13.1 Hz, A part additionally split by $J_{A,4′} = J_{A,6′}$ = 11.0 Hz ≡ $J_{ax,ax}$, B part additionally split by $J_{B,4′} = J_{B,6′}$ = 2.8 Hz ≡ $J_{eq,eq}$, A: 5′-H^{ax}, B: 5′-H^{eq} (*anti*-**23b**)], 1.68 [ddd, $^2J_{5′\text{-H(eq)},5′\text{-H(ax)}}$ = 13.0, $J_{5′\text{-H(eq)},4′} = J_{5′\text{-H(eq)},6′}$ = 2.3 Hz ≡ J_{eq}, A part additionally split by $J_{A,3}$ = 7.6 Hz, B part additionally split by $J_{B,3}$ = 6.3 Hz, 2-H_2 (*syn*-**23b**)]*, downfield-part superimposed by downfield part of AB signal [δ_A = 2.53, δ_B = 2.72, J_{AB} = 15.5 Hz, A part additionally split by $J_{A,3}$ = 9.2 Hz, B part additionally split by $J_{B,3}$ = 5.8 Hz, 2-H_2 (*anti*-**23b**)]*, 2.97 [ddd, $J_{3,2\text{-H(A)}} \approx J_{3,2\text{-H(B)}} \approx J_{3,4′} \approx$ 7 Hz, 3-H (*syn*-**23b**); broadened signal peaks due to not fully resolved allylic coupling]*, 3.14 [ddd, $J_{3,2\text{-H(A)}}$ = 9.9, $J_{3,2\text{-H(B)}} \approx J_{3,4′} \approx$ 7 Hz, 3-H (*anti*-**23b**); broadened signal peaks due to not fully resolved allylic coupling]*, AB signal [δ_A = 3.46, δ_B = 3.61, J_{AB} = 10.3 Hz, A part additionally split by $J_{A,6′}$ = 4.7 Hz, B part additionally split by $J_{B,6′}$ = 6.1 Hz, 1′′-H_2 (*syn*-**23b**)] both parts are overlapped by AB signal [δ_A = 3.47, δ_B = 3.61, J_{AB} = 10.2 Hz, A part additionally split by $J_{A,6′}$ = 4.8 Hz, B part additionally split by $J_{B,6′}$ = 5.9 Hz, 1′′-H_2 (*anti*-**23b**)], 3.803 [s, OMe (*syn*-**23b**)]*, 3.806 [s, OMe (*anti*-**23b**)]* overlapped by 3.78–4.10 [m, 4′-H, 6′-H, 1‴-H_2 (*syn*-**23b**) and (*anti*-**23b**)], extreme AB signal [δ_A = 4.49, δ_B = 4.53, J_{AB} = 11.7 Hz, 1⁗-H_2 (*syn*-**23b**); overlaps with another not fully resolved AB signal: 1⁗-H_2 (*anti*-**23b**)]*, 5.50 [s, 2′-H (*anti*-**23b**)]*, 5.52 [s, 2′-H (*syn*-**23b**)]*, 5.56 [d, $^2J_{5\text{-H(A)},5\text{-H(B)}}$ = 2.2 Hz, 5-H^A (*syn*-**23b**)]* overlapped by 5.57 [d, $^2J_{5\text{-H(A)},5\text{-H(B)}}$ = 2.0 Hz, 5-H^A (*anti*-**23b**)]*, 5.76 [d, $^2J_{5\text{-H(B)},5\text{-H(A)}}$ = 2.2 Hz, 5-H^B (*syn*-**23b**)]*, 5.78 [d, $^2J_{5\text{-H(B)},5\text{-H(A)}}$ = 2.0 Hz, 5-H^B (*anti*-**23b**)]*, 2 overlapping AA′BB′ signals centered at δ = 6.87 and 7.26 [2-$H^{Ar\text{-}1}$, 3-$H^{Ar\text{-}1}$, 5-$H^{Ar\text{-}1}$, 6-$H^{Ar\text{-}1}$, (*syn*-**23b**) and (*anti*-**23b**)], 7.29–7.37 and 7.47–7.51 ppm [2 m, 2-$H^{Ar\text{-}2}$, 3-$H^{Ar\text{-}2}$, 4-$H^{Ar\text{-}2}$, 5-$H^{Ar\text{-}2}$, 6-$H^{Ar\text{-}2}$, (*syn*-**23b**) and (*anti*-**23b**)]. *Assignment within a pair of signals to the corresponding diastereomer based on a comparison of integrals. The signal with the lower integral was assigned to the minor diastereomer *anti*-**23b** and vice versa. ^{13}C NMR (125.7 MHz, $CDCl_3$/$CDCl_3$): δ = –0.81 [$Si(CH_3)_3$ (*anti*-**23b**)]*, –0.79 [$Si(CH_3)_3$ (*syn*-**23b**)]*, 14.18 [C-2‴ (*syn*-**23b**)]*,A, 14.30 [C-2‴ (*anti*-**23b**)]*,A, 29.57 [C-5′ (*anti*-**23b**)]A, 32.41 [C-5′ (*syn*-**23b**)]A, 34.91 [C-2 (*anti*-**23b**)]A, 37.80 [C-2 (*syn*-**23b**)]A, 44.99 [C-3 (*anti*-**23b**)]A, 46.29 [C-3 (*syn*-**23b**)]A, 55.35 [OCH_3 (*syn*-**23b**) and (*anti*-**23b**)]A, 60.15 [C-1‴ (*syn*-**23b**)]*,A, 60.31 [C-1‴ (*anti*-**23b**)]*,A, 72.69 [C-1′′ (*syn*-**23b**)]*,A, 72.75 [C-1′′ (*anti*-**23b**)]*,A, 73.20 [C-1⁗ (*syn*-**23b**)]*,A, 73.25 [C-1⁗ (*anti*-**23b**)]*,A, 76.30 and 77.94 [C-4′, C-6′ (*anti*-**23b**)]*,A, 76.85 and 79.46 [C-4′, C-6′ (*syn*-**23b**)]*,A, 100.91 [C-2′ (*syn*-**23b**)]*, 101.15 [C-2′ (*anti*-**23b**)]*, 113.87 [C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$ (*syn*-**23b**) and (*anti*-**23b**)]**, 126.37 and 128.09 [C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$ (*syn*-**23b**)]*, 126.43 and 128.12 [C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$ (*anti*-**23b**)]*, 127.72 [C-5 (*anti*-**23b**)]A, 127.81 [C-5 (*syn*-**23b**)]A, 128.69 [C-4$^{Ar\text{-}2}$ (*syn*-**23b**); assignment and differentiation based on intensity, which is half as large as the intensities of the two preceding signals at δ = 126.37 and 128.09 ppm], 128.73 [C-4$^{Ar\text{-}2}$ (*anti*-**23b**); assignment and differentiation based on intensity, which is half as large as the intensities of the two preceding signals at δ = 126.43 and 128.12 ppm]*, 129.47 [C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$ (*syn*-**23b**)]*,**, 129.50 [C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$ (*anti*-**23b**)]*,**, 130.34 [C-1$^{Ar\text{-}1}$ (*syn*-**23b**) and (*anti*-**23b**); significantly lower intensity than the preceding signal]***, 136.16 [C-1$^{Ar\text{-}2}$ (*anti*-**23b**)]*,***, 138.60 [C-1$^{Ar\text{-}1}$ (*syn*-**23b**)]*,***, 150.47 [C-4 (*anti*-**23b**)]****, 151.43 [C-4 (*syn*-**23b**)]****, 158.49 [C-4$^{Ar\text{-}1}$ (*anti*-**23b**)]*,**, 159.32 [C-4$^{Ar\text{-}1}$ (*syn*-**23b**)]*,**, 172.63 [C-1 (*anti*-**23b**)]* 172.66 [C-1 (*syn*-**23b**)]* ppm. *Assignment within a pair of signals to the corresponding diastereomer based on integral heights; the signal with the smaller integral was assigned to the minor diastereomer *anti*-**23b** and vice versa. ** Assignment based on a comparison with chemical shifts resulting from a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 113.8 (C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$), 127.6 (C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$), 159.3 (C-4$^{Ar\text{-}1}$) ppm.[51] ***Assignment and differentiation by comparison with a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 130.7 (C-1$^{Ar\text{-}1}$), 138.3

