17. 3-Hydroxyglutarate and β,γ-Epoxy Esters as Substrates for Pig Liver Esterase (PLE) and α-Chymotrypsin

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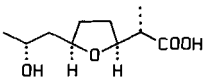
The pH dependence of the α-chymotrypsin-catalyzed hydrolysis of dimethyl 3-hydroxyglutarate (**3**) has been studied. The e.e. was determined by HPLC analysis of diastereoisomeric camphanoic-acid derivatives. Kinetic resolution of the β,γ-epoxy esters **10** and **24** by pig liver esterase has been shown to provide an alternative access to chiral β-hydroxy esters and acids of high optical purity. By this latter method, the unnatural enantiomer of γ-amino-β-hydroxybutyric acid (GABOB) has been synthesized. Finally, dimethyl *meso*-3,4-epoxyadipate (**19**) was hydrolyzed by pig liver esterase with almost 100% selectivity.

The ability of enzymes to catalyze reactions of *meso* and prochiral compounds with high stereoselectivity is now well established as a valuable method for the preparation of chiral synthons with high enantiomeric excess (e.e.). We [1] and others [2] have recently reported results on the enantioselective hydrolyses of such symmetric esters with pig liver esterase (PLE), α-chymotrypsin (α-chy), and esterases from microorganisms, respectively. As part of a programme designed to demonstrate the synthetic utility of this chemo-enzymatic approach, we had started a project directed to the synthesis of optically active nonactic acid (**1**) using methyl hydrogen (*R*)-3-hydroxyglutarate (**2**) as starting material[1]). *Rosen et al.* [4] have reported an assay for the determination of the optical purity of this half-ester which they used for studies of compounds related to compactin.



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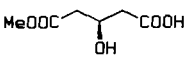

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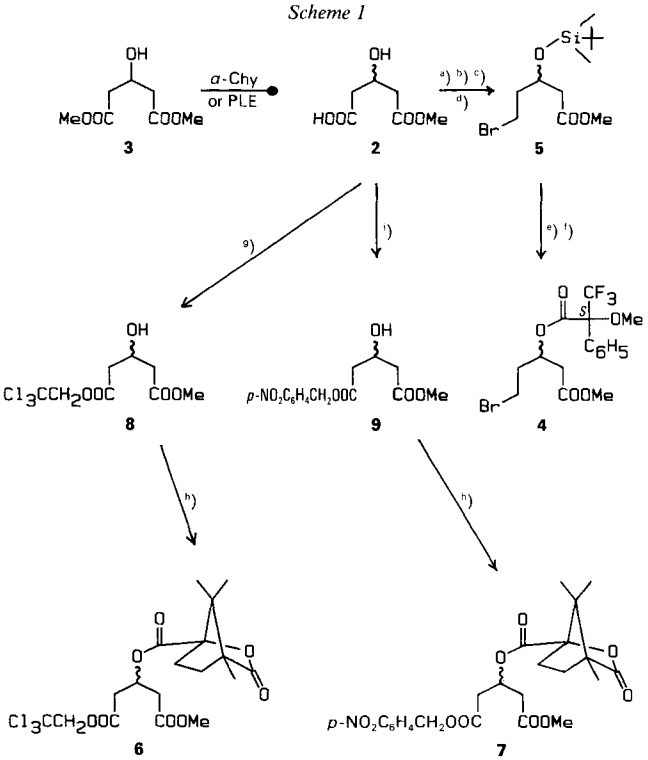
Our own results [1b] reported here concern two aspects: *1*) re-investigation [5] of the enantioselectivity of the enzymatic hydrolysis of dimethyl 3-hydroxyglutarate (**3**) including its pH dependence; *2*) complementary approach to 3-hydroxyalkanoates of high optical purity involving a kinetic resolution of 2,3-epoxy esters with PLE.

So far, we had determined the e.e. of **2** by comparing its optical rotation with the value reported in [5]. However, the low specific rotation of $[\alpha]_D^{22} = -1.7°$ ($c = 12.5$, $CHCl_3$) is an unreliable criterion for an exact optical purity evaluation of this viscous oil[2]). We have, therefore, looked for the formation of a derivative with an optically pure

[1]) For a recent example of a synthesis using (*R*)- and (*S*)-**2**, see [3].

[2]) *Rosen et al.*, moreover, have observed that the optical rotation of **2** is strongly dependent on the concentration [4].

Scheme 1



a) (*t*-Bu)Me_2SiCl, imidazole, DMF; b) K_2CO_3, MeOH, H_2O, THF; c) $BH_3 \cdot Me_2S$, THF; d) CBr_4, $P(C_6H_5)_3$, Py, Et_2O; e) HCl, H_2O, THF; f) 3,3,3-trifluoro-2-methoxy-2-phenylpropionyl chloride, Py, CH_2Cl_2; g) Cl_3CCH_2OH, DCC, CH_2Cl_2; h) Camphanoyl chloride, Py, CH_2Cl_2; i) *p*-$O_2NC_6H_4CH_2Br$, MeOH, H_2O.

reagent in order to obtain diastereoisomeric mixtures, which can be analyzed by appropriate techniques. According to *Scheme 1*, the (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionyl derivative **4** [6] and the camphanoates **6** and **7** were prepared *via* bromide **5** and *via* acylation of the diesters **8** and **9**, respectively, using routine transformations. Whereas **4** showed clear splittings in the 90-MHz ^{1}H-NMR spectrum which allowed the calculation of the e.e. value, neither the ^{1}H- nor the ^{13}C-NMR spectra of **6** and **7** were suited for the determination of the e.e. Ester **6** was decomposed during GC analysis, too. However, the diastereoisomeric triester **7**, obtained from **2** in two steps without crystalline intermediate, could be analyzed accurately by HPLC (*Partisil-5 NO$_2$*, hexane/Et_2O). The *Table*

Table. *Enzymatic Hydrolysis of Dimethyl 3-Hydroxyglutarate* (**3**), *e.e. Determination by HPLC of* **7**

Enzyme	pH Value	Abs. configuration of **2**	e.e. [%]
PLE	7.8	*S*	22
α-Chy	7.8	*R*	60
α-Chy	7.5	*R*	67.8
α-Chy	7.0	*R*	68.6
α-Chy	7.8	*R*	60[a])

[a]) Corresponds to the e.e. of **4**, determined by the ^{1}H-NMR spectroscopy.

summarizes the e.e. of **2** obtained from **3** with PLE and α-chymotrypsin, as determined by HPLC of **7**.

The following conclusions can be drawn: *1*) dimethyl 3-hydroxyglutarate (**3**) is, as already known [1] [2], an unsuitable substrate for PLE. *2*) Even with α-chymotrypsin, the hydrolysis is far away from being enantioselective as has been reported earlier [5]. *3*) The 'undesired' isomer is not only formed due to competing chemical hydrolysis, since a 6.3-fold decrease of the OH^- concentration caused only a diminuation of the amount of (*S*)-isomer formed from 20 to 15.7%. The enzymatic reaction is also lowered but only by a factor of *ca.* 2. *4*) Due to the high price and the large amounts of enzyme required (substrate/α-chymotrypsin 5:1 (*w/w*), reaction time 24 h), it is not opportune to work at pH values lower than 7. *5*) Esterases from *Corynebacterium equi* and *Acinetobactex lowfii*, studied recently by *Gopalan* and *Sih* [8], are superior to α-chymotrypsin.

