Tetrahedron Vol. 40, No. 8, pp. 1313 to 1324, 1984
Printed in Great Britain.

0040-4020/84 $3.00 + .00

α-ALKYLATION OF α-HETEROSUBSTITUTED CARBOXYLIC ACIDS WITHOUT RACEMIZATION[1]

EPC-SYNTHESES[2] OF TERTIARY ALCOHOLS AND THIOLS

DIETER SEEBACH,* RETO NAEF[3] and GIORGIO CALDERARI[4]
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule, ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich, Switzerland

(*Received in USA* 5 *May* 1983)

Abstract—α-Hydroxy- and α-mercapto–carboxylic acids are condensed with pivalaldehyde to give 2-t-butyl-5-substituted-1,3-dioxolanones or 1,3-oxathiolanones (**2**); the predominate *cis*-isomers are separated by crystallization. The *cis*-disubstituted heterocycles **2** derived from lactic, mandelic and malic acid furnish, after deprotonation with LDA, reaction with electrophiles such as alkyl halides, aldehydes and ketones, and hydrolysis α-branched α-hydroxy–carboxylic acids (**3, 6, 8, 9, 10**). These result from an overall substitution of the proton in the α-CO position with retention of configuration. The optically active carboxylic acids are α-alkylated without racemization and without employment of a chiral auxiliary ("self-reproduction of chirality", Scheme 1). The diastereoselectivities (ds) are generally > 95% (Table 1, 2, and **20–25**).

The three most important classes of compounds in the pool of chiral building blocks[5] are carbohydrates, aminoacids and hydroxy–carboxylic acids. In contrast to the carbohydrates, many representatives of the other two groups are now available in both enantiomeric forms, for instance lactic acid,[6,7] mandelic acid, malic acid,[8] tartaric acid,[2,9] and phenyl–lactic acid.[10] The variety is further increased by the fact that optically active aminoacids can readily be converted to α-hydroxy–carboxylic acids with retention of configuration.[11] Thus, it is not surprizing that compounds of this type are used frequently as starting materials for the synthesis of other enentiomerically pure products. The usefulness of α-hydroxy–carboxylic acids as building blocks for such EPC-syntheses[2] would be even larger, if methods became available, by which they could be α-alkylated without racemization and without employment of chiral auxiliaries. α-Branched α-hydroxy–carboxylic acids[12] have thus far been synthesized in optically active form by more or less elaborate asymmetric syntheses[13] or by multistep conversions of carbohydrates.[14]

As part of our investigations on chiral lithium enolates derived from optically active α- and β-heterosubstituted carboxylic acids,[1,15] we prepared acetal-type derivatives of α-hydroxy- and α-mercapto–carboxylic acids and alkylated them with self-reproduction of chirality, see Scheme 1. In this process, a carboxylic acid A is selectively converted to an acetal with *cis*- or *trans*-configuration derived from pivalaldehyde. The original asymmetric center can then be destroyed to form an enolate E which is non-racemic due to the auxiliary acetal-type center. This in turn can be expected to direct an incoming electrophile so that one of the possible diastereomeric products B prevails. The auxiliary center can then be sacrificed to give an enantiomerically pure or enriched product P. This product is related to the starting material A by a substitution of the α-proton either in a retention (A→*cis*→E→B→P) or in an inversion mode (A→*trans*→E→B→P). Both enantiomers P and $\bar{P}$ are thus available if (a) either the *cis*- or the *trans*-acetal is accessible from A selectively, or if (b) either one of the enantiomeric starting materials A or $\bar{A}$ can be employed.

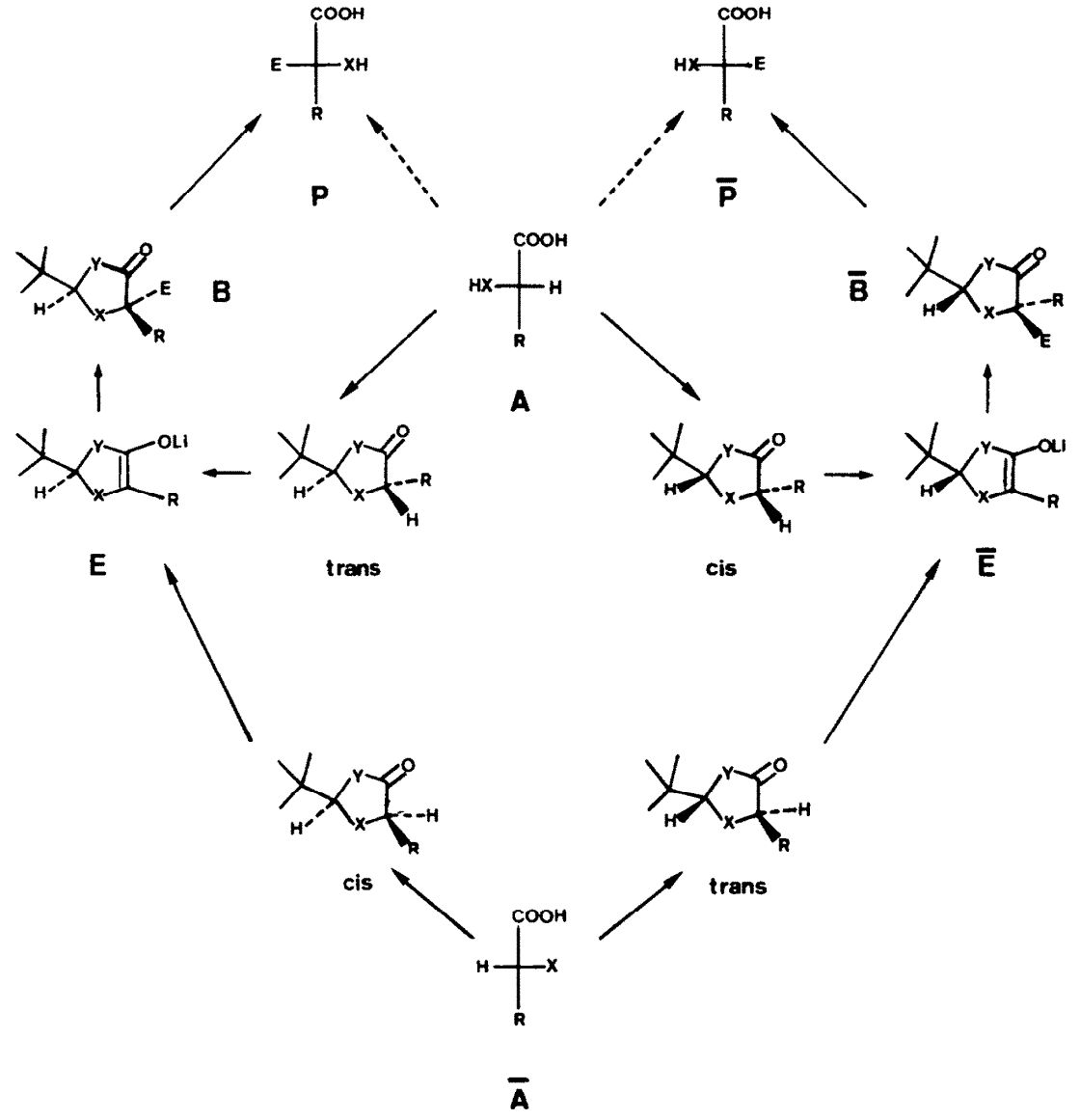
The present paper describes examples of the application of this principle to α-hydroxy- and α-mercapto–carboxylic acids. Instead of pivalaldehyde as a source of the auxiliary asymmetric C atom 2-ethyl–butanal or benzaldehyde may also be used.[16] The preparation and use of analogous α-aminoacid derivatives is described elsewhere[1c,1e], so is the application to a four step frontaline synthesis from lactic acid.[1d]

Preparation of the dioxolanones and oxathiolanones—configurational assignments

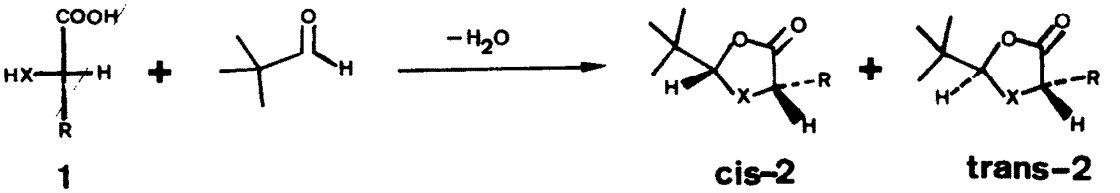
Acid catalyzed acetalization of pivalaldehyde with the α-hydroxy- and α-mercapto–carboxylic acids **1** in pentane, with azeotropic removal of the water-formed, produces mixtures of the *cis*- and *trans*-substituted heterocyclic compounds **2**. Except with **2g**, it was possible to separate the *cis*/*trans*-isomers by crystallization. The "undesired" isomer can be hydrolized back to the starting materials.

The configuration of the major diastereomer was determined to be *cis* or *l*[23] in the case of the lactic acid derived dioxolanone **2a** by NOE measurements: irradiation with the ^{1}H-NMR frequency of the t-butyl protons caused a 9% intensity increase of the quartet signal from the proton in 5-position of one isomer (*trans*) and no change with the other isomer (*cis*). The configurations of the major isomers of **2b** through **2f** are assigned to be *cis* by analogy with **2a**, by comparison with published ^{1}H-NMR data of dioxolanones and oxathiolanones,[24] and on the basis of generalizations about the steric course of reaction of enolates of type E (Scheme 1). In order to elaborate the last-mentioned point, we first have to examine some of the results of the alkylations and hydroxyalkylations of these enolates.

In eight cases the heterocyclic products **B** (Scheme 1) were chemically correlated for configurational assignment, see Scheme 2. Thus, in the overall processes, (*S*)-lactic acid was converted to the following compounds of known configuration: (*R*)-(−)-2-hydroxy-2-methyl-butanoic acid[25] (**3**), (*R*)-(+)-2-methyl-1,2-butandiol[26] (**4**) and -hexandiol[27] (**5**), (2*R*,3*S*)-(−)-2,3-*dihydroxy-pentanoic acid*[28] (**6**), and (*R*)-frontalin[1c] (**7**). Likewise, (*S*)-(+)-mandelic acid gave (*S*)-(+)-atrolactic acid[29,30] (**8**) and

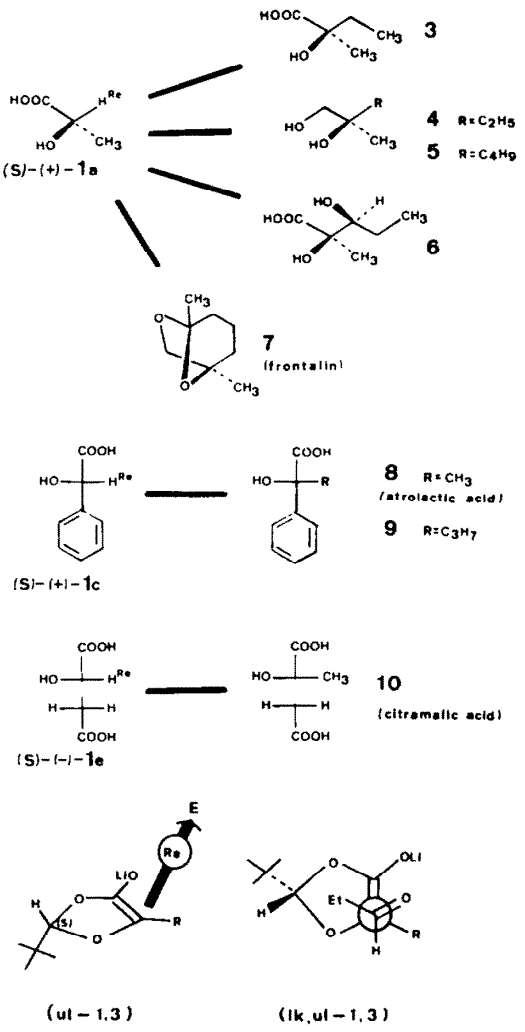


Scheme 1. α-Alkylation of an acid A to a product P with self-reproduction of chirality.



