79. Studies Directed toward the Synthesis of Phomenoic Acid

Part 1

Enantioselective Synthesis of the C(1)-to-C(6) Segment

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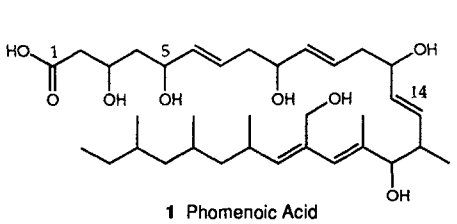
(9.III.94)

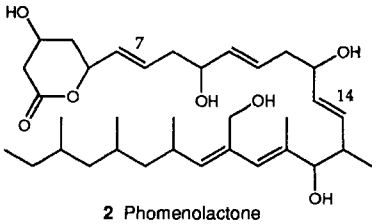
Based on a retrosynthetic analysis, a concept for the synthesis of all stereoisomers of the C(1)-to-C(6) segment of phomenoic acid has been developed. Both enantiomers of the chiral synthon **9** were prepared starting from *rac*-epoxy-diester **10**. They were converted to both enantiomers of the epoxyalcohol, **16** and **21**, respectively, using *Sharpless* epoxydation. They served as building blocks for the synthesis of the tetrol derivatives **20** and **22**, respectively. All four stereoisomers were obtained in optically pure form. They contain the correct assembly of protected functional groups, allowing selective deprotection in view of further transformations.

Introduction. – The fungus *Phoma lingam* TODE is a common pest of many species of the Cruciferea, *e.g.* turnip (*Brassica campestris var. rapifera*), cabbage (*Brassica oleracea*), and rapeseed (*Brassica rapa*). Systematic investigations of the biologically active secondary metabolites of *Phoma lingam* carried out by *Barbier* and coworkers [1] led to the isolation of the sirodesmins, phomamide [2], phomenoic acid, and phomenolactone [3]. The two latter compounds exhibit antifungal and antibiotic activity *in vitro*, in particular against *Candida albicans* [4]. However, the full range of the biological activity has not been elucidated yet.

On the basis of the ^{1}H- and ^{13}C-NMR data, the ozonolysis, and biosynthetic studies, especially incorporation experiments using [^{13}C]- and [^{14}C]-labelled acetates and [^{13}C- and ^{14}C-Me]-L-methionine, structure **1** was proposed for phomenoic acid [3a] and **2** for phomenolactone [3b]. However, the configuration of the nine chiral centers as well as of the diene chromophore has not been determined. To clarify the situation, we decided to synthesize at first the C(1)-to-C(14) segment **3** of **1**. The final goal is a stereocontrolled total synthesis of the microbial metabolite. Already the construction of the segment **3** represents an attractive synthetic challenge due to the presence of four chiral centers and

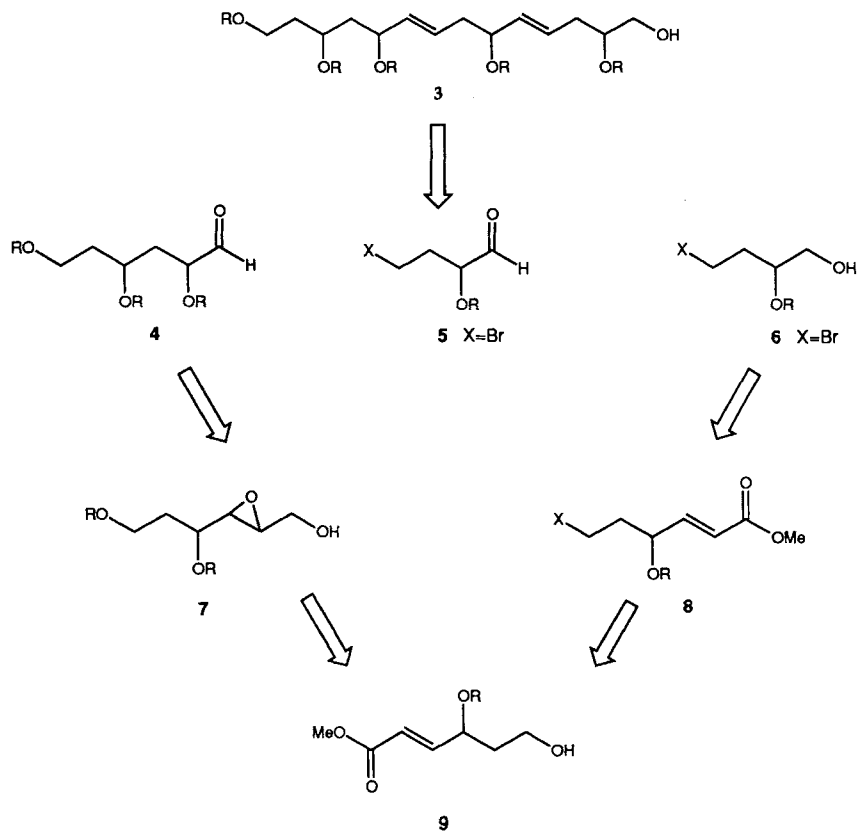


1 Phomenoic Acid



2 Phomenolactone

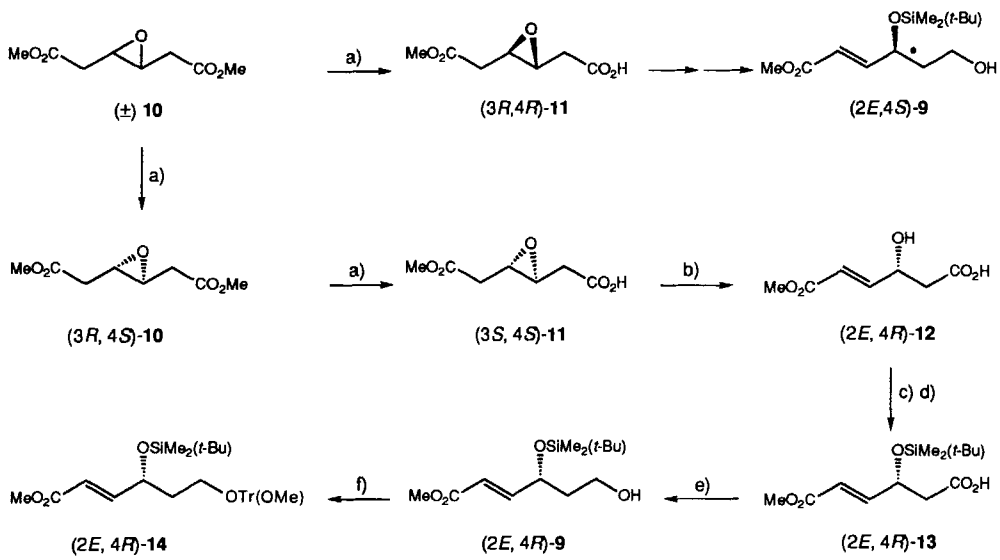
Scheme 1



C=C bonds within its C_{14}-skeleton. The synthetic concept is based on the retrosynthetic analysis which is outlined in *Scheme 1*. Cleavage of both C=C bonds of **3** leads to the aldehydes **4**, **5** and to the fragment **6**. The aldehyde **4** could be prepared from the epoxy-alcohol **7**. The fragments could be obtained by ozonolysis of the α,β-unsaturated ester **8**. Both compounds **7** and **8** are accessible from the key intermediate **9** by subsequent protection of the primary OH group, reduction of the ester group to the corresponding allylic alcohol, and asymmetric epoxydation [5] of the latter by which the configuration of the epoxide is controlled. Thus, all four stereoisomers of the aldehyde **4** could be obtained. According to this concept, the synthesis of intermediate **3** requires at first the preparation of the optically pure subtargets **4**, **5**, and **6** from the chiral synthon **9** followed by stereospecific coupling reactions. The synthetic plan would also allow to prepare all stereoisomers of segment **3**. They might be required in order to establish the unknown configuration of the chiral centers of the intermediate corresponding to the natural metabolite. In addition, the preparation of unnatural stereoisomers for biological testing would be possible.