(C-1^{Ar-1}) ppm.[51] ****Assignment based on a comparison with the chemical shifts resulting from a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 154.7 (C-4) ppm.[51] [A]The indicated nuclei, which are nonquaternary, were identified on the basis of an edHSQC analysis ("short-range C,H COSY spectrum"; 125.7/499.9 MHz, $CDCl_3$) by their cross-peaks with directly bonded protons (the latter had previously been assigned unequivocally) [δ_H(^{1}H) ↔ δ_C(^{13}C)]: δ_H = 1.12 [dd, 2‴-H$_2$ (*syn*-**23b**)] and δ_H = 1.21 [dd, 2‴-H$_2$ (*anti*-**23b**)] ↔ δ_C = 14.18 [C-2‴ (*syn*-**23b**)] and δ_C = 14.30 [C-2‴ (*anti*-**23b**)], δ_H = AB signal [δ_A = 1.46, δ_B = 1.52, A: 5′-H^{ax}, B: 5′-H^{eq} (*anti*-**23b**)] ↔ δ_C = 29.57 [C-5′ (*anti*-**23b**)], δ_H = 1.35 [ddd, 5′-H^{ax} (*syn*-**23b**)] and δ_H = 1.68 [ddd, 5′-H^{eq} (*syn*-**23b**)] ↔ δ_C = 32.41 [C-5′ (*syn*-**23b**)], δ_H = AB signal [δ_A = 2.53, δ_B = 2.72, 2-H$_2$ (*anti*-**23b**)] ↔ δ_C = 34.91 [C-2 (*anti*-**23b**)], δ_H = AB signal [δ_A = 2.41, δ_B = 2.74, 2-H$_2$ (*syn*-**23b**)] ↔ δ_C = 37.80 [C-2 (*syn*-**23b**)], δ_H = 3.14 [ddd, 3-H (*anti*-**23b**)] ↔ δ_C = 44.99 [C-3 (*anti*-**23b**)], δ_H = 2.97 [ddd, 3-H (*syn*-**23b**)] ↔ δ_C = 46.29 [C-3 (*syn*-**23b**)], δ_H = 3.803 [s, OMe (*syn*-**23b**)] and δ_H = 3.806 [s, OMe (*anti*-**23b**)] ↔ δ_C = 55.35 [OCH_3 (*syn*-**23b**) and (*anti*-**23b**)], δ_H =3.78–4.10 [m, 4′-H, 6′-H, 1‴-H$_2$ (*syn*-**23b**) and (*anti*-**23b**)] ↔ δ_C = 60.15 [C-1‴ (*syn*-**23b**)] and δ_C = 60.31 [C-1‴ (*anti*-**23b**)] and δ_C = 76.30 and δ_C = 77.94 [C-4′, C-6′ (*anti*-**23b**)] and δ_C = 76.85 and δ_C = 79.46 [C-4′, C-6′ (*syn*-**23b**)], δ_H = AB signal [δ_A = 3.46, δ_B = 3.61, 1″-H$_2$ (*syn*-**23b**)] and AB signal [δ_A = 3.47, δ_B = 3.61, 1″-H$_2$ (*anti*-**23b**)] ↔ δ_C = 72.69 [C-1″ (*syn*-**23b**)] and 72.75 [C-1″ (*anti*-**23b**)], δ_H = AB signal [δ_A = 4.49, δ_B = 4.53, 1⁗-H$_2$ (*syn*-**23b**); overlapped by another not fully resolved AB signal: 1⁗-H$_2$ (*anti*-**23b**)] ↔ δ_C = 73.20 [C-1⁗ (*syn*-**23b**)] and δ_C = 73.25 [C-1⁗ (*anti*-**23b**)], δ_H = 5.56 [d, 5-H^A (*syn*-**23b**)] overlapped by δ_H = 5.57 [d, 5-H^A (*anti*-**23b**)] and δ_H = 5.76 [d, $^2J_{5\text{-H(B)},5\text{-H(A)}}$ = 2.2, 5-H^B (*syn*-**23b**)] and δ_H = 5.78 [d, $^2J_{5\text{-H(B)},5\text{-H(A)}}$ = 2.0, 5-H^B (*anti*-**23b**)] ↔ δ_C = 127.72 [C-5 (*anti*-**23b**)] and δ_C = 127.81 [C-5 (*syn*-**23b**)] ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 3040, 2960, 2910, 2865, 2840, 1725, 1615, 1585, 1515, 1465, 1455, 1445, 1405, 1395, 1370, 1340, 1300, 1250, 1210, 1175, 1130, 1095, 1030, 935 cm^{-1}. $C_{29}H_{40}O_6Si$ (512.71): calcd. C 67.94, H 7.86; found C 67.66, H 7.85.

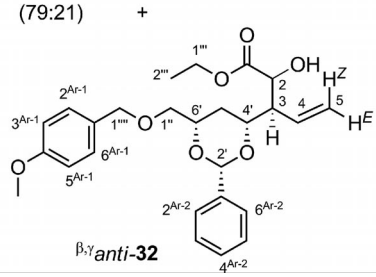
Ethyl (2*R*,3*S*)-2-Hydroxy-3-[(2*S*,4*R*,6*S*)-6-{[(4-methoxybenzyl)oxy]methyl}-2-phenyl-1,3-dioxan-4-yl]pent-4-enoate ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-32) in a 79:21 Mixture with an Unknown Diastereomer of Ethyl (2*S,3*R*)-2-Hydroxy-3-[(2*S*,4*R*,6*S*)-6-{[(4-methoxybenzyl)oxy]methyl}-2-phenyl-1,3-dioxan-4-yl]pent-4-enoate ($^{\beta,\gamma}$*anti*-32):** (*This configuration is not known.)

At –78 °C, a freshly prepared solution of KHMDS (0.45 M in THF, 5.6 mL, 2.5 mmol, 1.3 equiv.) was added dropwise to a solution of a 78:22 mixture (0.83 g, 1.88 mmol) of the diastereomeric esters $^{\beta,\gamma}$*syn*-**22b** and $^{\beta,\gamma}$*anti*-**22b** in THF (11 mL). The resulting solution was stirred at this temperature for 1 h. Solid Davis oxaziridine **29** (1.3 g, 5.0 mmol, 2.6 equiv.) was added in one portion. The reaction mixture was stirred until the starting material was completely consumed (as indicated by TLC control; 3 h). After adding aq. satd. NH_4Cl (20 mL), the mixture was allowed to warm to room temp. The phases were separated and the aqueous phase was extracted with *t*BuOMe (5 × 20 mL). The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (4.0 cm, C_6H_{12}/EtOAc, 7:1, from fraction 30, 5:1) to yield a 79:21 mixture* (fractions 28–46, 715 mg, 83%) of the diastereomers $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32** and $^{\beta,\gamma}$*anti*-**32**. This mixture (92 mg) was resubjected to a second flash chromatography (2.0 cm, C_6H_{12}/EtOAc, 7:1) to provide in fractions 37–44 the pure diastereomer $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32** (57 mg) as a colorless liquid and in fractions 45–57 a 43:57 mixture[I] of the diastereomers $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32** and $^{\beta,\gamma}$*anti*-**32** (34 mg). [I]This composition was determined from