1a: (*S*)-lactic acid
1b: (*S*)-phenyl lactic acid
1c: (*S*)-mandelic acid
1d: (*S*)-α-hydroxyisovaleric acid[17]
1e: (*S*)-malic acid
1f: (±)-thiolactic acid[19]
1g: (±)-thiomalic acid[19]

2a: R = CH_3, X = O (93%, 4:1)
2b: R = $CH_2C_6H_5$, X = O (87%, 5:1)
2c: R = C_6H_5, X = O (82%, 20:1)
2d: R = $CH(CH_3)_2$, X = O (50%, 5:1)
2e: R = CH_2COOH, X = O (95%, 3:2 or 50:1)[18]
2f: R = CH_3, X = S (92%, 2.5:1)
2g: R = CH_2COOH, X = S (72%, 1:1)[22]



Scheme 2. Configurational correlation of some products from S-lactic, S-mandelic, and S-malic acid.

(*S*)-(+)-2-propyl-mandelic acid[30] (**9**), and finally (*S*)-(−)-malic acid gave (*S*)-(+)-citramalic acid[31] (**10**), see Scheme 2. In all these cases, the α-carbonyl H atom sitting in the (*Re*)-half-space has been replaced in an electrophilic substitution by an alkyl or hydroxyalkyl group with retention of configuration. In all three cases, the major, thermodynamically more stable isomer of the dioxolanones **2a**, **2c** or **2e** was used as starting material, and the products were obtained with more than 90% enantiomeric excess (%ee), see Experimental.

Since the lactic-acid-derived major dioxolanone **2a** was assigned the *cis*-configuration, i.e. (*S*,*S*)-chirality when made from the (*S*)acid, the relative topicity of approach of the electrophiles on its enolate is specified[23] *ul*-1.3, see bottom part of Scheme 2. We assume that the same steric course, i.e. attack of the face opposite to the *t*-butyl-group, is followed in the other cases as well.[32] Although much more tentatively, we also propose the relative topicity[23] *lk* for all additions to aldehydes, as found for the bond formation between the two trigonal, two-dimensionally chiral centers of propanal and the enolate derived from lactic acid (right side at the bottom of Scheme 2); further results supporting this view will be presented below.

Alkylation of the enolates derived from the major isomer of **2**

The separated main-products **2** with *cis*-arrangement of the substituents are deprotonated in tetrahydrofuran (THF) with lithium diisopropylamide (LDA) or hexamethyldisilazide (LHMDS, recommended for **2b**) at −78°. A somewhat lower concentration and addition of the heterocycles **2** to the base are necessary in some cases in order to avoid self-addition (→**13**) from competing with formation of enolates[33] **11**. Primary alkyl, allyl and benzyl bromides and iodides can be used to introduce a second substituent in the 5-position of the dioxolanone by enolate alkylation. The products **12** are collected in Table 1. The diastereoselectivities are constantly high, mostly above 95% as determined by ^{1}H-NMR spectroscopy or capillary gas chromatography. In the case of the malic acid derivative, the carboxylic group is protected as the Li salt, see **14**. Some of the products derived from lactic acid were reduced[34] with lithium aluminium hydride (LAH) to the diols **4**, **5**, **15**, **16**, which in turn have been converted[34] to the 1,1-di-substituted oxiranes **17**—useful chiral building blocks. In some cases, products **19** of the enantiomeric series were also prepared through enolates **18**, see Table 2.

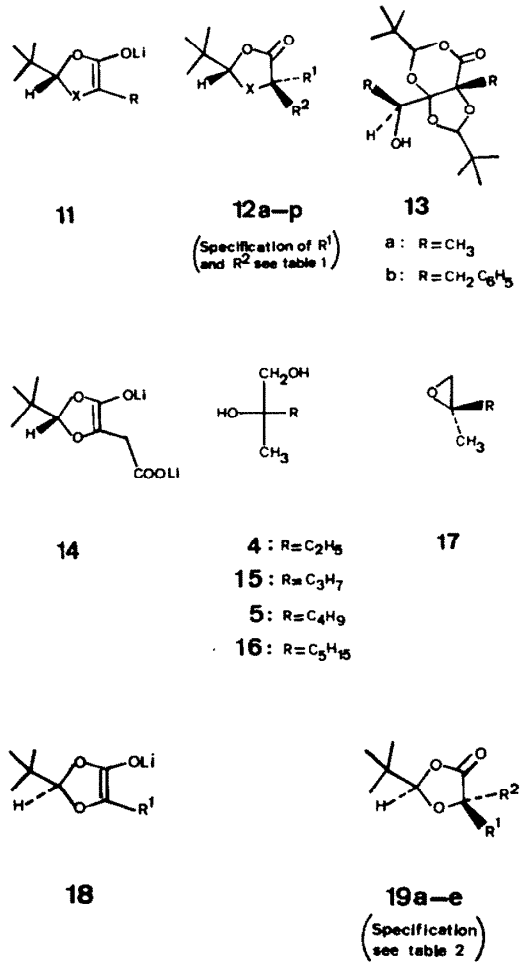


Table 1. Products **12** of alkylation of the enolates **11** derived from the major diastereomers **2**[a]

Product 12	R^1/X	R^2 (halide used)	yield [%]	% ds	$[\alpha]_D$
a	CH_3/O	C_2H_5 (I)	82	97	+43.8°
b	CH_3/O	C_3H_7 (I)	72	97	+28.8°
c	CH_3/O	C_4H_9 (I)	68	97	+26.6°
d	CH_3/O	C_7H_{15} (I)	84	96	+30.7°
e	CH_3/O	CH_2-CH=CH_2 (Br)	77	98	+52.9°
f	CH_3/O	CH_2-C_6H_5 (Br)	81	96	+57.6°
g	C_6H_5/O	C_3H_7 (I)	84	95	+29.9°
h	$CH_2C_6H_5/O$	CH_3 (I)	30	> 95	-27.5°
i	$CH_2C_6H_5/O$	C_2H_5 (I)	45	> 95	- 9.7°
k	$CH_2C_6H_5/O$	C_3H_7 (I)	40	> 95	-14.6°
l	$CH_2C_6H_5/O$	CH_2-CH=CH_2 (Br)	40	> 95	+ 5.2°
m	CH_2COOH/O	CH_3 (I)	79	> 95	+20.9°
n	CH_2COOH/O	$CH_2CH=CH_2$ (Br)	76	> 95	+66.0°
o	CH_2COOH/O	$CH_2C_6H_5$ (Br)	77	> 95	+65.3°
p	CH_3/S	$CH_2CH=CH_2$ (Br)	92	> 98	

[a]The yields are those of chromatographed, distilled or recrystallized material. If diastereoselectivities > 95% are given, no second isomer has been detected by 90 MHz ^{1}H-NMR spectroscopy, while specific % ds-values above 95% have been determined by capillary GC. The $[\alpha]_D$ values were measured with $CHCl_3$ solutions at ambient temperatures. The m.p. are uncorrected. For experimental details see general procedures. The yields of **12a–12l** and of **12p** were obtained with LDA, those of **12m, 12n, 12o** with LHMDS as the base for deprotonation. The yields of the phenyllactic acid derivatives **12h–12l** can be greatly improved by using the latter base (Table 2).

Reactions of enolates from **2** *with aldehydes and ketones*

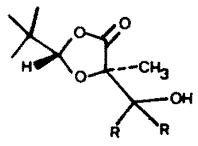
The enolates of type **11/14/18** are surprisingly nucleophilic and show little basicity, as evident from the good yields of adducts (**20a, 20b, 22, 24**) obtained with acetone, cyclopentanone and acetophenone. Additions to aldehydes[35] (→**21, 25**) and unsymmetrical ketones (→**22, 23**) furnish products containing three asymmetric C atoms. Of the possible four diastereomers, only two are formed, usually one with strong preference (see the % ds values under the *formulae*).

We assume that the sole adducts **20** to symmetrical ketones are formed with relative topicity *ul*-1.3—just

Table 2. Products **19** of alkylation of the enolates **18**[a]

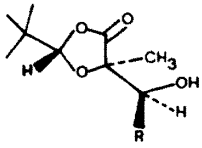
Product 19	R^1	R^2 (halide used)	yield [%]	$[\alpha]_D$
a	CH_3	$CH_2CON(CH_3)_2$ (Cl)	76	+53.5°
b	$CH_2C_6H_5$	C_2H_5 (I)	74	+ 9.8°
c	$CH_2C_6H_5$	CH_2-CH=CH_2 (Br)	78	- 5.1°
d	CH_2COOH	CH_2-CH=CH_2 (Br)	83	-61.6°
e	CH_2COOH	CH_2-C_6H_5 (Br)	84	-61.1°

[a]The enolates **18** were generated either (**19d, 19e**) from the minor (*trans*) diastereomer **2** or (**19a, 19b, 19c**) from the *cis*diastereomer obtained from (*R*)-acid rather than from (*S*)-acid **1**. Details as given in the legend of Table 1. In all but the first case (→**19a**) LHMDS was employed as base. All diastereoselectivities are above 95% ds.



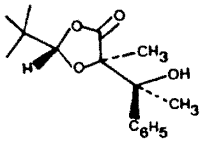
20

20a: R = CH_3 (83% y, > 95% ds)
20b: R – R = $(CH_2)_4$ (85% y, > 95% ds)
20c: R = C_6H_5 (87% y, > 95% ds)

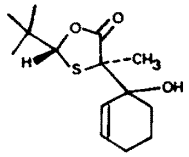


21

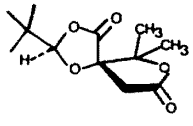
21a: R = CH_3 (84% y, 82% ds)
21b: R = C_2H_5 (80% y, 85% ds)
21c: R = t-C_4H_9 (83% y, 53% ds)
21d: R = CH_2=CH–C_6H_5 (66% y, 60% ds)
21e: R = C_6H_5 (85% y, 84% ds)
21f: R = 2,4,6-trimethylphenyl (65% y, 78% ds)



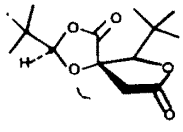
22 (81% y, 93% ds)



23 (65% y, 76% ds)



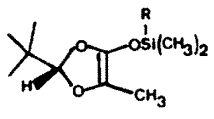
24 (53% y, 70%)



25 (72% y, 95% ds)

like the alkylated derivatives **12** and **19**. We propose the configurations of the main-products of addition to aldehydes and ketones as shown in the accompanying *formulae*. This assignment is made not only in analogy with the result of one correlation [(*S*)-(+)-(**1a**)→*cis*-dioxolanone **2a**→(*S*)-enolate **11** (X = 0)→**21b**→**6**, Scheme 2], but is also compatible with a ^{1}H-NMR comparison, see Table 3.

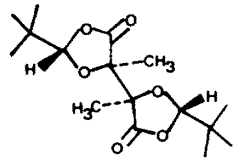
Silyl enol ethers have been shown to undergo certain transformations not possible with the corresponding lithium enolates.[36] In an attempt to perform some of these reactions, the enolate of the dioxolanone **2a** from lactic acid was silylated with chloro-trimethylsilane and t-butyldimethyl-chlorosilane to the ketene acetal derivatives **26**. The



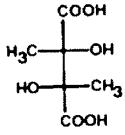
26

a : R = CH_3

b : R = t-C_4H_9



27



28

trimethylsilylated compound **26a** was treated in methylene chloride with 1,3,5-trioxane/$TiCl_4$ at −75°. Instead of the expected[37] hydroxymethylated compound, the dimer **27** was formed in good yield. Formally, this is an oxidative coupling[38,39] of lactic acid to (*R,R*)-2,3-dimethyl-tartaric acid (**28**).