Results. – For the synthesis of both enantiomers of synthon **9**, dimethyl (±)-3,4-epoxyhexanedioate ((±)-**10**) served as starting material (*Scheme 2*). A few years ago, the kinetic resolution of (±)-**10** by pig liver esterase (PLE) was reported [6] to afford the (+)-diester (3*R*,4*S*)-**10** and the (−)-monoester (3*R*,4*R*)-**11** with 95% ee. The latter has been converted to the protected synthon (2*E*,4*S*)-**9**. In a similar way, we now have prepared the enantiomeric synthon (2*E*,4*R*)-**9**. Treatment of the optically pure *meso*-diester **10** with PLE in phosphate buffer of pH 7 at room temperature afforded the epoxy acid (3*S*,4*S*)-**11** in 90% yield. It is worthwhile mentioning that the rate of the hydrolysis of (3*R*,4*S*)-**10** was much slower (30–40 h) than that of its enantiomer in the racemic mixture (±)-**10** (90 min). The reaction of (3*S*,4*S*)-**11** with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in CH_2Cl_2 at −50° → 0° led, after subsequent treatment with *Amberlyste* H^+, to the α,β-unsaturated ester (2*E*,4*R*)-**12** by a regioselective elimination. Selective protection

Scheme 2



Tr(OMe) = (4-methoxyphenyl)(diphenyl)methyl

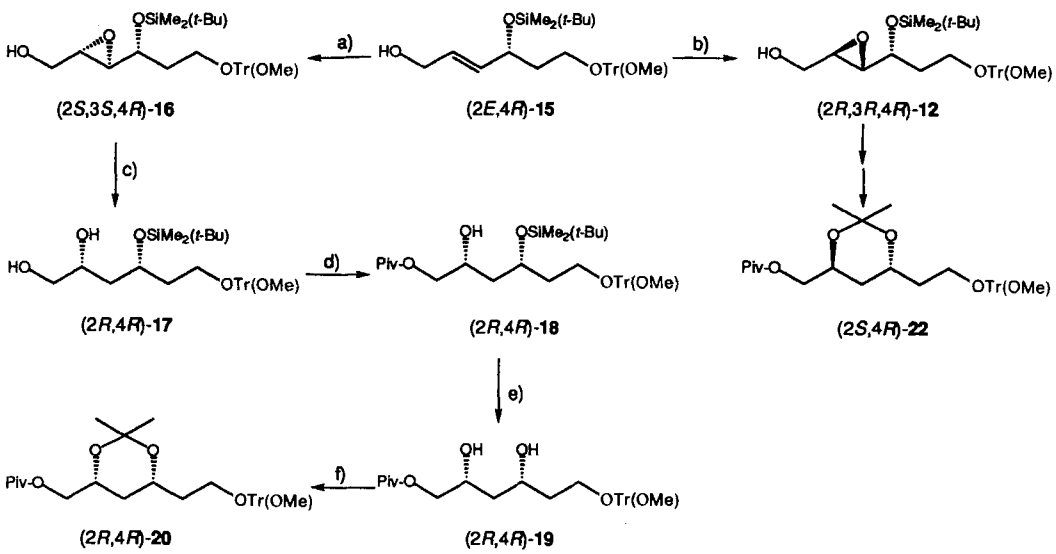
a) PLE, buffer phosphate pH 7; b) DBN, CH_2Cl_2, *Amberlyste* H^+; c) (*t*-Bu)Me_2SiCl, imidazole, DMF; d) K_2CO_3, MeOH/H_2O/THF 3:1:1; e) $BH_3 \cdot Me_2S$, THF; f) (MeO)TrCl, Py, r.t., 48 h.

of the secondary OH group with (*t*-Bu)Me_2SiCl and imidazole in DMF yielded (2*E*,4*R*)-**13**. Reduction of (2*E*,4*R*)-**13** with $BH_3 \cdot Me_2S$ in THF gave the required building block (2*E*,4*R*)-**9** $[\alpha]_D = +11.1$ (CH_2Cl_2; overall yield 44%). For the optical rotation of the enantiomer (2*E*,4*S*)-**9**, $[\alpha]_D = -12.5$ (CH_2Cl_2) had been reported [6]. However, it should be noted that the optical rotation of both enantiomers varies with the concentration of the solutions [7]. But the chromatographic behavior and spectral data were identical.

The next step was the synthesis of the protected building block (2*R*,4*R*)-**20**. It corresponds to the C(1)-to-C(6) segment of phomenoic acid (**1**) with (2*R*,4*R*)-configuration. After protection of the primary OH group of (2*E*,4*R*)-**9** by treatment with 4-

methoxytrityl chloride (= (4-methoxyphenyl)(diphenyl)methyl chloride, (MeO)TrCl) in pyridine, the unsaturated ester (2*E*,4*R*)-**14** obtained was reduced with diisobutylaminum hydride (DIBAL) to the allylic alcohol (2*E*,4*R*)-**15** in 88% yield. Subsequent asymmetric epoxydation with (i-PrO)$_4$Ti, *t*-BuOOH, and (+)-L-diethyl tartrate ((+)-DET) as chiral inducer [5] gave 77% of a mixture of epoxy alcohols consisting of 92% of (2*S*,3*R*,4*R*)-**16** with 84.0% de and 8% of its diastereoisomer as determined by ^{1}H-NMR (*Scheme 3*). The assignment of the configuration of the epoxide (2*S*,3*S*,4*R*)-**16** was confirmed by the subsequent transformations.

Scheme 3



Tr(OMe) = (4-methoxyphenyl)(diphenyl)methyl

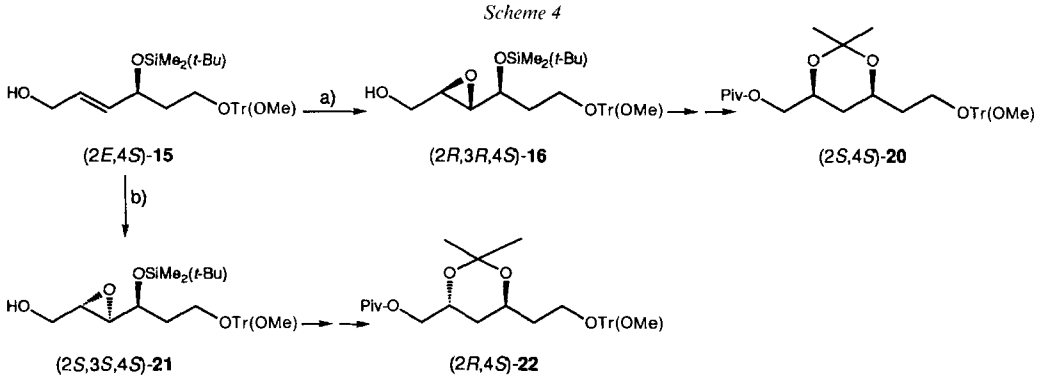
a) (+)-L-DET, CH_2Cl_2, (*i*-OPr)$_4$Ti, *t*-BuOOH, –23°, 24 h; b) (–)-D-DET, CH_2Cl_2, (*i*-OPr)$_4$Ti, *t*-BuOOH, –23°, 24 h; c) (*i*-OPr)$_4$Ti, $LiBH_4$, PhH; d) pivaloyl chloride, Py, 24 h, 0°; e) $Bu_4NF \cdot 3\ H_2O$, THF, 24 h; f) 2,2-dimethoxypropane, MeOH, TsOH.

The relatively high diastereoselectivity may be considered as a case in which the asymmetric epoxydation outweighs the effect of the adjacent center of chirality, if one compares with the results of the asymmetric expoxydation of an analogous structure [8]. Regioselective reductive opening of the epoxy group in (2*S*,3*S*,4*R*)-**16** with $LiBH_4$ and (i-OPr)$_4$Ti in benzene [9] afforded the 1,2-diol (2*R*,4*R*)-**17** (yield 76%). The 1,3-diol was formed as minor product. The ratio of 1,2-diol/1,3-diol of 87:13 was determined by an ^{1}H-NMR-analysis of the di-*O*-acetyl derivatives. In the 1,3-di-*O*-acetyl derivative, the signal of the methine appeared as a *dd* centered at 4.50 ppm, whereas in the 1,2-di-*O*-acetyl derivative it was located at 4.25 ppm as a *m* [10]. All attempts to separate the mixture of the two regioisomers on silica gel failed. Fortunately, purification was achieved by the conversion into (2*R*,4*R*)-**18**. It was possible to protect the primary OH group of (2*R*,4*R*)-**17** selectively by treatment with pivaloyl chloride in pyridine at 0° (yield

84%). Removal of the (*t*-Bu)Me_2Si group was achieved with Bu_4NF in THF yielding the diol (2*R*,4*R*)-**19**. The yield (36%) was low, because, unexpectedly, also deblocking of the pivaloyl group took place as a side reaction affording the 1,2,4-triol (yield 40%). For the success of the described and anticipated conversions the choice of suitable protecting groups proved to by crucial. (MeO)Tr was used for the protection of the primary OH group of (2*E*,4*R*)-**9**, because it is readily cleaved under mild acidic conditions [11] and stable, if the compounds are chromatographed on silica gel and to alkali. It is also a convenient marker on chromatograms, since it forms a yellow color upon spraying with H_2SO_4. For the protection of the primary OH group of (2*R*,4*R*)-**17**, the pivaloyl group was chosen, because it is readily removed by strong base [12] and, as we found, like the (*t*-Bu)Me_2Si group. For these reasons, compound (2*R*,4*R*)-**18** disposes of three different protecting groups which could be removed selectively in the course of the subsequent transformations. Treatment of the 1,3-diol (2*R*,4*R*)-**17** with 2,2-dimethoxypropane in the presence of a catalytic amount of TsOH in MeOH gave the acetonide (2*R*,4*R*)-**20**. The chemical shifts of the Me groups in the ^{13}C-NMR spectra confirmed the relative configuration [13]. It has been reported that the acetonide of a '*syn*'-1,3-diol adopts chair conformation, the equatorial Me appearing at 30.0 ppm and the axial at 20.0 ppm [14]. In contrast, the acetonide of an '*anti*'-1,3-diol adopts twist-boat conformation, both Me appearing at 25.0 ppm [15]. In the case of (2*R*,4*R*)-**20**, signals at 30.05 and 19.7 ppm were observed indicating the presence of a '*syn*'-1,3 diol. It is, therefore, reasonable to assume the (*R*)-configuration also for C(2).