$^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32**

(79:21) +

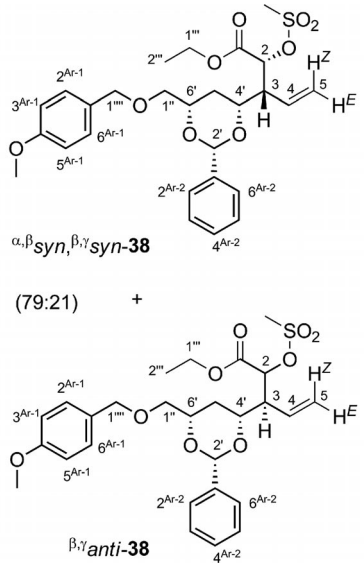


$^{\beta,\gamma}$*anti*-**32**

the ratio of the integrals over the following ^{1}H NMR signals: δ = 2.65 [ddd, $J_{3,4}$ = $J_{3,4'}$ = 9.8, $J_{3,2}$ = 2.2 Hz, 3-H ($^{\beta,\gamma}$*anti*-**32**)] versus δ = 2.78 [ddd, $J_{3,4}$ = $J_{3,4'}$ = 9.8, $J_{3,2}$ = 2.4 Hz, 3-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32**)] ppm. [α]$_D^{20}$ = –8.6 (*c* = 0.68, $CHCl_3$). [α]$_{20}^{365}$ = –31.1 (*c* = 0.68, $CHCl_3$). ^{1}H NMR (499.9 MHz, $CDCl_3$/Me_4Si): δ = 1.06 (t, $J_{2''',1'''}$ = 7.2 Hz, 2‴-H$_3$), 1.39 (ddd, $^2J_{5'\text{-H(ax)},5'\text{-H(eq)}}$ = 13.5, $J_{5'\text{-H(ax)},4'}$ = $J_{5'\text{-H(ax)},6'}$ = 11.6 Hz ≡ $J_{ax,ax}$, 5′-H^{ax}), 1.63 (ddd, $^2J_{5'\text{-H(eq)},5'\text{-H(ax)}}$ = 13.2, $J_{5'\text{-H(eq)},4'}$ = $J_{5'\text{-H(eq)},6'}$ = 2.4 Hz ≡ $J_{eq,eq}$, 5′-H^{eq}), 2.78 (ddd, $J_{3,4}$ = $J_{3,4'}$ = 9.8, $J_{3,2}$ = 2.4 Hz, 3-H), 3.17 (br. d, $J_{2\text{-OH},2}$ = 4.8 Hz, 2-OH), AB signal (δ_A = 3.48, δ_B = 3.61, J_{AB} = 10.3 Hz, A part additionally split by $J_{A,6'}$ = 4.5 Hz, B part additionally split by $J_{B,6'}$ = 6.0 Hz, 1″-H$_2$), 3.72 and 3.95 (2 m$_c$, 1‴-H$_2$) between 3.79 (s, OMe), 4.02 (dddd, $J_{6',5'\text{-H(ax)}}$ = 10.9, $J_{6',1\text{-H(B)}}$ = 6.4, $J_{6',1\text{-H(A)}}$ = 4.6, $J_{6',5'\text{-H(eq)}}$ = 2.1 Hz, 6′-H), 4.08 (ddd, $J_{4',5'\text{-H(ax)}}$ = 11.5, $J_{4',3}$ = 9.7, $J_{4',5'\text{-H(eq)}}$ = 2.1 Hz, 4′-H), 4.20 (br. dd, $J_{2,OH}$ = 4.3, $J_{2,3}$ = 2.2 Hz, 2-H), extreme AB signal (δ_A = 4.50, δ_B = 4.54, J_{AB} = 11.7 Hz, 1⁗-H$_2$), 5.22 (dd, $J_{5\text{-H}(E),4}$ = 10.2, $^2J_{5\text{-H}(E),5\text{-H}(Z)}$ = 1.7 Hz, 5-H^E), 5.27 (dd, $J_{5\text{-H}(Z),4}$ = 17.2, $^2J_{5\text{-H}(Z),5\text{-H}(E)}$ = 1.6 Hz, 5-H^Z), 5.46 (s, 2′-H), 5.75 (ddd, $J_{4,5\text{-H}(Z)}$ = 17.1, $J_{4,5\text{-H}(E)}$ = $J_{4,3}$ = 10.0 Hz, 4-H), AA′BB′ signal centered at δ = 6.87 and 7.26 (2-H^{Ar-1}, 3-H^{Ar-1}, 5-H^{Ar-1}, 6-H^{Ar-1}; contained solvent peak at δ = 7.26 ppm), 7.28–7.34 and 7.42–7.46 (2 m, 2-H^{Ar-2}, 3-H^{Ar-2}, 4-H^{Ar-2}, 5-H^{Ar-2}, 6-H^{Ar-2}) ppm. ^{13}C NMR (125.7 MHz, $CDCl_3$/$CDCl_3$): δ = 13.95 (C-2‴)^A, 32.29 (C-5′)^A, 53.31 (C-3)^A, 55.33 (OCH_3)^A, 61.54 (C-1‴)^A, 71.30 (C-2)^A, 72.59 (C-1″)^A, 73.21 (C-1⁗)^A, 74.02 (C-4′)^A, 76.23 (C-6′)^A, 100.83 (C-2′), 113.86 (C-3^{Ar-1}, C-5^{Ar-1})*, 119.38 (C-5)^A, 126.44 and 127.98 (C-2^{Ar-2}, C-3^{Ar-2}, C-5^{Ar-2}, C-6^{Ar-2}), 128.74 (C-4^{Ar-2}; assignment and differentiation based on intensity, which is half as large as the intensities of the two preceding signals at δ = 126.44 and 127.98 ppm), 129.47 (C-2^{Ar-1}, C-6^{Ar-1})*, 130.27 (C-1^{Ar-1}; significantly lower intensity than the preceding signal at δ = 129.47 ppm)*, 134.40 (C-4)^A, 138.35 (C-1^{Ar-2})**, 159.32 (C-4^{Ar-1})*, 174.07 ppm (C-1) ppm. *Assignment based on a comparison with chemical shifts resulting from a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 113.8 (C-3^{Ar-1}, C-5^{Ar-1}), 127.6 (C-2^{Ar-1}, C-6^{Ar-1}), 130.7 (C-1^{Ar-1}), 159.3 (C-4^{Ar-1}) ppm.[51] **Assignment and differentiation by comparison with a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 130.7 (C-1^{Ar-1}), 138.2 (C-1^{Ar-2}) ppm.[51] [A]The indicated nuclei, which are nonquaternary, were identified on the basis of an edHSQC analysis ("short-range C,H COSY spectrum"; 125.7/499.9 MHz, $CDCl_3$) by

their cross-peaks with directly bonded protons (the latter had previously been assigned unequivocally) [$\delta_H(^1H) \leftrightarrow \delta_C(^{13}C)$]: δ_H = 1.06 (d, 2‴-H_3) ↔ δ_C = 13.95 (C-2‴), δ_H = 1.39 (ddd, 5′-H^{ax}) and δ_H = 1.63 (ddd, 5′-H^{eq}) ↔ δ_C = 32.29 (C-5′), δ_H = 2.78 (ddd, 3-H) ↔ δ_C = 53.31 (C-3), δ_H = 3.79 (s, OMe) ↔ δ_C = 55.33 (OCH_3), δ_H = 3.72 and 3.95 (2 m, 1‴-H_2) ↔ δ_C = 61.54 (C-1‴), δ_H = 4.20 (br. dd, 2-H) ↔ δ_C = 71.30 (C-2), δ_H = AB signal (δ_A = 3.48, δ_B = 3.61, 1″-H_2) ↔ δ_C = 72.59 (C-1″), δ_H = AB signal (δ_a = 4.50, δ_B = 4.54, 1⁗-H_2) ↔ δ_C = 73.21 (C-1⁗), δ_H = 4.08 (ddd, 4′-H) ↔ δ_C = 74.02 (C-4′), δ_H = 4.02 (dddd, 6′-H) ↔ δ_C = 76.23 (C-6′), δ_H = 5.22 (dd, 5-H^E) and δ_H = 5.27 (dd, 5-H^Z) ↔ δ_C = 119.38 (C-5), δ_H = 5.75 (ddd, 4-H) ↔ δ_C = 134.40 (C-4), δ_H = AA′BB′ signal centered at δ = 6.87 and 7.26 (2-$H^{Ar\text{-}1}$, 3-$H^{Ar\text{-}1}$, 5-$H^{Ar\text{-}1}$, 6-$H^{Ar\text{-}1}$) ↔ δ_C = 113.86 (C-$3^{Ar\text{-}1}$, C-$5^{Ar\text{-}1}$) and δ_C = 129.47 (C-$2^{Ar\text{-}1}$, C-$6^{Ar\text{-}1}$), δ_H = 7.28–7.34 and 7.42–7.46 (2 m, 2-$H^{Ar\text{-}2}$, 3-$H^{Ar\text{-}2}$, 4-$H^{Ar\text{-}2}$, 5-$H^{Ar\text{-}2}$, 6-$H^{Ar\text{-}2}$) ↔ δ_C = 126.44 and 127.98 (C-$2^{Ar\text{-}2}$, C-$3^{Ar\text{-}2}$, C-$5^{Ar\text{-}2}$, C-$6^{Ar\text{-}2}$) and δ_C = 128.74 (C-$4^{Ar\text{-}2}$) ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 3690, 3510, 2980, 2935, 2875, 2810, 1725, 1615, 1515, 1490, 1455, 1445, 1415, 1385, 1350, 1300, 1280, 1250, 1180, 1175, 1150, 1115, 1080, 1040, 1025, 940, 845 cm^{-1}. $C_{26}H_{32}O_7$ (456.53): calcd. C 68.40, H 7.07; found C 68.43, H 6.97.

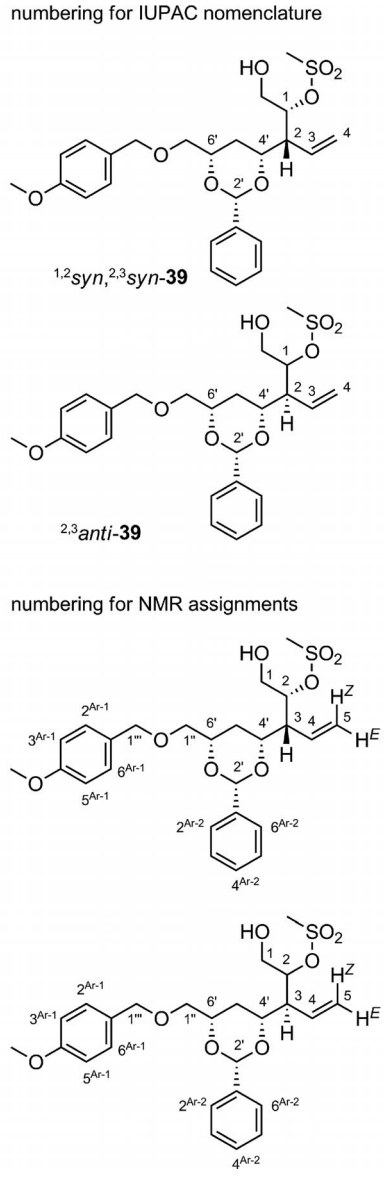
Ethyl (2*R*,3*R*)-2-[(Methanesulfonyl)oxy]-3-[(2*S*,4*R*,6*S*)-6-{[(4-methoxybenzyl)oxy]methyl}-2-phenyl-1,3-dioxan-4-yl]pent-4-enoate ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-38) in a 79:21 Mixture with an Unknown Diastereomer of Ethyl (2*S,3*S*)-2-[(Methanesulfonyl)oxy]-3-[(2*S*,4*R*,6*S*)-6-{[(4-methoxybenzyl)oxy]methyl}-2-phenyl-1,3-dioxan-4-yl]pent-4-enoate ($^{\beta,\gamma}$*anti*-38):** (*This configuration is not known.)



