Asymmetric Nucleophilic Acylation of Aldehydes via 1,1-Heterodisubstituted Alkenes

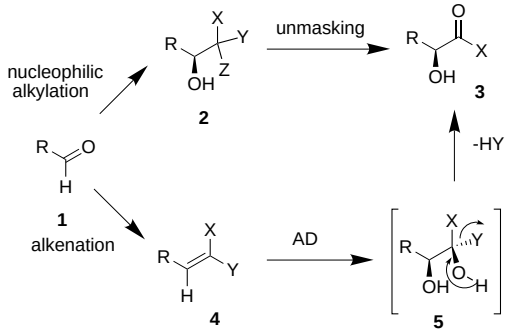
Holger Monenschein, Gerald Dräger, Alexander Jung, and Andreas Kirschning*[a]

Abstract: Aldehydes are asymmetrically acylated by a two step sequence that is initiated by a homologation step to 1,1-heterodisubstituted alkenes followed by asymmetric dihydroxylation. Thus, ketene *O*,*S*-acetals are efficiently prepared from aldehydes by a Peterson olefination with lithiated methoxy-phenylthiotrimethylsilyl methane **14** as the C-1 source. Although they are dihydroxylated with the Sharpless catalyst with moderate to good enantioselectivity (62–80% *ee*), the process is not efficient owing to the low chemical yields of the desired α-hydroxy methyl esters (7–37%). Use of the corresponding sulfoxide **24** or sulfon **25** led to an improved chemical yield of α-hydroxy methyl ester **19**, but the stereoselectivity was diminished. In contrast, intermediate ketene *O*,*O*-acetals are prepared by a Horner–Wittig reaction with phosphine oxide **31** and are dihydroxylated both with good chemical and stereochemical yield. The concept is applicable to aromatic, aliphatic, and chiral aldehydes. For example, this short sequence allows exclusive and independent preparation of both diastereomeric heptoses **69a** and **69b**.

Keywords: aldehydes · asymmetric synthesis · C–C coupling · dihydroxylations · Wittig reactions

Introduction

Homologation of aldehydes by the use of various C nucleophiles is a key transformation in organic synthesis.[1] Appropriate substitution of the nucleophilic carbanion with two or three heteroatoms (X–Z) leads to *masked* formyl-anion equivalents. In the presence of aldehydes **1**, these carbanions can be used for the preparation of masked α-hydroxy aldehydes, carboxylic acids, or esters **2**, which subsequently have to be unmasked to give **3** (Scheme 1). The most commonly used heteroatoms for these d^1 synthons are sulfur,[2] tin,[3] and to a lesser extent silicon[4] in some cases in connection with oxygen substituents.[5] Additionally, the carbanion can be stabilized by nitrogen,[6] which is often part of a heterocycle, namely in benzothiazole[7] or 2-trimethylsilyl-thiazole.[8] Control of the configuration of the newly formed stereogenic center at C-2 as well as liberation of the aldehyde from the primary adducts are still the major challenges for all methods developed so far. One strategy for performing the acylation of aldehydes in an asymmetric mode uses an α-positioned chiral center in the substrate (substrate control).[9] In particular Dondoni and co-workers elegantly applied this approach, using substituted thiazoles as formyl-anion equivalents.[10] Alternatively, when chiral formyl-anion equivalents are employed (reagent control) more stereochemical flexibility is gained because achiral aldehydes can be used and both stereochemical series become principally accessable. Typical examples for this strategy are the use of C_2-symmetric *trans*-1,3-dithiane *S*,*S*-dioxides,[11] chiral *O*,*S*-acetals,[12] and amino cyanides $\{[R^1C(NR^*_2)CN]^-[M]^+\}$ or formaldehyde SAMP-hydrazones.[13] Corey and Jones described a very different three step approach by utilizing a nucleophilic chiral alkinylmethyl borane in an addition reaction with aldehydes. After protection and ozonolysis of the resulting 1,2-dienyl carbinols, α-hydroxyaldehydes are generated in up to 99% *ee*. However, these reagent-based strategies are often hampered by irreversible loss of the chiral auxiliary.



Scheme 1. Concepts of asymmetric acylations of aldehydes.

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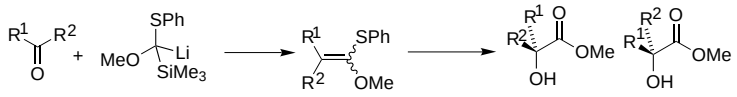
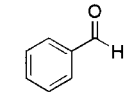
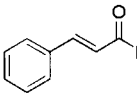
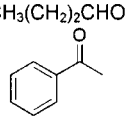
Recently, we disclosed a new acylation concept[15] that circumvents most of the drawbacks described for the classical approaches via intermediate **2**. The fundamental difference lies in the fact that homologation and build-up of the stereogenic center at C-2 are separated in time. This new strategy utilizes a formyl-anion equivalent that in the reaction with aldehydes affords a prochiral 1,1-heterodisubstituted alkene **4**. Now, the stage is set for asymmetrically introducing the hydroxy group at C-2, by the means of the Sharpless asymmetric dihydroxylation (AD).[16] The intermediate diol **5** formed spontaneously collapses to the corresponding α-hydroxy ester **3** if the vinylic substituents X and Y have leaving-group properties. This report presents detailed investigations with various 1,1-heterodisubstituted alkenes as intermediates and improvements of the general concept.

Table 1. Asymmetric acylation of aldehydes **7**, **11**, **12**, and ketone **13** via ketene *O*,*S*-acetals: yields, configurations and enantioselectivities.



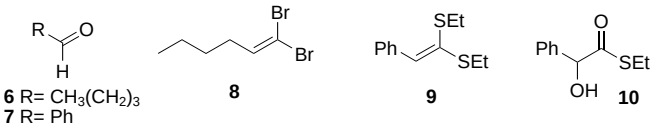
7, **11**-**13** **14** **15**-**18** **19**-**22**

Aldehyde (Ketone)		Ketene *O*,*S*-acetal (yield) [%][a] (*E*:*Z* ratio)[b]	Hydroxyester (yield) [%][a]	AD-mix α[(DHQ)$_2$PHAL]		AD-mix β[(DHQD)$_2$PHAL]	
				ee[%]	config	*ee*[%]	config
	**7**	**15** (97, 2 : 1)	**19** (37)	76.8	2 *S*	80.0	2 *R*
	**11**	**16** (89, 1 : 4)	**20** (30)	75.0	2 *S*	80.3	2 *R*
$CH_3(CH_2)_2CHO$	**12**	**17** (99, 1 : 1)	**21** (7)	62.3	2 *S*	72.8	2 *R*
	**13**	**18** (93, 1 : 4)	**22** (18)	12.1	2 *S*[c]	11.0	2 *R*[c]

[a] Yield of isolated products after column chromatography. [b] Determined from the ^{1}H NMR spectra. [c] Determined by comparison with other examples.

Results and Discussion

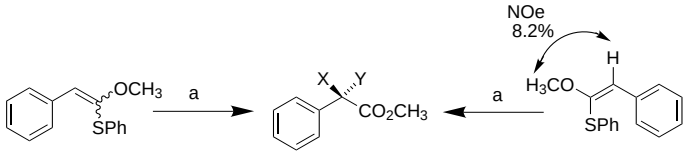
Preparation and asymmetric dihydroxylation of ketene *O*,*S*-acetals: Initial studies in our laboratories rapidly revealed that 1,1-dibromo alkene **8**, which is conveniently prepared from pentanal **6** with the Corey–Fuchs alkenation methodology,[17] is not a suitable substrate for the Sharpless asymmetric dihydroxylation; formation of the desired α-hydroxy hexanoic acid is not observed. In fact, Sharpless and co-workers pointed



6 R= $CH_3(CH_2)_3$
7 R= Ph
8 **9** **10**

out that halogenated alkenes are poor substrates for the asymmetric dihydroxylation.[18] It is assumed that for 1,1-dibromoalkenes steric hinderance in connection with the reduced nucleophilicity of the olefinic double bond are responsible for this lack of reactivity. Therefore, we turned our attention to the use of ketene *S*,*S*-acetal **9**, conveniently prepared from benzaldehyde **7** by the Horner–Emmons olefination with $[(EtO)_2P(O)C(SEt)_2]Li$ as a nucleophile.[19] However, also **9** could not be transformed into α-hydroxy thiol ester **10** under the typical asymmetric dihydroxylation conditions and in fact was almost quantitatively recovered.