As mentioned above dimethyl 3-hydroxyglutarate (**3**) is rapidly hydrolyzed by PLE but with virtually no selectivity, whereas the 3-amino analogue suffers from concomitant non-enzymatic hydrolysis [9]. In sharp contrast, all other 3-monosubstituted dimethyl glutarates studied so far [1] [2] [9] (except those containing bulky substituents in the 3-position) are attacked almost exclusively at the *pro-S*-methoxycarbonyl group. We have reasoned that a chiral or a prochiral β,γ-epoxy ester, which can serve, owing to its reactivity towards nucleophiles, as a synthetic precursor of a 3-hydroxy ester, could behave similary against PLE as 'normal' 3-monosubstituted glutarates and could hence be hydrolyzed with high selectivity. To test this hypothesis, we have briefly examined (±)-dimethyl 3,4-epoxyhexanedioate (**10**) as substrate for PLE *(Scheme 2)*. This racemic ester, easily accessible from commercially available (*E*)-3-hexenedioic acid, has a C_2 axis, hence the two COOMe groups are homotopic. However, if the enantiomeric ratio $(E)^3)$ of the hydrolysis of (±)-**10** with PLE is high enough, both diester **10** and acid **11** can be obtained in high optical purity. This was found to be the case.

When (±)-**10** was incubated with PLE at pH 7.0, a rapid hydrolysis took place, which nearly stopped after consumption of 0.5 equiv. of base. Extraction with AcOEt afforded in good yield (caution: the starting material is quite soluble in H_2O and sensitive to acids and bases) the ester (+)-**10** ($[\alpha]_D^{r.t.} = +28.4°$ ($c = 1.27$, EtOH); *cf. Scheme 2*). For the determination of the absolute configuration and the optical purity, (+)-**10** was transformed into the known lactone **12**. Base-catalyzed elimination with 1,5-diazabicyclo-[4.3.0]non-5-ene (DBN) yielded smoothly the hydroxy diester (+)-**13** ($\leq 2\%$ (*Z*)-isomer) from (+)-**10**. After hydrogenation and cyclization in the presence of TsOH, **12** ($[\alpha]_D^{r.t.} = +35.6°$ ($c = 0.54$, EtOH) was obtained indicating, according to [11] ($[\alpha]_D^{r.t.} = -36.4°$ ($c = 1$, EtOH) for the (*R*)-isomer), the (*S*)-configuration in 98% purity. To confirm this result unambiguously, the propionyl derivative **14** [6] was prepared and analyzed by ^{1}H-NMR. Whereas a sample synthesized from racemic (±)-**13** showed clearly four singlets for COOMe groups, in the spectrum of **14** derived from optically active (+)-**13**, only two singlets appeared. Therefore, the e.e. must be $\geq 95\%$. The β-hydroxy ester (+)-**13** was also methylated under *Fráter-Seebach* conditions [12] to yield the *threo*-ester **15** in excellent selectivity (*ca.* 97:3).

The unstable epoxy acid (−)-**11** should be an even more versatile chiral synthon than (+)-**10**. It can be obtained from the enzymatic reaction mixture by acidifying the aqueous

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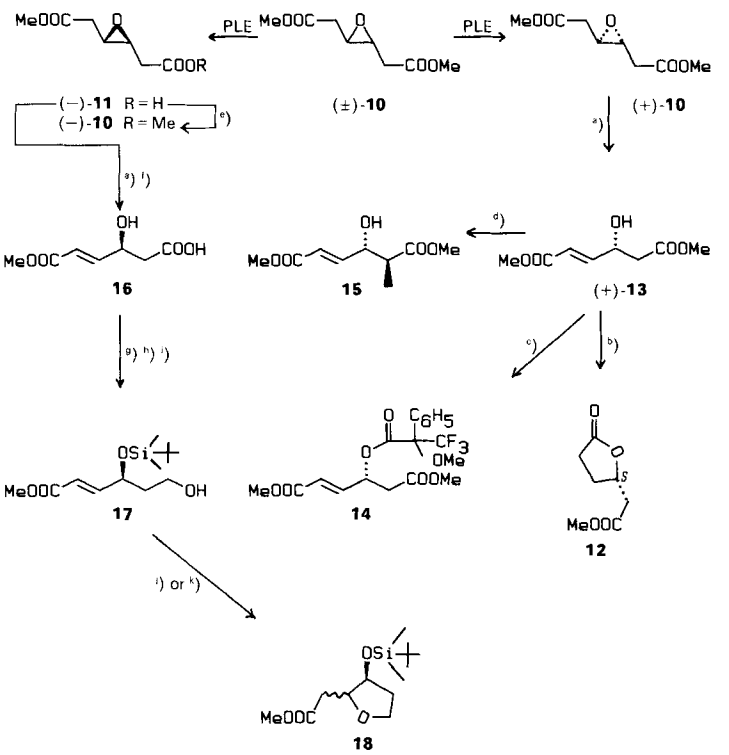
3) For a definition of *E* and a mathematical treatment of such kinetic resolutions, *cf.* [10].

Scheme 2

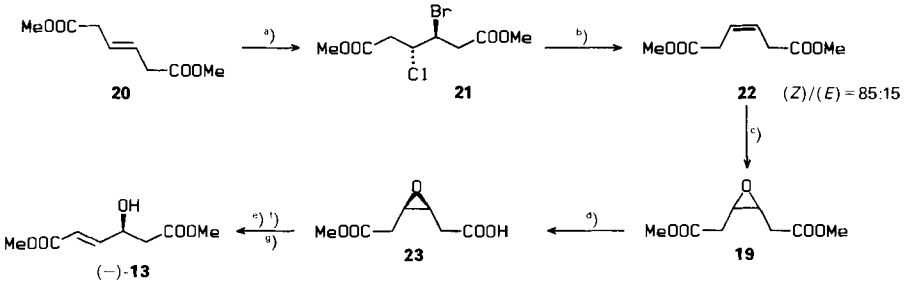


a) DBN, CH_2Cl_2 (− 50°→0°); b) Pd/C, AcOEt; TsOH, CH_2Cl_2; c) 3,3,3-trifluoro-2-methoxy-2-phenylpropionic acid, DCC, Me_2NPy, CH_2Cl_2; d) 2.5 equiv. of LiN(i-Pr)$_2$, THF, MeI; e) CH_2N_2; f) *Amberlyste* H^+; g) (*t*-Bu)-Me_2SiCl, imidazole, DMF; h) K_2CO_3, MeOH, H_2O, THF; i) $BH_3 \cdot Me_2S$, THF; j) NaOMe, MeOH; k) 1 equiv. of BuLi, THF, − 78°→ − 40° (5 h).

layer to pH 2.5 and extraction with large amounts of AcOEt. Last traces of diester (+)-**10** of opposite configuration are easily removed at a later stage. Direct treatment of (−)-**11** with CH_2N_2 yielded (−)-**10**, for which $[\alpha]_D^{rt.} = -27.0°$ ($c = 1.48$, EtOH) was determined. The numerical-value range was within experimental error with that found for (+)-**10**, whose optical purity was shown to be $\geq 95\%$. Careful exposure of (−)-**11** to DBN (CH_2Cl_2, − 50°→0°) induced a regio- and stereoselective elimination to form, after treatment with *Amberlyste* H^+, the unsaturated ester **16**, a chiral C_6-building block possessing four different functional groups. It was, for instance, transformed into the monoprotected diol **17** using standard procedures. The latter yielded a 35:65 mixture of disubstituted tetrahydrofurans **18** upon treatment with NaOMe/MeOH (thermodynamic conditions). After reduction of **17** to the allylic alcohol, stereoselective epoxidation [14] and – to some extent – hydroxylation [15] should be possible.