At 0 °C, NEt_3 (0.81 mL, 0.59 g, 5.9 mmol, 3.0 equiv.), methanesulfonyl chloride (196 μL, 290 mg, 2.53 mmol, 1.3 equiv.), and DMAP (24 mg, 0.19 mmol, 0.1 equiv.) were added successively to a solution of an 81:19 mixture (0.89 g, 1.95 mmol) of hydroxy esters $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*- and $^{\beta,\gamma}$*anti*-**32** in CH_2Cl_2 (40 mL). The reaction mixture was stirred at 0 °C for 3 h, after which time TLC showed that the substrate was completely consumed. The reaction mixture was poured into a mixture of CH_2Cl_2 (50 mL) and aq. HCl (1 M, 25 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were washed with aq. satd. $NaHCO_3$ (25 mL), dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash chromatography (4.0 cm, C_6H_{12}/EtOAc, 4:1) to furnish in fractions 26–37 a 79:21 mixture[I] (1.03 g, 98%) of the diastereomers $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*- and $^{\beta,\gamma}$*anti*-**38**. [I]The composition of this mixture was determined from the averaged ratios of the integrals over the following ^{1}H NMR signals: δ = 2.87 [ddd, 3-H ($^{\beta,\gamma}$*anti*-**38**)] versus 3.02 [ddd, $J_{3,4}$ = $J_{3,4'}$ = 9.6, $J_{3,2}$ = 2.4 Hz, 3-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], δ = 5.20 [ddd, 5-H^Z ($^{\beta,\gamma}$*anti*-**38**)] and 5.25 [dd, 5-H^E (*iso*-**193**)] versus 5.31 [dd, 5-H^E ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] and 5.34 [ddd, 5-H^Z ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] ppm. ^{1}H NMR (400.1 MHz, $CDCl_3$/Me_4Si): δ = 1.03 [t, $J_{2''',1'''}$ = 7.1 Hz, 2‴-H_3 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*], 1.25 [t, $J_{2''',1'''}$ = 7.2 Hz, 2‴-H_3 ($^{\beta,\gamma}$*anti*-**38**)*], 1.39 [ddd, $^2J_{5'\text{-H(ax)},5'\text{-H(eq)}}$ = 13.2, $J_{5'\text{-H(ax)},4'}$ = $J_{5'\text{-H(ax)},6'}$ = 11.4 Hz ≡ $J_{ax,ax}$, 5′-H^{ax} ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)]^A, 1.65 [ddd, $^2J_{5'\text{-H(eq)},5'\text{-H(ax)}}$ = 13.3, $J_{5'\text{-H(ax)},4'}$ = $J_{5'\text{-H(ax)},6'}$ = 2.4 Hz ≡ $J_{eq,eq}$, 5′-H^{eq} ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*], 1.70 [ddd, $^2J_{5'\text{-H(eq)},5'\text{-H(ax)}}$ = 13.3, $J_{5'\text{-H(ax)},4'}$ = $J_{5'\text{-H(ax)},6'}$ = 2.4 Hz ≡ $J_{eq,eq}$, 5′-H^{eq} ($^{\beta,\gamma}$*anti*-**38**)*], 2.87 [ddd, $J_{3,4}$ = $J_{3,4'}$ = 10.0, $J_{3,2}$ = 2.5 Hz, 3-H ($^{\beta,\gamma}$*anti*-**38**)*], 3.02 [ddd, $J_{3,4}$ = $J_{3,4'}$ = 9.6, $J_{3,2}$ = 2.4 Hz, 3-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*], 3.16 [s, 2-OSO_2Me ($^{\beta,\gamma}$*anti*-**38**)*], 3.17 [s, 2-OSO_2Me ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*], AB signal [δ_A = 3.48, δ_B = 3.60, J_{AB} = 10.3 Hz, A part additionally split by $J_{A,6'}$ = 4.5 Hz, B part additionally split by $J_{B,6'}$ = 5.9 Hz, 1″-H_2 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*] partly overlapped with AB signal [δ_A = 3.52, δ_B = 3.65, J_{AB} = 10.5 Hz, A part additionally split by $J_{A,6'}$ = 4.8 Hz, B part additionally split by $J_{B,6'}$ = 5.7 Hz, 1″-H_2 ($^{\beta,\gamma}$*anti*-**38**)*], 3.73 and 3.84 [2 m_c, 1‴-H_2 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)]^A, 3.800 [s, OMe ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*] not fully separated from 3.803 [s, OMe ($^{\beta,\gamma}$*anti*-**38**)*], 3.93–4.11 [m, 4′-H, 6′-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)]^A, 4.19 [m_c, 1‴-H_2 ($^{\beta,\gamma}$*anti*-**38**)]^A, extreme AB signal [δ_A = 4.50, δ_B = 4.53, J_{AB} = 11.7 Hz, 1⁗-H_2 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*] overlapping with extreme AB signal [δ_A = 4.52, δ_B = 4.56, J_{AB} = 11.7 Hz, 1⁗-H_2 ($^{\beta,\gamma}$*anti*-**38**)*], 5.07 [d, $J_{2,3}$ = 2.4 Hz, 2-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*], 5.20 [ddd, $J_{5\text{-H}(Z),4}$ = 17.1, $^2J_{5\text{-H}(Z),5\text{-H}(E)}$ = 1.6, $^4J_{5\text{-H}(Z),3}$ = 0.5 Hz, 5-H^Z ($^{\beta,\gamma}$*anti*-**38**)*], 5.25 [dd, $J_{5\text{-H}(E),4}$ = 10.4, $^2J_{5\text{-H}(E),5\text{-H}(Z)}$ = 1.8 Hz, 5-H^E ($^{\beta,\gamma}$*anti*-**38**)*], 5.31 [dd, $J_{5\text{-H}(E),4}$ = 10.2, $^2J_{5\text{-H}(E),5\text{-H}(Z)}$ = 1.5 Hz, 5-H^E ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*], 5.34 [ddd, $J_{5\text{-H}(Z),4}$ = 17.1, $^2J_{5\text{-H}(Z),5\text{-H}(E)}$ = 1.4, $^4J_{5\text{-H}(Z),3}$ = 0.7 Hz, 5-H^Z ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*], 5.49 [s, 2′-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], 5.60 [s, 2′-H ($^{\beta,\gamma}$*anti*-**38**)] superimposed by 5.64 [ddd, $J_{4,5\text{-H}(Z)}$ = 17.3, $J_{4,5\text{-H}(E)}$ = $J_{4,3}$ = 10.2 Hz, 4-H ($^{\beta,\gamma}$*anti*-**38**)*] partly overlapping with 5.71 [ddd, $J_{4,5\text{-H}(Z)}$ = 17.1, $J_{4,5\text{-H}(E)}$ = $J_{4,3}$ = 10.0 Hz, 4-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*] overlapping with 5.67 [d, $J_{2,3}$ = 3.3 Hz, 2-H ($^{\beta,\gamma}$*anti*-**38**)*], two overlapping AA′BB′ signals centered at δ = 6.87 and 7.26 [2-$H^{Ar\text{-}1}$, 3-$H^{Ar\text{-}1}$, 5-$H^{Ar\text{-}1}$, 6-$H^{Ar\text{-}1}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**); contained solvent peak at δ = 7.26], 7.28–7.38, 7.42–7.46 and 7.55–7.59 [3 m, 2-$H^{Ar\text{-}2}$, 3-$H^{Ar\text{-}2}$, 4-$H^{Ar\text{-}2}$, 5-$H^{Ar\text{-}2}$, 6-$H^{Ar\text{-}2}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)] ppm. *Assignments to the respective diastereomer within pairs of signals based on integral height comparisons. The signal with the small integral was assigned to the minor diastereomer $^{\beta,\gamma}$*anti*-**38** and vice versa. [A]The indicated protons were distinguished by means of a DQF COSY analysis ["H,H COSY spectrum" (400.1 MHz, $CDCl_3$)] by their cross-peaks with protons, which had been assigned unequivocally [$\delta_H(^1H) \leftrightarrow \delta_H(^1H)$]: δ = 1.65 [ddd, 5′-H^{eq} ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] ↔ δ = 1.39 [ddd, 5′-H^{ax} ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)], δ = 1.70 [ddd, 5′-H^{eq} ($^{\beta,\gamma}$*anti*-**38**)] ↔ δ = 1.39 [ddd, 5′-H^{ax} ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)], δ = 1.65 [ddd, 5′-H^{eq} ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] ↔ δ = 3.93–4.11 [m, 4′-H, 6′-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)], δ = 1.70 [ddd, 5′-H^{eq} ($^{\beta,\gamma}$*anti*-**38**)] ↔ δ = 3.93–4.11 [m, 4′-H, 6′-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)], δ = 1.39 [ddd, 5′-H^{ax} ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)] ↔ δ = 3.93–4.11 [m, 4′-H, 6′-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)], δ = 1.03 [t, 2‴-H_3 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] ↔ δ = 3.73 and 3.84 [2 m_c, 1‴-H_2 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], δ = 1.25 [t, 2‴-H_3 ($^{\beta,\gamma}$*anti*-**38**)] ↔ 4.19 [m_c, 1‴-H_2 ($^{\beta,\gamma}$*anti*-**38**)] ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$/$CDCl_3$): δ = 13.82 [C-2‴ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)]^A, 14.24 [C-2‴ ($^{\beta,\gamma}$*anti*-**38**)]^A, 32.14 [C-5′ ($^{\beta,\gamma}$*anti*-**38**)*]^A, 32.18 [C-5′ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*]^A, 39.32 [OSO_2CH_3 ($^{\beta,\gamma}$*anti*-**38**)*]^A, 39.45 [OSO_2CH_3 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*]^A, 51.80 [C-3 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)]^A, 52.07 [C-3 ($^{\beta,\gamma}$*anti*-**38**)]^A, 55.33 [OCH_3 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)]^A, 61.68 [C-1‴ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)]^A, 61.97 [C-1‴ ($^{\beta,\gamma}$*anti*-**38**)]^A, 72.47 [C-1″ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)*]^A, 73.24 [C-1⁗ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)*]^A, 73.59 and 75.98 [C-4′, C-6′ ($^{\beta,\gamma}$*anti*-**38**)]^A, 73.82 and 76.08 [C-4′, C-6′ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)]^A, 76.67 [C-2 ($^{\beta,\gamma}$*anti*-**38**)]^A, 78.59 [C-2 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)]^A, 100.62 [C-2′ ($^{\beta,\gamma}$*anti*-**38**)], 100.91 [C-2′ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], 113.89 [C-$3^{Ar\text{-}1}$, C-$5^{Ar\text{-}1}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and