Ketene *O*,*S*-acetals **15**–**18** turned out to be the first 1,1-heterodisubstituted alkenes that could be applied for the new acylation strategy (Table 1). First of all, they are prepared in excellent yield from aldehydes **7**, **11**, and **12** or ketone **13** by the Peterson olefination with silyl-substituted carbanion **14** as the nucleophile.[20] Secondly, they react with osmium tetroxide under the Sharpless conditions to give α-hydroxy methyl esters **19**–**22**. However, the yields of this process are far from satisfactory. A careful search for other oxidation products was conducted and led to the isolation of diphenyldisulfide. In some cases, methyl esters like **23** were isolated that derive from the regioselective addition of water to the ketene double bond and displacement of the thiolate ion (Scheme 2). α-



15 (*E*:*Z*= 2:1) (2*R*)-**19** X= OH, Y= H **23** X= Y= H (*Z*)-**15**

Scheme 2. a) AD-mix β, H_2O, *t*BuOH, $MeSO_2NH_2$, 0 °C, 12 h; from (*E*/*Z* 2:1)-**15**: 37%, 80.0% *ee*; from (*Z*)-**15**: 31%, 80.3% *ee*.

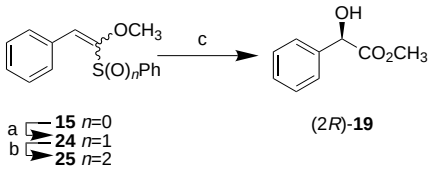
Hydroxy phenylthiol esters, which would be generated alternatively if the methoxy substituent acts as a leaving group during fragmentation of the intermediate diols, were not detected. The high pH value of the dihydroxylation mixture may cause hydrolysis of a possible intermediate thiol ester. Therefore, we studied the stability of phenylacetic acid thiol ester under basic and under hydrolysis conditions. At pH 10.5 not more than 5% of phenylacetic acid was generated within 12 h. A mixture of phenylacetic acid thiol ester in H_2O/*t*BuOH (1:1) or Na_2SO_3 left the starting material unaltered after 12h. A similar set of experiments was performed with an *E*/*Z* mixture (2:1) of ketene *O*,*S*-acetal **15**. In fact, they are stable under basic conditions (pH = 10.5) and in the presence of $[K_4Fe(CN)_6]\cdot 3H_2O$, but OsO_4 causes oxidation to diphenyldisulfide and various unidentified products. The enantio-

purities of the hydroxylation products were moderate with *ee* values between 62–80%. When acetophenone **13** was employed as the starting carbonyl compound, the asymmetric dihydroxylation furnished atrolactinic acid methyl ester **22** in low isolated and stereochemical yield. The latter value is in accordance with other examples of tetrasubstituted alkenes, which are poor substrates for the AD process.[21]

For raising the efficiency of the acylation strategy with ketene *O*,*S*-acetals, it was necessary to improve both the isolated yield and enantioselectivity of the dihydroxylation step. However, neither performing the asymmetric dihydroxylation at $-10\,^{\circ}C$ instead of $0\,^{\circ}C$ nor a larger molar ratio of the dihydroxylation mixture gave improved results.

We reasoned that the moderate stereoselectivity observed for the oxidation of ketene *O*,*S*-acetals **15**–**17** may be owing to the fact that the *E*/*Z* mixtures obtained during the alkenation step were employed. To test this hypothesis, the *E*/*Z* isomers of alkene **15** were separated by flash column chromatography on neutral Al_2O_3. Then, the enantiopurity of the dihydroxylation product **19** obtained from the pure *Z* isomer of **15** was compared with the ee value of mandelic methyl ester formed from a 2:1 starting mixture (Scheme 2). The ee ratios were determined by gas chromatography with a modified chiral β-cyclodextrin column and were judged to be almost identical [2:1 *E*/*Z* mixture **15**: 80.0% *ee*; (*Z*)-**15**: 80.3% *ee*]. These results show that ketene *O*,*S*-acetals can be employed as diastereomeric mixtures for the AD process, but they also mean that the enantiopurities listed in Table 1 are already close to the optimal values.

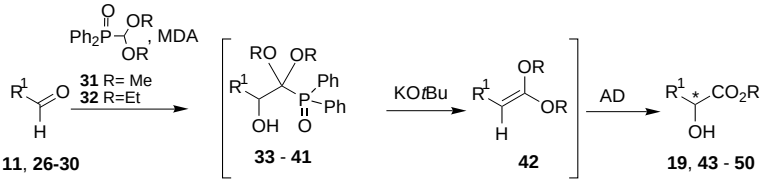
The sensitivity of the phenylthio group towards oxidants could be another reason for the low isolated yields. In order to improve the acylation method in this respect, the ketene *O*,*S*-acetal **15** was converted into sulfoxide **24** and sulfone **25**. In fact, in terms of yields, these 1,1-heterodisubstituted alkenes are much better substrates than **15**. However, the oxidation furnished mandelic methyl ester **19** with only low enantiopurity (Scheme 3).

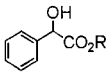
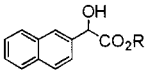
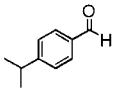
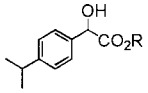
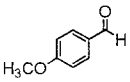
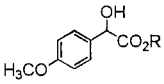
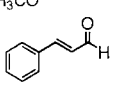
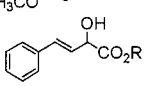
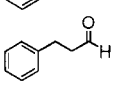
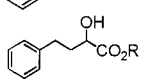
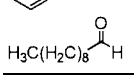
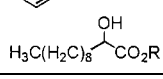


Scheme 3. a) $NaIO_4$, MeOH, H_2O (1:1), THF, RT, 36 h, 82%; b) *m*CPBA, CH_2Cl_2, RT, 48 h; c) AD-mix β, H_2O, *t*BuOH, $MeSO_2NH_2$, $0\,^{\circ}C$, 12 h; from **24**, 80%, 4.3% *ee*, from **25**, 55%, 2.0% *ee*.

Preparation and asymmetric dihydroxylation of ketene *O*,*O*-acetals: We extended our concept to the utilization of ketene *O*,*O*-acetals **42** (Table 2).[15] Indeed, these 1,1-heterodisubstituted alkenes are ideally suited for this concept, because of the excellent nucleophilicity of the alkenic double bond and the small size of the two geminal alkoxy groups. They can conveniently be prepared from aldehydes by the Horner–Wittig reaction[22] with the dialkoxymethyl diphenyl phosphine oxides **31** and **32**[23] Furthermore, they are ideal substrates in the Sharpless asymmetric dihydroxylation[24]

Table 2. Asymmetric acylation of aldehydes **10**, **11**, and **26**–**31** via ketene *O*,*O*-acetals: yields, configurations and enantioselectivities.



Aldehyde		Cation[a]	R	Phosphinoxide (yield) [%][b]	Hydroxyester (yield) [%][b]		AD-mix α[(DHQ)$_2$PHAL]		AD-mix β[(DHQD)$_2$PHAL]	
							ee [%]	config	*ee* [%]	config
	**7**	K	Me	**33** (91)		**19** (90)	93.0	2 *S*	96.0	2 *R*
		K	Et	**34** (89)		**43** (76)	98.4	2 *S*	99.9	2 *R*
	**26**	K	Et	**35** (84)		**44** (68)	93.0[c]	2 *S*	95.0[c]	2 *R*
	**27**	K	Me	**36** (78)		**45** (93)	91.0	2 *S*	96.0	2 *R*
		K	Et	**37** (72)		**46** (88)	69.7	2 *S*	80.3	2 *R*
	**28**	K	Et	**38** (92)		**47** (71)	86.1	2 *S*	88.0	2 *R*
	**11**	Li	Et	**39** (72)		**48** (73)	95.7	2 *S*	93.5	2 *R*
	**29**	Li	Me	**40** (71)		**49** (34)[d]	93.0	2 *S*	94.0	2 *R*
	**30**	Li	Me	**41** (73)		**50** (70)	92.0	2 *S*	98.0	2 *R*

[a] Optimal cation. [b] Yield of isolated product after column chromatography. [c] Determined from the ^1H NMR spectra of both diastereomeric Mosher esters. [d] Not optimized.