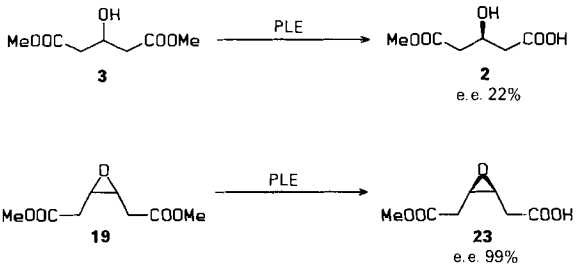
We next briefly examined the synthesis of epoxy diester **19** which has a plane of symmetry. We anticipated that **19** would be, like the *trans*-epoxide (±)-**10**, a good substrate for PLE. In principle, the total amount of starting material can be transformed into a desired target molecule. The preparation according to [16] *via* reduction of a triple

Scheme 3



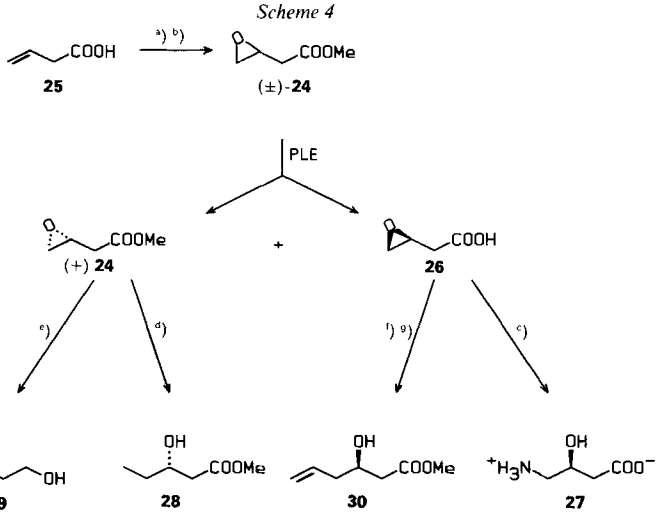
a) NBS, HCl; b) NaI, DMF 70°; c) *m*-chloroperbenzoic acid; d) PLE; e) DBN; f) *Amberlyste* H^+; g) CH_2N_2.

bond seemed to us too cumbersome. Therefore, we investigated the inversion of the double bond of dimethyl (*E*)-3-hexendioate (**20**) *(Scheme 3)* by the method described by *Sonnet* and *Oliver* [17]. Treatment with *N*-bromosuccinimide (NBS) and gaseous HCl ($-78° \rightarrow -20°$) yielded the crystalline bromo-chloro compound **21**, which, on exposure to an excess of NaI in DMF, underwent S_N2 displacement followed by elimination to afford the desired (*Z*)-olefin **22**. However, the product was contaminated with 15% of the (*E*)-isomer and traces of dimethyl (*E,E*)-2,4-hexadienedioate. The latter was easily removed at the next stage, since it resisted the subsequent epoxidation with *m*-chloroperbenzoic acid. After column chromatography, **19** was obtained in an isomeric purity of $\geq 95\%$. It was rapidly hydrolyzed by PLE to the half-ester **23** in 90% yield, whose absolute configuration and optical purity was determined by transformation into (−)-**13**. The optical rotation was found to be $[\alpha]_D^{r.t.} = -5.71°$ ($c = 1.5$, $CHCl_3$). This value excellently correlates with that measured for (+)-**13** ($[\alpha]_D^{r.t.} = +5.47°$ ($c = 1.9$, $CHCl_3$)) prepared from (+)-**10**. Hence the optical purity must be $\geq 99\%$. This result demonstrated that, with respect to the prochiral C(β)-atom bonded to an O-atom, the enzyme PLE cleaves the same ester group as in the case of 3-hydroxyglutarate, but with much higher selectivity:



According to the very simple model which we recently have proposed [1], only substituents in α- and/or β-position with respect to COOMe group, which is cleaved, are essential for the selectivity of the enzymatic hydrolysis with PLE. If this assumption is correct, also (±)-methyl 3,4-epoxybutanoate (**24**) should be a good substrate for the enzyme. This ester, which was prepared from commercially available 3-butenoic acid (**25**) in two steps without isolation of the intermediate *(Scheme 4)*, was indeed hydrolyzed by PLE albeit at a somewhat slower rate than (±)-**10**. Workup after consumption of *ca.* 0.5

Scheme 4



a) DCC, MeOH, Me_2NPy, CH_2Cl_2; b) *m*-chloroperbenzoic acid, CH_2Cl_2; c) NH_3; d) Me_2CuLi, Et_2O; e) $LiAlH_4$, Et_2O; f) vinylmagnesium bromide 0.1 equiv. of CuI, THF, $-50° \rightarrow 0°$; g) MeOH/HCl.

equiv. of base (the hydrolysis did not stop completely after 0.5 equiv. indicating that the enantiomeric ratio *E* is not as high as in the case of (±)-**10**) as described above, yielded *ca.* 40% of ester (+)-**24** and 30% of acid **26**. For the determination of the absolute configuration, the latter was treated with conc. NH_3 [18] to afford (+)-γ-amino-β-hydroxybutyric acid (**27**), the unnatural form of the hypotensive agent GABOB. $[\alpha]_D^{r.t.} = +19.6°$ ($c = 0.52$, H_2O) (m.p. 203–205° (dec.)) was found after crystallization from $EtOH/H_2O$ ([18]: $[\alpha]_D^{r.t.} = -20.11°$ ($c = 1.0$, H_2O), m.p. 212° (dec.)) indicating 97% optical purity of the (*S*)-isomer. Again, our predictions were at least qualitatively fulfilled. The remaining ester (+)-**24** was reacted with Me_2CuLi and $LiAlH_4$ to yield the hydroxy ester **28** and diol **29** of the (*S*)-series, respectively. Diol **29** obtained without crystalline intermediate had, according to the optical rotation, an optical purity of 74% ($[\alpha]_D^{r.t.} = +23.0°$ ($c = 1$ EtOH); [19]: $[\alpha]_D^{r.t.} = -31°$ ($c = 1.5$, EtOH)), whereas the optical purity of methyl 3-hydroxypentanoate (**28**) seemed to be 82% ($[\alpha]_D^{r.t.} = +30.9°$ ($c = 1.3$, $CHCl_3$); [20]: $[\alpha]_D^{r.t.} = -37.8°$ ($c = 1.3$, $CHCl_3$)). We believe that (+)-**24** and **26**, both available in high optical purity simply by stopping the enzymatic reaction after 40 or 60% transformation, respectively, are valuable building blocks for the construction of natural products owing to the synthetic versatility of the epoxy group. Coupling of **26** with vinylmagnesium bromide (2 equiv.) in the presence of CuI [21] yielded, after esterification, methyl (*R*)-3-hydroxy-5-hexeneoate (**30**), which represents a synthetic equivalent of **2**, but available in higher enantiomeric excess.