($^{\beta,\gamma}$*anti*-**38**)]**, 121.07 [C-5 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)]^{A}, 121.88 [C-5 ($^{\beta,\gamma}$*anti*-**38**)]^{A}, 126.27 and 128.19 [C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$ ($^{\beta,\gamma}$*anti*-**38**)*], 126.49 and 128.02 [C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*], 128.75 [C-4$^{Ar\text{-}2}$ ($^{\beta,\gamma}$*anti*-**38**)*; assignment and differentiation based on intensity, which is half as large as the intensities of the two preceding signals at δ = 126.27 and 128.19 ppm], 128.85 [C-4$^{Ar\text{-}2}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*; assignment and differentiation based on intensity, which is half as large as the intensities of the two preceding signals at δ = 126.49 and 128.02 ppm], 129.47 [C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$ ($^{\beta,\gamma}$*anti*-**38**)*]**, 129.49 [C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*]**, 130.23 [C-1$^{Ar\text{-}1}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*; significantly lower intensity than the preceding signal at δ = 129.49 ppm]**, 130.30 [C-1$^{Ar\text{-}1}$ ($^{\beta,\gamma}$*anti*-**38**)*; significantly lower intensity than the preceding signal at δ = 129.47 ppm]**, 130.43 [C-4 ($^{\beta,\gamma}$*anti*-**38**)*]^{A}, 132.29 [C-4 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*]^{A}, 138.14 [C-1$^{Ar\text{-}2}$ ($^{\beta,\gamma}$*anti*-**38**)*]***, 138.20 [C-1$^{Ar\text{-}2}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)*]***, 159.36 [C-4$^{Ar\text{-}1}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)]**, 168.03 [C-1 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)]^{A}, 168.76 [C-1 ($^{\beta,\gamma}$*anti*-**38**)]^{A} ppm. *Assignment within a pair of signals to the corresponding diastereomer based on a comparison of integrals. The signal with the lower integral was assigned to the minor diastereomer $^{\beta,\gamma}$*anti*-**38** and vice versa. **Assignment based on a comparison with chemical shifts resulting from a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 113.8 (C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$), 127.6 (C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$), 130.7 (C-1$^{Ar\text{-}1}$), 159 (C-4$^{Ar\text{-}1}$) ppm.[51] ***Assignment and differentiation by comparison with a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 130.7 (C-1$^{Ar\text{-}1}$), 138.2 (C-1$^{Ar\text{-}2}$) ppm.[51] ^{A}The indicated nuclei, which are nonquaternary, were identified on the basis of an edHSQC analysis ("short-range C,H COSY spectrum"; 100.6/400.1 MHz, $CDCl_3$) by their cross-peaks with directly bonded protons (the latter had previously been assigned unequivocally) [δ_H(^{1}H) $\leftrightarrow$ δ_C(^{13}C)]: δ_H = 1.03 [t, 2‴-H$_3$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] $\leftrightarrow$ δ_C = 13.82 [C-2‴ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], δ_H = 1.25 [t, 2‴-H$_3$ ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 14.24 [C-2‴ ($^{\beta,\gamma}$*anti*-**38**)], δ_H = 1.39 [ddd, 5′-H^{ax} ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)] and δ_H = 1.65 [ddd, 5′-H^{eq} ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] and δ_H = 1.70 [ddd, 5′-H^{eq} ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 32.14 [C-5′ ($^{\beta,\gamma}$*anti*-**38**)] and δ_C = 32.18 [C-5′ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], δ_H = 3.16 [s, 2-OSO$_2$Me ($^{\beta,\gamma}$*anti*-**38**)] and δ_H = 3.17 [s, 2-OSO$_2$Me ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] $\leftrightarrow$ δ_C = 39.32 [OSO$_2$CH$_3$ ($^{\beta,\gamma}$*anti*-**38**)] and δ_C = 39.45 [OSO$_2$CH$_3$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], δ_H = 2.87 [ddd, 3-H ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 51.80 [C-3 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], δ_H = 2.87 [ddd, 3-H ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 52.07 [C-3 ($^{\beta,\gamma}$*anti*-**38**)], δ_H = 3.800 [s, OMe ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] and δ_H = 3.803 [s, OMe ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 55.33 [OCH$_3$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)], δ_H = 3.73 and 3.84 [2 m$_c$, 1‴-H$_2$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] $\leftrightarrow$ δ_C = 61.68 [C-1‴ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], δ_H = 4.19 [m$_c$, 1‴-H$_2$ ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 61.97 [C-1‴ ($^{\beta,\gamma}$*anti*-**38**)], δ_H = AB signal [δ_A = 3.48, δ_B = 3.60, 1″-H$_2$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] and δ_H = AB signal [δ_A = 3.52, δ_B = 3.65, 1″-H$_2$ ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 72.47 [C-1″ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)], δ_H = AB signal [δ_A = 4.50, δ_B = 4.53, 1⁗-H$_2$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] overlapped by AB signal [δ_A = 4.52, δ_B = 4.56, 1⁗-H$_2$ ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 73.24 [C-1⁗ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)], δ_H = 3.93–4.11 [m, 4′-H, 6′-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 73.59 and 75.98 [C-4′, C-6′ ($^{\beta,\gamma}$*anti*-**38**)] and δ_C = 73.82 and 76.08 [C-4′, C-6′ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], δ_H = 5.67 [d, 2-H ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 76.67 [C-2 ($^{\beta,\gamma}$*anti*-**38**)], δ_H = 5.07 [d, 2-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] $\leftrightarrow$ δ_C = 78.59 [C-2 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], δ_H = 5.31 [dd, 5-H^{E} ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] and δ_H = 5.34 [ddd, 5-H^{Z} ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] $\leftrightarrow$ δ_C = 121.07 [C-5 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], δ_H = 5.20 [ddd, 5-H^{Z} ($^{\beta,\gamma}$*anti*-**38**)] and δ_H = 5.25 [dd, 5-H^{E} ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 121.88 [C-5 ($^{\beta,\gamma}$*anti*-**38**)], δ_H = 5.64 [ddd, 4-H ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 130.43 [C-4 ($^{\beta,\gamma}$*anti*-**38**)], δ_H = 5.71 [ddd, 4-H ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] $\leftrightarrow$ δ_C = 132.29 [C-4 ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], δ_H = two overlapping AA′BB′-signals centered at δ = 6.87 and 7.26 [2-H$^{Ar\text{-}1}$, 3-H$^{Ar\text{-}1}$, 5-H$^{Ar\text{-}1}$, 6-H$^{Ar\text{-}1}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 113.89 [C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)] and δ_C = 129.47 [C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$ ($^{\beta,\gamma}$*anti*-**38**)] and δ_C = 129.49 [C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)], δ_H = 7.28–7.38, 7.42–7.46, and 7.55–7.59 [3 m, 2-H$^{Ar\text{-}2}$, 3-H$^{Ar\text{-}2}$, 4-H$^{Ar\text{-}2}$, 5-H$^{Ar\text{-}2}$, 6-H$^{Ar\text{-}2}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 126.27 and 128.19 [C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$ ($^{\beta,\gamma}$*anti*-**38**)] and δ_C = 128.75 [C-4$^{Ar\text{-}2}$ and ($^{\beta,\gamma}$*anti*-**38**)], δ_H = 7.28–7.38, 7.42–7.46, and δ_H = 7.55–7.59 [3 m, 2-H$^{Ar\text{-}2}$, 3-H$^{Ar\text{-}2}$, 4-H$^{Ar\text{-}2}$, 5-H$^{Ar\text{-}2}$, 6-H$^{Ar\text{-}2}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**) and ($^{\beta,\gamma}$*anti*-**38**)] $\leftrightarrow$ δ_C = 126.49 and 128.02 [C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] and δ_C = 128.85 [C-4$^{Ar\text{-}2}$ ($^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**)] ppm. IR ($CDCl_3$): $\tilde{\nu}$ = 3155, 2985, 2900, 1815, 1795, 1755, 1640, 1610, 1560, 1515, 1470, 1380, 1300, 1250, 1215, 1175, 1095, 990, 930 cm^{-1}. $C_{27}H_{34}O_9S$ (534.62): calcd. C 60.66, H 6.41; found C 60.45, H 6.36.