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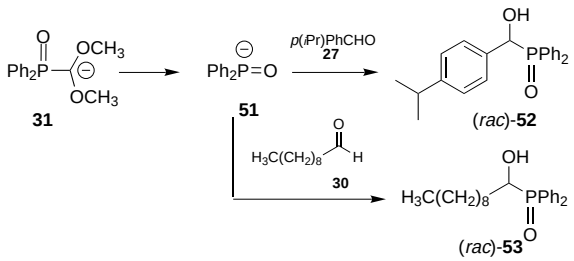
giving intermediate diols that spontaneously collapse to α-hydroxy carboxylates (Table 2).

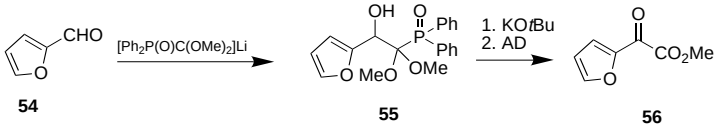
For this two step sequence, the Horner–Wittig alkenation turned out to be the yield-determinig reaction. Quantitative formation of the metallated dialkoxymethyl diphenylphosphine oxide was best achieved by use of lithium diisopropyl amide (LDA) or potassium diisopropyl amide (KDA) in THF at $-110\,^{\circ}C$. Under these conditions the dark red anion is quantitatively generated. Metallation with alternate bases like *n*BuLi, or lithium or potassium hexamethyldisilazide (LHMDA or KHMDA) was incomplete. Addition of aldehydes **7**, **11**, and **26–30** to the carbanion afforded stable phosphine oxides **33–41**, which after aqueous workup, could be chromatographed on silica gel and fully characterized or directly used for the next step (Table 2). Aromatic aldehydes **7** and **26–28** gave slightly better yields with the potassium salt of diethoxymethyl diphenylphosphine oxide. In initial studies with enolizable aldehydes, only moderate yields in the reaction with anion **32** were achieved,[15] so that a modified procedure had to be developed. Attempts to improve the yield by adding metal salts like $ZnBr_2$, $MgBr_2OEt_2$, or $Ti(OiPr)_4$ and transmetallating the lithiated diphenylphosphine oxide **31** did not give better yields or were unsuccessful. Only when a threefold excess of lithiated **31** was employed, could the yield for the primary adducts be raised to a satisfactory 70–80%. In the following, the corresponding ketene acetals **42** were liberated by KO*t*Bu-promoted elimination. Alternatively, **42** can also be prepared by direct elimination of the metallated primary coupling product at elevated temperature. However, we found that this procedure gave a reduced yield of α-hydroxy carboxylic esters after AD. After the elimination was complete the reaction mixture was concentrated at $0\,^{\circ}C$, and the crude product was enantioselectively oxidized, affording the α-hydroxy carboxylates **19** and **43–50** in good overall yield and excellent enantiopurity (Table 2).[25] The intermediate 1,1-dimethoxy ketene *O*,*O*-acetals are slightly better substrates for the AD process than the corresponding diethoxy derivatives, which are generated from carbanion **32**. The reduced ee values for dihydroquinine (DHQ) ligand relative to the dihydroquinidine (DHQD) ligand is a phenomenon often observed for the AD process.[26] It is noteworthy, that in most cases proton-induced hydrolysis of the ketene acetals to the corresponding carboxylates did not occur. However, oxidation is best performed in an inverse manner by adding the precooled AD mixture to **42**.

To obtain the best results, it is also essential to control the reaction time and temperature in the Horner–Wittig step. Otherwise, fragmentation of carbanions **31** and **32** to lithiated phosphine oxide **51** occurs; this can subsequently attack aldehydes like **27** or **30**, for which isolation of byproducts **52** and **53**, respectively, are a clear proof (Scheme 4).

When aromatic aldehydes like **27**, **28**, or **54** are employed overoxidation can occur under prolonged reaction times in the dihydroxylation step leading to the corresponding α-ketoesters. In fact, ketoester **56** was the only oxidation product obtained after applying the acylation sequence on furfural **54** via intermediate **55** (Scheme 5). Attempts to suppress overoxidation by reducing the reaction time and the temperature were not successful.[27]

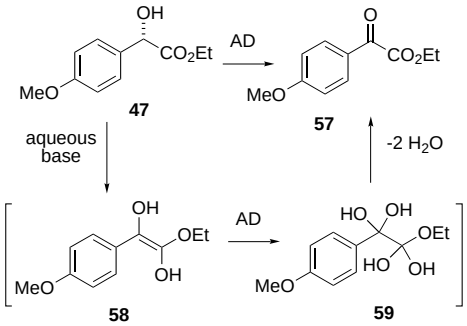


Scheme 4. Fragmentation of carbanion **31** and subsequent nucleophilic addition of metallated phosphine oxide **51** to aldehydes **27** and **30**.



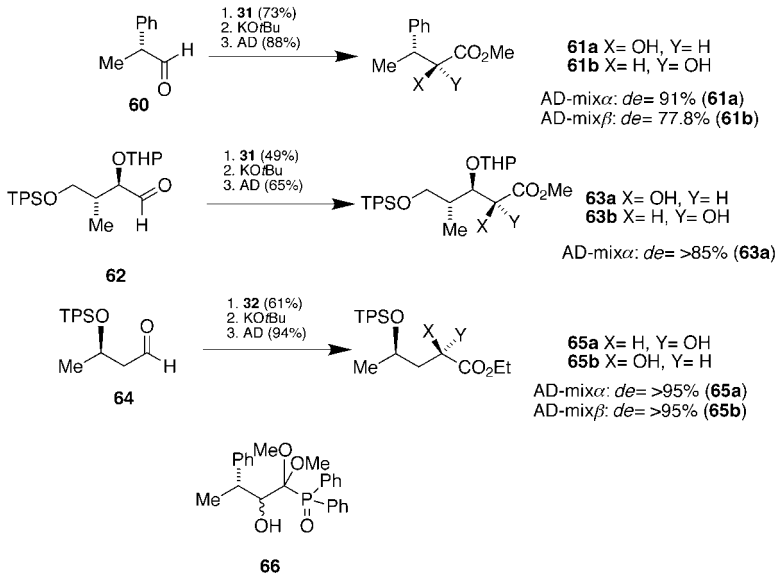
Scheme 5. Overoxidation of intermediate aromatic ketene *O*,*O*-acetal.

Insights into the mechanism of overoxidation were gained from experiments carried out with 4-methoxy mandelic acid ethyl ester **47** (Scheme 6). Ester **47** was prepared in 57% overall yield from aldehyde **28** (Table 2) along with keto ester **57**, which was formed in 23% yield during the asymmetric hydroxylation. The yield for **47** could be improved to 71% yield if the reaction time for the asymmetric dihydroxylation was reduced to three hours. When pure (2*S*)-α-hydroxy ester **47** was subjected to the Sharpless mixture again, this time for 12 h, 20% of **47** was reisolated. Additionally, the reaction furnished keto ester **57** in substantial amounts (23%). This observation may be rationalized on the basis of the assumption of partial tautomerization of **47** to enol **58** under the basic dihydroxylation conditions. If this isomer is dihydroxylated again, the intermediate diol **59** would collapse spontaneously to give α-keto ester **57**. Support for this hypothesis comes from our observation that aromatic α-hydroxy esters tend to racemize rapidly.[15]



Scheme 6. Proposed mechanism of overoxidation.