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Experimental Part

General. Water- and air-sensitive reactions were carried out under inert gas. PLE was purchased from *Boehringer* and α-chymotrypsin from *Sigma*. Capillary GC: crosslinked-dimethylsilicone (12.5 m) and phenylsilicone (25 m) columns, He as carrier gas. HPLC: *Partisil-5 NO_2* column *(Knauer)*, Et_2O/hexane, UV detection at 265 nm. $[\alpha]_D$: *Perkin-Elmer* model-*141* polarimeter. IR spectra (cm^{-1}): *Perkin-Elmer* model-*781* IR spectrophotometer. ^{1}H-NMR Spectra: *Varian EM 360* (60 MHz) and *EM 390* (90 MHz) spectrometer; FT-^{1}H-NMR (90 MHz): *Bruker WH 90*. ^{13}C-NMR spectra: *Bruker WH-90* (22.63 MHz). Chemical shifts of NMR spectra are given in ppm rel. to internal TMS, if indicated in parentheses, otherwise rel. to the *s* of $(CH_3)_2Si$ of silylated compounds. GC/MS: *Hewlett-Packard 5970* mass spectrometer; compounds of low volatility were recorded with a *VG-70-250* spectrometer.

Enzymatic hydrolysis of dimethyl 3-hydroxyglutarate (**3**) was performed as described in [1] and [7] except that the pH was kept constant at different values (see the *Table*). After 24 h, the mixture was extracted with Et_2O at pH 9, the aq. layer acidified (HCl) to pH 2.5 and evaporated at r.t. The semisolid residue was extracted 3 times with Et_2O and dried. Evaporation of the solvent yielded 80–90% of pure **2**.

*1-Methyl Hydrogen 3-[(*tert*-Butyl)dimethylsilyloxy]glutarate.* To a soln. of 8.4 g (51.8 mmol) of **2** in 100 ml of DMF, 17.6 g (116 mmol) of (*t*-Bu)Me_2SiCl and 16.4 g (240 mmol) of imidazole were added, and the mixture was kept for 12 h at r.t. The soln. was diluted with Et_2O and crushed ice, the org. layer washed with sat. NH_4Cl soln. and dried. Evaporation of the solvent yielded 19.4 g of bissilylated intermediate, which was directly hydrolyzed by stirring it in 500 ml of MeOH/THF/H_2O 3:1:1 containing 10 g of K_2CO_3. After 1 h at r.t., the volume was reduced *i.v.* to *ca.* 1/4 and the alkaline soln. extracted with Et_2O. Under cooling with ice, the aq. phase was acidified with HCl to pH 2.5 and extracted with Et_2O. Drying and evaporation of the solvent afforded 12.3 g (84%) of the title compound. IR (film): 3500–2500, 2955, 2930, 2900, 2860, 1740, 1710, 1440. ^{1}H-NMR (90 MHz, $CDCl_3$, $\delta(CHCl_3) = 7.25$): 0.05 (*s*, $(CH_3)_2Si$); 0.85 (*s*, $(CH_3)_3C$); 2.55, 2.6 (2*d*, $CH_2(2)$, $CH_2(4)$); 3.65 (*s*, CH_3OOC); 4.45 (*quint.*, H–C(3)); 9.2 (br. *s*, COOH).

*Methyl 3-[(*tert*-Butyl)dimethylsilyloxy]-5-hydroxypentanoate.* A soln. of 2.75 g (10 mmol) of methyl hydrogen 3-[(*tert*-butyl)dimethylsilyloxy]glutarate in 10 ml of abs. THF was treated with 1.2 ml (12 mmol) of $BH_3 \cdot Me_2S$ ($T \leq 20°$). After 1.5 h, 15 ml of H_2O were added, followed by K_2CO_3 to dissolve the precipitate. Extraction with Et_2O afforded, after drying and evaporation of the solvents, 2.0 g (76%) of a clean oil, which was used without further purification, although it was contaminated with small amounts of 3-(silyloxy)valerolactone. IR (film): 3600–3200, 2960, 2930, 2860, 1740, 1440, 1255, 835, 775. ^{1}H-NMR (90 MHz, $CDCl_3$, TMS): 0.1 (2*s*, $(CH_3)_2Si$); 0.9 (*s*, $(CH_3)_3C$); 1.85 (*m*, $CH_2(4)$); 2.3 (br. *s*, OH); 2.6 (*d*, $J = 7$, $CH_2(2)$); 3.75 (*s*, CH_3OOC); 3.85 (br. *t*, $CH_2(5)$); 4.4 (*quint.*, $J = 7$, H–C(3)).

*Methyl 5-Bromo-3-[(*tert*-butyl)dimethylsilyloxy]pentanoate* (**5**). To 2.02 g (10 mmol) of methyl 3-[(*tert*-butyl)dimethylsilyloxy]-5-hydroxypentanoate in 50 ml of abs. Et_2O were subsequently added 5.52 g (20 mmol) of Ph_3P, 6.62 g (20 mmol) of CBr_4, and 2 ml (25 mmol) of pyridin. After stirring at r.t. for 2 h, the precipitate was filtered off and the volume of the Et_2O soln. reduced *i.v.* to 1/4. After filtration through *Celite*, the solvents were evaporated. The residue was dissolved in CH_2Cl_2 and washed with 1N HCl and brine. Drying and evaporation of the solvent yielded a crude product, which was purified by CC (CH_2Cl_2) to afford 2.3 g (71%) of pure **5** ($\geq 98\%$ GC). IR (film): 2970, 2940, 2870, 1750, 1440, 785. ^{1}H-NMR (90 MHz, $CDCl_3$, TMS): 0.1 (2*s*, $(CH_3)_2Si$); 0.8 (*s*, $(CH_3)_3C$); 1.95 (*q*, $J = 7$, $CH_2(4)$); 2.35 (*d*, $J = 7$, $CH_2(2)$); 3.35 (*t*, $J = 7$, $CH_2(5)$); 3.5 (*s*, CH_3OOC); 4.2 (*quint.*, $J = 7$, H–C(3)). EI-MS (70 eV): 327, 325 ($M^{+\cdot} + H$), 311, 309, 269, 267, 227, 225.

Methyl 5-Bromo-3-hydroxypentanoate. ^{1}H-NMR (90 MHz, $CDCl_3$, TMS): 2.0 (*m*, $CH_2(4)$); 2.5 (*d*, $CH_2(2)$); 3.15 (br. *d*, OH); 3.55 (*t*, $CH_2(5)$); 3.7 (*s*, CH_3OOC); 4.25 (*m*, H–C(3)). ^{13}C-NMR (22.63 MHz, $CDCl_3$, TMS): 29.5 (*t*, C(4)); 39.4 (*t*, C(2)); 41.1 (*t*, C(5)); 51.8 (*d*, C(3)); 66.1 (*q*, CH_3OOC); 172.8 (*s*, C(1)).