EXPERIMENTAL

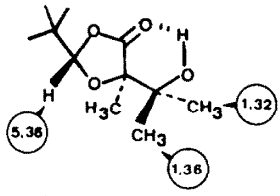
General remarks. M.ps and b.ps are uncorrected. M.p. were determined on a Büchi 510 m.p. apparatus. B.ps are air-bath-temps of the Kugelrohr distillations using a Büchi-GKR-50 apparatus. Spectra were recorded with the following instruments: IR: Perkin–Elmer-Spectrophotometer 297; ^{1}H-NMR: Varian-EM-390 (90 MHz), and Varian XL-100 (100 MHz); ^{13}C-NMR:Varian-CFT-20 (20 MHz); MS: Hitachi Perkin–Elmer RMU-6M. IR data are presented in cm^{-1}. NMR spectra were recorded with $(CH_3)_4Si$ as internal standard. Optical rotations were determined with a Perkin–Elmer Model 241 polarimeter. The diastereomeric composition (% ds = diastereoselectivity) of crude products was determined by ^{1}H-, ^{13}C-NMR (a) or by capillary GC, using a 20 m CW 1000 column (b). The anisochronous NMR-signals of the minor diastereomer are reported oblique. All reactions involving Li derivatives were carried out under anhydrous conditions in an argon atmosphere. Flash chromatography was performed according to the method described by Still *et al.*[40] Molecular weight determinations in solution were done osmometrically.

Acetalization of α-heterosubstituted carboxylic acids. General procedure. A mixture of 0.5 mol of carboxylic acid, 1 mol of pivalaldehyde, 1 g of *p*-toluenesulfonic acid, 2 drops of conc. H_2SO_4 and 400 ml of pentane was refluxed with azeotropic removal of the water formed. The resulting soln was washed with water (2 × 200 ml), dried ($MgSO_4$) and concentrated at reduced pressure.

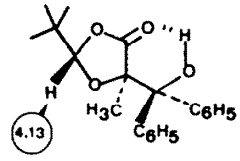
(2S,5S) - 2 - (t - *Butyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (*cis*-**2a**). From 45 g (0.50 mol) of freshly distilled *S*-**1a** and 86 g (1.00 mol) of pivalaldehyde 73.5 g (93%) **2a** of a 4:1 (a) (*cis*/*trans*) mixture was obtained after a Kugelrohr distillation. Two recrystallizations from ether–pentane at −78° gave 48 g of *cis*-**2a** (96% ds (b)). The residue of the concentrated mother liquor was treated with 1 g of *p*-toluenesulfonic acid and 20 ml of water. After refluxing for 3 hr, the resulting mixture was used for acetalization as described in the general procedure, m.p. ~ 5°; b.p. 80°/20 mm Hg. $[\alpha]_D^{20}$ + 44.8° (*c* = 1.83; $CHCl_3$). IR ($CHCl_3$): 2970 s, 1795 s, 1300 m, 1200 s, 1115 m, 970 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.14 (d, J = 1 Hz, 1 H), 4.45 (d × q,

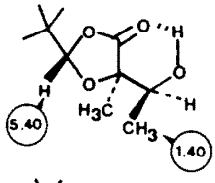
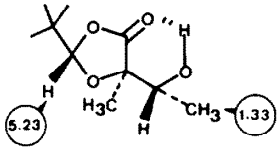
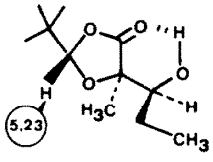
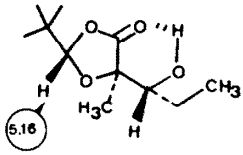
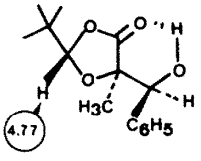
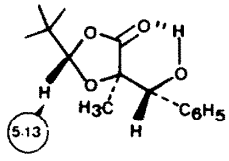
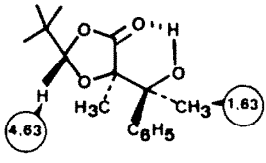
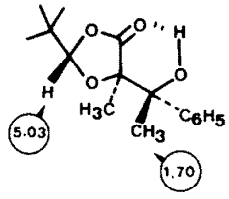
Table 3. Comparison of the ^{1}H-NMR shifts (circled values, in ppm) of some characteristic signals from the adducts of the (*S*)-lactic acid derived enolate with aldehydes and ketones[a]

20a



20c



MAJOR (u)	DIASTEREOMER	MINOR (l)
	**21a**	
	**21b***	
	**21e**	
	**22**	

* Cf. chemical correlation with **6**

[a]The main-conformers are assumed to be the hydrogen-bonded ones shown in all cases. The acetal hydrogen of the *u*-isomer obtained with aliphatic aldehydes appears at lower field than that of the l-isomer; with the products from benzaldehyde and acetophenone a reversed behaviour is observed.

$J_1 = 1$ Hz, $J_2 = 7$ Hz, 1 H), 1.48 (d, J = 7 Hz, 3 H), 0.98 (s, 9 H). ^{13}C-NMR ($CDCl_3$): δ 173.17 s, 109.07 d, 71.36 d, 34.16 s, 30.40 q, 16.14 q. MS *m/e*: 114, 101, 73, 57, 45. (Found: C, 60.74; H, 9.02. Calc for $C_8H_{14}O_3$: C, 60.74, H, 8.92%.)

trans-**2a**: ^{1}H-NMR ($CDCl_3$): δ 5.30 (d, J = 1 Hz, 1 H), 4.36 (d × q, $J_1 = 1$ Hz, $J_2 = 7$ Hz, 1H), 1.44 (d, J = 7 Hz, 3 H), 0.96 (s, 9 H).

(2S,5S) - 5 - *Benzyl* - 2 - (*t* - *butyl*) - 1,3 - *dioxolan* - 4 - *one* (*cis*-**2b**). From 35 g (210 mmol) of *S*-(−)-**1b** and 43 g (500 mmol) of pivalaldehyde 43 g (87%) of **2b** as a 5:1 (a) (*cis*/*trans*) mixture was obtained. After two recrystallizations from ether/pentane at −30°, 33 g (67%) of *cis*-**2b** (ds 99% (b)) was obtained, m.p. 56–58°. $[\alpha]_D^{25}$ − 45.9° (*c* = 1.80; $CHCl_3$). IR (KBr): 3060 w, 2960 m, 1785 s, 1220 m, 1195 m, 1185 m, 1105 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 7.25 (s, 5 H), 5.09 (d, 1 Hz, 1 H), 4.50–4.38 (m, 1 H), 2.30–2.76 (m, 1 H), 0.85 (s, 9 H). MS *m/e*: 234, 121, 91, 57. (Found: C, 71.82; H, 7.90. Calc for $C_{13}H_{18}O_3$: C, 71.76; H, 7.74%.)

trans-**2b**: ^{1}H-NMR ($CDCl_3$): δ 7.25 (s, 5 H), 4.82 (d, J = 1 Hz, 1 H), 4.50–4.38 (m, 1 H), 3.30–2.76 (m, 2 H), 0.85 (s, 9 H).

(2S,5S) - 2 - (*t* - *Butyl*) - 5 - *phenyl* - 1,3 - *dioxolan* - 4 - *one* (*cis*-**2c**). From 18.6 g (122 mmol) of (*S*)-(+)-**1c** and 43 g (500 mmol) of pivalaldehyde 25.8 g of crude *cis*-dioxolanon **2c** (98% ds (b)) was obtained. One recrystallization from ether/pentane gave 22.0 g (82%) of *cis*-**2c** as colourless crystals. (> 99% ds (b)), m.p. 140°. $[\alpha]_D^{25}$ + 88.7° (*c* = 1.2; $CHCl_3$). IR(KBr): 2980 m, 1800 s, 1205 m, 1090 m, 975 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 7.28 (m, 5 H), 5.28 (d, J = 1.5 Hz, 1 H), 5.19 (d, J = 1.5 Hz, 1 H), 1.04 (s, 9 H). ^{13}C-NMR ($CDCl_3$): δ 171.72 s, 133.73 s, 129.11 d, 128.70 d, 127.09 d, 109.27 d, 77.00 d, 34.46 s, 23.63 q. MS *m/e*: 220, 135, 107, 70, 57. (Found: C, 70.94; H, 7.44. Calc for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32%.)

(2S,5S) - 2 - (*t* - *Butyl*) - 5 - (*isopropyl*) - 1,3 - *dioxolan* - 4 - *one* (*cis*-**2d**). From 20 g (170 mmol) of *S*-(+)-**1d** and 30 g (340 mmol) of pivalaldehyde 15.7 g (50%) of **2d** was obtained after Kugelrohr distillation as a 5:1 (a) (*cis*/*trans*) mixture. Recrystallization from ether/pentane at −78° gave 11.2 g (36%) of *cis*-**2d** (> 95% ds (a)), b.p. 110°/0.1 mm Hg. $[\alpha]_D^{25}$ − 6.9° (*c* = 2.9; $CHCl_3$). IR (CCl_4): 2990 m, 1795 s, 1100 m, 990 m. ^{1}H-NMR ($CDCl_3$): 5.10 (s, 1 H), 4.06 (d, J = 5 Hz, 1 H), 2.20 (m, 1 H), 1.10 (d, J = 7 Hz, 3 H), 1.05 (d, J = 7 Hz, 3 H), 1.00 (s, 9 H). (Found: C, 64.47; H, 9.69. Calc for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74%.)

(2S,5S) - 2 - (*t* - *Butyl*) - 5 - (*methoxycarbonyl*) - 1,3 - *dioxolan* - 4 - *one* (*cis*-**2e**). To a suspension of 40 g (300 mmol) of *S*-(−)-malic acid in 500 ml of pentane 40 g (465 mmol) of pivalaldehyde, 5 g of *p*-toluenesulfonic acid and 5 drops of conc. sulfuric acid were added. After acetalization under the usal conditions, the cooled resulting suspension was filtered. The filter cake was dissolved in 400 ml of CH_2Cl_2 and washed twice with 200 ml of 8% aqueous phosphoric acid. The soln was dried over $MgSO_4$ and concentrated to half the volume under reduced pressure. Crystallization at −80° gave 40.2 g (67%) (> 98% ds (a)) of *cis*-**2e** as colurless crystals. The combined mother liquors yielded 16 g (28%) of a diastereomeric mixture which could be recycled as described above, m.p. 102–104°. $[\alpha]_D^{25}$ − 2.3° (*c* = 1.3, $CHCl_3$). IR ($CHCl_3$): 2960 s, (br.), 1790 s, 1720 s, 115 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 10.6 (br. s, 1 H), 5.20 (s, 1 H), 4.16 (dd, J_1 = 4 Hz, J_2 = 4 Hz, 1 H), 3.17–2.60 (m, 2 H), 1.00 (s, 9 H).

trans-**2d**: m.p. 114–117°. $[\alpha]_D^{25}$ + 23.1° (*c* = 1.1; $CHCl_3$). ^{1}H-NMR ($CDCl_3$): δ 10.3 (br. s, 1 H), 5.34 (d, J = 2 Hz, 1 H), 4.63 (d × t, J_1 = 2 Hz, J_2 = 5 Hz, 1 H), 2.94 (d, J = 5 Hz, 2 H), 0.98 (s, 9 H). (Found: C, 53.52; H, 6.94. Calc for $C_9H_{14}O_5$: C, 53.46; H, 6.98%.)

2 - (*t* - *Butyl*) - 5 - *methyl* - 1,3 - *thioxolan* - 4 - *one* (*cis*-**2f**). Racemic thiolactic acid (**1f**) (52 g, 0.5 mol) and 86 g (1 mol) of pivalaldehyde gave, after Kugelrohr distillation, **2f** (80 g, 92%) as a mixture of two diastereomers (71% ds (b)). Recrystallization from ether/pentane at −80° gave the same *cis* diastereomer **2f**. B.p. 57°/1 mm Hg. IR ($CHCl_3$): 2960 s, 1755 s, 1365 m, 1275 m, 1035 m, 1015 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.23 (s, 1 H), 4.00 (q, J = 7 Hz, 1 H), 1.57 (d, J = 7 Hz, 3 H), 1.03 (s, 9 H). ^{13}C-NMR ($CDCl_3$): 175.17 s, 87.99 d, 41.14 d, 34.86 s, 25.04 q, 17.18 q. MS *m/e*: 174, 117, 89, 57, 41. (Found: C, 54.79; H, 8.72. Calc for $C_8H_{14}O_2S$: C, 55.09; H, 8.10%.)

trans-**2f**: ^{1}H-NMR ($CDCl_3$): 5.23 (s, 1 H), 3.90 (q, J = 7 Hz, 1 H), 1.60 (d, J = 7 Hz, 3 H), 1.03 (s, 9 H). ^{13}C-NMR ($CDCl_3$): 175.78 s, 87.99 d, 40.62 d, 36.53 s, 24.75 q, 19.43 q.