The use of chiral aldehydes is particularly important when introducing a new acylation method, as numerous applications in natural-product synthesis can be envisaged. Therefore, chiral aldehydes containing an α-aryl- (**60**), α-alkoxy- (**62**), and β-siloxy-substituents (**64**) were transformed into the corresponding α-hydroxy esters **61**, **63**, and **65** under the standard conditions developed for enolizable aldehydes (Scheme 7). Except for **62**, which was employed as a 3:1 mixture epimeric at the THP group, all examples proceeded

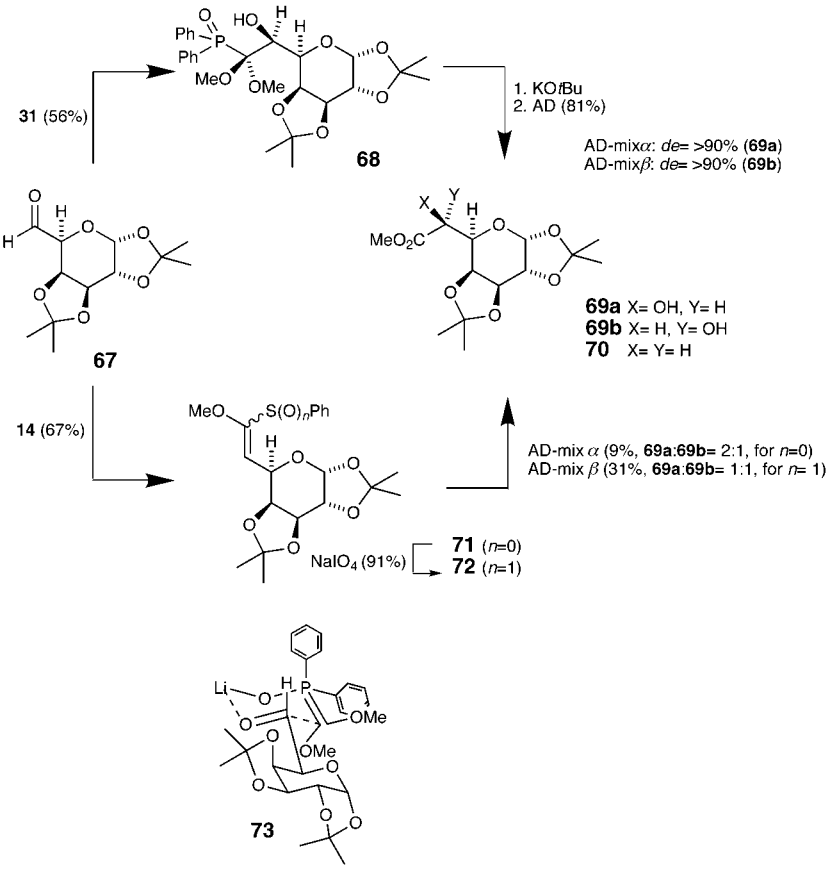


Scheme 7. Asymmetric acylation of chiral aldehydes **60**, **62**, and **64** via ketene *O*,*O*-acetals

with similar yields relative to the model systems listed in Table 2. The stereo directing power of the two chiral Sharpless ligands is particularly well-demonstrated in the first example, (2*R*)-2-phenylpropanal **60**. When dihydroquinine 1,4-phthalazinediyl diether (DHQ-PHAL) is employed, catalyst control and substrate control work in the same direction (matched case), leading to the corresponding acylation product with good diastereoselectivity.[28] However, even the stereochemically opposite mismatched series, with the dihydroquinidine ligand (DHQD-PHAL), is still practical, furnishing a diastereoselectivity close to 80%. When the stereogenetic center is moved one carbon further away to the β-position as in aldehyde **64**, stereocontrol at the newly formed chiral carbon at C-2 is overwhelmingly exerted by the dihydroxylation mixture so that both diastereomers **65a** and **65b** can be prepared separately with high diastereoselectivity.

Particular challenging substrates are hexose-derived aldehydes, which would lead to the corresponding heptoses. These naturally rare glycosidic moieties play a role as biosynthetic intermediates[29] or as components of enterobacterial lipopolysaccharides of Gram-negative bacteria.[30] Furthermore, they can serve as transition-state-analogue inhibitors of glycosyltransferases.[31]

Still, no high yielding and especially stereoselective homologation methods for aldehydes like **67** are known that are so flexible so as to create both possible diastereomers independently.[32, 33] Thus, we extended our asymmetric homologation method to α-D-*galacto*-dialdopyranose **67**. It was first treated with carbanion **31** to give phosphine oxide adduct **68** as a single isomer (Scheme 8). The sequence was terminated in the usual manner and afforded methyl esters **69a** and **69b** with remarkably high diastereofacial selectivity for both series. However, under the dihydroxylation conditions typically employed, the intermediate ketene *O*,*O*-acetal was hydrolyzed to yield heptose **70** as the major product (78%). The isolated yield for **69** (81%) could only be improved, by the suppression of the formation of **70** (6%), when the amount of the dihydroxylation mixture employed was tripled. It is noteworthy, that the nucleophilic addition of **31** to dialdopyranose **67** stereoselectively afforded **68** with a stereochemistry that is consistent with an *anti*-



Scheme 8. Preparation of heptoses **69** by asymmetric acylation of aldehyde **67**.

0947-6539/99/0508-2274 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 8

diastereofacial approach and the transition state model **73**. In order to validate the route via ketene *O*,*O*-acetals, the alternate procedure via ketene *O*,*S*-acetals **71** and **72** was also investigated. As shown in Scheme 8, alkenation of **67** with silyl-stabilized anion **14** proceeds in good yield to afford ketene acetal **70** as a 1:1 mixture of diastereomers. Again, however, asymmetric dihydroxylation proceeded with low efficiency to yield both diastereomeric isomers **69a** and **69b**. Oxidation of **71** to the corresponding sulfoxide **72** followed by dihydroxylation with AD-mix β proceeded with better yield and furnished a 1:1 mixture of heptose esters **69a** and **69b**. Finally, it should be noted that our acylation route of dialdopyranoses via ketene *O*,*O*-acetals is comparable in terms of shortness and stereoselectivity with the method developed by the group of Dondoni,[32] while the yields for the homologation step need further improvement.

In conclusion, we have developed a very competitive strategy for asymmetrically transforming and homologating aldehydes to the corresponding α-hydroxy carboxylic esters. The strength of the transformation described here lies in its shortness. This is particularly evident from the fact that the ester functionality is spontaneously liberated during the stereoselective introduction of the hydroxy group. Furthermore, the use of an external tool for asymmetric induction, which is available in both enantiomeric forms, allows for the straightforward preparation of both stereochemical series. Although the synthesis and oxidation of the intermediate ketene *O*,*O*-acetals requires careful handling the method should be widely applicable for a diverse number of aldehydes and should prove very useful in natural product synthesis.

Experimental Section

General techniques: All temperatures quoted are uncorrected. Optical rotations: Perkin–Elmer 243b polarimeter. ^{1}H NMR, ^{13}C NMR spectra: Bruker DPX200, AMX400 spectrometer. ^{13}C NMR multiplities: DEPT135 method; they are reported with the following abbreviations: o = singlet (due to quaternary carbon), + = doublet and quartet (methine, methyl), − = triplet (methylene). MS: HP5989B MASS Hewlett–Packard (DIP-MS) and Finnigan A 311, 70 eV (EI-MS). Unless otherwise stated, all reactions were run under a nitrogen atmosphere. All solvents used were of reagent grade and were further dried. Reactions were monitored by TLC on silica gel 60PF^{254} (E. Merck, Darmstadt) and detected either by UV-absorption or by staining with H_2SO_4/4-methoxybenzaldehyde in ethanol. Preparative column chromatography (CC): silica gel 60 (E. Merck, Darmstadt). GC: HPGC series 5890 Hewlett–Packard equipped with column RTX-50 (30 m) and FID 19231 D/E. Chiral GC: HPGC series 5890 Hewlett–Packard equipped with FID 19231 D/E; column: heptakis-(2,6-di-*O*-methyl-3-*O*-pentyl)-β-cyclodextrin (25 m); gas: helium; conditions: isothermal, $P_{(column)} = 175$ kPa, $P_{He} = 3.5$ bar, $P_{H_2} = 1.5$ bar, flow rate. The absolute configuration was deduced from comparison of CD spectra with those of authentic (2*R*)-**43** [positive Cotton effect for (2*S*)-**19**–**21** and **44**–**50**, and negative Cotton effect for (2*R*)-**19**–**21** and **44**–**50**]. Compounds **8**[17] and **9**[19] were synthesized according to literature procedures. Lithiated **14** was prepared as described by Hackett and Livinghouse.[20] Aldehydes **60** (97%), **62** (86%), **64** (88%), and **67** (88%) were obtained from the corresponding alcohols with the use of the Dess–Martin reagent.[34] α-Hydroxy esters **19** and aldehydes **6**, **7**, **11**, **12**, and **26**–**30**, ketone **13**, and ester **23** are commercially available.