Methyl 5-Bromo-3-{[(S)-3,3,3-trifluoro-2-methoxy-2-phenylpropionyl]oxy}pentanoate (**4**). ^{1}H-NMR (90 MHz, $CDCl_3$, TMS): 2.3 (*m*, $CH_2(4)$); 2.75 (2*d*, $CH_2(2)$); 3.35 (2*t*, $CH_2(5)$); 3.55 (2*s*, CH_3O–C(2)); 3.65 (2*s*, CH_3OOC); 5.6 (*m*, H–C(3)); 7.45 (*m*, 5 arom. H).

p-*Nitrobenzyl Methyl 3-Hydroxyglutarate* (**9**). To a soln. of 2.4 g (14.8 mmol) of **2** in 25 ml of H_2O, whose pH had been adjusted to 6.0, were added 3.24 g (15 mmol) of *p*-nitrobenzyl bromide in 20 ml of EtOH. The mixture was gently refluxed (*ca.* 1 h), until all solid had dissolved. Most of the EtOH was evaporated and the residue extracted with Et_2O. The org. layer was dried and evaporated i.v. CC (petroleum ether/Et_2O 1:4) yielded 1.7 g of pure **9**. IR (film): 3650–3300, 2960, 1740, 1610, 1525, 1440, 1350, 910, 735. ^{1}H-NMR (90 MHz, $CDCl_3$, TMS): 2.6, 2.7 (2*d*, $J = 6$, $CH_2(2)$, $CH_2(4)$); 3.55 (br. *d*, OH); 3.7 (*s*, CH_3OOC); 4.55 (*m*, H–C(3)); 5.3 (*s*, $NO_2C_6H_4CH_2$); 7.8 (*AA'BB'*, 4 arom. H). EI-MS (70 eV): 298 ($M^{+\cdot} + H$), 248, 137, 127 (100%). CI-MS (NH_3): 315 (100, $[M + NH_4]^+$), 298 ($M^{+\cdot} + H$), 283, 106.

p-Nitrobenzyl Methyl 3-(Camphanoyloxy)glutarate (**7**). A soln. of 124 mg (0.42 mmol) of **9** in 1 ml of abs. CH_2Cl_2 was treated subsequently with 0.5 ml of pyridine and 97 mg (0.45 mmol) of (−)-camphanoyl chloride. The mixture was kept for 24 h at r.t. Crushed ice and Et_2O were added, and the org. layer was subsequently washed with 1N HCl, 1N NaOH, and brine. Drying and evaporation of the solvent yielded 190 mg (94%) of pure **7** as a slightly yellow oil, which was analyzed by HPLC for d.e. determination. ^{1}H-NMR (90 MHz, $CDCl_3$, TMS): 0.95, 1.1, 1.15 (3*s*, CH_3(8′), CH_3(9′), CH_3(10′)); 1.55–2.4 (*m*, CH_2(5′), CH_2(6′)); 2.77, 2.9 (2*d*, CH_2(2), CH_2(4)); 3.7 (*s*, CH_3OOC); 5.2 (*s*, $NO_2C_6H_4CH_2$); 5.65 (*quint.*, H–C(3)); 7.8 (*AA′BB′*, 4 arom. H). ^{13}C-NMR (22.63 MHz, $CDCl_3$, TMS): 9.6, 16.5, 16.6 (3*q*, C(8′), C(9′), C(10′)); 29.0, 30.8 (2*t*, C(5′), C(6′)); 38.2, 38.4 (2*t*, C(2), C(4)); 51.9 (*d*, C(3)); 51.2, 54.9 (2*s*, C(4′), C(7′)); 65.3 (*t*, $NO_2C_6H_4CH_2$); 68.3 (*q*, CH_3OOC); 90.9 (*s*, C(1′)); 123.8, 128.7 (2*d*, 4 arom. C); 142.8, 148.0 (2*s*, 2 arom. C); 166.5, 169.1, 169.8, 177.4 (4*s*, 4COO). EI-MS (70 eV): 478 ($M^{+\cdot}$ + H), 446, 431, 416, 288, 127 (100). CI-MS (NH_3): 495 ($[M + NH_4]^+$), 216 (100).

Methyl 2,2,2-Trichloroethyl 3-Hydroxyglutarate (**8**). ^{1}H-NMR (90 MHz, $CDCl_3$, TMS): 2.6, 2.7 (2*d*, CH_2(2), CH_2(4)); 3.5 (br. *s*, OH); 3.7 (*s*, CH_3O); 4.5 (*m*, CH(3)); 4.8 (*s*, CCl_3CH_2OO).

Methyl 2,2,2-Trichloroethyl 3-(Camphanoyloxy)glutarate (**6**). ^{1}H-NMR (90 MHz, $CDCl_3$, TMS): 0.95, 1.1, 1.15 (3*s*, CH_3(8′), CH_3(9′), CH_3(10′)); 1.6–2.5 (*m*, CH_2(5′), CH_2(6′)); 2.85, 2.95 (2*d*, J = 6, CH_2(2), CH_2(4)); 3.7 (*s*, CH_3OOC); 4.75 (*s*, Cl_3CCH_2OOC); 5.7 (*quint.*, J = 6, H–C(3)). ^{13}C-NMR (22.63 MHz, $CDCl_3$, TMS): 9.6, 16.5, 16.6 (3*q*, C(8′), C(9′), C(10′)); 29.0, 30.8 (2*t*, C(5′), C(6′)); 38.0, 38.1 (2*t*, C(2), C(4)); 51.9 (*d*, C(3)); 54.2, 54.8 (2*s*, C(4′), C(7′)); 67.9 (*q*, CH_3OOC); 74.3 (*t*, Cl_3CCH_2OO); 90.8 (*s*, C(1′)); 94.7 (*s*, Cl_3CCH_2OOC); 166.5, 167.9, 169.7, 177.8, (4*s*, 4COO). EI-MS (70 eV): 475, 473 ($M^{+\cdot}$ + H), 446, 444, 325, 295, 293, 83 (100). CI-MS (NH_3): 492, 490 ($[M + NH_4]^+$), 458, 456, 216 (100).

Dimethyl (±)-*3,4-Epoxyadipate* ((±)-**10**). IR (film): 3005, 2960, 2850, 1740, 1440, 1260, 1200, 1175. ^{1}H-NMR (60 MHz, $CDCl_3$, TMS): 2.55 (*d*, J = 6, CH_2(2), CH_2(4)); 2.9–3.25 (*m*, H–C(3), H–C(4)); 3.7 (*s*, $2CH_3OOC$). GC/MS (EI): 156 ($M^{+\cdot}$ − MeOH), 129, 117, 87, 59 (100).

Kinetic Resolution of (±)-**10**. The enzymatic hydrolysis was carried out as described in [1]. The pH was kept constant at 7.0 by adding 1N NaOH. After consumption of 0.5 equiv. of base, the rate decreased dramatically, and the aq. soln. was extracted with AcOEt. Drying and evaporation of the solvent yielded *ca.* 40% (80% of the theor. amount) of (+)-**10** (≥ 97%, GC) $[\alpha]_D^{r.t.}$ = + 28.4° (*c* = 1.27, EtOH).