The same sequence of reactions was applied to the key intermediate (2*E*,4*S*)-**9** in order to provide also the (2*S*,4*S*)-segment of **20** (*Scheme 4*). The spectroscopic and chromatographic data of the resulting derivatives (2*E*,4*S*)-**14** to (2*S*,4*S*)-**20** were identical with those of the corresponding enantiomers (*Scheme 3*). However, asymmetric epoxydation of (2*E*,4*S*)-**15** with *t*-BuOOH, (i-OPr)$_4$Ti, and (−)-DET in CH_2Cl_2 (−23°, 24 h) yielded a 8:1 mixture of the epoxides (2*R*,3*R*,4*S*)-**16** and its diastereoisomer (yield 77%). On the other hand, epoxidation of (2*E*,4*R*)-**15** (*Scheme 3*) with (−)-DET gave a 5:1 mixture of (2*R*,3*R*,4*R*)-**21** and its diastereoisomer (yield 66%) under the same conditions, the de

Scheme 4



Tr(OMe) = (4-methoxyphenyl)(diphenyl)methyl

a) (−)-D-DET, CH_2Cl_2, (*i*-PrO)$_4$Ti, *t*-BuOOH, −23°, 24 h; b) (+)-L-DET, CH_2Cl_2, (*i*-PrO)$_4$Ti, *t*-BuOOH, −23°, 24 h.

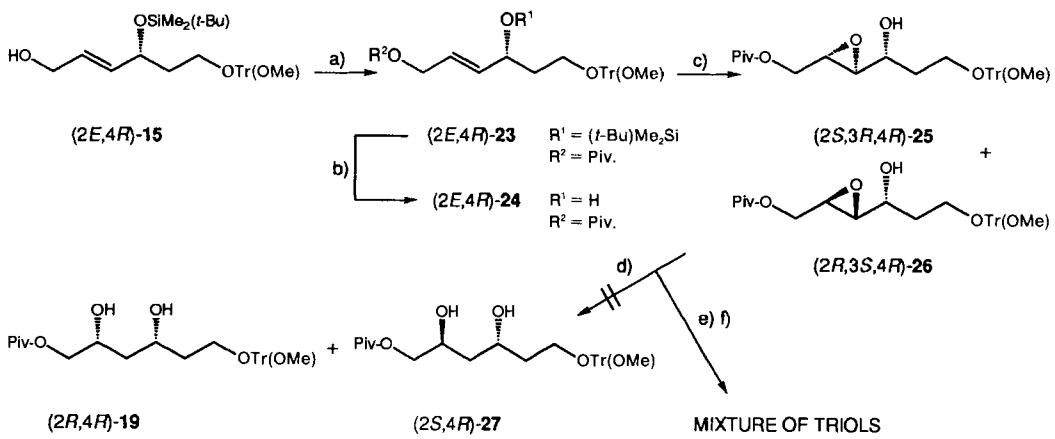
value of 84.0 and 67.0% for (2*S*,3*S*,4*R*)-**16** and (2*R*,3*R*,4*R*)-**21** and of 75.0 and 64.0% for their enantiomers, respectively, were readily determined by the integration of the signals at 0.0 (2*s*, Me_2Si) and 0.85 ppm (*s*, *t*-BuSi), the ratio of intensities being 11.5:1; 8:1; 5:1, and 4.5:1, respectively. The differences of the values of the optical rotation correlated well with the NMR data.

It is known that *Sharpless* epoxidation of chiral (*E*)-allylic alcohols give normally epoxy alcohols in similar yields and high stereoselectivity ($\geq$ 90% ee) with both (+)- and (−)-DET [16]. However, cases are known in which this is not valid [16b] [17]. The difference in stereoselectivity demonstrates the double asymmetric character [18]. For example, the epoxydation of (2*R*,4*R*)-**15**, mediated by (+)-DET, is reasonably stereoselective (11.5:1; *Scheme 3*), whereas the reaction of (2*E*,4*S*)-**15** using (−)-DET is considerably less stereoselective (5:1). They represent matched and mismatched stereochemical pairing, respectively [19]. It is interesting to note that diastereoselectivities observed in our work are reasonable. They do not seem to be exceptional for cases of sterically crowded *trans*-allylic alcohols [8a] [17] [20].

Starting from the expoxy alcohol (2*R*,3*R*,4*R*)-**21** and its enantiomer (2*S*,3*S*,4*S*)-**21**, it is possible to obtain not only (2*S*,4*R*)-**22** (*Scheme 3*) but also (2*R*,4*S*)-**22** (*Scheme 4*), respectively, which now are available for further transformations.

In this connection, the stereoselectivity of the asymmetric epoxidation catalyzed by V^{5+} of the secondary allylic alcohol (2*E*,4*R*)-**24** was of interest. Therefore, the primary OH group of (2*E*,4*R*)-**15** was protected by the pivaloyl group (*Scheme 5*).

Scheme 5



Tr(OMe) = (4-methoxyphenyl)(diphenyl)methyl

a) $(CH_3)_3CCOCl$, Py, r.t.; b) $Bu_4NF \cdot 3\ H_2O$, THF; c) $VO(acac)_2$, benzene, *t*-BuOOH, 50°; d) Red-Al (1 equiv.)/(in THF, 0° or in 1,2-dimethoxyethane, r.t.); e) LAH, Et_2O, 0°, 2 h; f) Red-Al (3 equiv.), THF, r.t., 2 h.

Removal of the (*t*-Bu)Me_2Si in (2*E*,4*R*)-**23** was achieved with subsequent treatment with Bu_4NF in THF yielding (2*E*,4*R*)-**24**. Epoxidation of the latter with *t*-BuOOH/$VO(acac)_2$ in benzene at 50° yielded a mixture of both diastereoisomeric epoxides (2*S*,3*R*,4*R*)-**25** and (2*R*,3*S*,4*R*)-**26** in a ratio of 3:1 (yield 81%), determined by ^{1}H-NMR in $CDCl_3$ focussing of H–C(4) which appeared as a *dd* at 4.3 ppm. The same sequence of

reactions was applied to the enantiomer (2*E*,4*R*)-**24** giving finally both corresponding diastereoisomeric epoxides (2*R*,3*S*,4*S*)-**25** and (2*S*,3*R*,4*S*)-**26** in the expected ratio. The *erythro*/*threo*-selectivity of the V^{5+}-catalyzed epoxidation of acyclic secondary allylic alcohols is well documented [21]. The poor stereoselectivity observed for both (2*E*,4*R*)- and (2*E*,4*S*)-**15** is not surprising considering the results of extensive studies of other cases [22].

Regio- and stereoselective reductive ring opening in the epoxides **25** and **26** leading to the 1,3-diols **19** and **27**, respectively, was unsuccessful. They did not react with 1 equiv. of Na bis(2-methoxyethoxy)aluminum hydride (Red-Al) neither in THF at 0° nor in 1,2-dimethoxyethane at room temperature [23]. Treatment with $LiAlH_4/AlCl_3$ in Et_2O [24] or with 3 equiv. Red-Al at room temperature gave a mixture of different triols which were not separated.

Since the selectivity of the epoxidation of the secondary allylic alcohol **24** is not high enough, and the regiospecific ring opening proved to be difficult, the procedure described for the primary allylic alcohol **15** is much more suitable for further transformations which will be described in a subsequent paper.

Financial support of these investigations by the *Swiss National Science Foundation* is gratefully acknowledged.

Experimental Part

General. All reactions under anh. conditions were performed under N_2 or Ar if not stated otherwise. CH_2Cl_2 and Et_2O were dried by passing through an Al_2O_3 column, THF by distilling over Na/K alloy. All org. extracts were dried (Na_2SO_4) and evaporated below 50°. Pig liver esterase (EC. 3.1.1.1) was purchased from *Boehringer Mannheim GmbH*. TLC: Silica gel *60* F_{254} (*Merck*), spots detected by UV light and/or spraying with a soln. of $KMnO_4$ (2 g), $NaHCO_3$ (4 g) in H_2O (100 ml), or 10% H_2SO_4 in MeOH followed by heating. Column chromatography (CC): silica gel 60 (0.063–0.200 mm, *Merck*) and silica gel 60 (0.040–0.063 mm) for flash chromatography; PE = petroleum ether. Silica gel *60* F_{254} precoated places (0.5 mm) were used for the prep. TLC. $[\alpha]_D$: *Perkin-Elmer* polarimeter model *141*. Anal. GC: *Hewlett-Packard-5890* equipped with a flame-ionization detector and a cap. column of 5% phenyl-methylsilicone (0.2 mm × 25 m) and chiral L-val column (0.22 mm × 25 m) using He as carrier gas. IR [cm^{-1}]: *Perkin-Elmer-781* spectrometer. NMR: *Varian-EM-360* (^1H, 60 MHz), *Varian-EM-390* (^1H, 90 MHz), *Varian Gemini-300* (^1H, 300 MHz; ^{13}C, 75 MHz), *Varian VXR-400* (^1H, 400 MHz; ^{13}C, 101 MHz); chemical shifts in ppm rel. to internal Me_4Si (= 0 ppm) or Me_3CSi. MS (*m*/*z* (%)): *VG 70-250* spectrometer.