General procedure for the preparation of ketene *O*,*S* acetals: 1,10-Phenanthroline (4 mg mmol^{-1}) and dry TMEDA (1 equiv) was added to a solution of phenoxy(phenylthio)(trimethylsilyl)methane[20] (1 equiv) in absolute THF (2.5 mL mmol^{-1}) under nitrogen. The solution was cooled to −78 °C and then treated with *sec*-butyl lithium until the color of the solution changed. At this point, additional *sec*-butyl lithium (1.44 M in cyclohexane, 1.3 equiv) was added dropwise. The reaction temperature was monitored throughout the addition and did not exceed −75 °C. After 2.5 h at ambient temperature freshly purified aldehyde (1.1 equiv) was added to the dark red solution. The reaction mixture was allowed to warm to RT overnight and was diluted with saturated aqueous NH_4Cl. After phase separation and extraction of the aqueous phase with dichloromethane (5 times), the combined organic extracts were washed with water, dried ($MgSO_4$), and concentrated in vacuo. Further purification of the residue was performed by column chromatography.

(*E*,*Z*)-1-Methoxy-2-phenyl-1-(phenylthio)ethene (15): Aldehyde **7** (265 mg, 2.5 mmol) was used to prepare the title compound **15** (587 mg, 2.43 mmol, 97%; *E*/*Z* = 2:1) with the general procedure described above. Purification and separation of the two isomers was achieved by flash column chromatography on neutral Al_2O_3 (petroleum ether/ethyl acetate 50:1).

Isomer (*E*)-**15**:[20] Oil; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.55$–7.00 (m, 10H, Ph), 6.09 (s, 1H, =CH), 3.59 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 158.7$ (+, C-2), 151.4 (o, C-1), 136.5–127.0 (o and +, Ph), 57.8 (+, OCH_3); $C_{15}H_{14}OS$: calcd C 74.34, H 5.82; found C 74.31, H 5.88.

Isomer (*Z*)-**15**:[35] Oil; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.55$–7.00 (m, 10H, Ph), 6.19 (s, 1H, =CH), 3.64 (s, 3H, OCH_3).

(1-*E*,*Z*; 3-*E*)-1-Methoxy-4-phenyl-1-(phenylthio)-1,3-butadiene (16): Aldehyde **11** (330 mg, 2.5 mmol) was used to prepare the title compound **16** (596 mg, 2.23 mmol, 89%; *E*/*Z* = 1:4) by the general procedure described above. Purification was achieved by column chromatography (petroleum ether/ethyl acetate 38:1).

Isomer (*E*)-**16**:[20] Oil; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.49$–7.10 (m, 10H, Ph), 6.58 (s, 1H, 2-H), 6.50 (d, $J = 15.7$ Hz, 1H, 4-H), 6.07 (d, $J = 15.7$ Hz, 1H, 3-H), 3.65 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 149.6$ (o, C-1), 149.6 (+, C-4), 139.8 (+, C-2), 138.6–125.5 (o and +, Ph), 116.9 (+, C-3), 56.9 (+, OCH_3).

Isomer (*Z*)-**16**:[20] ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.49$–7.10 (m, 10H, Ph), 6.61 (s, 1H, 2-H), 6.56 (d, $J = 15.7$ Hz, 1H, 4-H), 6.10 (d, $J = 15.7$ Hz, 1H, 3-H), 3.69 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 151.1$ (+, C-4), 149.6 (o, C-1), 139.8 (+, C-2), 138.6–125.5 (o and +, Ph), 118.2 (+, C-3), 56.9 (+, OCH_3). $C_{17}H_{16}OS$: calcd C 76.08, H 6.01; found C 76.31, H 6.24.

(*E*,*Z*)-1-Methoxy-1-(phenylthio)-1-pentene (17): Aldehyde **12** (200 mg, 2.32 mmol) was used to prepare the title compound **17** (510 mg, 2.29 mmol, 99%; *E*/*Z* = 1:1) by the general procedure described above. Purification was achieved by column chromatography (petroleum ether/ethyl acetate 1:10).

Isomer (*E*)-**17**: Oil; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.37$–7.08 (m, 5H, Ph), 5.27 (t, $J = 7.5$ Hz, 1H, 2-H), 3.53 (s, 3H, OCH_3), 2.15 (q, $J = 7.5$ Hz, 2H, 3-H), 1.36 (sep, $J = 7.5$ Hz, 2H, 4-H), 0.89 (t, $J = 7.4$ Hz, 3H, 5-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 146.7$ (o, C-1), 135.2 (+, C-2), 128.8–123.6 (o and +, Ph), 56.6 (+, OCH_3), 28.4, 22.5 (−, C-3, C-4), 13.8 (+, C-5).

Isomer (*Z*)-**17**: Oil; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.37$–7.08 (m, 5H, Ph), 5.37 (t, $J = 7.5$ Hz, 1H, 2-H), 3.58 (s, 3H, OCH_3), 2.23 (q, $J = 7.5$ Hz, 2H, 3-H), 1.38 (sep, $J = 7.5$ Hz, 2H, 4-H), 0.91 (t, $J = 7.4$ Hz, 3H, 5-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 149.0$ (o, C-1), 134.5 (+, C-2), 128.8–123.6 (o and +, Ph), 57.0 (+, OCH_3), 30.7, 22.5 (−, C-3, C-4), 13.7 (+, C-5); $C_{13}H_{18}OS$: calcd C 70.22, H 8.16; found C 70.09, H 8.02.

(*E*,*Z*)-1-Methoxy-2-phenyl-1-(phenylthio)-1-propene (18): Ketone **13** (300 mg, 2.5 mmol) was used to prepare the title compound **18**[36] (595 mg, 2.32 mmol, 93%; *E*/*Z* = 1:4) by the general procedure described above. Purification was achieved by column chromatography (petroleum ether/ethyl acetate 30:1).

Isomer (*E*)-**18**: Oil; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.43$–6.97 (m, 10H, Ph), 3.28 (s, 3H, OCH_3), 2.17 (s, 3H, $=CCH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 144.2$ (o, C-1), 135.3 (+, C-2), 131.2–125.7 (o and +, Ph), 57.0 (+, OCH_3), 21.1 (+, CH_3).

Isomer (*Z*)-**18**: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.43$–6.97 (m, 10H, Ph), 3.50 (s, 3H, OCH_3), 2.07 (s, 3H, $=CCH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 141.7$ (o, C-1), 131.5 (+, C-2), 131.2–125.7 (o and +, Ph), 57.0

(+, OCH_3), 19.2 (+, CH_3); $C_{16}H_{16}OS$: calcd C 74.96, H 6.19; found C 75.11, H 6.03.

(*E*/*Z*)-(2′*S*,3′*R*,4′*R*,5′*R*,6′*R*)-2-[2′(3′,4′,5′,6′-Di-*O*-isopropylidene)tetrahydropyranyl]-1-methoxy-1-phenylthio ethene (71): Aldehyde **67** (646 mg, 2.5 mmol) was used to prepare the title compound **71** (655 mg, 1.66 mmol, 67 %; *E*/*Z* = 1:1) by the general procedure described above. Purification was achieved by column chromatography (petroleum ether/ethyl acetate 15:1).