The aq. layer was acidified with HCl to pH 2.5 and extracted with large amounts of AcOEt. Thereby, 40% (80% of the theor. amount) of *methyl hydrogen (S)-3,4-epoxyadipate* ((−)-**11**) were obtained as colourless oil. IR (film): 3500–2800, 3010, 2960, 1740, 1715 (sh), 1440, 1175, 960. ^{1}H-NMR (60 MHz, $CDCl_3$, TMS): 2.55 (2*d*, CH_2(2), CH_2(5)); 3.15 (br. *t*, J = 5, H–C(3), H–C(4)); 3.7 (*s*, CH_3OOC); 10.6 (br. *s*, COOH). Esterification with CH_2N_2 in Et_2O yielded (−)-**10** (97%, GC), $[\alpha]_D^{r.t.}$ = − 27.0° (*c* = 1.48°, EtOH).

Dimethyl (E,R)-4-Hydroxy-2-hexenedioate ((+)-**13**). A soln. of 320 mg (1.7 mmol) of (+)-**10** in 3 ml of CH_2Cl_2 was cooled to − 40°, and 225 µl (1.8 mmol) of DBN were added. After stirring for 1/4 h at − 40° and 1/2 h at 0°, the mixture was quenched with 2N HCl and extracted with Et_2O. After washing with H_2O, drying, and evaporation of the solvents, 270 mg (85%) of (+)-**13** were obtained as colourless oil (≥ 98% GC). $[\alpha]_D^{r.t.}$ = + 5.47° (*c* = 1.9, $CHCl_3$). IR (film): 3600–3200, 3005, 2960, 1730, 1665, 1440, 1275, 1170, 1110. ^{1}H-NMR (60 MHz, $CDCl_3$, TMS): 2.55 (*d*, J = 6, CH_2(5)); 3.4 (br. *s*, OH); 3.7 (*s*, CH_3OOC); 4.5–5.0 (*m*, H–C(4)); 6.1 (*dd*, J = 15, 1.5, H–C(2)); 6.9 (*dd*, J = 15, 4.5, H–C(3)). GC/MS (EI): 170 ($M^{+\cdot}$ − H_2O), 157 ($M^{+\cdot}$ − MeO), 156 ($M^{+\cdot}$ − MeOH), 128, 125, 115, 87 (100).

Methyl (E,S)-5-Oxo-2,3,4,5-tetrahydrofuran-2-acetate (**12**). At r.t. and 1 atm, 42 mg (0.22 mmol) of (+)-**13** were hydrogenated in 2 ml of AcOEt over 10 mg of Pd/C. Filtration through silica gel yielded 41 mg of crude product, which consisted, according to ^{1}H-NMR, mainly of the sat. hydroxydiester. Addition of a few crystals of TsOH induced ring closure to the δ-lactone. CC (Et_2O) yielded 27 mg (77%) of pure **12** (≥ 98%, GC). $[\alpha]_D^{r.t.}$ = + 35.6 (*c* = 0.54, EtOH). IR (film): 2960, 2930, 2855, 1780, 1740, 1440, 1355, 1170, 1040. ^{1}H-NMR (60 MHz, $CDCl_3$, TMS): 1.5–2.9 (*m*, 6H); 3.7 (*s*, CH_3OOC); 4.85 (*m*, H–C(5′)). GC/MS (EI): 140 ($M^{+\cdot}$ − H_2O), 130, 127 ($M^{+\cdot}$ − MeO), 126, 85 (100).

Dimethyl (E,4R)-4-{[(S)-3,3,3-Trifluoro-2-methoxy-2-phenylpropionyl]oxy}-2-hexenedioate (**14**). To 18 mg (0.09 mmol) of (+)-**13** in 1 ml of CH_2Cl_2 were added subsequently 30 mg of (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionic acid (0.13 mmol), 10 mg of 4-(dimethylamino)pyridine and 40 mg (0.19 mmol) of *N,N*-dicyclohexylcarbodiimide (DCC). After stirring for 24 h at r.t., the mixture was directly poured on a silica-gel column and eluted with petroleum ether/Et_2O 2:1: 24 mg (65%) of **14**. ^{1}H-NMR (90 MHz, $CDCl_3$, TMS): 2.75 (*m*, CH_2(5)); 3.55 (*d*, J = 1, CH_3O–C(2′)); 3.74, 3.69 (2*s*, $2CH_3OOC$); 5.9 (*dd*, J = 15.5, 1.5, H–C(2)); 6.0 (*m*, H–C(4)); 6.85 (*dd*, J = 15.5, 5.5, H–C(3)); 7.45 (*m*, 5 arom. H); the spectrum of an authentic sample prepared in the same way from (±)-**13** indicated a 1:1 diastereoisomeric mixture and showed that no kinetic resolution had occurred during esterification; *e.g.*, the $4CH_3OOC$ signals appeared at 3.754, 3.737, 3.686, and 3.616 ppm.

*Dimethyl (*E,*4*S,*5*S*)-4-Hydroxy-5-methyl-2-hexenedioate* (**15**). A soln. of 280 mg (1.48 mmol) of (+)-**13** in 2 ml of THF was added at − 78° to 3.7 mmol of LiN(i-Pr)$_2$ in THF/hexane. After stirring for 15 min, 190 µl (3 mmol) of MeI were injected to the dark brown soln. of the enolate. After 10 min, the cooling bath was removed and as soon as the internal temp. reached − 20°, the mixture was quenched with sat. NH_4Cl soln. The crude product consisted, according to GC, of 20% of (+)-**13** and 80% of **15** (*erythro/threo* 3:97). Separation was possible by CC (Et_2O/petroleum ether 1:1). ^{1}H-NMR (60 MHz, $CDCl_3$, TMS): 1.2 (*d*, *J* = 7, $CH_3C(2)$); 2.6 (br. *quint.*, *J* = 7, H−C(2)); 2.9 (br. *s*, OH); 3.7 (2*s*, $2CH_3OOC$); 4.35 (br. *t*, *J* = 6, H−C(3)); 6.1 (*dd*, *J* = 15.5, 1, H−C(5)); 6.9 (*dd*, *J* = 15.5, 5, H−C(4)). GC/MS (EI): 171 ($M^{+\cdot}$ − MeO), 170 ($M^{+\cdot}$ − MeOH), 139, 115, 88 (100).

*Methyl Hydrogen (*E,S*)-4-Hydroxy-2-hexenedioate* (**16**). To a soln. of 850 mg (4.88 mmol) of (−)-**11** (see above) in 10 ml of CH_2Cl_2 at − 50°, 1.31 ml (11 mmol) of DBN were added. The mixture was kept at − 50° for 15 min and 0° for 30 min. Then, 5 g of *Amberlyste* (H^+ form) were added (caution: exothermic!). After stirring over night, the resin was filtered off and washed thoroughly with CH_2Cl_2. Evaporation to dryness yielded 587 mg (70%) of **16** contaminated with traces of (+)-**13**, derived from (+)-**10**, which was as impurity in the starting material. It was removed at a later stage. IR (film): 3600–2800, 2960, 1750–1700, 1665, 1440, 1110. ^{1}H-NMR (60 MHz, $CDCl_3$, TMS): 2.6 (br. *d*, *J* = 6, $CH_2(5)$); 3.7 (*s*, CH_3OOC); 4.55–4.95 (*m*, H−C(4)); 6.1 (*dd*, *J* = 15.5, 1, H−C(2)); 6.8 (br. *s*, OH, COOH); 6.85 (*dd*, *J* = 15.5, 4.5, H−C(3)).