Enzymatic Hydrolysis of Dimethyl (+)-3,4-Epoxyadipate ((3*R*,4*S*)-**10**). To 300 mg (1.42 mmol) of (3*R*,4*S*)-**10** suspended in 8.1 ml of 0.1M phosphate buffer of pH 7 were added 40 units of PLE with vigorous stirring. The pH value was kept within the 7.0–7.5 range by addition of 1N NaOH. After consumption of 1.0 equiv. of base during 30 h, the mixture was homogeneous. The aq. phase was extracted with 2 ml of AcOEt. The org. layer was washed with H_2O, and the combined aq. solns. were acidified to pH 2.5 with 2N HCl and extracted with AcOEt (5 × 25 ml), dried, and evaporated to dryness to afford 249 mg (90%) of *hydrogen methyl (3S,4S)-3,4-epoxyadipate* ((3*S*,4*S*)-**11**). IR (film): 3480, 2960–2850, 1730, 1440, 1270, 1170, 1050. ^1H-NMR (60 MHz, $CDCl_3$): 2.55 (*2d*, 2 H–C(2), 2 H–C(5)); 2.9–3.2 (*m*, H–C(3), H–C(4)); 3.7 (*s*, Me); 9.5 (*s*, COOH).

Hydrogen Methyl (2E,4R)-4-Hydroxyhex-2-enedioate ((2*E*,4*R*)-**12**). To a soln. of 185 mg (1.06 mmol) of (3*S*,4*S*)-**10** in 5 ml of CH_2Cl_2 at −50°, 285 µl (2.39 mmol) of DBN were added. The mixture was stirred at −50° for 15 min and at 0° for 30 min, then 1 g of *Amberlyst 15* (H^+ form) was added. After stirring overnight at r.t., the resin was filtered off and washed thoroughly with CH_2Cl_2. Evaporation to dryness yielded 138 mg (75%) of crude (2*E*,4*R*)-**12**. It was purified at a later stage. IR (film): 3500, 2960, 1780, 1730, 1660, 1440, 1280, 1170, 1050. ^1H-NMR (60 MHz, $CDCl_3$): 2.6 (*d*, *J* = 6, 2 H–C(5)); 3.7 (*s*, Me); 4.55–4.95 (*m*, H–C(4)); 6.1 (*dd*, *J* = 15.5, 2. H–C(2)); 6.85 (*dd*, *J* = 15.5, 4, H–C(3)); 7.1 (br. *s*, COOH).

Hydrogen Methyl (2E,4R)-4-{[(tert-Butyl)dimethylsilyl]oxy}hex-2-enedioate ((2*E*,4*R*)-**13**). To a soln. of 80 mg (0.45 mmol) of (2*E*,4*R*)-**12** in 3 ml of DMF, 300 mg of (*t*-Bu)Me_2SiCl (1.97 mmol) and 300 mg (4.3 mmol) of imidazole were added, and the mixture was stirred at r.t. for 24 h. The soln. was diluted with Et_2O (15 ml) and crushed ice (20 g), then the org. layer washed with sat. NH_4Cl soln., and dried. Evaporation yielded 1.2 g of

disilylated intermediate, which was directly hydrolyzed by stirring it in 35 ml of MeOH/THF/H_2O 3:1:1 containing 200 mg of K_2CO_3. After 1 h at r.t., the volume was reduced to ¼ of its volume and the alkaline soln. extracted with 2 ml of Et_2O. After addition of ice, the aq. phase was acidified with 1N HCl to pH 2.5 and extracted with Et_2O (4 × 25 ml). After drying and evaporation 67 mg (51%) of (2*E*,4*R*)-**13** was obtained. IR (film): 3400, 2960–2860, 1740, 1700, 1665, 1475, 1440, 1360, 1120, 975, 840, 780. ^{1}H-NMR (60 MHz, $CDCl_3$): 0.0 (*s*, Me_2Si); 0.80 (*s*, *t*-Bu); 2.46 (*d*, *J* = 6, 2 H–C(5)); 3.7 (*s*, Me); 4.5–4.9 (*m*, H–C(4)); 5.9 (*dd*, *J* = 15, 2, H–C(2)); 6.8 (*dd*, *J* = 15, 5, H–C(3)); 10.5 (br. *s*, COOH).

*Methyl (2*E*,4*R*)-4-{[(*tert*-Butyl)dimethylsilyl]oxy}-6-hydroxyhex-2-eneoate* ((2*E*,4*R*)-**9**). To 500 mg (1.75 mmol) of (2*E*,4*R*)-**13** in 5 ml of THF were injected 375 µl of $BH_3 \cdot Me_2S$ (3.75 mmol). After stirring for 3 h at r.t., 5 drops of H_2O were added, and the mixture was evaporated to dryness. The residue was dissolved in AcOEt dried, and evaporated. After purification of the crude product by CC (PE/Et_2O 1:1) 178 mg (37.5%) of (2*E*,4*R*)-**8** was obtained as colorless oil (90% purity, GC). $[\alpha]_D = +11.1$ (*c* = 1.0, CH_2Cl_2). Reported value [6] for enantiomer (2*E*,4*S*)-**9** (93% purity, GC): $[\alpha]_D = -12.5$ (*c* = 0.7, CH_2Cl_2). IR (film): 3450, 2950, 2890, 2860, 1730, 1660, 1470, 1460, 1435, 1360, 1270, 1200, 1160, 1120, 1090, 830. ^{1}H-NMR (90 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.85 (*s*, *t*-Bu); 1.16 (br. *s*, OH); 1.5–1.9 (*m*, 2 H–C(5)); 3.7 (*s*, Me); 3.7 (*t*, *J* = 6, 2 H–C(6)); 4.26–4.6 (*m*, H–C(4)); 6.1 (*dd*, *J* = 15.5, 2, H–C(2)); 6.85 (*dd*, *J* = 15.5, 4, H–C(3)). CI-MS: 292 (44.1, $[M + NH_4]^+$), 275 (100, $[M + 1]^+$), 260 (4.2), 244 (5.9), 217 (3.6), 187 (6.6), 160 (46.4), 143 (44.9), 132 (8.7), 125 (5.4), 114 (1.7).

*Methyl (2*E*,4*R*)-4-{[(*tert*-Butyl)dimethylsilyl]oxy}-6-[(4-methoxyphenyl)(diphenyl)methoxy]hex-2-enoate* ((2*E*,4*R*)-**14**) *and Enantiomer (2*E*,4*S*)-***14***. Enantiomer (2*E*,4*R*)-***14***.* To a soln. of 50 mg (0.182 mmol) (2*E*,4*R*)-**9** in 3 ml of dry pyridine, 112 mg (0.364 mmol) of (4-methoxydiphenyl)(diphenyl)methyl chloride was added. After stirring for 24 h at r.t., the solvent was removed under high vacuum. The crude product was purified by CC (PE/Et_2O 9:1) to afford 84 mg (84.3%) of (2*E*,4*R*)-**14** as a colorless oil. $[\alpha]_D = -1.1$ (*c* = 2.0, CH_2Cl_2). IR (film): 3060–2860, 1730, 1670, 1610, 1510, 1490, 1470, 1450, 1360, 1300, 1260, 1220, 1170, 1040, 900, 840, 780, 710. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.85 (*s*, *t*-Bu); 1.61–1.91 (*m*, 2 H–C(5)); 3.18 (*t*, *J* = 7, 2 H–C(6)); 3.75 (*s*, MeO); 3.82 (*s*, Me); 4.50 (*m*, H–C(4)); 5.95 (*dd*, *J* = 18, 5, H–C(2)); 6.85 (*d*, *J* = 9, 2 arom. H); 6.95 (*dd*, *J* = 16, 5, H–C(3)); 7.22–7.35 (*m*, 8 arom. H); 7.46 (*d*, *J* = 7, 4 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): –5.4; –4.9; 17.86; 25.56; 37.80; 51.36; 55.11; 59.76; 69.22; 113.17; 119.44; 126.94; 127.91; 128.56; 130.47; 136.14; 144.90; 151.36; 158.79; 167.32. FAB-MS: 585 (4.5, $[M + K]^+$), 546 (0.7, M^+), 274 (24.2), 273 (100), 229 (3.1), 165 (3.1), 73 (30.8).