1st fraction: (*Z*)-**71**: Oil; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.39 – 7.18 (m, 5H, Ph), 5.56 (d, *J* = 8.6 Hz, 1H, =CH), 5.05 (d, *J* = 5.2 Hz, 1H, 6′-H), 4.87 (dd, *J* = 1.6, 8.4 Hz, 1H, 2′-H), 4.61 (dd, *J* = 2.4, 8.0, 1H, 4′-H), 4.31 (dd, *J* = 2.4, 5.2 Hz, 1H, 5′-H), 4.24 (dd, *J* = 1.6, 8.4 Hz, 1H, 3′-H), 3.57 (s, 3H, OCH_3), 1.58, 1.48, 1.36, 1.35 (4s, 12H, $2C(CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 154.3 (o, *C*(OMe)SPh), 136.0 (+, =CH), 132.2 – 126.6 (o and +, Ph), 109.3, 108.7 (o, $2C(CH_3)_2$), 96.6 (+, C-6′), 73.8 (+, C-2′), 70.9 (+, C-3′), 70.3 (+, C-5′), 67.3 (+, C-4′), 26.0, 25.1, 24.4, 24.3 (+, $2C(CH_3)_2$).

2nd fraction: (*E*)-**71**: Oil; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.37 – 7.10 (m, 5H, Ph), 5.33 (d, *J* = 7.0 Hz, 1H, =CH), 5.55 (d, *J* = 5.0 Hz, 1H, 6′-H), 4.83 (dd, *J* = 1.6, 7.0 Hz, 1H, 2′-H), 4.61 (dd, *J* = 2.5, 8.4, 1H, 4′-H), 4.31 (dd, *J* = 2.5, 5.0 Hz, 1H, 5′-H), 4.19 (dd, *J* = 1.6, 8.4 Hz, 1H, 3′-H), 3.63 (s, 3H, OCH_3), 1.54, 1.50, 1.35, 1.32 (4s, 12H, $2C(CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 155.7 (o, *C*(OMe)SPh), 132.8 (+, =CH), 132.2 – 127.2 (o and +, Ph), 109.7, 109.3 (o, $2C(CH_3)_2$), 97.0 (+, C-6′), 74.3 (+, C-2′), 71.4 (+, C-3′), 70.7 (+, C-5′), 67.7 (+, C-4′), 26.4, 26.3, 25.5, 24.7 (+, $2C(CH_3)_2$); $C_{20}H_{26}O_6S$: calcd C 60.89, H 6.64; found C 60.55, H 6.73.

(*E*/*Z*)-(2′*S*,3′*R*,4′*R*,5′*R*,6′*R*)-Benzenesulfoxyl-2-[2′(3′,4′,5′,6′-di-*O*-isopropylidene)tetrahydropyranyl]-1-methoxy ethene (72): A suspension of **71** (300 mg, 0.76 mmol) and molecular sieves (3 Å, 50 mg) in dry methanol (8 mL) at RT was treated with $NaIO_4$ (195 mg, 0.91 mmol). Stirring was continued for 12 h at RT, while excluding light. Another batch of $NaIO_4$ (86 mg, 0.4 mmol) was added and stirring was continued. After 4 d the reaction mixture was filtered and washed with water. The aqueous phase was extracted with dichloromethane (5 times). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification was achieved by flash column chromatography (petroleum ether/ethyl acetate 11:1) and yielded the title compound **72** (223 mg, 0.70 mmol; 91 %) as a colorless oil, which was directly used for the next step, the asymmetric dihydroxylation.

(*E*,*Z*)-2-Benzenesulfoxyl-2-methoxystyrene (24): Ketene *O*,*S*-acetal **15** (484 mg, 2.0 mmol) was suspended in H_2O/MeOH (1:1). THF was added until a clear, colorless solution resulted. After addition of $NaIO_4$ (512 mg, 2.4 mmol) stirring was continued at RT for 12 h. Another batch of $NaIO_4$ (512 mg, 2.4 mmol) was added. After 24 h the reaction mixture was filtered and washed with dichloromethane (5 times). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification was achieved by flash column chromatography (petroleum ether/ethyl acetate 5:1)and yielded the title compound **24** (428 mg, 1.66 mmol; 82 %) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.80 – 7.21 (m, 10H, Ph), 6.41, 6.30 (s, 1H, =CH, *E*/*Z*-isomers), 3.78, 3.70 (s, 3H, OCH_3, *E*/*Z* isomers); $C_{15}H_{14}O_2S$: calcd C 69.74, H 5.46; found C 69.54, H 5.68.

(*E*,*Z*)-2-Benzenesulfonyl-2-methoxystyrene (25): *m*CPBA (36 mg, 0.21 mmol) was added to a solution of ketene *O*,*S*-acetal **24** (50 mg, 0.19 mmol) in dry CH_2Cl_2 at RT. After 48 h the reaction mixture was filtered, washed with an aqueous $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated under reduced pressure. The analytical data of **25** were in accordance with the literature.[37] The title compound was sufficiently pure for further use in the dihydroxylation step.

General procedure for the asymmetric dihydroxylation of ketene *O*,*S*-acetals: Ketene *O*,*S*-acetal (1 equiv) was added to a suspension of AD-mix [1 mol % $(DHQ)_2$-PHAL for AD-mix α or $(DHQD)_2$-PHAL for AD-mix β] and methanesulfonamide (1.02 equiv) in water (5 mL mmol^{-1}), *tert*-butanol (4 mL mmol^{-1}), and acetonitrile (1 mL mmol^{-1}) at −10 °C. The suspension was vigorously stirred for 6 h at 0 °C and reduced with sodium sulfite (1.5 g mmol^{-1}). Stirring was continued for 30 min at 0 °C, and after additional 15 min at RT water (5 mL mmol^{-1}) and dichloromethane (20 mL mmol^{-1}) were added. The aqueous layer was extracted with dichloromethane (5 times) and the combined organic extracts were washed with KOH (2 M), dried ($MgSO_4$), concentrated under reduced pressure, and purified by column chromatography on silica gel.

Mandelic acid methyl ester (19): Ketene *O*,*S*-acetal **15** (242 mg, 1.0 mmol) was used to prepare the title compound **19** (62 mg, 0.37 mmol, 37 %) by the general procedure described above. Purification was achieved by column chromatography (petroleum ether/ethyl acetate 14:1) to afford an oil. The enantiomeric excess was determined by chiral GC: isothermal 111 °C, 26.04 min (2*S*), 24.32 min (2*R*); AD-mix α: $ee_{(S)}$ = 76.8 %; AD-mix β: $ee_{(R)}$ = 80.0 %.

Sulfoxide **24** (50 mg, 0.19 mmol) and sulfone **25** (50 mg, 0.18 mmol) were dihydroxylated with AD-mix β according to the general procedure described above to afford **19** (25 mg, 0.15 mmol, 79.6 %, 4.3 % ee from **24**; 17 mg, 0.1 mmol, 54.7 %, 2.0 % ee from **25**).

(*E*)-2-Hydroxy-4-phenyl-but-3-enoic acid methyl ester (20): Ketene *O*,*S*-acetal **16** (126 mg, 0.47 mmol) was used to prepare the title compound **20**[38] (27 mg, 0.14 mmol, 30 %) by the general procedure described above. Purification was achieved by column chromatography (petroleum ether/ethyl acetate 11:1). The enantiomeric excess was determined by chiral GC: isothermal 124 °C, 28.36 min (2*S*), 25.98 min (2*R*); AD-mix α: $ee_{(S)}$ = 75.0 %; AD-mix β: $ee_{(R)}$ = 80.3 %; oil; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.45 – 7.21 (m, 5H, Ph), 6.77 (dd, *J* = 15.4, 1.2 Hz, 1H, C-4), 6.19 (dd, *J* = 15.4, 5.2 Hz, 1H, C-3), 4.77 (ddd, *J* = 5.6, 5.2, 1.2 Hz, 1H, C-2), 3.62 (s, 3H, OCH_3), 3.51 (br, 1H, OH); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 176.0 (o, CO), 149.3 (+, C-4), 136.4 – 126.2 (o and +, Ph), 119.7 (+, C-3), 70.8 (CHOH), 52.3 (OCH_3).