2 - (*t* - *Butyl*) - 5 - (*methoxycarbonyl*) - 1,3 - *thioxolan* - 4 - *one* (**2g**). From 75.0 g (0.5 mol) of racemic thiomalic acid and 86.0 g (1.0 mol) of pivalaldehyde 93.7 g (86%) of **2g**, as a *cis*/*trans* mixture (50% ds (a)), was prepared according to the procedure for the malic acid acetalization. It was not possible to separate the diastereomers, m.p. 103–110°. IR ($CHCl_3$): 3100 m (br.), 2970 m, 1720 s, 1400 m, 1195 m, 1040 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 9.80 (br. s, 1 H), 5.30 (s, 1 H), 4.46–4.06 (m, 1 H), 3.15–2.63 (m, 3 H), 1.02 (s, 9 H). MS *m/e*: 218, 161, 151, 87, 70, 57, 41. (Found: C, 49.48; H, 6.54; S, 14.56. Calc for $C_9H_{14}O_4S$: C, 49.54; H, 6.47; S, 14.69%.)

General procedure for reactions of the enolate from the dioxolanone **2** *with various electrophiles.* A 10 mmol run is described. Unless noted otherwise, 10 mmol of **2** was added to a soln of 10.5 mmol of LDA in 70 ml THF–hexane (9:1) at −78°. After 45 min at −78°, 15 mmol of the electrophile was added and the temp was allowed to warm up to *ca* −20° over a period of 3 h. The reaction soln was poured into 100 ml of half-sat ammonium chloride soln and extracted twice with 100 ml of ether. The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo*. Specific details are given for each compound.

(2S,5R) - 2 - (*t* - *Butyl*) - 5 - *ethyl* - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**12a**). EtI (2.4 g, 15 mmol) and 1.58 g (10 mmol) of *cis*-**2a** gave, after Kugelrohr distillation the product **12a** (1.53 g, 82%) (97% ds (b)) as a colourless liquid. B.p. 110°/16 mm Hg. $[\alpha]_D^{25}$ + 43.8° (*c* = 2.52, $CHCl_3$). IR ($CDCl_3$): 2980 m, 1775 s, 1145 m, 1075 m, 975 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.16 (s, 1 H), 1.90–1.64 (m, 2 H), 1.40 (s, 3 H), 1.00 (t, J = 7 Hz, 3 H), 0.94 (s, 9 H). MS *m/e*: 187, 129, 101, 73, 57, 43. (Found: C, 64.32; H, 9.76. Calc for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74%.)

(2S,5R) - 2 - (*t* - *Butyl*) - 5 - *methyl* - 5 - *propyl* - 1,3 - *dioxolan* - 4 - *one* (**12b**). PrI (5.1 g, 30 mmol) and 4 g (25 mmol) of *cis*-**2a** were used. Kugelrohr distillation afforded 3.6 g (72%) **12b** as a colourless liquid (97% ds (b)), b.p. 105°/19 mm Hg. $[\alpha]_D^{20}$ + 28.8° (*c* = 2.46; $CHCl_3$). IR (film): 2960 s, 1795 s, 1635 m, 1345 m, 1180 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.17 (s, 1 H), 1.80–1.45 (m, 4 H), 1.40 (s, 3 H), 1.00–0.88 (m, 3 H), 0.92 (s, 9 H). MS *m/e*: 201, 173, 115, 87, 57. (Found: C, 65.91; H, 10.00. Calc for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07%.)

(2S,5R) - 5 - *Butyl* - 2 - (*t* - *butyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**12c**). From BuI (7.4 g, 40 mmol) and 4.6 g (29 mmol) of *cis*-**2a** 4.4 g (69%) of **12c** was obtained as a colourless liquid (97% ds (b)), b.p. 100°/16 mm Hg. $[\alpha]_D^{20}$ + 26.6° (*c* = 4.48; $CHCl_3$). IR (film): 2950 s, 2920 s, 1795 s, 1480 s, 1155 s, 980 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.15 (s, 1 H), 1.60–1.85 (m, 2 H), 1.40 (s, 1 H), 1.10–1.50 (m, 7 H), 0.92 (s, 9 H). MS *m/e*: 215, 202, 158, 102, 57. (Found: C, 67.18; H, 10.40. Calc for $C_{11}H_{22}O_3$: C, 67.23; H, 10.35%.)

(2S,5R) - 2 - (*t* - *Butyl*) - 5 - *heptyl* - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**12d**). Heptyl iodide (9.0 g, 30 mmol) and 4.0 g (25 mmol) of *cis*-**2a** gave, after Kugelrohr distillation, the product **12d** (5.3 g, 84%) as a pale yellow liquid (96% ds (b)), b.p. 120°/16 mm Hg. $[\alpha]_D^{20}$ + 30.7° (*c* = 1.05; $CHCl_3$). IR (film): 2960 s, 2930 s, 2840 s, 2820 s, 1800 s, 1175 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.16 (s, 1H), 1.52–1.90 (br., m, 4 H), 1.40 (s, 3 H), 1.18–1.36 (br., s, 8 H), 0.94 (s, 9 H), 0.84–0.90 (m, 3 H). MS *m/e*: 212, 199, 143, 125, 57.

(2S,5R) - 5 - *Allyl* - 2 - (*t*- *-butyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**12e**). Allylbromide (1.8 g, 15 mmol) and 1.58 g (10 mmol) of *cis*-**2a** were used. Kugelrohr distillation afforded 0.96 g (77%) of **12e** (98% ds (b)) as a colourless oil, b.p. 130°/12 mm Hg. $[\alpha]_D^{25}$ + 52.9° (*c* = 2.23; $CHCl_3$). IR ($CHCl_3$): 2970 m, 1770 s, 1165 m, 1080 m, 985 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 6.04–5.58 (m, 1 H), 5.32–5.06 (m, 2 H), 5.18 (s, 1 H), 2.60–2.32 (m, 2 H), 1.42 (s, 3 H), 0.92 (s, 9 H). ^{13}C-NMR ($CDCl_3$): δ 174.73 s, 130.80 s, 119.91 t, 108.12 d, 79.39 s, 40.47 t, 34.22 s, 22.95 q, 22.41 q. MS *m/e*: 198, 157, 129, 113, 87, 57, 43. (Found: C, 66.57; H, 9.32. Calc for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%.)

(2S,5R) - 5 - *Benzyl* - 2 - (*t* - *butyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**12f**). From benzylbromide (1.9 g, 11 mmol) and 1.58 g (10 mmol) of *cis*-**2a** 2.0 g (81%) of **12f** was obtained (96% ds (b)) after Kugelrohr distillation as a pale yellow resin. B.p. 140°/0.001 mm Hg. $[\alpha]_D^{25}$ + 57.6° (*c* = 2.48; $CHCl_3$). IR ($CHCl_3$): 2960 w, 1775 s, 1135 s, 1070 m, 975 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 7.25 (s, 5 H), 4.44 (s, 1 H), 3.11 (d, H = 13 Hz, 1 H), 2.83 (d, J = 13 Hz, 1 H), 1.41 (s, 3 H), 0.83 (s, 9 H). ^{13}C-NMR ($CDCl_3$): δ 175.19 s, 134.96

s, 130.28 d, 128.41 d, 127.28 d, 108.60 d, 80.75 s, 42.73 t, 34.32 s, 23.63 q. 23.17 q. MS *m/e*: 291, 248, 135, 91, 87, 43. (Found: C, 72.64; H, 8.17. Calc for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12%.)

(2S,5S) - 2 - (*t* - *Butyl*) - 5 - *phenyl* - 5 - *propyl* - 1,3 - *dioxolan* - 4 - *one* (**12g**). A soln of 1.1 g (5 mmol) of *cis*-**2c** was cooled to −78° and 5.5 ml of 1 M LDA-soln (THF–hexane; 1:3) was added. After 30 min 1.7 g (10 mmol) of 1-iodopropane was added, and the temp was allowed to warm up to 5° over a period of 2 hr. After usual work up, Kugelrohr distillation give 1.1 g (84%) of **12g** (95% ds (b)) as a colourless resin, b.p. 95°/0.001 mm Hg. $[\alpha]_D^{25}$ + 29.9° (*c* = 1.0; $CHCl_3$). IR ($CHCl_3$): 2960 m, 1780 s, 1345 m, 1140 m, 1080 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): *δ* 7.75–7.20 (m, 5 H), 5.34 (s, 1 H), 2.26–1.90 (m, 2 H), 1.56–1.16 (m, 2 H), 0.99 (s, 9 H), 0.90 (t, J = 7 Hz, 3 H).^{13}C-NMR ($CDCl_3$): *δ* 173.73 s, 138.37 s, 128.17 d, 127.29 d, 124.95 d, 108.60 d, 80.52 s, 40.82 t, 35.01 s, 23.57 q, 17.09 t, 13.83 q. MS *m/e*: 263, 219, 177, 150, 105, 57. (Found: C, 73.06; H, 8.59. Calc for $C_{16}H_{22}O_3$: C, 73.25; H, 8.46%.)

General procedure for reactions of the enolate from the dioxolanone cis-**2b** *with various electrophiles.* A 10 mmol run is described. Unless stated otherwise, a soln of 2.34 g (10 mmol) of *cis*-**2b** in 10 ml of THF was added to a soln of 10.5 mmol of LDA in 60 ml THF–hexane 8:1 at −78°. After 15 min at −78°, 15 mmol of the electrophile was added and the temp was allowed to warm to −10° over a period of 3 hr. The reaction soln was poured into 100 ml of half-saturated aqueous ammonium chloride soln and extracted twice with 100-ml portions of ether. The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo*. Specific details are given for each compound.

Note: the reaction was contaminated by the formation of two byproducts, which could be fully identified as the self-addition product **13b** and as an addition product of the enolate from *cis*-**2b** to pivalaldehyde. The formation of these byproducts could be avoided by generation of the enolate with LHMDS. This procedure was similar to the one described above.

(2S,5S) - 5 - *Benzyl* - 2 - (*t* - *butyl*) - 5 - *methyl–dioxolan* - 4 - *one* (**12h**). MeI (2.12 g, 15 mmol) and 2.34 g (10 mmol) of *cis*-**2b** gave, after flash-chromatography (pentane–ether 15:1, R_f = 0.32), **12h** (0.75 g, 30%) (> 95% ds (a)) as colourless crystals: m.p. 47–49°. $[\alpha]_D^{20}$ − 27.5° (*c* = 1.30; $CHCl_3$). IR (KBr): 2980 m, 2960 m, 1785 s, 1195 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): *δ* 7.21 (s, 5 H), 5.10 (s, 1 H), 2.34–3.14 (d × d, J = 14 Hz, 2 H), 1.37 (s, 3 H), 0.75 (s, 9 H). MS *m/e*: 249, 248, 191, 135, 57. (Found: C, 72.37; H, 8.09. Calc for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12%.)

(2S,5S) - 5 - *Benzyl* - 2 - (*t* - *butyl*) - 5 - *ethyl* - 1,3 - *dioxolan* - 4 - *one* (**12i**). EtI (2.43 g, 15 mmol) and 2.34 g (10 mmol) of *cis*-**2b** were used. Flash-chromatography of the distilled product with pentane–ether (20 : 1, R_f 0.33) gave 1.2 g (45%) (> 95% ds (a)) of **12i** as a colourless liquid; b.p. 120°/0.01 mm Hg. $[\alpha]_D^{20}$ − 9.7° (*c* = 1.55, $CHCl_3$). IR (film): 2970 s, 1790 s, 1485 m, 1170 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): *δ* 7.20 (s, 5 H), 5.12 (s, 1 H), 2.86–3.10 (d × d, J = 14 Hz), 1.66–1.90 (q, J = 7 Hz, 2 H), 0.96–1.10 (t, J = 7 Hz, 3 H), 0.75 (s, 9 H). MS *m/e*: 262, 205, 170, 57. (Found: C, 73.29; H, 8.54. Calc for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45%.)