*Enantiomer (2*E*,4*S*)-***14***.* As described above, (2*E*,4*S*)-**9** (425 mg, 1.58 mmol) was converted into 735 mg (85%) of (2*E*,4*S*)-**13**. $[\alpha]_D = +1.25$ (*c* = 2.0, CH_2Cl_2). IR (film): 3060–2860, 1730, 1670, 1610, 1510, 1490, 1470, 1450, 1360, 1300, 1260, 1220, 1170, 1140, 1070, 1040, 900, 840, 780, 710. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.88 (*s*, *t*-Bu); 1.80–1.99 (*m*, 2 H–C(5)); 3.22 (*t*, *J* = 7, 2 H–C(6)); 3.78 (*s*, MeO); 3.85 (*s*, Me); 4.51 (*m*, H–C(4)); 5.95 (*dd*, *J* = 15, 4, H–C(2)); 6.87 (*d*, *J* = 8, 2 arom. H); 6.95 (*dd*, *J* = 16, 5, H–C(3)); 7.27–7.48 (*m*, 8 arom. H); 7.50 (*d*, *J* = 8, 4 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): –5.4; –4.9; 17.84; 25.53; 37.74; 51.34; 55.05; 59.71; 69.16; 86.40; 113.11; 119.38; 126.92; 127.89; 128.51; 130.43; 136.0; 144.83; 151.36; 158.74; 167.31. FAB-MS: 585 (3.0, $[M + K]^+$), 546 (0.4, M^+), 273 (100), 229 (4.6), 195 (3.9), 165 (6.8), 152 (3.2), 105 (5.6), 89 (9.3), 77 (4.1).

*(2*E*,4*R*)-4-{[(*tert*-Butyl)dimethylsilyl]oxy}-6-[(4-methoxyphenyl)(diphenyl)methoxy]hex-2-en-1-ol* ((2*E*,4*R*)-**15**) *and Enantiomer* ((2*E*,4*S*)-**15**). *Enantiomer (2*E*,4*R*)-***15***.* DIBAL (193 µl, 1.5M in hexane, 0.275 mmol) was injected slowly during 30 min to (2*E*,4*R*)-**14** (30 mg, 0,055 mmol) in hexane (2 ml) at –70°. After stirring for 1 h, 5 drops of MeOH were added, and the mixture was warmed to r.t. Sat. aq. NH_4Cl (3 ml) was added, followed by 5 ml of Et_2O. The org. layer was washed once with 0.5N HCl, brine, and then dried. Evaporation to dryness gave crude (2*E*,4*R*)-**15** which was purified on CC (PE/Et_2O 1:1, R_f 0.38) to afford pure (2*E*,4*R*)-**15** (25 mg, 88%) as a colorless oil. $[\alpha]_D = -3.2$ (*c* = 2.0, CH_2Cl_2). IR (film): 3340, 3020–2860, 1610, 1580, 1510, 1450, 1390, 1300, 1250, 1180, 1070, 1030, 970, 830, 770, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.82 (*s*, *t*-Bu); 1.59 (br. *s*, OH); 1.77–1.88 (*m*, 2 H–C(5)); 3.1 (*m*, 2 H–C(6)); 3.80 (*s*, MeO); 4.05 (*d*, *J* = 4, 2 H–C(1)); 4.33 (*m*, H–C(4)); 5.65 (*m*, H–C(2), H–C(3)); 6.8 (*dd*, *J* = 8, 2 arom. H); 7.21–7.33 (*m*, 8 arom. H); 7.43 (*d*, *J* = 8, 4 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): –4.9; –4.25; 18.15; 25.84; 38.60; 55.21; 60.25; 63.16; 70.25; 86.20; 112.96; 126.73; 127.69; 128.40; 130.27; 134.99; 136.0; 144.77; 158.42. FAB-MS: 557 (0.9, $[M + K]^+$), 273 (100), 243 (2.2), 213 (4.9), 197 (3.3), 165 (10.0), 135 (4.1), 105 (6.6), 89 (7.1), 77 (7.8).

*Enantiomer (2*E*,4*S*)-***15***.* Enantiomer (2*E*,4*S*)-**15** was obtained in 90% yield starting from (2*E*,4*S*)-**14** (610 mg, 1.17 mmol) as described above. $[\alpha]_D = +2.4$ (*c* = 2.0, CH_2Cl_2). IR (film): 3400, 3060–2860, 1610, 1580, 1510, 1485, 1450, 1410, 1390, 1360, 1300, 1250, 1180, 1070, 830, 770, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.82 (*s*, *t*-Bu); 1.26 (br. *s*, OH); 1.75–1.9 (*m*, 2 H–C(5)); 3.12 (*m*, 2 H–C(6)); 3.79 (*s*, MeO); 4.05 (*d*, *J* = 4, 2 H–C(1)); 4.33 (*m*, H–C(4)); 5.66 (*m*, H–C(2), H–C(3)); 6.82 (*d*, *J* = 9, 2 arom. H); 7.21–7.33 (*m*, 8 arom. H); 7.4

(*d*, *J* = 7, 4 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): –5.21; –4.60; 17.91; 25.64; 38.45; 55.10; 60.17; 63.05; 70.21; 86.22; 113.08; 126.90; 127.90; 128.65; 130.45; 135.14; 136.28; 144.99; 158.71. FAB-MS: 557 (2.0, $[M+K]^+$), 273 (100), 241 (3.5), 229 (3.1), 213 (4.9), 195 (5.5), 165 (10.0), 105 (7.7), 77 (7.8).

(2S,3S,4R)-4-{[(tert-Butyl)dimethyl]silyloxy}-2,3-epoxy-6-[(4-methoxyphenyl)(diphenyl)methoxy]hexanol ((2*S*,3*S*,4*R*)-**16**), *Its Enantiomer (2R,3R,4S)-***16**, *and Diastereoisomers (2R,3R,4R)-***21** *and (2S,3S,4S)-***21**. *Enantiomer (2S,3S,4R)-***16**. To a cold (–23°) soln. of (i-PrO)$_4$Ti (168 µl, 160 mg, 0.565 mmol) in CH_2Cl_2 (3 ml) was added a soln. of (+)-L-diethyl tartarate (97 µl, 116.8 mg, 0.565 mmol) in 0.25 ml of CH_2Cl_2. After 10 min at –23°, (2*E*,4*R*)-**15** (293 mg, 0.565 mmol) in 0.5 ml of CH_2Cl_2 and 3M anh. *t*-BuOOH (400 µl, 1.2 mmol) in 0.5 of CH_2Cl_2 were added dropwise to the soln. The mixture was stored at –20° overnight in a sealed flask, then stirred again at –23° and 1.25 ml of 10% tartaric acid was added. After 30 min, the soln. was allowed to warm up and stirred for 1 h. The org. layer was diluted with CH_2Cl_2, washed with H_2O, dried, and evaporated *in vacuo* to give a colorless oil. To a soln. in 5 ml of Et_2O, 1N NaOH (1 ml) was added and the mixture stirred for 30 min at 0°. The org. layer was diluted with Et_2O, washed with H_2O and sat. aq. NaCl, dried, and evaporated. The residue gave after purification on CC (PE/Et_2O 1:1) 232 mg of a colorless oil (77.0%): a mixture of 11.5:1 of (2*S*,3*S*,4*R*)-**16** and its diastereoisomer. $[\alpha]_D = -9.9$ (*c* = 2.0, CH_2Cl_2). IR (film): 3440, 3060–2850, 1610, 1580, 1510, 1490, 1460, 1440, 1300, 1230, 1180, 1150, 1030, 830, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.85 (*s*, *t*-Bu); 1.80 (br. *s*, OH); 1.80–1.93 (*m*, 2 H–C(5)); 2.89 (*m*, H–C(2)); 3.17 (*m*, H–C(3), 2 H–C(6)); 3.37–3.62 (*m*, 2 H–C(1)); 3.75 (*dd*, *J* = 13, 2, 2 H–C(4)); 3.79 (*s*, MeO); 6.83 (*d*, *J* = 9, 2 arom. H); 7.37–7.20 (*m*, 8 arom. H); 7.44 (*d*, *J* = 7, 4 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): –4.47; –3.81; 18.71; 26.43; 36.0; 55.82; 56.90; 59.68; 60.38; 61.79; 72.05; 86.94; 113.67; 127.47; 128.35; 128.94; 130.82; 136.39; 145.05; 159.10. FAB-MS: 573 (5.1, $[M+K]^+$), 273 (100), 195 (3.4), 165 (5.0), 105 (4.2), 77 (2.7).