2-Hydroxy-pentanoic acid methyl ester (21): Ketene *O*,*S*-acetal **17** (208 mg, 1.0 mmol) was used to prepare the title compound **21**[39] (9 mg, 0.07 mmol, 7 %) by the general procedure described above. Purification was achieved by column chromatography (petroleum ether/ethyl acetate 4:1). The enantiomeric excess was determined by chiral GC: isothermal 107 °C, 17.21 min (2*S*), 13.62 min (2*R*); AD-mix α: $ee_{(S)}$ = 62.3 %; AD-mix β: $ee_{(R)}$ = 72.8 %; oil; ^{1}H NMR (200 MHz, $CDCl_3$, TMS): δ = 5.15 (dt, *J* = 4.8, 1.6 Hz, 1H, 2-H), 3.61 (s, 3H, OCH_3), 2.71 (br, 1H, OH), 2.31 (dt, *J* = 2.4, 7.6 Hz, 2H, 3-H), 1.56 (sep, *J* = 7.4 Hz, 2H, 4-H), 0.96 (t, *J* = 7.2 Hz, 3H, 5-H).

2-Hydroxy-2-phenyl-propionic acid methyl ester (22): Ketene *O*,*S*-acetal **18** (256 mg, 1.0 mmol) was used to prepare the title compound **22**[40] (32 mg, 0.18 mmol, 18 %) by the general procedure described above. Purification was achieved by column chromatography (petroleum ether/ethyl acetate 13:1). The enantiomeric excess was determined by chiral GC: isothermal 100 °C, 24.27 min (2*S*), 25.20 min (2*R*); AD-mix α: $ee_{(S)}$ = 12.1 %; AD-mix β: $ee_{(R)}$ = 11.0 %; oil; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.50 – 7.45, 7.32 – 7.15 (m, 5H, Ph), 3.71 (s, 3H, OCH_3), 3.67 (br, 1H, OH), 1.72 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 176.1 (o, CO), 142.7 (o, Ph), 128.3 – 125.1 (+, Ph), 75.7 (o, COH), 53.3 (+, OCH_3), 26.6 (+, CH_3).

Dimethoxymethyldiphenylphosphine oxide (31) and diethoxymethyldiphenylphosphine oxide (32): *p*-Chlorodiphenylphosphine (1 equiv) was added dropwise (caution: exothermic) to freshly distilled trialkylorthoformiate (1 equiv) under nitrogen at RT. The reaction mixture solidified and was heated for 2 h at 110 °C, by which alkyl chloride was removed. After cooling to RT, the yellow solid was recrystallized (petroleum ether/toluene 100:1) to afford the title compounds.

Compound **31**:[23] (scale: 50 mmol; yield: 11.45 g, 41.5 mmol; 83 %); colorless crystals; m.p. 86 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.0 – 7.80 (m, 4H, Ph), 7.60 – 7.30 (m, 6H, Ph), 4.93 (d, J_{P-H} = 7.8 Hz, 1H, $CH(OMe)_2$), 3.57 (2s, 6H, $2OCH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 131.1, 129.1 (o, Ph), 132.0 – 128.2 (+, Ph), 106.1 (+, d, J_{P-C} = 117.1 Hz, $PCH(OMe)_2$), 58.4, 58.2 (+, $2OCH_3$).

Compound **32**:[41] (scale: 50 mmol; yield: 12.7 g, 45.4 mmol; 90.7 %); colorless crystals; m.p. 74 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.03 – 7.86 (m, 4H, Ph), 7.60 – 7.38 (m, 6H, Ph), 5.07 (d, J_{P-H} = 7.6 Hz, 1H, $CH(OEt)_2$), 3.87, 3.71 (dq, *J* = 9.5, 7.0 Hz, 4H, $2OCH_2CH_3$), 1.23 (t, *J* = 7 Hz, 6H, $2CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 131.4, 129.5 (o, Ph), 132.2 – 128.1 (+, Ph), 103.6 (+, d, J_{P-C} = 118.6 Hz, $PCH(OEt)_2$), 66.6, 66.4 (−, $2OCH_2CH_3$), 15.1, 15.0 (+, $2CH_3$).

General procedure for the asymmetric nucleophilic acylation via ketene *O*,*O*-acetals: Dialkoxymethyl diphenylphosphine oxide (1.2 equiv) in absolute THF (2 mL mmol^{-1}) was added over a period of 30 min to a solution of LDA or KDA (1.1 equiv) in dry THF (15 mL mmol^{-1}) under nitrogen at −110 °C (KDA was prepared by addition of freshly sublimed

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KO*t*Bu in THF to an equal amount of LDA at −110 °C). During the addition, the temperature must not raise above −110 °C. After 1 h at that temperature freshly purified aldehyde (1 equiv for aromatic aldehydes **7**, **26**–**28**, and **11**; 0.3 mmol for aliphatic aldehydes **29**, **30**, **60**, **62**, **64**, and **67**) in dry THF (2 mL mmol^{-1}) was added to the dark red solution. The reaction mixture, which decolorized immediately, was hydrolyzed after 15 min with water (4 mL mmol^{-1}) and was allowed to warm to RT. After addition of brine (10 mL mmol^{-1}) and dichloromethane (10 mL mmol^{-1}), the layers were separated. The aqueous phase was treated with dichloromethane (5 times), and the combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. In most cases the crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate 1:1). Alternatively, the crude product was used directly for the next reaction. In this case, traces of water were removed by co-distillation with toluene prior to use.

The adduct was dissolved in absolute THF (15 mL mmol^{-1}) under nitrogen and was treated with freshly sublimed potassium *tert*-butoxide (1.1 equiv) in THF (2 mL mmol^{-1}) at 0 °C. After 15 min the solution was concentrated in an ice bath under reduced pressure to a volume of approximately 1 mL. A suspension of AD-mix [1 mol% $(DHQ)_2$-PHAL for AD-mix α or $(DHQD)_2$-PHAL for AD-mix β] in water (5 mL mmol^{-1}) and *tert*-butanol (5 mL mmol^{-1}) was prepared at RT, cooled to 0 °C and added to the precooled ketene acetal. After addition of methanesulfonamide (1.02 equiv) the suspension was vigorously stirred overnight at 0 °C and reduced with sodium sulfite (1.5 g mmol^{-1}). Stirring was continued for 30 min at 0 °C, and after additional 15 min at RT water (5 mL mmol^{-1}) and dichloromethane (20 mL mmol^{-1}) were added. The aqueous layer was extracted with dichloromethane (5 times), and the combined organic extracts were dried ($MgSO_4$), concentrated under reduced pressure, and purified by column chromatography on silica gel.

1,1-Dimethoxy-2-hydroxy-2-phenyl-ethyl-1-(diphenylphosphine oxide) (33) and mandelic acid methyl ester (19): Aldehyde **7** (318 mg, 3.0 mmol) was used to prepare the title compound **33** (1.04 g, 2.73 mmol, 91%) by the general procedure described above. Colorless crystals; m.p. 142 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.87–7.61 (m, 4H, Ph), 7.56–7.20 (m, 8H, Ph), 7.09–6.99 (m, 3H, Ph), 5.59 (d, J = 7.3 Hz, 1H, OH), 5.06 (dd, J = 7.3, J_{P-H} = 13.3 Hz, 1H, C*H*OH), 3.37 and 3.28 (2s, 6H, $2OCH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.5–130.2 (o, Ph), 132.7–127.2 (+, Ph), 103.4 (o, d, J_{P-C} = 109.5 Hz, $C(OMe)_2$), 76.1 (+, d, J_{P-C} = 12.2 Hz, CHOH), 52.9, 50.5 (+, d, J_{P-C} = 3.9 and 8.3 Hz, $PC(OCH_3)_2$).