(2R,5R) - 5 - *Benzyl* - 2 - (*t* - *butyl*) - 5 - *ethyl* - 1,3 - *dioxolan* - 4 - *one* (**19b**). Alkylation of the enolate derived from the enantiomer of *cis*-**2b** with ethyl iodide and with LHMDS as a base gave **19b** in 74% yield. The absolute values for $[\alpha]_D$ and the spectral data were identical for the two enantiomers **12i** and **19b**.

(2S-5S) - 5 - *Benzyl* - 2 - (*t* - *butyl*) - 5 - *propyl* - 1,3 - *dioxolan* - 4 - *one* (**12k**). PrI (2.62 g, 15 mmol) and 2.34 g (10 mmol) of *cis*-**2b** gave, after flash-chromatography (pentane–ether 20:1; R_f 0.34), product **12k** (1.1 g, 40%) as a colourless liquid: b.p. 95°/0.01 mm Hg. $[\alpha]_D^{20}$ − 14.6° (*c* = 0.70, $CHCl_3$). IR (film): 2860 s, 1795 s, 1480 m, 1170 m, 700 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): *δ* 7.23 (s, 5 H); 5.16 (s, 1 H), 2.86–3.10 (d × d, J = 14 Hz, 2 H), 1.34–1.70 (m, 4 H), 0.74–1.00 (t, J = 6 Hz, 3 H), 0.75 (s, 9 H). MS *m/e*: 276, 219, 71, 57, 43. (Found: C, 73.80; H, 8.73. Calc for $C_{17}H_{24}O_3$: C, 73.88, H, 8.75%.)

(2S,5S) - 5 - *Allyl* - 5 - *benzyl* - 2 - (*t* - *butyl*) - 1,3 - *dioxolan* - 4 - *one* (**12l**). Allyl bromide (1.8 g, 15 mmol) and 2.34 g (10 mmol) of *cis*-**2b** were used. Flash-chromatography of the distilled product with pentane–ether (15:1, R_f 0.35) gave 1.1 g (40%) of **12l** as a colourless liquid: b.p. 150°/0.3 mm Hg. $[\alpha]_D^{20}$ + 5.2° (*c* = 2.53, $CHCl_3$). IR (film): 2960 m, 1795 s, 1190 s, 700 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): *δ* 7.20 (s, 5 H), 5.64–6.07 (m, 1 H), 5.15 (s, 1 H), 5.08–5.22 (m, 2 H), 2.88–3.12 (d × d, J = 14 Hz), 2.40–2.56 (m, 2 H), 0.76 (s, 9 H). MS *m/e*: 274, 233, 91, 69, 57. (Found: C, 74.57; H, 8.23. Calc for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08%.)

(2R,5R) - 5 - *Allyl* - 5 - *benzyl* - 2 - (*t* - *butyl*) - 1,3 - *dioxolan* - 4 - *one* (**19c**). Alkylation of the enolate derived from the minor diastereomer *trans*-**2b** with allyl bromide and with LHMDS as a base gave (2*R*,5*R*) enantiomer **19c** in 78% yield. The absolute values for $[\alpha]_D$ and the spectral data were identical for the two enantiomers **12l** and **19c**.

(2S,5S) - 2 - (*t* - *Butyl*) - 5 - (*methoxycarbonyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**12m**). To a −78° cold stirred soln of 1.01 g (5 mmol) of *cis*-**2e** in 60 ml of THF 21.0 ml of 0.5 M lithium examethyldisilazide in THF–hexane 3:1 was added. After 20 min, 1.50 g (10.5 mmol) of MeI was added, and the temp was allowed to warm to −20° over a period of 3 hr. The resulting mixture was partitioned between dichloromethane and 1 N HCl. The organic layer was dried over $MgSO_4$ and the solvent removed *in vacuo*. Recrystallization from ether–pentane gave 0.85 g (79%) of **12m** as a single diastereomer (a). M.p. 139°. $[\alpha]_D^{28}$ + 20.9° (*c* = 1.4; $CHCl_3$). IR (KBr): 3400 m (br.), 2980 m (br.), 1795 s, 1715 s, 1180 s, cm^{-1}. ^{1}H-NMR ($CDCl_3$): *δ* 10.00 (s, br., 1 H), 5.16 (s, 1 H), 2.83 (AB, J_{AB} = 15 Hz, 2 H), 1.47 (s, 3 H), 0.97 (s, 9 H). ^{13}C-NMR ($CDCl_3$): *δ* 174.17 s, 110.00 d, 77.53 s, 41.36 t, 34.23 s, 23.64 q, 19.62 q. MS *m/e*: 217, 159, 103, 85, 70, 57. (Found: C, 55.42; H, 7.46. Calc for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46%.)

(2S,5S) - 5 - *Allyl* - 2 - (*t* - *butyl*) - 5 - (*methoxycarbonyl*) - 1,3 - *dioxolan* - 4 - *one* (**12n**). Allyl bromide (1.30 g, 10.5 mmol) and 1.01 g (5 mmol) of *cis*-**2e** were used (for procedure see **12m**) to give after Kugelrohr distillation, **12n** (0.96 g, 76%) (> 95% ds (a)) as a colourless resin. A (C-2)-epimeric mixture (85% ds) resulted after Kugelrohr distillation. B.p. 110°/0.02 mm Hg. $[\alpha]_{D_{crude}}^{25}$ + 66.0° (*c* = 0.5; $CHCl_3$); $[\alpha]_{D_{dist.}}^{25}$ + 47.2° (*c* = 0.45; $CHCl_3$). IR ($CHCl_3$): 2970 m (br.), 1795 s, 1720 s, 1410 m, 1165 m, 970 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): *δ* 10.5 (s, br., 1 H), 6.10–5.60 (m, 1 H), 5.40–5.10 (m, 3 H), 2.83 (s, 2 H), 2.56 (d, J = 7 Hz, 2 H), 0.95 (s, 9 H). ^{13}C-NMR ($CDCl_3$): *δ* 173.82 s, 173.50 s, 130.23 d, 121.10 t, 108.46 d, 79.95 s, 39.63 t, 38.20 t, 34.39 s, 23.61 q. MS *m/e*: 243, 225, 185, 129, 111, 87, 57, 41.

(2R,5S)-**12n**: ^{1}H-NMR ($CDCl_3$): 2.80 (s, 2 H), 2.50 (d, J = 6 Hz, 2 H), other signals are identical. ^{13}C-NMR ($CDCl_3$): 174.46 s, 173.36 s, 130.51 d, 120.64 t, 110.25 d, 79.95 s, 42.27 t, 39.64 t, 34.66 s, 23.61 q. (Found: C, 59.40; H, 7.41. Calc for $C_{12}H_{18}O_5$: C, 59.47; H, 7.49%.)

(2S,5S) - 5 - *Benzyl* - 2 - (*t* - *butyl*) - 5 - (*methoxycarbonyl*) - 1,3 - *dioxolan* - 4 - *one* (**12o**). Following the procedure used for **12m** 1.01 g (5 mmol) of *cis*-**2e** and 1.80 g (10 mmol) of benzyl bromide gave 1.12 g (77%) of **12o** (after recrystallziation from ether–pentane) (> 95% ds (a)), m.p. 136°. $[\alpha]_D^{25}$ + 65.3° (*c* = 1.1; $CHCl_3$). IR (KBr): 3300 m (br.), 2980 w, 1775 s, 1740 w, 1170 m cm^{-1}. ^{1}H.NMR ($CDCl_3$): *δ* 11.20 (br., s, 1 H); 7.29 (s, 5 H), 4.58 (s, 1 H), 3.10 (AB, J_{AB} = 14 Hz, 2 H), 2.80 (AB, J_{AB} = 15 Hz, 2 H), 0.86 (s, 9 H), MS *m/e*: 292, 235, 206, 162, 119, 57. (Found: C, 65.68; H, 6.90. Calc for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90%.)

1 - 5 - *Allyl* - 2 - (*t* - *butyl*) - 5 - *methyl* - 1,3 - *thioxolan* - 4 - *one* (**12p**). A soln of 1.74 g (10 mmol) of **2f** in 60 ml of THF was cooled to −78° and 10.5 ml of a 1 M LDA soln (THF–hexane 1:3) was added. After stirring for 30 min, allyl bromide (1.4 g, 12 mmol) was added and the temp was allowed to warm to −20°. After usual work up Kugelrohr

distillation afforded 1.97 g (92%) of **12p** (98% ds (a)) as a colourless liquid, b.p. 95°/0.5 mm Hg. IR ($CHCl_3$): 2960 s, 1750 s, 1280 m, 1135 m, 1040 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 6.23–5.56 (m, 2 H), 5.40–5.03 (m, 2 H), 5.16 (s, 1 H), 2.83–2.47 (m, 2 H), 1.56 (s, 3 H), 1.03 (s, 9 H). ^{13}C.NMR ($CDCl_3$): δ 176.62 s, 132.10 d, 120.16 t, 86.38 d, 54.70 s, 44.98 t, 35.07 s, 25.63 q, 24.85 q. MS *m/e*: 214, 173, 124, 100, 85, 59. (Found: C, 61.54; H, 8.43; S, 14.80. Calc for $C_{11}H_{18}O_2S$: C, 61.64; H, 8.42; S, 14.96%.)

(1'S,6R) - 3,8 - *Di* - (*t* - *butyl*) - 6 - [1' - *hydroxyethyl*] - 2,4,7,9 - *tetraoxabicyclo*[4,3,0]*nonan* - 5 - *one* (**13a**). To a stirred soln of 1.58 g (10 mmol) of *cis*-**2a** in 40 ml of THF at −78°, 5 ml of 1 M LDA soln in THF–hexane 1:3 was added. The temp was allowed to warm to −30° over a period of 2 hr. After usual work up and recrystallization from ether–pentane, 1.42 g (89%) of **13** was obtained as a pure diastereomer, m.p. 147°. $[\alpha]_D^{24}$ + 21.1° (*c* = 0.9; $CHCl_3$). IR (KBr): 3480 m (br.), 2970 m, 1775 s, 1180 m, 1045 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.32 (s, 1 H), 4.51 (s, 1 H), 4.34 (q, J = 6 Hz, 1 H), 3.06 (s, 1 H), 1.40 (s, 3 H), 1.33 (d, J = 6 Hz, 3 H), 0.95 (s, 9 H), 0.88 (s, 9 H). ^{13}C-NMR ($CDCl_3$): δ 172.40 s, 110.06 d, 109.81 d, 102.10 s, 83.10 s, 75.82 d, 34.52 s, 33.53 s, 24.07 q, 23.25 q, 18.86 q, 13.96 q. MS *m/e*: 315, 259, 158, 145, 87, 70. Mass determination gave 311. (Calc for $C_{16}H_{28}O_6$: 316.) (Found: C, 60.78; H, 9.02. Calc for $C_{16}H_{28}O_6$: C, 60.78; H, 8.92%.)

(1'S,6R) - 3,8 - 6 - *Benzyl* - 1 - (2' - *phenyl* - 1' - *hydroxyethyl*) - 3,8 - *di* - (*t* - *butyl*) - 2,4,7,9 - *tetraoxabicyclo*[4,3,0]*nonan* - 5 - *one* (**13b**). Chromatography (pentane–ether 2:1, R_f 0.38) of the residue from the distillation of **12l** gave the dimer **13b** in 20% yield. Subl. point: 209–211°. $[\alpha]_D^{20}$ − 38.9° (*c* = 1.40, $CHCl_3$). IR (KBr): 3450 s, br., 2980 s, 2960 s, 1770 s, 1150 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 7.26 (s, 5 H), 7.18 (s, 5 H), 5.30 (s, 1 H), 4.52 (s, 1 H), 3.33–2.94 (m, 5 H), 1.60 (s, 1 H), 0.93 (s, 9 H), 0.50 (s, 9 H). MS *m/e*: 411, 235, 91, 57. (Found: C, 71.27; H, 7.81. Calc for $C_{28}H_{36}O_6$: C, 71.77, H, 7.74%. Molecular weight: Found 460; Calc 468.)