(1*S*,2*S*)-1-(Hydroxymethyl)-2-[(2*S*,4*R*,6*S*)-6-{[(4-methoxybenzyl)oxy]methyl}-2-phenyl-1,3-dioxan-4-yl]but-3-enyl Methanesulfonate (^{1,2}*syn*,^{2,3}*syn*-39) and an Unknown Diastereomer of (1*S,2*S*)-1-(Hydroxymethyl)-2-[(2*S*,4*R*,6*S*)-6-{[(4-methoxybenzyl)oxy]methyl}-2-phenyl-1,3-dioxan-4-yl]but-3-enyl Methanesulfonate (^{2,3}*anti*-39):** (*This configuration is not known.)



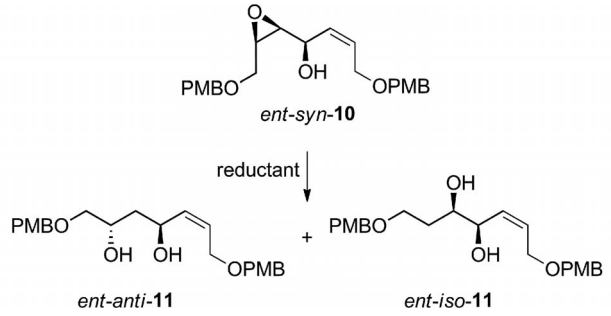
At –20 °C, a solution of a 79:21 mixture of the esters (1.00 g, 1.87 mmol) $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*- and $^{\beta,\gamma}$*anti*-**38** in THF (10 mL) was added within 30 min to a suspension of $LiAlH_4$ (213 mg, 5.61 mmol, 3.0-fold molar amount) in THF (20 mL). The resulting mixture was stirred for 30 min until TLC control indicated a complete conversion of the starting material. Aq. H_2SO_4 (1.0 M, 25 mL) and *t*Bu-

OMe (25 mL) were added with care. The resulting mixture was warmed to room temp. After phase separation the aqueous phase was extracted with *t*BuOMe (6 × 20 mL). The combined organic phases were dried with $MgSO_4$. The organic phase was concentrated under reduced pressure. The residue was purified by flash chromatography (5.0 cm, C_6H_{12}/EtOAc, 2:1). Fractions 17–23 provided the ^{2,3}*anti*-**39** (169 mg, 18%; relative to the fraction of pure $^{\beta,\gamma}$*anti*-**38**: 88%) and fractions 26–41 furnished ^{1,2}*syn*,^{2,3}*syn*-**39** (721 mg, 78%; relative to the fraction of pure $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**38**: 99%). The total yield was 96% and the diastereomeric ratio of the separated diastereomers ^{1,2}*syn*,^{2,3}*syn*-**39** and ^{2,3}*anti*-**39** was 81:19.

^{1,2}*syn*,^{2,3}*syn*-**39:** $[\alpha]_D^{20}$ = –15.0 (*c* = 1.08, $CHCl_3$). $[\alpha]_{20}^{365}$ = –45.2 (*c* = 1.08, $CHCl_3$). ^{1}H NMR (400.1 MHz, $CDCl_3$/Me_4Si): δ = 1.47 (ddd, $^2J_{5'\text{-H(ax)},5'\text{-H(eq)}}$ = 13.3, $J_{5'\text{-H(ax)},4'} = J_{5'\text{-H(ax)},6'}$ = 11.4 Hz ≡ $J_{ax,ax}$, 5′-H^{ax}), 1.66 (ddd, $^2J_{5'\text{-H(eq)},5'\text{-H(ax)}}$ = 13.3, $J_{5'\text{-H(ax)},4'} = J_{5'\text{-H(ax)},6'}$ = 2.5 Hz ≡ $J_{eq,eq}$, 5′-H^{eq}), 2.40 (br. s. 1-OH), 2.74 (ddd, $J_{3,4}$ = 9.7, $J_{3,4'}$ = 8.3, $J_{3,2}$ = 4.3 Hz, 3-H), 3.02 (s, 2-OSO_2Me), AB signal (δ_A = 3.48, δ_B = 3.60, J_{AB} = 10.3 Hz, A part additionally split by $J_{A,6'}$ = 4.5 Hz, B part additionally split by $J_{B,6'}$ = 5.9 Hz, 1′′-H$_2$)^A, 3.79 (s, OMe), extreme AB signal (δ_A = 3.84, δ_B = 3.89, J_{AB} = 12.7 Hz, A part additionally split by $J_{A,2}$ = 6.9 Hz, B part additionally split by $J_{B,2}$ = 4.0 Hz, 1-H$_2$; signals broadened due to not fully resolved coupling with 1-OH)^A, 4.00 (ddd, $J_{4',5'\text{-H(ax)}}$ = 11.1, $J_{4',3}$ = 8.3, $J_{4',5'\text{-H(eq)}}$ = 2.5 Hz, 4′-H) partly overlapping with 4.05 (dddd, $J_{6',5'\text{-H(ax)}}$ = 11.3, $J_{6',1''\text{-H(B)}}$ = 5.7, $J_{6',1''\text{-H(A)}}$ = 4.5, $J_{6',5'\text{-H(eq)}}$ = 2.4 Hz, 6′-H)^A, extreme AB signal (δ_A = 4.48, δ_B = 4.53, J_{AB} = 11.7 Hz, 1′′′-H$_2$), 4.96 (ddd, $J_{2,1\text{-H(A)}}$ = 6.8, $J_{2,1\text{-H(B)}} = J_{2,3}$ = 4.1 Hz, 2-H), 5.23–5.30 (m, 5-H$_2$), 5.54 (s, 2′-H), 5.68 (m$_c$, 4-H), AA′BB′ signal centered at δ = 6.87 and 7.26 (2-H$^{Ar\text{-}1}$, 3-H$^{Ar\text{-}1}$, 5-H$^{Ar\text{-}1}$, 6-H$^{Ar\text{-}1}$; contained solvent peak at δ = 7.26 ppm), 7.31–7.39 and 7.45–7.49 (2 m, 2-H$^{Ar\text{-}2}$, 3-H$^{Ar\text{-}2}$, 4-H$^{Ar\text{-}2}$, 5-H$^{Ar\text{-}2}$, 6-H$^{Ar\text{-}2}$) ppm. ^{A}The indicated protons were distinguished by means of a DQF COSY analysis ["H,H COSY spectrum" (400.1 MHz, $CDCl_3$)] by their cross-peaks with protons, which had been assigned unequivocally [δ_H(^{1}H) ↔ δ_H(^{1}H)]: AB signal (δ_A = 3.48, δ_B = 3.60, 1′′-H$_2$) ↔ δ = 4.05 (dddd, 6′-H), δ = 4.05 (dddd, 6′-H) ↔ δ = 1.47 (ddd, 5′-H^{ax}), δ = 4.05 (dddd, 6′-H) ↔ δ = 1.66 (ddd, 5′-H^{eq}), extreme AB signal (δ_A = 3.84, δ_B = 3.89, 1-H$_2$) ↔ δ = 4.96 (ddd, 2-H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$/$CDCl_3$): δ = 32.06 (C-5′)^A, 38.51 (2-OSO_2CH_3)^A, 51.68 (C-3)^A, 55.33 (OCH_3)^A, 62.96 (C-1)^A, 72.40 (C-1′′)^A, 73.22 (C-1′′′)^A, 75.44 (C-4′)^A, 76.20 (C-6′)^A, 83.96 (C-2)^A, 100.93 (C-2′), 113.86 (C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$)^I, 120.80 (C-5)^A, 126.21 and 128.34 (C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$), 129.00 (C-4$^{Ar\text{-}2}$; assignment and differentiation based on intensity, which is half as large as the intensities of the two preceding signals at δ = 126.21 and 128.34 ppm and the following signal at δ = 129.50 ppm), 129.50 (C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$)^I, 130.14 (C-1$^{Ar\text{-}1}$; significantly lower intensity than the preceding signal at δ = 129.50 ppm)^{I,II}, 132.47 (C-4)^A, 138.03 (C-1$^{Ar\text{-}2}$)^{II}, 159.32 ppm (C-4$^{Ar\text{-}1}$)^I ppm. ^{I}Assignment based on a comparison with chemical shifts resulting from a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 113.8 (C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$), 127.6 (C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$), 130.7 (C-1$^{Ar\text{-}1}$), 159.3 (C-4$^{Ar\text{-}1}$) ppm.[51] ^{II}Assignment and differentiation by comparison with a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 130.7 (C-1$^{Ar\text{-}1}$), 138.2 (C-1$^{Ar\text{-}2}$) ppm.[51] ^{A}The indicated nuclei, which are nonquaternary, were identified on the basis of an edHSQC analysis ("short-range C,H COSY spectrum"; 100.6/400.1 MHz, $CDCl_3$) by their cross-peaks with directly bonded protons (the latter had previously been assigned unequivocally) [δ_H(^{1}H) ↔ δ_C(^{13}C)]: δ_H = 1.47 (ddd, 5′-H^{ax}) and δ_H = 1.66 (ddd, 5′-H^{eq}) ↔ δ_C = 32.06 (C-5′), δ_H = 3.02 (s, 2-OSO_2Me) ↔ δ_C = 38.51 (2-OSO_2CH_3), δ_H = 2.74 (ddd, 3-H) ↔ δ_C = 51.68 (C-3), δ_H = 3.79 (s, OMe) ↔ δ_C = 55.33 (OCH_3), δ_H = AB signal (δ_A = 3.84, δ_B = 3.89, 1-H$_2$) ↔ δ_C = 62.96 (C-1), δ_H = AB signal (δ_A = 3.48, δ_B = 3.60, 1′′-H$_2$) ↔ δ_C = 72.40 (C-1′′), δ_H = AB signal (δ_A = 4.48, δ_B = 4.53, 1′′′-H$_2$) ↔ δ_C = 73.22 (C-1′′′), δ_H = 4.00 (ddd, 4′-H) ↔ δ_C = 75.44 (C-4′), δ_H = 4.05 (dddd, 6′-H) ↔ δ_C = 76.20 (C-6′), δ_H = 4.96 (ddd, 2-H) ↔ δ_C = 83.96 (C-2), δ_H = 5.23–5.30 (m, 5-H$_2$) ↔ δ_C = 120.80 (C-5), δ_H = 5.68 (m$_c$, 4-H) ↔ δ_C = 132.47 (C-4), δ_H = AA′BB′ signal centered at δ = 6.87 and 7.26 (2-H$^{Ar\text{-}1}$, 3-H$^{Ar\text{-}1}$, 5-H$^{Ar\text{-}1}$, 6-H$^{Ar\text{-}1}$) ↔ δ_C = 113.86 (C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$) and δ_C = 129.50 (C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$), δ_H = 7.31–7.39 and 7.45–7.49 (2 m, 2-H$^{Ar\text{-}2}$, 3-H$^{Ar\text{-}2}$, 4-H$^{Ar\text{-}2}$, 5-H$^{Ar\text{-}2}$, 6-H$^{Ar\text{-}2}$) ↔ δ_C = 126.21 and 128.34 (C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$) and δ_C = 129.00 (C-4$^{Ar\text{-}2}$) ppm. IR (film): $\tilde{\nu}$ = 3430, 2980, 2870, 1610, 1515, 1455, 1345, 1300, 1250, 1175, 1140, 1090, 1030, 970, 915, 815, 760, 700 cm^{-1}. $C_{25}H_{32}O_8S$ (492.58): C 60.96, H 6.55, S 6.51; found C 61.06, H 6.66, S 6.32.