*Methyl Hydrogen (*E,S*)-4-[(*tert*-Butyl)dimethylsilyloxy]-2-hexenedioate.* In analogy to the procedure given for hydroxy acid **2**, **16** was silylated in 60% yield. IR (film): 3400–2800, 2960, 2935, 2900, 2860, 1740–1700, 1665, 1475, 1440, 1365, 1260, 1120, 975, 840, 780, 735. ^{1}H-NMR (60 MHz, $CDCl_3$): 0.0 (*s*, $(CH_3)_2Si$); 0.85 (*s*, $(CH_3)_3C$); 2.55 (*d*, *J* = 6.5, $CH_2(5)$); 3.7 (*s*, CH_3OOC); 4.55–4.9 (*m*, H−C(4)); 6.0 (*dd*, *J* = 15.5, 1, H−C(2)); 6.95 (*dd*, *J* = 15.5, 5, H−C(3)); 10.5 (br. *s*, COOH).

*Methyl (*E,S*)-4-[(*tert*-Butyl)dimethylsilyloxy]-6-hydroxy-2-hexeneoate* (**17**). To 400 mg (1.39 mmol) of the above prepared silyl ether of **16** in 3 ml of THF were injected 300 µl of $BH_3 \cdot Me_2S$ (*ca.* 3 mmol). After 3 h at r.t., 5 drops of H_2O were added and the solvent was evaporated. The residue was dissolved in AcOEt, dried, and evaporated to dryness. CC of the crude product (petroleum ether/Et_2O 1:1), yielded 66% of **17** as colourless oil ($\geq$ 95%, GC), $[\alpha]_D^{r.t.} = -24.9°$ (*c* = 1.6, $CHCl_3$). IR (film): 3600–3300, 2960, 2940, 2900, 2860, 1730, 1660, 1475, 1440, 1360, 1260, 1165, 1125, 840, 780. ^{1}H-NMR (60 MHz, $CDCl_3$): 0.0 (2*s*, $(CH_3)_2Si$); 0.85 (*s*, $(CH_3)_3C$); 1.55–1.9 (*m*, $CH_2(5)$); 2.2 (*s*, OH); 3.7 (*s*, CH_3OOC); 3.7 (*t*, $CH_2(6)$); 4.5 (*m*, CH(4)); 5.9 (*dd*, *J* = 15.5, 1, H−C(2)); 6.9 (*dd*, *J* = 15.5, 4.5, H−C(3)). GC/MS (EI): 243 ($M^{+\cdot}$ − MeO), 217 ($M^{+\cdot}$ − *t*-Bu), 185, 155, 75 (100).

*Methyl (*3S*)-3-[(*tert*-Butyl)dimethylsilyloxy]-2,3,4,5-tetrahydrofuran-2-acetate* (**18**). To 80 mg (0.28 mmol) of **17** were added 4 ml of MeOH containing a few crystals of NaOMe. After 24 h at r.t., the soln. was diluted with Et_2O and washed with H_2O. Drying and evaporation left 80 mg (GC 100%) of a 65:35 diastereoisomeric mixture. Treatment of this sample for additional 2 d did not change the isomeric ratio. ^{1}H-NMR (60 MHz, $CDCl_3$): 0.0 (*s*, $(CH_3)_2Si$); 0.85 (*s*, $(CH_3)_3C$); 1.6–2.3 (*m*, $CH_2(4')$); 2.4–2.7 (*m*, $CH_2(2)$); 3.65 (*s*, CH_3COOC); 3.8–4.5 (*m*, H−C(2'), $CH_2(5')$). GC/MS (EI): first eluted isomer: 259 ($M^{+\cdot}$ − Me), 243 ($M^{+\cdot}$ − MeO), 217 (78, $M^{+\cdot}$ − *t*-Bu), 157, 89 (100); secondly eluted isomer: 259 ($M^{+\cdot}$ − Me), 243 ($M^{+\cdot}$ − MeO), 217 (100, $M^{+\cdot}$ − *t*-Bu), 157, 89 (61).

*Dimethyl (*3R**,4S**)-3-Bromo-4-chloroadipate* (**21**). Through a soln. of 1.1 g (6.4 mmol) of dimethyl (*E*)-3-hexenedioate (**20**) in 10 ml of CH_2Cl_2, dry HCl was bubbled for 10 min at − 78°. All at once, 1.2 g (6.7 mmol) of NBS were added, and stirring was continued for 30 min. The cooling bath was then removed, and, as soon as the internal temp. reached − 20°, the mixture was quenched with ice-cold Na_2SO_3 soln. The org. layer was separated, washed with 1N Na_2CO_3 and H_2O, dried, and evaporated. Recrystallization of the crude product (1.8 g) from Et_2O/petroleum ether yielded 1.17 g (64%) of **21** as white needles (GC, $\geq$ 99%) m.p. 80–82° (corr.). IR (KBr): 3000, 2960, 2930, 2855, 1735, 1440, 1390, 1240, 1160, 1060, 970, 900, 725, 690, 630. ^{1}H-NMR (60 MHz, $CDCl_3$, TMS): 2.6–3.6 (*m*, $CH_2(2)$, $CH_2(5)$); 3.7 (*s*, $2CH_3OOC$); 4.5 (*m*, H−C(3), H−C(4)). GC/MS (EI): 257, 255 ($M^{+\cdot}$ − MeO), 253, 251 ($M^{+\cdot}$ − Cl), 221, 220, 219, 218, 177, 175, 171 (100, $M^{+\cdot}$ − HCl − Br).

Dimethyl meso-*3,4-Epoxyadipate* (**19**). To 500 mg (1.74 mmol) of **21** in 2 ml of DMF were added 5 g of NaI, and the soln. was kept at 70° for 24 h. The semisolid mixture was taken up in Et_2O/H_2O 1:1 and washed subsequently with $Na_2S_2O_3$ soln. and H_2O. Drying and evaporation of the solvent yielded 250 mg of crude product, which consisted, according to GC of 80% of **22**, 10–15% of **20** and $\leq$ 5% of dimethyl (*E,E*)-2,4-hexadienedioate. Epoxidation with *m*-chloroperbenzoic acid (1.2 equiv.) in CH_2Cl_2 at r.t., when stopped before completeness, slightly raised the ratio of the desired to the non-desired epoxide, since the (*Z*)-isomer **22** was oxidized faster than **20**. Filtration, washing with $NaHSO_3$ soln., 2N Na_2CO_3, and H_2O, drying, and evaporation of the solvent yielded 250 mg of crude epoxide, which consisted, according to GC, of 85% of *cis*-epoxide **19**, 9.5% of *trans*-epoxide/dimethyl (*E,E*)-2,4-hexadienedioate and 6% of olefin mixture. CC (AcOEt/petroleum ether 2:7) yielded 50% (from **21**) of **19** of $\geq$ 95% purity. IR (film): 3005, 2960, 1740, 1435, 1335, 1265, 1195, 1170. ^{1}H-NMR (60 MHz, $CDCl_3$,

TMS): 2.55 (*d*, J = 6, CH_2(2), CH_2(5)); 3.25–3.55 (*m*, H–C(3), H–C(4)); 3.7 (*s*, $2CH_3OOC$). GC/MS (EI): 170 ($M^{+\cdot} - H_2O$), 157 ($M^{+\cdot}$ – MeO), 156 ($M^{+\cdot}$ – MeOH), 125, 117, 87 (100), 59 (100).