(2R,5S) - 2 - (*t* - *Butyl*) - 5 - (*dimethylcarbamoylmethyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**19a**). From 1.58 g (10 mmol) of the enantiomer of *cis*-**2a** obtained from (R)-(−) lactic acid and 1.50 g (12 mmol) of N,N-dimethylchloroacetamide 1.85 g (76%) of **19a** (> 95% ds (a)) was obtained as colourless crystals after Kugelrohr distillation. M.p. 79°; b.p. 100°/0.05 mm Hg. $[\alpha]_D^{25}$ + 53.5° (*c* = 1.89; $CHCl_3$). IR ($CHCl_3$): 2970 m (br.), 1785 s, 1650 s, 1400 m, 990 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.43 (s, 1 H), 3.10–2.87 (m, 8 H), 1.50 (s, 3 H), 0.97 (s, 9 H). MS *m/e* 244, 243, 186, 140, 130, 72, 46. (Found: C, 59.42; H, 8.67; N, 5.86. Calc for $C_{12}H_{21}NO_4$: C, 59.24; H, 8.70; N, 5.76%.)

(2R,5R) - 5 - *Allyl* - 2 - (*t* - *butyl*) - 5 - (*methoxycarbonyl*) - 1,3 - *dioxolan* - 4 - *one* (**19d**). Allyl bromide (1.30 g, 10.5 mmol) and 1.01 g (5 mmol) of *trans*-**2e** gave 1.00 g (83%) of crude **19d**. $[\alpha]_D^{25}$ − 61.6° (*c* = 0.68; $CHCl_3$). All other physical data are identical with **12n**.

(2R,5R) - 5 - *Benzyl* - 2 - (*t* - *butyl*) - 5 - (*methoxycarbonyl*) - 1,3 - *dioxolan* - 4 - *one* (**19e**). From 1.01 g (5 mmol) of *trans*-**2e** and 1.80 g (10.5 mmol) of benzyl bromide 1.22 g (84%) of **19e** was obtained. $[\alpha]_D^{25}$ − 61.1° (*c* = 1.3, $CHCl_3$). All other physical data are identical with **12o**.

(2S,5R) - 2 - (*t* - *Butyl*) - 5 - (1' - *hydroxy* - 1' - *methylethyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**20a**). Acetone (1.16 g, 20 mmol) and 1.58 g (10 mmol) of *cis*-**2a** gave, after recrystallization from ether–pentane, 1.80 g (83%) of **20a** (> 95% ds (a)) as colourless crystals, m.p., 95°. $[\alpha]_D^{25}$ + 26.3° (*c* = 0.93; $CHCl_3$). IR (KBr): 2480 m (br.), 2970 m, 1770 s, 1355 m, 1155 m, 970 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.32 (s, 1 H), 1.94 (s, 1 H), 1.40 (s, 3 H), 1.36 (s, 3 H), 1.32 (s, 3 H), 0.93 (s, 9 H). MS *m/e*: 215, 158, 87, 85, 70, 57, 43. (Found: C, 60.97; H, 9.25. Calc for $C_{11}H_{20}O_4$: C, 61.08; H, 9.32%.)

(2S,5R) - 2 - (*t* - *Butyl*) - 5 - (1' - *hydroxycyclopentyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**20b**). Cyclopentanone (0.93 g, 11 mmol) and 1.58 g (10 mmol) of *cis*-**2a** gave after recrystallization from ether–pentane 2.06 g (85%) of **20b** (> 95% ds (a)) as colourless cyrstals, m.p. 85°. $[\alpha]_D^{24}$ + 9.3° (*c* = 1.68; $CHCl_3$). IR ($CHCl_3$): 3550 m (br.), 2940 s (br.), 1765 s, 1345 m, 1150 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.33 (s, 1 H), 2.00 (s, 1 H), 1.77 (br., s, 8 H), 1.51 (s, 3 H), 1.00 (s, 9 H). MS *m/e*: 158,139,111, 87, 70, 57, 43. (Found: C, 64.22; H, 9.15. Calc for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15%.)

(2S,5R) - 2 - (*t* - *Butyl*) - 5 - *methyl* - 5 - (1' - *hydroxydiphenylmethyl*) - 1,3 - *dioxolan* - 4 - *one* (**20c**). Benzophenone (1.91 g, 10 mmol) and 1.58 g (10 mmol) of *cis*-**2a** gave after recrystallization from ether–pentane, 2.97 g (87%) of **20c** (> 95% ds (a)) as colourless crystals, m.p. 90°. $[\alpha]_D^{25}$ + 88.7° (*c* = 0.73, $CHCl_3$). IR ($CHCl_3$): 3500 m (br.), 2940 m (br.), 1755 s, 1140 s, 1030 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 7.93–7.16 (m, 10 H), 4.36 (br., s, 1 H), 4.13 (s, 1 H), 1.63 (s, 3 H), 0.89 (s, 9 H). MS *m/e*: 340, 209, 183, 158, 105, 77, 57, 43. (Found: C, 73.99; H, 7.08. Calc for $C_{21}H_{24}O_4$: C, 74.04; H, 7.11%.)

(1'S,2S,5R) - 2 - (*t* - *Butyl*) - 5 - (1' - *hydroxyethyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**21a**). Acetaldehyde (0.9 g, 20 mmol) and 1.58 g (10 mmol) of *cis*-**2a** were used and gave, after Kugelrohr distillation, 1.66 g (84%) of **21a** (82% ds (a)) as a colourless liquid. B.p. 90°/0.005 mm Hg. $[\alpha]_D^{25}$ + 23.5° (*c* = 1.71; $CHCl_3$). IR ($CHCl_3$): 3600 w (br.), 2960 m, 1775 s, 1150 s, 1075 m, 980 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.40/5.23 (s, 1 H), 4.01 (m, 1 H), 2.66/2.40 (br., s, 1 H), 1.40/1.33 (d, J = 10 Hz, 3 H), 1.00 (s, 9 H). MS *m/e*: 203, 158, 145, 89, 87, 70, 57. (Found: C, 59.44; H, 9.10. Calc for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97%.)

(1'S,2S,5R) - 2 - (*t* - *Butyl*) - 5 - (1' - *hydroxypropyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**21b**). Propanal (0.87 g, 15 mmol) and 1.58 g (10 mmol) of *cis*-**2a** gave, after Kugelrohr distillation, the product **21b** (1.73 g, 80%) as a colourless liquid (83% ds (a)). It was not possible to separate the two diastereomers by distillation or chromatography, b.p. 120°/0.03 mm Hg. $[\alpha]_D^{20}$ + 16.3° (*c* = 0.95, $CHCl_3$). IR (film): 3500 s, br., 2980 s, 1785 s, 1485 s, 985 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.32/5.16 (s, 1 H), 3.50–3.80 (m, 1 H), 2.18–2.60 (m, 1 H), 1.50–1.53 (m, 2 H), 1.40/1.32 (s, 3 H), 0.94–1.10 (t, J = 8 Hz, 3 H), 0.92 (s, 9 H). MS *m/e*: 218, 217, 158, 70, 57. (Found: C, 60.75; H, 8.99. Calc for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32%.)

(2S,5R) - 2 - (*t* - *Butyl*) - 5 - (1' - *hydroxy* - 2',2' - *dimethylpropyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**21c**). From 1.58 g (10 mmol) of *cis*-**2a** and 1.12 g (13 mmol) of pivalaldehyde 2.02 g (83%) of **21c** (53% ds (a)) was obtained after recrystallization from ether–hexane as colourless crystals, m.p. 43–46°. $[\alpha]_D^{25}$ + 19.6° (*c* = 1.02; $CHCl_3$). IR ($CHCl_3$): 3500 m (br.), 2900 s (br.), 1765 s, 1350 m, 1140 m, 975 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.39/5.26 (s, 1 H), 3.57/3.51 (s, 1 H), 2.70 (br., s, 1 H), 1.51 (d, J = 5 Hz, 3 H), 1.09 (s, 9 H), 0.99 (s, 9 H). MS *m/e*: 245, 187, 158, 87, 70, 57, 43. (Found: C, 63.67; H, 9.89. Calc for $C_{13}H_{24}O_4$: C, 63.91; H, 9.90%.)

(2S,5R) - 2 - (*t* - *Butyl*) - 5 - (1' - *hydroxy* - 3' - *phenyl* - 2' - *propenyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**21d**). Cinnamaldehyde (2.0 g, 15 mmol) and 1.5 g (9.5 mmol) of *cis*-**2a** gave after Kugelrohr distillation **21d** (6.5 mmol, 68%) as a yellow resin (60% ds (a)). B.p. 160–170°/0.01 mm Hg. $[\alpha]_D^{20}$ + 45.66° (*c* = 1.30, $CHCl_3$). Three recrystallizations (ether–pentane 1:1, −30°) gave 0.96 g (35%) of the major diastereomer (> 95% (a)) as colourless crystals; m.p. 136–137°. $[\alpha]_D^{20}$ + 101.2° (*c* = 1.00; $CHCl_3$). The mother liquor gave 0.65 g (23%) of a diastereomeric mixture with the minor diastereomer in excess (66% ds (a)) as colourless crystals: m.p. 112–117°.$[\alpha]_D^{20}$ + 10.8° (1.10, $CHCl_3$). IR (KBr): 3480 s, 2960 m, 1770 s, 1370 s, 1360 s, 1200 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 7.25–7.45 (m, 5 H), 6.10–6.75 (m, 2 H), 5.45/5.40 (s, 1 H); 4.35–4.50 (m, 1 H), 2.10–2.14 (d, J = 4 Hz, 1 H), 1.40 (s, 2 H), 1.34 (s, 1 H), 0.94 (s, 9 H). MS *m/e*: 291, 290, 158, 133, 57. (Found: C, 70.23; H, 7.53. Calc for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64%.)

(1'S,2S,5R) - 2 - (*t* - *Butyl*) - 5 - (1' - *hydroxy* - 1' - *phenylmethyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**21e**). Benzaldehyde (1.1 g, 10 mmol) and 1.58 g (10 mmol) of

cis-**2a** were used and gave, after flash-chromatography, 2.25 g (85%) of **21e** (84% ds (a)) as colourless crystals, m.p. 88–95°. R_f (ether–pentane = 3:1): 0.3. $[\alpha]_D^{25} + 31.1°$ ($c = 0.83$; $CHCl_3$). IR ($CHCl_3$): 3550 m (br.), 2900 m (br.), 1770 s, 1345 m, 1135 s, 975 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 7.34 (s, 5 H), 5.35/4.83 (s, 1 H), 5.13/4.77 (s, 1 H), 2.45 (s, br., 1 H), 1.40 (s, 3 H), 0.93/0.88 (s, 9 H). MS *m/e*: 158, 133, 87, 70, 57, 43. (Found: C, 68.06; H, 7.73. Calc for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63%.)