*Enantiomer (2R,3R,4S)-***16**. Epoxidation was carried out as described for (2*S*,3*S*,4*R*)-**16** from (2*E*,4*S*)-**15** except for using (–)-D-DET instead of (+)-L-DET. A 8:1 mixture of (2*R*,3*R*,4*S*)-**16** and its diastereoisomer (analyzed by ^{1}H-NMR in $CDCl_3$) was obtained (77% yield). $[\alpha]_D = +7.4$ (*c* = 2.0, CH_2Cl_2). IR (film): 3400, 3080–2860, 1610, 1510, 1450, 1300, 1250, 1180, 1070, 1030, 900, 830, 770, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.85 (*s*, *t*-Bu); 1.80–1.92 (*m*, 2 H–C(5)); 1.93 (br. *s*, OH); 2.88 (*m*, H–C(2)); 3.16 (*m*, H–C(3), 2 H–C(6)); 3.40–3.60 (*m*, 2 H–C(1)); 3.75 (*dd*, *J* = 13, 3, H–C(4)); 3.80 (*s*, MeO); 6.83 (*d*, *J* = 9, 2 arom. H); 7.38–7.20 (*m*, 8 arom. H); 7.44 (*d*, *J* = 6, 4 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): –5.08; –4.43; 18.0; 25.80; 32.63; 35.43; 55.21; 56.21; 59.08; 59.79; 61.22; 71.45; 86.0; 113.08; 126.77; 127.72; 128.35; 130.21; 135.82; 145.0; 158.55. FAB-MS: 573 (3.3, $[M+K]^+$), 289 (2.8), 273 (100), 213 (2.4), 195 (1.9), 165 (5.1), 105 (5.0), 77 (4.1).

*Diastereoisomer (2R,3R,4R)-***21**. Epoxidation was carried out as described for (2*R*,3*R*,4*R*)-**21** starting from (2*E*,4*R*)-**15** except for using (–)-D-DET instead of (+)-L-DET to give a 5:1 mixture of (2*R*,3*R*,4*R*)-**21** and its diastereoisomer (analyzed by ^{1}H-NMR in $CDCl_3$) in 66% yield. It was purified by prep. TLC (PE/Et_2O 1:1). $[\alpha]_D = +4.8$ (*c* = 0.5, Et_2O). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.81 (*s*, *t*-Bu); 1.48 (br. *s*, OH); 1.88 (*m*, 2 H–C(5)); 2.94 (*m*, H–C(2)); 3.15 (*m*, H–C(3), 2 H–C(6)); 3.59 (*m*, H–C(4)); 3.80 (*s*, MeO); 3.90–3.83 (*m*, 2 H–C(1)); 6.83 (*d*, *J* = 9, 2 arom. H); 7.40–7.20 (*m*, 8 arom. H); 7.44 (*d*, *J* = 7, 4 arom. H).

*Diastereoisomer (2S,3S,4S)-***21**. Epoxidation was carried out as described for (2*S*,3*S*,4*S*)-**21** starting from (2*E*,4*S*)-**15** using (+)-L-DET to afford 64.0% yield of 4.5:1 mixture of (2*S*,3*S*,4*S*)-**21** and its diastereoisomer (analyzed by ^{1}H-NMR in $CDCl_3$). It was purified by prep. TLC (PE/Et_2O 1:1). $[\alpha]_D = -3.6$ (*c* = 0.5, Et_2O). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.81 (*s*, *t*-Bu); 1.94–1.60 (*m*, 2 H–C(5), OH); 2.94 (*m*, H–C(2)); 3.19 (*m*, H–C(3), 2 H–C(6)); 3.60 (*m*, H–C(4)); 3.80 (*s*, MeO); 3.87 (*m*, 2 H–C(1)); 6.84 (*d*, *J* = 7, 2 arom. H); 7.41–7.22 (*m*, 8 arom. H); 7.45 (*d*, *J* = 8, 4 arom. H).

(2R,4R)-4-{[(tert-Butyl)dimethyl]silyloxy}-6-[(4-methoxyphenyl)(diphenyl)methoxy]hexane-1,2-diol- ((2*R*,4*R*)-**17**), *and Enantiomer (2S,4S)-***17**. *Enantiomer (2R,4R)-***17**. (i-PrO)$_4$Ti (70 µl, 0.235 mmol) was added to a soln. of (2*S*,3*S*,4*R*)-**16** (84 mg, 0.157 mmol) in 3 ml of benzene. After 10 min stirring at r.t., a benzene soln. of $LiBuH_4$ (13 mg, 0.6 mmol in 1 ml) was added and the mixture stirred for 20 h. It was diluted with Et_2O, and 2 ml of 1N HCl were added under vigorous stirring. The Et_2O layer was washed once with brine, dried, and evaporated to dryness. The crude product was purified by CC (AcOEt/PE, 4:10) to give (2*R*,4*R*)-**17** in 76% yield as a colorless oil. $[\alpha]_D = -11.3$ (*c* = 2.0, CH_2Cl_2). The ratio 1,2 diol/1,3 diol was 87:13 according to the ^{1}H-NMR analysis of the diacetyl derivatives. IR (film): 3400, 3080–2840, 1610, 1580, 1510, 1450, 1300, 1250, 1180, 1110, 1030, 830, 770, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.85 (*s*, *t*-Bu); 1.65–2.05 (*m*, 2 H–C(5), 2 H–C(3), OH); 2.60 (br. *s*, OH); 3.16 (*m*, 2 H–C(6)); 3.60 (*m*, H–C(2)); 3.75 (*m*, H–C(4)); 3.81 (*s*, MeO); 3.84 (*t*, *J* = 4, 2 H–C(1)); 6.84 (*d*, *J* = 9, 2 arom. H); 7.21–7.35 (*m*, 8 arom. H); 7.43 (*d*, *J* = 8, 4 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): –4.6; –4.1; 17.84; 25.77; 38.17; 39.37; 55.19; 60.05; 61.71; 66.94; 70.35; 70.96; 86.37; 113.05; 126.81; 127.74; 128.34; 130.24; 135.85; 144.55; 158.50. FAB-MS: 575 (3.3, $[M+K]^+$), 273 (100), 228 (1.3), 213 (4.4), 165 (4.5), 105 (4.7), 77 (3.1).

*Enantiomer (2S,4S)-***17**. Following the procedure described above, (2*S*,4*S*)-**17** was prepared starting from (2*R*,3*R*,4*S*)-**16** in 70% yield. $[\alpha]_D = +6.4$ ($c = 1.0$, CH_2Cl_2). IR (film): 3400, 3080–2860, 1610, 1510, 1450, 1300, 1250, 1180, 1070, 830, 770, 740, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.88 (*s*, *t*-Bu); 1.95–1.30 (*m*, 2 H–C(5), 2 H–C(3), OH); 2.59 (br. *s*, OH); 3.19–3.01 (*m*, 2 H–C(6)); 3.36–3.23 (*m*, H–C(2)); 3.57–3.50 (*m*, H–C(4)); 3.73 (*s*, MeO); 3.76 (*m*, 2 H–C(1)); 6.77 (*d*, $J = 8$, 2 arom. H); 7.26–7.13 (*m*, 8 arom. H); 7.36 (*d*, $J = 8$, 4 arom. H). FAB-MS: 575 (5.6, $[M + K]^+$), 289 (3.7), 273 (100), 259 (2.1), 213 (4.4), 165 (4.4), 115 (4.3), 105 (3.9), 77 (2.6).

*(2*R*,4*R*)-4-{[(*tert*-Butyl)dimethyl]silyloxy}-2-hydroxy-6-[(4-methoxyphenyl)(diphenyl)methoxy]hexyl 2,2-Dimethylpropanoate* ((2*R*,4*R*)-**18**) *and Enantiomer (2*S*,4*S*)-***18***. Enantiomer (2*R*,4*R*)-***18***.* Pivaloyl chloride (17.7 µl, 0.144 mmol) was added at 0° to a soln. of (2*R*,4*R*)-**17** (77.4 mg, 0.144 mmol) in 3 ml of pyridine. The mixture was stored in a sealed flask at −5° for 48 h, then 2 drops of MeOH were added, and the solvent was evaporated. The residue was dissolved in CH_2Cl_2, washed once with sat. $NaHCO_3$ and H_2O and dried. After evaporation, the crude product was purified by CC (PE/AcOEt 4:1) to afford (2*R*,4*R*)-**18** (yield 84%) as a colorless oil. $[\alpha]_D = -2$ ($c = 2.0$, CH_2Cl_2). IR (film): 3400, 3060–2860, 1730, 1610, 1510, 1480, 1440, 1280, 1250, 1150, 1070, 1030, 830, 770, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.86 (*s*, *t*-Bu); 1.23 (*s*, *t*-Bu); 1.58–2.21 (*m*, 2 H–C(3), 2 H–C(5), OH); 3.17 (*t*, $J = 7$, 2 H–C(6)); 3.75 (*m*, H–C(2)); 3.83 (*s*, MeO); 3.96–4.24 (*m*, 2 H–C(1), H–C(4)); 6.8 (*d*, $J = 7$, 2 arom. H); 7.22–7.34 (*m*, 8 arom. H); 7.45 (*d*, $J = 8$, 4 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): –4.62; –4.58; 17.87; 25.78; 27.20; 37.94; 39.99; 55.19; 60.32; 68.56; 69.47; 72.80; 86.41; 113.05; 126.81; 127.74; 128.36; 130.22; 135.89; 144.58; 158.49; 178.50. FAB-MS: 659 (2.2, $[M + K]^+$), 289 (2.8), 273 (100), 213 (4.2), 195 (1.9), 165 (4.6), 115 (3.2), 105 (4.9), 77 (3.4).