Kinetic resolution of (±) *methyl 3,4-epoxybutyrate* ((±)-**24**) was performed as in the case of (±)-**10**. By AcOEt extraction at pH 7.0, after consumption of *ca.* 0.5 equiv. of base, were isolated about 40% of (+)-*methyl 3,4-epoxybutyrate* ((+)-**24**). $[\alpha]_D^{r.t.}$ = + 10.67° (c = 1.8, $CHCl_3$). IR (film): 3060, 3010, 2960, 1740, 1440, 1330, 1270, 1200, 1180, 1010. ^{1}H-NMR (60 MHz, $CDCl_3$, TMS): 2.50 (*d*, J = 6, CH_2(2)); 2.5 (overlapped, H–C(4)); 2.80 (*t*, J = 4.5, H–C(4), 3.25 (*m*, H–C(3)); 3.70 (*s*, CH_3OOC). GC/MS (EI): 88 ($M^{+\cdot}$ – 28), 85 ($M^{+\cdot}$ – MeO), 84, 74, 58 (100).

Acidification to pH 2.8 and extraction with AcOEt yielded *ca.* 30% of *3,4-epoxybutyric acid* (**26**). IR (film): 3500–2500, 3010, 2930, 1720, 1410, 1265, 1190, 855. ^{1}H-NMR (60 MHz, $CDCl_3$, TMS): 2.55 (*d*, J = 6, CH_2(2)); 2.5 (overlapped, H–C(4)); 2.80 (*t*, J = 4.5, H–C(4)); 3.25 (*m*, H–C(3)); 9.7 (br. *s*, COOH).

(S)-4-Amino-3-hydroxybutyric Acid ((+)-GABOB, **27**). For 2 h, 85 mg (0.83 mmol) of **26** were heated on a steam bath in 2 ml of conc. NH_3. Evaporation of the solvent left a semisolid, which was twice recrystallized from EtOH/H_2O to yield *ca.* 20 mg of (**27**). $[\alpha]_D^{r.t.}$ = + 19.6° (c = 0.52, H_2O). M.p. 203–205° (dec.; corr.). IR (KBr): 3600–2300, 2180, 1660, 1570 (br.), 1450, 1400 (br.), 1340, 1280, 1165, 1120, 1050, 980. ^{1}H-NMR (200 MHz, D_2O): 4.6 (*s*, HOD); 3.97 (*m*, H–C(3)); 2.93 (*dd*, J = 3.5, 13.5, H–C(4)); 2.71 (*dd*, J = 9, 13.5, H–C(4)); 2.20 (*d*, J = 6.5, CH_2(2)). ^{13}C-NMR (22.63 MHz, D_2O/dioxane): 43.1 (C(2)); 45.1 (C(4)); 66.3 (C(3)); 179.1 (C(1)).

Methyl (S)-3-Hydroxypentanoate (**28**). At 0°, 150 mg (1.3 mmol) of (+)-**24** were treated with 3.5 equiv. of Me_2CuLi in 12 ml of Et_2O. Usual workup after 2 h followed by CC (petroleum ether/Et_2O 3:1) yielded 50 mg of pure **28**. $[\alpha]_D^{r.t.}$ = + 30.9° (c = 1.3, $CHCl_3$). IR (film): 3450 (br.), 2970, 2940, 2880, 1735, 1440, 1280, 1170, 980. ^{1}H-NMR (60 MHz, $CDCl_3$, TMS): 1.0 (br. *t*, J = 7, CH_3(5)); 1.2–1.7 (*m*, CH_2(4)); 2.45 (*m*, CH_2(2)); 2.75 (br. *s*, OH); 3.70 (*s*, CH_3OOC); 3.95 (br. *quint.*, J = 6, H–C(3)). GC/MS (EI): 103 ($M^{+\cdot} - C_2H_5$), 101 ($M^{+\cdot}$ – MeO), 83, 74, 71, 61, 59, 43 (100).

(S)-1,3-Butanediol (**29**). To a slurry of excess of $LiAlH_4$ in 4 ml of dry Et_2O, 45 mg of (+)-**24** were added. After 1 h at 0°, 5 drops of conc. NaOH soln. were added and stirring continued for a few h. Filtration from the precipitated Al_2O_3 and evaporation of the solvent left a residue, which was purified by CC (Et_2O): 20 mg of pure **29**. $[\alpha]_D^{r.t.}$ = + 23.0° (c = 1, EtOH). ^{1}H-NMR (60 MHz, $CDCl_3$, TMS): 1.20 (*d*, J = 6.5, CH_3); 1.70 (br. *q*, J = 5.5, CH_2(2)); 2.7 (br., 2OH); 3.2–4.2 (*m*, CH_2(1), H–C(3)).

Methyl (R)-3-Hydroxy-5-hexenoate (**30**). The reaction was carried out at lower temp. than described in [20] in order to suppress halohydrin formation. To a slurry of 95 mg of CuI in 2 ml of THF were added at – 30° 4.2 ml of 1.2M vinylmagnesium bromide/THF. After cooling to – 70°, 210 mmol of acid **26** in 2 ml of THF were injected. The temp. was slowly raised to – 20° and kept at – 20° for 48 h. After addition of 1N HCl and Et_2O, the mixture was stirred until 2 homogeneous layers separated. Drying and evaporation of the org. solvent left 300 mg of crude acid, which were esterified by reaction with 20 ml of MeOH, which had been treated with 50 µl of AcCl. After 5 h at r.t., usual workup yielded 290 mg of crude product, which consisted, according to GC, of 65% of **30** and 25% of methyl 4-bromo-3-hydroxybutyrate. Pure **30** could be isolated by CC (petroleum ether/Et_2O 5:2). $[\alpha]_D^{r.t.}$ = – 12.55° (c = 1.3, $CHCl_3$). IR (film): 3450 (br.), 3080, 2960, 1740, 1645, 1440, 920. ^{1}H-NMR (60 MHz, $CDCl_3$, TMS): 2.2–2.8 (*m*, CH_2(2), CH_2(4)); 3.0 (br. *s*, OH); 3.70 (*s*, CH_3OOC); 4.10 (br. *quint.*, J = 6, H–C(3)); 5.0, 5.2 (*m*, CH_2(6)); 5.5–6.2 (*m*, H–C(5)). GC/MS (EI): 126 ($M^{+\cdot} - H_2O$), 113 ($M^{+\cdot}$ – MeO), 103 (63), 71 (86), 43 (100).

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