(1'S,2S,5R) - 2 - (*t* - *Butyl*) - 5 - (1' - *hydroxy* - 1' - *mesitylmethyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**21f**). From mesitaldehyde (0.9 g, 6 mmol) and 0.9 g (5.6 mmol) of *cis*-**2a** 1.2 g (69%) of **21f** was obtained as a yellow resin (78% ds (a)). B.p. 120°/0.005 mm Hg. $[\alpha]_D^{20} + 97.7°$ ($c = 1.10$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): δ 6.79–6.84 (br., d, J = 5 Hz, 2 H), 5.52/4.40 (s, 1 H), 5.46 (br., s, 1 H), 3.07 (s, 3 H), 2.31 (s, 3 H), 2.23 (s, 3 H), 2.13 (s, 1 H), 1.60/1.20 (s, 3 H), 0.91/0.83 (s, 9 H). ^{13}C-NMR ($CDCl_3$): δ 176.60/174.84, 138.76, 137.44, 136.97, 131.88, 131.16, 130.17, 129.05, 110.69/109.51, 84.65/84.47, 75.44, 73.62, 34.15/34.32, 23.31/23.20, 21.87/21.33, 20.60. Two recrystallizations of the diastereomeric mixture gave 0.55 g (32%) of the major diastereomer with >99% ds (a): m.p. 138–139°. $[\alpha]_D^{20} + 118.4°$ ($c = 1.70$, $CHCl_3$). IR (KBr): 3575 s, 3440 s, 2980 s, 1780 s, 1760 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 6.79–6.84 (br., d, J = 5 Hz, 2 H), 5.52 (s, 1 H), 5.44 (d, J = 4 Hz, 1 H), 3.07 (s, 3 H), 2.31 (s, 3 H), 2.18 (s, 1 H), 2.23 (s, 3 H), 1.20 (s, 3 H), 0.91 (s, 9 H). MS *m/e*: 307, 306, 158, 149. (Found: C, 70.52; H, 8.45. Calc for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55%.)

(1'S,2S,5R) - 2 - (*t* - *Butyl*) - 5 - (1' - *hydroxy* - 1' - *phenylethyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**22**). From 1.58 g (10 mmol) of *cis*-**2a** and 1.32 g (11 mmol) of acetophenone in 10 ml THF 2.25 g (81%) (93% ds (a)) was obtained after recrystallization from ethanol–water, m.p. 91–98°. $[\alpha]_D^{25} + 51.2°$ ($c = 1.2$; $CHCl_3$). IR ($CHCl_3$): 3540 m (br.), 2950 m (br.), 1770 s, 1140 s, 1070 m, 980 m cm^{-1}. ^{1}H-NMR($CDCl_3$): δ 7.60–7.10 (m, 5 H), 5.03/4.63 (s, 1 H), 2.93 (br., s, 1 H), 1.70/1.63 (s, 3 H), 1.36 (s, 3 H), 0.85 (s, 9 H). ^{13}C-NMR ($CDCl_3$): δ 174.60 s, 142.67 s, 127.98 d, 127.67 d, 126.26 d, 109.89 d, 84.65 s, 77.32 s, 34.71 s, 25.24 q, 23.25 q, 20.17 q. MS *m/e*: 173, 158, 121, 87, 70, 57, 43. (Found: C, 69.04; H, 8.05. Calc for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97%.)

2 - (*t* - *Butyl*) - 5 - (1' - *hydroxy* - 2' - *cyclohexenyl*) - 5 - *methyl* - 1,3 - *dioxolan* - 4 - *one* (**23**). To a cold soln of the enolate of *cis*-**2a** (1.58 g, 10 mmol), prepared according to the procedure for **12p**, 1.06 g (11 mmol) of 2-cyclohexenone was added. After 30 min stirring at dry ice temp, the mixture was worked up in the usuall manner. Flash-chromatography afforded 1.76 g (65%) of **23** (76% ds (a)) as a mixture of two diastereomers. 1,4-addition products were not observed. IR ($CHCl_3$): 3600 w, 2960 s, 1750 s, 1290 m, 1040 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 6.30–5.96 (m, 1 H), 5.80/5.66 (s, 1 H), 5.30/5.24 (s, 1 H), 2.70 (br., s, 1 H), 2.32–1.50 (m, 6 H), 1.55 (s, 3 H), 1.03 (s, 9 H). ^{13}C-NMR ($CDCl_3$): δ 176.11/176.82 s, 134.45/133.57 d, 128.42/127.46 d, 87.68/87.55 d, 75.00/74.92 s, 64.03 s, 35.24 s, 31.65/30.93 q, 25.11 t, 24.86 q, 23.35 t, 18.55 t. MS *m/e*: 252, 174, 117, 89, 68, 57, 41. (Found: C, 62.25; H, 8.41; S, 11.69. Calc for $C_{14}H_{22}O_3S$: C, 62.19; H, 8.20; S, 11.86%.)

(2R,5S) - 2 - (*t* - *Butyl*) - 6,6 - *dimethyl* - 1,3,7 - *trioxaspiro*[4.4]*nonan* - 4,8 - *dione* (**24**). To a soln of enolate **14** (5 mmol), prepared from the enantiomer of *cis*-**2e** according to procedure for **12m**, at −78° 0.40 g (7 mmol) of acetone in 5 ml of THF was added. Kugelrohr distillation gave 0.69 g (53%) of **24** (70% ds). After one recrystallization from ether–pentane 0.37 g of pure **24** was obtained (> 95% ds (a)), b.p. 100°/0.2 mm Hg, m.p. 97° $[\alpha]_D^{25} + 34.8°$ ($c = 0.8$; $CHCl_3$). IR (KBr): 2970 m, 1775 s, 1260 s, 1205 m, 1120 m, 1075 m. ^{1}H-NMR ($CDCl_3$): δ 5.23 (s, 1 H), 3.00 (AB, J_{AB} = 18 Hz, 2 H), 1.54 (s, 3 H), 1.51 (s, 3 H), 0.97 (s, 9 H). MS *m/e*: 243, 184, 156, 87, 57, 43. (Found: C, 59.50; H, 7.52. Calc for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49%.) Minor diastereomer: ^{1}H-NMR ($CDCl_3$): 5.13 (s, 1 H), 2.95 (AB, J_{AB} = 18 Hz, 2 H), 1.57 (s, 3 H). The other signals were identical with those of the main diastereomer.

(2R,5S,6R) - 2,6 - *Di* - (*t* - *butyl*) - 1,3,7 - *trioxaspiro*[4.4]*nonan* - 4,8 - *dione* (**25**). From 1.01 g (5 mmol) of *cis*-**2e** and 0.52 g (6 mmol) of pivalaldehyde (for procedure see **24**) 0.97 g (72%) of **25** (> 95% ds (a)) was obtained after sublimation (80°/0.01 mm Hg), m.p. 129°. $[\alpha]_D^{25} - 31°$ ($c = 1.2$, $CHCl_3$). IR (KBr): 2960 m, 1800 s, 1780 s, 1260 m, 1195 m, 1130 m, 1030 m cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.30 (s, 1 H), 4.28 (s, 1 H), 2.92 (AB, J_{AB} = 18 Hz, 2 H), 1.06 (s, 9 H), 0.94 (s, 9 H). ^{13}C-NMR ($CDCl_3$): δ 171.07 s, 171.00 s, 110.04 d, 90.22 d, 83.08 s, 42.42 t, 35.04 s, 33.97 s, 25.95 q, 23.06 q. MS *m/e*: 270, 184, 156, 86, 57, 41. (Found: C, 62.21; H, 8.18. Calc for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20%.)

(2S) - 2 - (*t* - *Butyl*) - 5 - *methyl* - 4 - (*trimethylsilyloxy*) - 1,3 - *dioxa* - 4 - *cyclopentene* (**26a**). *cis*-**2a** (1.58 g, 10 mmol) was added to a soln of 10.5 mmol of LDA in 70 ml of THF–hexane 9:1 at −78°. After 30 min at −78°, 1.32 g (12 mmol) of chlorotrimethylsilane was added and the temp was allowed to warm up to room temp and stirring continued for an additional hr. The solvent was removed by evaporation. The residue, which was fairly pure apart from the presence of lithium chloride, was directly used without further purification, due to the high sensitivity of **26a** to hydrolysis as well as to thermolysis. ^{1}H-NMR ($CDCl_3$): δ 5.16 (s, 1 H), 1.70 (s, 3 H), 0.92 (s, 9 H), 0.20 (s, 9 H) ($CHCl_3$ as internal standard).

(2S) - 2 - (*t* - *Butyl*) - 4 - (*t* - *butyldimethylsilyloxy*) - 5 - *methyl* - 1,3 - *dioxa* - 4 - *cyclopentene* (**26b**). To a soln of 10.5 mmol of LDA in 70 ml of THF–hexane 9:1 T −78° *cis*-**2a** (1.58 g, 10 mmol) was added. After stirring for 15 min, the soln was quenched by the addition of 1.6 g (10.6 mmol) of t-butylchlorodimethylsilane in 10 ml of THF. Within *ca* 1 hr, the temp was raised to room temp and stirring was continued for an additional hr. The reaction soln was poured onto 100 ml of ice cold water and extracted twice with 100-ml portions of ether. Drying over $MgSO_4$ and evaporation of the solvents *in vacuo* gave 2.45 g (90%) of fairly pure **26b** as a colourless liquid. Attempted distillation and chromatography resulted in decomposition of the product. ^{1}H-NMR ($CDCl_3$): δ 5.14 (s, 1 H), 1.72 (s, 3 H), 0.90 (s, 18 H), 0.14 (s, 6 H) ($CHCl_3$ as internal standard).

(2S,5R,2'S,5'R) - 5 - [3' - (*t* - *Butyl* - 1' - *methyl* - 5 - *oxo* - 2',4' - *dioxolanyl*] - 2 - (*t* - *butyl*) - 5 - *methyl* - 1,3 - *dioxolan*-5 - *one* (**27**). A suspension of 5.7 g (30 mmol) of titanium tetrachloride in 5 ml of CH_2Cl_2 and 2.7 g (30 mmol) of trioxane (which proved to be essential for the dimerisation although originally it was meant to achieve hydroxymethylation of the ketene acetal) was cooled to −78° and the crude trimethylsilyl ketene acetal **26a** (*ca* 10 mmol, *cf* formation of **26a**) dissolved in 10 ml of CH_2Cl_2 was added (also cooled to −78°). The resulting deep green mixture was stirred for 3 hr at −78° and then hydrolysed by the addition of 100 ml of H_2O. Extraction of the purple soln with ether, washing of the combined organic layers with H_2O, drying ($MgSO_4$) and removal of the solvent afforded, after Kugelrohr distillation, 0.94–1.10 g (60–70%) (> 95% ds (a)) of **27** as colourless crystals which was recrystallized from ether–pentane (1:1): m.p. 123–125°; b.p. 120°/0.03 mm Hg. $[\alpha]_D^{20} + 52.9$ ($c = 1.95$, $CHCl_3$). IR (KBr): 2960 s, 2910 s, 1790 s, 1480 s, 1200 s cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 5.12 (s, 2 H), 1.62 (s, 6 H), 0.92 (s, 18 H). ^{13}C-NMR ($CDCl_3$): δ 171.47, 110.50, 83.06, 34.97, 23.30, 19.44. MS *m/e*: 315, 257, 158, 57. (Found: C, 61.11; H, 8.36. Calc for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34%.) Molecular weight: Found 317. Calc for $C_{16}H_{26}O_6$: 314.

Configural correlations

(2R)-2-*Hydroxy*-2-*methyl*-*butanoic acid* (**3**). Alkaline hydrolysis of **12a** and recrystallization of the crude product gave the pure **3**, m.p. 72–73°; $[\alpha]_D^{25} - 6.6°$ ($c = 1.4$, 0.2 N NaOH). *Cf.* lit.[25]: m.p. 73.5°; $[\alpha]_D - 6.9°$

(*R*)-(+)-2-*Methyl*-1,3-*butandiol* (**4**). LAH reduction of

12a gave the diol **4**. B.p. 105°/14 mm Hg. $[\alpha]_D^{20} + 8.7°$ ($c = 1.35$, $CHCl_3$), *cf.* lit.[26]: $[\alpha]_D^{22} + 5.9$ (ee 49%).

(R)-(+)-*2-Methyl-1,2-hexandiol* (**5**). LAH reduction of **12c** gave the diol **5**. B.p. 140°/15 mm Hg. $[\alpha]_D^{20} + 4.4$ ($c = 0.97$, $CHCl_3$), *cf* lit.[27]: $[\alpha]_D^{27}$: $[\alpha]_D + 4.0$.