^{2,3}*anti*-**39**: $[\alpha]_D^{20}$ = +11.1 (*c* = 1.05, $CHCl_3$). ^{1}H NMR (400.1 MHz, $CDCl_3$/Me_4Si): δ = 1.35 (ddd, $^2J_{5'\text{-H(ax)},5'\text{-H(eq)}}$ = 13.3, $J_{5'\text{-H(ax)},4'} = J_{5'\text{-H(ax)},6'}$ = 11.4 Hz ≡ $J_{ax,ax}$, 5′-H^{ax}), 1.66 (ddd, $^2J_{5'\text{-H(eq)},5'\text{-H(ax)}}$ = 13.3, $J_{5'\text{-H(ax)},4'} = J_{5'\text{-H(ax)},6'}$ = 2.4 Hz ≡ $J_{eq,eq}$, 5′-H^{eq}), 2.12 (br. dd. $J_{OH,1\text{-H(A)}} = J_{OH,1\text{-H(B)}}$ = 5.9 Hz, 1-OH), 2.39 (ddd, $J_{3,4} = J_{3,4'}$ = 9.9, $J_{3,2}$ = 2.0 Hz, 3-H), 3.08 (s, 2-OSO_2Me), AB signal (δ_A = 3.51, δ_B = 3.63, J_{AB} = 10.4 Hz, A part additionally split by $J_{A,6'}$ = 4.6 Hz, B part additionally split by $J_{B,6'}$ = 5.7 Hz, 1′′-H$_2$)^A downfield part overlapped by upfield part of the following AB signal (therefore the upfield part of the following AB signal is not sufficiently resolved), AB signal (δ_A = 3.60–3.66, δ_B = 3.77, J_{AB} = 12.9 Hz, B part additionally split by $J_{B,2}$ = 8.3, $J_{B,OH}$ = 4.8 Hz, 1-H$_2$; signal peaks are broadened due to not fully resolved coupling with 1-OH)^A overlapped by 3.80 (s, OMe), 3.96 (ddd, $J_{4',5'\text{-H(ax)}}$ = 11.4, $J_{4',3}$ = 9.7, $J_{4',5'\text{-H(eq)}}$ = 2.2 Hz, 4′-H), 4.06 (dddd, $J_{6',5'\text{-H(ax)}}$ = 11.3, $J_{6',1''\text{-H(B)}}$ = 5.8, $J_{6',1''\text{-H(A)}}$ = 4.8, $J_{6',5'\text{-H(eq)}}$ = 2.3 Hz, 6′-H)^A, extreme AB signal (δ_A = 4.51, δ_B = 4.55, J_{AB} = 11.7 Hz, 1′′′-H$_2$), 5.17 (dd, $J_{5\text{-H}(Z),4}$ = 17.12, $^2J_{5\text{-H}(Z),5\text{-H}(E)}$ = 1.6 Hz, 5-H^Z), 5.27 (dd, $J_{5\text{-H}(E),4}$ = 10.3, $J_{5\text{-H}(E),5\text{-H}(Z)}$ = 1.7 Hz, 5-H^E), 5.30 (ddd, $J_{2,1\text{-H(B)}}$ = 8.3, $J_{2,1\text{-H(A)}}$ = 3.5, $J_{2,3}$ = 2.0 Hz, 2-H)^A, 5.58 (s, 2′-H) overlapping with 5.63 (ddd, $J_{4,5\text{-H}(Z)}$ = 17.1, $J_{4,5\text{-H}(E)} = J_{4,3}$ = 10.2 Hz, 4-H), AA′BB′ signal centered at δ = 6.87 and 7.27 (2-H$^{Ar\text{-}1}$, 3-H$^{Ar\text{-}1}$, 5-H$^{Ar\text{-}1}$, 6-H$^{Ar\text{-}1}$; contained solvent peak at δ = 7.26 ppm), 7.29–7.39 and 7.54–7.58 (2 m, 2-H$^{Ar\text{-}2}$, 3-H$^{Ar\text{-}2}$, 4-H$^{Ar\text{-}2}$, 5-H$^{Ar\text{-}2}$, 6-H$^{Ar\text{-}2}$) ppm. ^{A}The indicated protons were distinguished by means of a DQF COSY analysis ["H,H COSY spectrum" (400.1 MHz, $CDCl_3$)] by their cross-peaks with protons, which had been assigned unequivocally [δ_H(^{1}H) ↔ δ_H(^{1}H)]: δ = 5.30 (ddd, 2-H) ↔ δ = 2.39 (ddd, 3-H), AB signal (δ_A = 3.51, δ_B = 3.63, 1′′-H$_2$) ↔ δ = 4.06 (dddd, 6′-H), δ = 4.06 (dddd, 6′-H) ↔ δ = 1.35 (ddd, 5′-H^{ax}), δ = 4.06 (dddd, 6′-H) ↔ δ = 1.66 (ddd, 5′-H^{eq}), AB signal (δ_A = 3.60–3.66, δ_B = 3.77, J_{AB} = 12.9 Hz, 1-H$_2$) ↔ 5.30 (ddd, 2-H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$/$CDCl_3$): δ = 32.29 (C-5′)^A, 38.53 (2-OSO_2CH_3)^A, 51.75 (C-3)^A, 55.35 (OCH_3)^A, 64.38 (C-1)^A, 72.50 (C-1′′)^A, 73.23 (C-1′′′)^A, 73.84 (C-4′)^A, 76.04 (C-6′)^A, 81.23 (C-2)^A, 100.66 (C-2′), 113.88 (C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$)^I, 121.53 (C-5)^A, 126.28 and 128.23 (C-2$^{Ar\text{-}2}$, C-3$^{Ar\text{-}2}$, C-5$^{Ar\text{-}2}$, C-6$^{Ar\text{-}2}$), 128.80 (C-4$^{Ar\text{-}2}$; assignment and differentiation based on intensity, which is half as large as the intensities of the two preceding signals at δ = 126.28 and 128.23 ppm and the following signal at δ = 129.47 ppm), 129.47 (C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$)^I, 130.30 (C-1$^{Ar\text{-}1}$; significantly lower intensity than the preceding signal at δ = 129.47 ppm)^{I,II}, 131.06 (C-4)^A, 138.25 (C-1$^{Ar\text{-}2}$)**, 159.33 (C-4$^{Ar\text{-}1}$)^I ppm. ^{I}Assignment based on a comparison with chemical shifts resulting from a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 113.8 (C-3$^{Ar\text{-}1}$, C-5$^{Ar\text{-}1}$), 127.6 (C-2$^{Ar\text{-}1}$, C-6$^{Ar\text{-}1}$), 130.7 (C-1$^{Ar\text{-}1}$), 159.3 (C-4$^{Ar\text{-}1}$) ppm.[51] ^{II}Assignment and differentiation by comparison