*Enantiomer (2*S*,4*S*)-***18***.* As described above, (2*S*,4*S*)-**18** was obtained, in 67% yield, as a colorless oil. $[\alpha]_D = +1.2$ ($c = 2.0$, CH_2Cl_2), starting from (2*S*,4*S*)-**17**. IR (film): 3400, 3080–2860, 1730, 1610, 1510, 1450, 1280, 1250, 1160, 1070, 1030, 830, 770, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.82 (*s*, *t*-BuSi); 1.19 (*s*, *t*-Bu); 1.96–1.52 (*m*, 2 H–C(3), 2 H–C(5), OH); 3.13 (*t*, $J = 7$, 2 H–C(6)); 3.75 (*m*, H–C(2)); 3.79 (*s*, MeO); 4.22–3.93 (*m*, 2 H–C(1), H–C(4)); 6.83 (*d*, $J = 7$, 2 arom. H); 7.31–7.18 (*m*, 8 arom. H); 7.42 (*d*, $J = 8$, 4 arom. H). FAB-MS: 659 (3.2, $[M + K]^+$), 289 (3.9), 273 (100), 259 (2.5), 229 (2.4), 213 (5.1), 165 (5.1), 115 (4.2), 105 (5.7), 77 (4.0).

*(2*R*,4*R*)-2,4-Dihydroxy-6-[(4-methoxyphenyl)(diphenyl)methoxy]hexyl 2,2-Dimethylpropanoate* ((2*R*,4*R*)-**19**) *and Enantiomer (2*S*,4*S*)-***19***. Enantiomer (2*R*,4*R*)-***19***.* To a soln. of (2*R*,4*R*)-**18** (50 mg, 0.08 mmol) dissolved in 5 ml of THF, 75 mg (0.24 mmol) of $Bu_4NF \cdot 3\,H_2O$ were added portionwise and stirred at r.t. for 24 h. H_2O was added (1 ml) and the mixture extracted with Et_2O. The org. layer was separated, washed with H_2O and brine, dried, and evaporated. The crude product was purified by CC (AcOEt/PE 2:3) to give (2*R*,4*R*)-**19** (yield 36%) as a colorless oil. $[\alpha]_D = -6.4$ ($c = 1.0$, CH_2Cl_2). IR (film): 3400, 3060–2860, 1730, 1610, 1510, 1450, 1280, 1250, 1170, 1070, 1030, 830, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.18 (*s*, *t*-Bu); 1.73–1.90 (*m*, 2 H–C(3), 2 H–C(5)); 2.66 (*d*, $J = 6$, OH); 3.22 (*d*, $J = 5$, OH); 3.28–3.45 (*m*, 2 H–C(6)); 3.47 (*m*, H–C(4)); 3.65 (*m*, H–C(2)); 3.79 (*s*, MeO); 4.15 (*m*, 2 H–C(1)); 6.83 (*d*, $J = 9$, 2 arom. H); 7.20–7.32 (*m*, 8 arom. H); 7.41 (*d*, $J = 7$, 4 arom. H). FAB-MS: 545 (7.9, $[M + K]^+$), 506 (2.6, M^+), 289 (2.9), 273 (100), 242 (18.6), 235 (2.6), 213 (7.6), 165 (4.5), 105 (5.6), 77 (3.7).

*Enantiomer (2*S*,4*S*)-***19***.* Enantiomer (2*S*,4*S*)-**19** was obtained as described above, in 33% yield, starting from (2*S*,4*S*)-**18**. $[\alpha]_D = +4.4$ ($c = 1.0$, CH_2Cl_2). IR (film): 3400, 3060–2840, 1730, 1610, 1510, 1450, 1280, 1250, 1160, 1070, 1030, 830, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.18 (*s*, *t*-Bu); 1.70–1.91 (*m*, 2 H–C(3), 2 H–C(5)); 2.67 (br. *s*, OH); 3.22 (br. *s*, OH); 3.25–3.40 (*m*, 2 H–C(6)); 3.45 (*m*, H–C(4)); 3.63 (*m*, H–C(2)); 3.79 (*s*, MeO); 4.16 (*m*, 2 H–C(1)); 6.83 (*d*, $J = 9$, 2 arom. H); 7.22–7.36 (*m*, 8 arom. H); 7.41 (*d*, $J = 7$, 4 arom. H). FAB-MS: 545 (9.1, $[M + K]^+$), 506 (1.8, M^+), 289 (3.4), 273 (100), 242 (75.5), 213 (8.7), 184 (7.8), 165 (6.6), 142 (14.3), 105 (10.9), 77 (9.8).

*(2*R*,4*R*)-2,4-Isopropylidenedioxy-6-[(4-methoxyphenyl)(diphenyl)methoxy]hexyl 2,2-Dimethylpropanoate* ((2*R*,4*R*)-**20**). A soln. of 17 mg (0.035 mmol) of (2*R*,4*R*)-**19** in 2 ml of MeOH and 1 ml of 2,2-dimethoxypropane in presence of 2 mg of TsOH was stirred at r.t. for 24 h. The mixture was evaporated and the crude product purified by CC (PE/AcOEt 12:1) to afford (2*R*,4*R*)-**20** (yield 37%) as a colorless oil. $[\alpha]_D = -2.7$ ($c = 1.0$, Et_2O). IR (film): 3060–2860, 1730, 1600, 1500, 1440, 1370, 1280, 1240, 1150, 760, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.19 (*s*, *t*-Bu); 1.35 (*s*, Me); 1.43 (*s*, Me); 1.71–1.84 (*m*, 2 H–C(3), 2 H–C(5)); 3.05–3.24 (*m*, 2 H–C(6)); 3.79 (*s*, MeO); 4.0 (*d*, $J = 2$, 2 H–C(1)); 4.08–4.20 (*m*, H–C(2), H–C(4)); 6.82 (*d*, $J = 9$, 2 arom. H); 7.18–7.32 (*m*, 8 arom. H); 7.42 (*d*, $J = 8$, 4 arom. H). ^{13}C-NMR (101 MHz, $CDCl_3$): 19.69; 27.15; 30.05; 33.49; 36.91; 55.19; 58.91; 61.48; 65.72; 66.80; 67.38; 98.63; 108.26; 113.02; 126.78; 127.68; 128.38; 130.27; 136.0; 144.62; 144.69; 144.71; 144.84; 158.43; 178.3.

*(2*E*,4*R*)-4-{[(*tert*-Butyl)dimethyl]silyloxy}-6-[(4-methoxyphenyl)(diphenyl)methoxy]hex-2-enyl 2,2-Dimethylpropanoate* ((2*E*,4*R*)-**23**) *and Enantiomer (2*E*,4*S*)-***23***. Enantiomer (2*E*,4*R*)-***23***.* Pivaloyl chloride (246 µl, 2.0 mmol) was added dropwise to a stirred soln. of (2*E*,4*R*)-**15** (280 mg, 0.540 mmol) in 3 ml of pyridine at r.t.

Stirring was continued overnight, 1 ml of MeOH added, and the mixture evaporated. The residue was dissolved in Et_2O, washed with H_2O, dried, and evaporated. The crude product was purified by CC (PE/Et_2O 9:1) to yield 283 mg (87%) of (2*E*,4*R*)-**23** as a colorless oil. IR (film): 3080–2840, 1730, 1610, 1510, 1480, 1450, 1250, 830, 770, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.82 (*s*, *t*-BuSi); 1.18 (*s*, *t*-Bu); 1.80 (*m*, 2 H–C(5)); 3.12 (*t*, *J* = 7, 2 H–C(6)); 3.79 (*s*, MeO); 4.34 (*dd*, *J* = 15, 5, H–C(4)); 4.47 (*d*, *J* = 5, 2 H–C(1)); 5.65 (*m*, H–C(2), H–C(3)); 6.81 (*d*, *J* = 9, 2 arom. H); 7.21–7.32 (*m*, 8 arom. H); 7.42 (*d*, *J* = 8, 4 arom. H). FAB-MS: 641 (1.9, $[M + K]^+$), 289 (2.9), 273 (100), 259 (2.2), 241 (2.3), 229 (2.0), 195 (4.4), 165 (7.6), 135 (2.9), 115 (5.7), 77 (4.6).