(2R,3S) - 2,3 - *Dihydroxy* - 2 - *methylpentanoic acid* (**6**). Acidic hydrolysis of **21b** (86% ds) and recrystallization of the crude product to constant m.p. and $[\alpha]_D$ gave the pure (2*R*,3*S*)-diastereomer **6**, m.p. 105–106°, $[\alpha]_D^{20} - 24.0°$ ($c = 1.00$, H_2O). The (2*R*,3*R*)-isomer has a m.p. of 149–151° and an $[\alpha]_D$-value of +13°.[28]

(R)-(+)-*Frontalin* (**7**). Synthesis from *S*-(+)-lactic acid and refs are described in 1*c*. $[\alpha]_D^{25} + 53.45°$ ($c = 2.17$; ether), *cf* lit.[41]: $[\alpha]_D + 53.4°$.

2-*Hydroxy*-2-*methylsuccinic acid* (**10**). Acidic hydrolysis of **12m** gave **10** as a noncrystallizable resin. $[\alpha]_D^{25} + 20.8°$ ($c = 2.9$; H_2O), *cf* lit. [31]: m.p. 112°. $[\alpha]_D + 23.6°$ ($c = 3.0$; H_2O).

Acknowledgements—We gratefully acknowledge financial support by the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung and by the Sandoz AG (Basel). The following companies generously supplied chemicals: BASF AG (Ludwigshafen) [pivalaldehyde], Degussa (Hanau) [phenyllactic acid], Hoechst AG (Frankfurt–Hoechst) [pivalaldehyde, Cl-containing solvents], Ruhrchemie AG (Oberhausen) [pivalaldehyde]. We thank the following gentlemen for performing some of the experiments: A. Bernhard, S. Ebner, G. Huber, G. Steiner. The NOE measurements were done by F. Bangeter, the elemental analyses and the osmometric measurements of mol weights were carried out by D. Manser.

REFERENCES

[1]Previous and other papers on this subject are: [a]D. Seebach and R. Naef, *Helv. Chim. Acta* **64**, 2704 (1981); [b]D. Seebach, M. Boes, R. Naef and W. B. Schweizer, *J. Am. Chem. Soc.* **105**, 5390 (1983); [c]R. Naef and D. Seebach, *Liebigs Ann. Chem.* 1983, 1930; [d]R. Naef and D. Seebach, *Helv. Chim. Acta*, in preparation.

[2]D. Seebach and E. Hungerbühler, *Modern Synthetic Methods* 1980 (Edited by R. Scheffold), Vol. 2, pp. 91–171. Salle + Sauerländer, Aarau, Switzerland (1980).

[3]Part of the Ph.D. thesis of R.N., ETH Zürich, No. 7442, 1983.

[4]Partly from the Master's Thesis of G.C.

[5]D. Seebach and H.-O. Kalinowski, *Nachr. Chem. Tech.* **24**, 415 (1976).

[6]C. H. Halten, *Lactic Acid.* Verlag Chemie, Weinheim (1971).

[7]M. A. K. Patterson, R. P. Szajewski and G. M. Whitesides, *J. Org. Chem.* **46**, 4682 (1981), in preparation.

[8a]E. Hungerbühler, D. Seebach and D. Wasmuth, *Helv. Chim. Acta* **64**, 1467 (1981); [b]H. Wynberg and E. G. Staring, *J. Am. Chem. Soc.* **104**, 166 (1982).

[9]P. Barre, *Ann. Technol. Agr.* **15**, 203 (1966).

[10]H. Arakawa, *Naturwissenschaften* **50**, 441 (1963).

[11a]A. Neuenberger, *Advances in Protein Chemistry* (Edited by M. L. Anson and J. T. Edsall), Vol. 4, p. 333. Academic Press, New York (1948); [b]P. Brewster, F. Hiron, E. D. Huges, C. K. Ingold and P. A. D. S. Rao, *Nature* **166**, 179 (1950).

[12]For a general discussion and review about transformations leading to products with quarternary centers see: [a]S. F. Martin, *Tetrahedron* **36**, 419 (1980); for more recent examples see: [b]K. Tomioka, Y.-S- Cho, F. Sato and K. Koga, *Chem. Lett.* 1621 (1981); [c]D. Seebach and L. Widler, *Helv. Chim. Acta* **65**, 1972 (1982).

[13]See for instance: [a]E. L. Eliel, J. K. Koskimies and B. Lohri, *J. Am. Chem. Soc.* **100**, 1614 (1978); [b]Y. Sakito and T. Mukayama, *Chem. Lett.* 1027 (1979).

[14]Examples are found in: [a]R. Méric and J. P. Vigneron, *Bull. Soc. Chim. France* 327 (1973); [b]S. Jarosz, D. R. Hicks and B. Fraser-Reid, *J. Org. Chem.* **47**, 935 (1982).

[15a]Acetonide of tartaric esters: R. Naef and D. Seebach, *Angew. Chem.* **93**, 1113 (1981); *Ibid. Int. Ed. Engl.* **20**, 1030 (1981); [b]Malic ester: D. Seebach and D. Wasmuth, *Helv.Chim. Acta* **63**, 197 (1980); [c]D. Wasmuth, D. Arigoni and D. Seebach, *Ibid.* **65**, 344 (1982); [d]β-Hydroxy–butyric ester: M. Züger, Th. Weller and D. Seebach, *Ibid.* **63**, 2005 (1980); [e]N-Formylaspartic ester: D. Seebach and D. Wasmuth, *Angew. Chem.* **93**, 1007 (1981); *Ibid. Int. Ed. Engl.* **20**, 971 (1981).

[16](*S*)-Lactic acid was also condensed with benzaldehyde and with 2-ethylbutanal. In the first case, a 2.5:1 mixture of (2S,5S)-5-methyl-2-phenyl-1.3-dioxolan-4-one and the (2*R*)-epimer was formed. Recrystallization from ether pentane gave the pure *cis*-isomer (m.p. 46°, $[\alpha]_D^{20} - 9.30$ ($c = 3.4$; $CHCl_3$)). In the second case, a 2:1 mixture of isomers was formed which was benzylated ($C_6H_5CH_2Br$) with 78% diastereoselectivity. Mandelic acid and benzaldehyde were also condensed to give a 1:1 mixture of *cis*- and *trans*-2,5-diphenyl-1,3-dioxolan-4-one which was deprotonated to the corresponding racemic enolate and methylated (MeI) with 83% ds. Recrystallization of the 1:1 mixture of the non-methylated diphenyl–dioxolanones gave one pure isomer (m.p. 84°; $[\alpha]_D^{25} + 66.6°$ ($c = 0.77$; $CHCl_3$).

[17]Prepared from valine: C. G. Barker *et al.*, *J. Am. Chem. Soc.* **73**, 1336 (1951).

[18]The (3:2)-ratio is that of the equilibrium mixture obtained if the acetalization is carried out in benzene. The heterogeneous conditions of acetalization in pentane produce the pure *cis*-isomer which epimerizes upon warming to 80°.

[19]This compound was employed as a racemic mixture. For resolution of thiolactic acid and of thiomalic acid, see Refs. 20 and 21, respectively.

[20]J. M. Lovén, *J. prakt. Chem.* **78**, 63 (1908).

[21]A. Fredga, *Arkiv Kemi* **B14**, no. 27 (1941).

[22]In this case, the mixture of diastereomers could not be separated by crystallization.

[23]D. Seebach and V. Prelog, *Angew. Chem.* **94**, 696 (1982); *Ibid. Int. Ed. Engl.* **21**, 654 (1982).

[24]K. Pilgram and M. Zupan, *J. Heterocyclic Chem.* **14**, 1035 (1977).

[25]W. Christen and A. Kjaer, *Acta Chem. Scand.* **16**, 2466 (1962).

[26]W. Kirmse, H. Arrold and B. Kornrumpf, *Chem. Ber.* **109**, 1783 (1971).

[27]R. Pappo *et al.*, *Chemistry, Biochemistry and Pharmacological Activity of Prostanoids* (Edited by M. Standley, R. and F. Scheinmann). Pergamon Press, Oxford (1979).

[28]R. M. Smith *et al.*, *Tetrahedron Letters* 1029 (1970).

[29]G. Fráter, U. Müller and W. Günther, *Tetrahedron Letters* 4221 (1981).

[30]These correlations were carried out by G. Fráter *et al.* (see Ref. 29) who have done some similar experiments to those described here. See also: [a]A. McKenzie and G. W. Clogh, *J. Chem. Soc.* **97**, 1016 (1910); [b]A. I. Meyers and J. Slade, *J. Org. Chem.* **45**, 2785 (1980).

[31a]H. A. Barker and A. H. Blair, *Biochem. Preparations* **9**, 21 (1962); [b]P. A. Stadler, A. J. Frey and A. Hofmann, *Helv. Chim. Acta* **46**, 2300 (1963).

[32]We also prepared the γ-lactone derived from 4-hydroxy-5,5-dimethylhexanoic acid, the analogue of **2** without the second ring oxygen. Its enolate was methylated with 96% ds, i.e. with the same degree of selectivity as that derived from **2**.

[33]The achiral enolates of 2,2,5-trimethyl-1,3-dioxolan-4-one and -1,3-thioxolan-4-one have been used previously [A. Schultz and Y. Yee, *J. Org.Chem.* **41**, 4044 (1976)], there is however no statement about the diastereoselectivity with which they add to cyclohexenone in a 1,2- or 1,4-fashion. For other achiral α-heterosubstituted enolates see: [a]R. Lohmar and W. Steglich, *Chem. Ber.* **113**, 3706 (1980) and

earlier papers in this series; [b]K. Rühlmann, K. Kaufmann and K. Ickert, *Z. Chem.* **10**, 392, 393 (1970); [c]K. Rühlmann and G. Kuhrt, *Angew. Chem.* **80**, 797 (1968); *Ibid. Int. Ed. Engl.* 7, 809 (1968); [d]P. Bey and J. Vevert, *Tetrahedron Letters* 1455 (1977); [e]K. Shepard and J. Stevens, *J. Chem. Soc.*, Chem. Commun. 951 (1971); [f]M. Touzin, *Tetrahedron Letters* 1477 (1975); [g]W. Adam, L. Encarnacion and H. Fick, *Synthesis* 828 (1978); [h]A. Duggan, M. Adams, P. Brynes and J. Meinwald, *Tetrahedron Letters* 4323 (1978); *Ibid.* 4327 (1978); [i]L. Ciochetto, D. Bergbreiter and M. Newcomb, *J. Org. Chem.* **42**, 2948 (1977); [k]M. Newcomb and D. Bergbreiter, *Ibid.* **42**, 3963 (1978).

[34]These reactions were conducted under the usual conditions, they are not described in the experimental section. Details are avialable as supplementary material from the authors. The primary HO-group of the diol from the LAH reduction was tosylated (pyridine–TosCl, 0°) and the filtered solution treated with KOH in MeOH–H_2O at 20°.

[35]The achiral enolates of esters of RO-protected lactic acid also add highly diastereoselectively (85 to > 97% ds) to various aldehydes: C. H. Heathcock *et al.*, *J. Am. Chem. Soc.* **103**, 4972 (1981).

[36]For a recent review article see: M. T. Reetz, *Angew. Chem.* **94**, 97 (1982); *Ibid. Int. Ed. Engl.* **21**, 96 (1982).

[37]T. Mukaiyama and M. Hayashi, *Chem. Lett.* 15 (1974).

[38]Other examples of oxidative coupling of silyl–enol–ethers by $TiCl_4$ are: [a]T. H. Chan and I. H. M. Wallace, *Tetrahedron Letters* 799 (1982); [b]S. Inaba and I. Ojima, *Ibid.* 2009 (1977); [c]K. Hirai and I. Ojima, *Ibid.* 785 (1983).

[39]Review articles on the use of titanium, zorconium and vanadium derivatives in organic synthesis: D. Seebach, B. Weidmann and L. Widler, In *Modern Synthetic Methods* 1983 (Edited by R. Scheffold), Vol. 3, p. 217. Salle Sauerländer, Aarau, Switzerland and Wiley, New York (1983); D. Seebach, A. K. Beck, M. Schiess, L. Widler and A. Wonnacott, *Pure & Appl. Chem.* **55**, 1807 (1983).

[40]W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.* **43**, 2923 (1978).

[41]K. Mori, *Tetrahedron* **31**, 1381 (1975).