Table 3. Reductive epoxide ring-opening of mirror-image *ent-syn*-**10** of the epoxy alcohol *syn*-**10**, the RedAl® reduction of which is shown in Scheme 1.[a]



Reductant	Solvent	*T*	*t* [h]	Result
RedAl®	toluene	room temp.	2	recovered starting material (91%)
DIBAH	toluene	–20 °C	3	decomposition
$LiALH_4$	THF	0 °C → room temp.	1+3	diols *ent-iso*-**11** + *ent-anti*-**11** (61:39 mixture, 93%)
$LiBH_4/Ti(OiPr)_4$	THF	0 °C	20	diols *ent-iso*-**11** + *ent-anti*-**11** (95:5 mixture, 72%)

[a] For comments, see ref.[19]

with a simulation of the ^{13}C NMR spectrum with the program ACD C NMR-Predictor, which provided δ = 130.7 (C-1^{Ar-1}), 138.2 (C-1^{Ar-2}) ppm.[51] [A]The indicated nuclei, which are nonquaternary, were identified on the basis of an edHSQC analysis ("short-range C,H COSY spectrum"; 100.6/400.1 MHz, $CDCl_3$) by their cross-peaks with directly bonded protons (the latter had previously been assigned unequivocally) [$\delta_H(^1H) \leftrightarrow \delta_C(^{13}C)$]: δ_H = 1.35 (ddd, 5′-H^{ax}) and δ_H = 1.66 (ddd, 5′-H^{eq}) $\leftrightarrow \delta_C$ = 32.29 (C-5′), δ_H = 3.08 (s, 2-OSO$_2$Me) $\leftrightarrow \delta_C$ = 38.53 (2-OSO$_2$CH$_3$), δ_H = 2.39 (ddd, 3-H) $\leftrightarrow \delta_C$ = 51.75 (C-3), δ_H = 3.80 (s, OMe) $\leftrightarrow \delta_C$ = 55.35 (OCH$_3$), δ_H = AB signal (δ_A = 3.60–3.66, δ_B = 3.77, 1-H$_2$) $\leftrightarrow \delta_C$ = 64.38 (C-1), δ_H = AB signal (δ_A = 3.51, δ_B = 3.63, 1′′-H$_2$) $\leftrightarrow \delta_C$ = 72.50 (C-1′′), δ_H = AB signal (δ_A = 4.51, δ_B = 4.55, 1′′′-H$_2$) $\leftrightarrow \delta_C$ = 73.23 (C-1′′′), δ_H = 3.96 (ddd, 4′-H) $\leftrightarrow \delta_C$ = 73.84 (C-4′), δ_H = 4.06 (dddd, 6′-H) $\leftrightarrow \delta_C$ = 76.04 (C-6′), δ_H = 5.30 (ddd, 2-H) $\leftrightarrow \delta_C$ = 81.23 (C-2), δ_H = 5.17 (dd, 5-H^Z) and δ_H = 5.27 (dd, 5-H^E) $\leftrightarrow \delta_C$ = 121.53 (C-5), δ_H = 5.63 (ddd, $J_{4,5\text{-}H(Z)}$ = 17.1, $J_{4,5\text{-}H(E)} = J_{4,3}$ = 10.2 Hz, 4-H) $\leftrightarrow \delta_C$ = 131.06 (C-4), δ_H = AA′BB′ signal centered at δ = 6.87 and 7.27 (2-H^{Ar-1}, 3-H^{Ar-1}, 5-H^{Ar-1}, 6-H^{Ar-1}) $\leftrightarrow \delta_C$ = 113.88 (C-3^{Ar-1}, C-5^{Ar-1}) and δ_C = 129.47 (C-2^{Ar-1}, C-6^{Ar-1}), δ_H = 7.29–7.39 and 7.54–7.58 (2 m, 2-H^{Ar-2}, 3-H^{Ar-2}, 4-H^{Ar-2}, 5-H^{Ar-2}, 6-H^{Ar-2}) $\leftrightarrow \delta_C$ = 126.29 and 128.23 (C-2^{Ar-2}, C-3^{Ar-2}, C-5^{Ar-2}, C-6^{Ar-2}) and δ_C = 128.80 (C-4^{Ar-2}) ppm. IR (film): $\tilde{\nu}$ = 3520, 2990, 2940, 2870, 1610, 1585, 1515, 1455, 1345, 1300, 1250, 1170, 1140, 1090, 1030, 910, 815, 760, 700 cm^{-1}. $C_{25}H_{32}O_8S$ (492.58): C 60.96, H 6.55, S 6.51; found C 61.05, H 6.55, S 6.37.

Supporting Information (see footnote on the first page of this article): Experimental details for compounds not on the direct pathway to the final product, NMR spectra, and X-ray data for **36**.

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[9] See ref. 9 and 10 in ref.[8].

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[15] The complementary Sharpless epoxidation **9**→*ent-anti*-**10** was employed in our synthesis of the "eastern moiety" of the naturally configured aglycons **1**–**5**.[8].

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[18] The unreactive epoxy alcohol *syn*-**10** reacted with Red-Al® at 60 °C, delivering the 1,3-diol *syn*-**13** in 51% yield (Scheme 1, reaction c). This kind of (over-)reduction was first described by S. Hatakeyama, K. Satoh, S. Takano, *Tetrahedron Lett.* **1993**, *34*, 7425–7428. It involves an epoxide ring-opening via the trialkoxyaluminate **12** and an S_N' displacement of the allylic *p*-methoxybenzyloxy group by the reductant. However, the yield of this tandem reduction (51%) was lower than the yield of the analogous tandem reduction of the (more) reactive epoxy alcohol *anti*-**10** (→*syn*-**13**; Scheme 1, reaction c), which proceeded in 83% yield. This yield might result from the greater steric hindrance in the trialkoxyaluminate intermediate **12** compared with *iso*-**12**.

[19] RedAl® did not reduce epoxy alcohol *ent-syn*-**10** even at room temp. (Table 3, entry 1, located in the Exp. Sect. after the description of the formation of diol *syn*-**11** by DIBAH reduction of the ca. 25:75 mixture of epoxy alcohol diastereomers *syn*- and *anti*-**10**). A 300 MHz ^{1}H NMR spectrum (300 MHz, $CDCl_3$/TMS) of the crude product showed no 1,3-diol *ent-anti*-**11** whatsoever. DIBAH[16a] caused decomposition of the epoxy alcohol *ent-syn*-**10** (entry 2). $LiAlH_4$ reduced the epoxy alcohol *ent-syn*-**10** (entry 3; 93% yield) giving more 1,2-diol (*ent-iso*-**11**) than 1,3-diol (*ent-anti*-**11**). Treatment of the crude mixture with $NaIO_4$ led to the cleavage of the 1,2-diol *ent-iso*-**11** and 37% yield of pure 1,3-diol *ent-anti*-**11**. A combination of $LiBH_4$ and $Ti(OiPr)_4$ reduced the epoxy alcohol *ent-syn*-**10** to give 72% of a 95:5 mixture of 1,2-diol *ent-iso*-**11** and 1,3-diol *ent-anti*-**11** (entry 4).[20]

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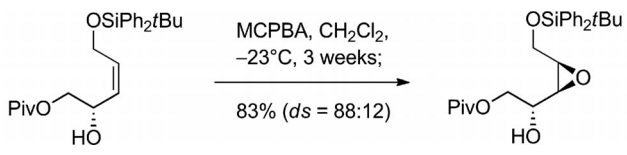

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[33] The *syn* configuration of the major addition product *syn*-**22b** was proved by its subsequent transformation via $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**33** (see Scheme 4) into the *p*-bromobenzoate **36** (Scheme 5), which was analyzed by X-ray diffraction (cf. ref.[50]).

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[38] The asymmetric induction in the 1,4-addition of vinylmagnesium chloride to the *tert*-butyl ester (*E*)-**7c** is too small to attribute the *syn* configuration to the major product diastereomer on the grounds of the unambiguous *syn* selectivity[33] starting from the ethyl ester (*E*)-**7b** and the plausible *syn* selectivity[37] starting from the methyl ester (*E*)-**7a**.

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[45] We became aware of these differences when we treated the α-hydroxy ester $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*syn*-**32** further, assuming (incorrectly) that it was $^{\alpha,\beta}$*syn*,$^{\beta,\gamma}$*anti*-**32**, with $LiALH_4$ and the transformations of Scheme 5 to give the desired building block **6**.

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