*Enantiomer (2*E,*4S)*-**23**. As described above, (2*E*,4*S*)-**23** was obtained in 85% yield starting from (2*E*,4*S*)-**15**. IR (film): 3080–2840, 1730, 1610, 1580, 1510, 1460, 1450, 1360, 1280, 1250, 1150, 1070, 1030, 1000, 970, 830, 770, 700. ^{1}H-NMR (60 MHz, $CDCl_3$): 0.0 (2*s*, Me_2Si); 0.80 (*s*, *t*-BuSi); 1.20 (*s*, *t*-Bu); 1.87 (*m*, 2 H–C(5)); 3.1 (*t*, *J* = 6, 2 H–C(6)); 3.8 (*s*, MeO); 4.50 (*m*, H–C(4), 2 H–C(1)); 5.70 (*m*, H–C(2), H–C(3)); 6.8 (*d*, *J* = 8, 2 arom. H); 7.20–7.60 (*m*, 12 arom. H). FAB-MS: 641 (1.9, $[M + K]^+$), 273 (100), 259 (3.0), 241 (1.4), 229 (1.4), 215 (1.5), 195 (1.7), 159 (4.6), 85 (3.7).

*(2*E,*4*R*)-4-Hydroxy-6-[(4-methoxyphenyl)(diphenyl)methoxy]hex-2-enyl 2,2-Dimethylpropanoate* ((2*E*,4*R*)-**24**) *and Enantiomer (2*E,*4*S*)*-**24**. *Enantiomer (2*E,*4*R*)*-**23**. $Bu_4NF \cdot 3\ H_2O$ (503 mg, 1.59 mmol) was added portionwise within 20 min to a stirred soln. of (2*E*,4*R*)-**23** (320 mg, 0.531 mmol) in 10 ml of THF. Stirring was continued at r.t. for 24 h, then H_2O (2 ml) was added and the mixture extracted with Et_2O. The org. phase was washed with H_2O and brine, dried, and evaporated. The crude product was purified by CC (PE/Et_2O 1:1) to afford 119 mg (46%) of (2*E*,4*R*)-**22**. $[\alpha]_D = -6.8$ (*c* = 2.0, CH_2Cl_2). IR (film): 3400, 3080–2840, 1730, 1610, 1510, 1480, 1450, 1400, 1370, 1280, 1250, 1150, 1070, 1030, 970, 900, 830, 770, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.19 (*s*, *t*-Bu); 1.83 (*q*, *J* = 12, 6, 2 H–C(5)); 2.99 (br. *s*, OH); 3.23–3.33 (*m*, 2 H–C(6)); 3.79 (*s*, MeO); 4.36 (*m*, H–C(4)); 4.50 (*d*, *J* = 4, 2 H–C(1)); 5.75 (*m*, H–C(2), H–C(3)); 6.83 (*d*, *J* = 9, 2 arom. H); 7.19–7.32 (*m*, 8 arom. H); 7.42 (*d*, *J* = 8, 4 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$). 15.26; 27.19; 36.61; 55.20; 61.68; 64.15; 70.95; 87.01; 113.14; 124.42; 126.96; 127.89; 128.25; 130.22; 135.41; 135.87; 144.16; 158.57; 178.23. FAB-MS: 527 (5.1, $[M+K]^+$), 488 (3.4, M^+), 411 (4.5), 289 (3.2), 273 (100), 213 (6.3), 197 (3.0), 183 (3.4), 165 (5.9), 135 (5.5), 105 (11.2), 77 (4.3).

*Enantiomer (2*E,*4*S*)*-**24**. Similarly, the enantiomer (2*E*,4*S*)-**24** was obtained in 51% yield. $[\alpha]_D = +6.2$ (*c* = 2.0, CH_2Cl_2). IR (film): 3400, 3060–2840, 1730, 1610, 1580, 1510, 1480, 1445, 1400, 1360, 1280, 1250, 1210, 1150, 1070, 1030, 970, 900, 830, 790, 760, 700. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.19 (*s*, *t*-Bu); 1.82 (*m*, 2 H–C(5)); 3.05 (br. *s*, OH); 3.25–3.35 (*m*, 2 H–C(6)); 3.79 (*s*, MeO); 4.37 (*m*, H–C(4)); 4.51 (*d*, *J* = 4, 2 H–C(1)); 5.58–5.76 (*m*, H–C(2), H–C(3)); 6.83 (*d*, *J* = 8, 2 arom. H); 7.21–7.35 (*m*, 8 arom. H); 7.43 (*d*, *J* = 9, 4 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 26.97; 36.42; 38.55; 55.07; 61.55; 64.08; 70.86; 87.0; 113.24; 124.56; 127.11; 128.41; 130.38; 135.62; 136.07; 144.40; 158.83; 178.60. FAB-MS: 527 (6.3, $[M + K]^+$), 489 (3.3, $[M + 1]^+$), 411 (2.8), 273 (100), 213 (3.2), 195 (1.3). EI-MS: 488 (1.1, M^+), 411 (4.0), 273 (100), 229 (3.6), 213 (6.5), 197 (4.6), 165 (7.7), 135 (5.2), 105 (10.5), 77 (4.6).

*(2*S,*3*R,*4*R*)-2,3-Epoxy-4-hydroxy-6-[(4-methoxyphenyl)(diphenyl)methoxy]hexyl 2,2-Dimethylpropanoate* ((2*S*,3*R*,4*R*)-**25**) *and Enantiomer (2*R,*3*S,*4*S*)*-**25**. *Enantiomer (2*S,*3*R,*4*R*)*-**25**. To a soln. of (2*E*,4*R*)-**24** (180 mg, 0.368 mmol) in benzene (10 ml) was added a freshly prepared soln. of $[VO(acac)_2]$ (0.514 mg, 1.8×10^{-3} mmol) in benzene (100 µl), followed by a soln. of *t*-BuOOH (3M, 200 µl, 0.6 mmol) in benzene (500 µl). After heating for 24 h at 50°, the mixture was filtered through a short column of *Florisil* (200–300 mesh, 2 g, Et_2O). After evaporation, the crude product was purified by CC (PE/Et_2O 1:1) to afford 150 mg (81%) of (2*S*,3*R*,4*R*)-**25** as a colorless oil. $[\alpha]_D = +0.6$ (*c* = 2.0, CH_2Cl_2). IR (film): 3400, 3080–2840, 1730, 1610, 1510, 1450, 1400, 1370, 1280, 1250, 1150, 1070, 1030, 900, 830, 800, 770, 700. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.20 (*s*, *t*-Bu); 1.86 (*m*, 2 H–C(5)); 2.84 (br. *s*, OH); 2.88 (*m*, H–C(3)); 3.20 (*m*, H–C(2)); 3.30–3.40 (*m*, 2 H–C(6)); 3.79 (*s*, MeO); 3.88 (*m*, 2 H–C(1)); 4.33 (*dd*, *J* = 13, 3, H–C(4)); 6.83 (*d*, *J* = 7, 2 arom. H); 7.20–7.31 (*m*, 8 arom. H); 7.42 (*d*, *J* = 6, 4 arom. H). ^{13}C-NMR (101 MHz, $CDCl_3$): 27.18; 33.42; 38.82; 52.77; 55.22; 58.04; 61.24; 64.0; 68.39; 87.01; 113.19; 127.01; 127.86; 128.25; 128.33; 130.22; 135.38; 144.17; 158.62; 178.17. FAB-MS: 543 (7.6, $[M + K]^+$), 504 (3.7, M^+), 273 (100), 215 (3.8), 165 (4.2), 135 (2.8), 113 (4.0), 105 (7.6), 77 (4.5).

*Enantiomer (2*R,*3*S,*4*S*)*-**25**. Similarly, the enantiomer (2*R*,3*S*,4*S*)-**25** was obtained as a colorless oil. Yield 67%. $[\alpha]_D = -0.6$ (*c* = 2.0, CH_2Cl_2). IR (film): 3450, 3060–2820, 1730, 1610, 1580, 1510, 1445, 1400, 1360, 1280, 1250, 1150, 1070, 1030, 900, 830, 790, 750, 700. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.21 (*s*, *t*-Bu); 1.86 (*m*, 2 H–C(5)); 2.82 (br. *s*, OH); 2.88 (*m*, H–C(3)); 3.20 (*m*, H–C(2)); 3.30–3.40 (*m*, 2 H–C(6)); 3.79 (*s*, MeO); 3.88 (*m*, 2 H–C(1)); 4.33 (*dd*, *J* = 13, 3, H–C(4)); 6.83 (*d*, *J* = 9, 2 arom. H); 7.20–7.39 (*m*, 8 arom. H); 7.41 (*d*, *J* = 8, 4 arom. H). ^{13}C-NMR (101 MHz, $CDCl_3$): 26.93; 33.19; 38.63; 52.64; 55.08; 57.92; 61.11; 63.9; 68.30; 87.0; 113.28; 128.08; 128.40; 130.38; 135.55; 144.44; 158.87; 178.54. FAB-MS: 543 (8.1, $[M + K]^+$), 504 (2.7, M^+), 289 (3.0), 273 (100), 229 (2.1), 215 (6.5), 195 (3.8), 165 (6.1), 135 (4.6), 105 (10.3), 77 (5.6).

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