Elimination and asymmetric dihydroxylation of **33** (1 mmol) according to the standard protocol afforded the title compound **19** (149 mg, 0.9 mmol, 90%) after column chromatography (petroleum ether/ethyl acetate 8:1). The enantiomeric excess was determined by chiral GC: isothermal 108 °C, 30.78 min (2*S*), 28.93 min (2*R*); AD-mix α: $ee_{(S)}$ = 93.0%, $[\alpha]_D^{23.5} = +150°$ (c = 0.42, $CHCl_3$); AD-mix β: $ee_{(R)}$ = 96.0%, $[\alpha]_D^{23.5} = -168°$ (c = 0.5, $CHCl_3$). The spectroscopic data were in accordance with those listed above.

1,1-Diethoxy-2-hydroxy-2-phenyl-ethyldiphenylphosphine oxide (34) and mandelic acid ethyl ester (43): Aldehyde **7** (318 mg, 3.0 mmol) was used to prepare the title compound **34** (1.11 g, 2.67 mmol, 89%) by the general procedure described above. Colorless crystals; m.p. 139 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.89–7.19 (m, 4H, Ph), 7.58–7.19 (m, 8H, Ph), 7.12–6.99 (m, 3H, Ph), 5.54 (d, J = 6.8 Hz, 1H, OH), 5.04 (dd, J = 6.8, J_{P-H} = 12.3 Hz, 1H, C*H*OH), 3.86–3.56 (m, 4H, $2OCH_2CH_3$) 1.17, 1.14 (t, J = 7.0 Hz, 6H, $2CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.8–130.4 (o, Ph), 132.6–127.1 (+, Ph), 103.3 (o, d, J_{P-C} = 109.3 Hz, $C(OEt)_2$), 76.4 (+, d, J_{P-C} = 11.2 Hz, CHOH), 60.6, 58.4 (−, d, J_{P-C} = 4.4 and 7.3 Hz, $PC(OCH_2CH_3)_2$), 15.2, 14.9 (+, $2C(OCH_2CH_3)_2$).

Elimination and asymmetric dihydroxylation of **34** (1 mmol) according to the standard protocol afforded the title compound **43** (157 mg, 0.87 mmol, 87%) after column chromatography (petroleum ether/ethyl acetate 8:1). The enantiomeric excess was determined by chiral GC: isothermal 99 °C, 52.7 min (2*S*), 48.6 min (2*R*); AD-mix α: $ee_{(S)}$ = 98.4%, $[\alpha]_D^{21} = +118.6°$ (c = 1.02, $CHCl_3$); AD-mix β: $ee_{(R)}$ = 99.9%, $[\alpha]_D^{21} = -121.4°$ (c = 0.92, $CHCl_3$). The spectroscopic data were in accordance with those listed above.

1,1-Diethoxy-2-hydroxy-2-naphtylethyldiphenylphosphine oxide (35) and 2-hydroxy-2-naphtylacetic acid ethyl ester (44): Aldehyde **26** (468 mg, 3.0 mmol) was used to prepare the title compound **35** (1.089 g, 2.52 mmol, 84%) by the general procedure described above. Amorphous solid; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.80–7.28 (m, 14H, naph), 7.16–6.90 (m, 3H, Ph), 5.77 (d, J = 6.8 Hz, 1H, OH), 5.22 (d, J = 6.8 Hz, 1H, C*H*OH), 3.86–3.40 (m, 4H, $2OCH_2CH_3$), 1.25, 1.14 (t, J = 7.0 Hz, 6H, $2CH_3$).

Elimination and asymmetric dihydroxylation of **35** (1 mmol) according to the standard protocol afforded the title compound **44** (156 mg, 0.68 mmol, 68%) after column chromatography (petroleum ether/ethyl acetate 15:1). The enantiomeric excess was determined by preparing the Mosher esters of both diastereomers[42] followed by ^{1}H NMR analysis: AD-mix α: $ee_{(S)}$ = 92.7%; AD-mix β: $ee_{(R)}$ = 94.7; amorphous solid; m.p. 85 °C (lit. 87 °C[43]); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.93–7.72 (m, 4H, naph), 7.56–7.38 (m, 3H, naph), 5.31 (d, J = 5.6 Hz, 1H, C*H*OH), 4.19, 4.11 (dq, J = 7.2, 10.6 Hz, 2H, OCH_2CH_3), 3.77 (d, J = 5.6 Hz, 1H, OH), 1.18 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 175.7 (o, C=O), 132.1–122.3 (+, naph), 75.8 (+, CHOH), 62.7 (−, OCH_2CH_3), 14.3 (+, OCH_2CH_3).

1,1-Dimethoxy-2-hydroxy-2-(4-isopropylphenyl)ethyldiphenylphosphine oxide (36), **1-hydroxy-1-(4-isopropylphenyl)methyldiphenylphosphine oxide (52)**, **and 2-hydroxy-2-(4-isopropylphenyl)acetic acid methyl ester (45)**: Aldehyde **27** (444 mg, 3.0 mmol) was used to prepare the title compounds **36** (983 mg, 2.32 mmol, 78%) and **52** (123 mg, 0.4 mmol, 13%) by the general procedure described above.

1st fraction **36**: colorless crystals; m.p. 135 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.81–7.55 (m, 4H, Ph), 7.54–7.17 (m, 8H, Ph), 6.90–6.80 (m, 2H, Ph), 5.60 (br, 1H, OH), 5.06 (d, J_{P-H} = 14.3 Hz, 1H, C*H*OH), 3.45, 3.27 (2s, 6H, $2OCH_3$), 2.72 (sep, J = 7.0 Hz, 1H, $CH(CH_3)_2$), 1.13 (d, J = 7.0 Hz, 6H, $2CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 147.8–130.1 (o, Ph), 132.8–125.2 (+, Ph), 103.5 (o, d, J_{P-C} = 109.8 Hz, $C(OMe)_2$), 75.9 (+, d, J_{P-C} = 11.6 Hz, CHOH), 52.6, 50.4 (+, d, J_{P-C} = 3.9 and 8.8 Hz, $PC(OCH_3)_2$), 33.6 (+, $C(CH_3)_2$), 23.9 (+, $C(CH_3)_2$).

2nd fraction **52**: colorless crystals; m.p. 162 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.84–7.24 (m, 11H, Ph), 7.10–6.98 (m, 3H, Ph), 5.44 (d, J_{P-H} = 5.3 Hz, 1H, PC*H*OH), 4.29 (br, 1H, OH), 2.83 (sep, J = 6.8 Hz, 1H, $CH(CH_3)_2$), 1.19 (d, J = 6.8 Hz, 6H, $2CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 148.8–127.5 (o, Ph), 132.9–126.5 (+, Ph), 73.8 (+, d, J_{P-C} = 81.2 Hz, P*C*HOH), 33.8 (+, $C(CH_3)_2$), 23.9, 23.6 (+, $C(CH_3)_2$); $C_{22}H_{23}O_2P$: calcd C 75.41, H 6.62; found C 75.36, H 6.71.

Elimination and asymmetric dihydroxylation of **36** (1 mmol) according to the standard protocol afforded the title compound **45**[44] (193 mg, 0.93 mmol, 93%) after column chromatography (petroleum ether/ethyl acetate 8:1). The enantiomeric excess was determined by chiral GC: isothermal 130 °C, 41.13 min (2*S*), 38.89 min (2*R*); AD-mix α: $ee_{(S)}$ = 91.0%, $[\alpha]_D^{21} = +124.3°$ (c = 1.0, $CHCl_3$); AD-mix β: $ee_{(R)}$ = 96.0%, $[\alpha]_D^{21} = -127.2°$ (c = 1.0, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.37–7.17 (m, 4H, Ph), 5.14 (d, J = 5.8 Hz, 1H, C*H*OH), 3.74 (s, 3H, OCH_3), 3.49 (d, J = 5.8 Hz, 1H, OH), 2.30 (sep, J = 6.9 Hz, 1H, $CH(CH_3)_2$), 1.24 (d, J = 6.9 Hz, 6H, $2CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 174.2 (o, C=O), 149.2, 135.6 (o, Ph), 126.7, 126.5 (+, Ph), 72.7 (+, CHOH), 52.8 (+, OCH_3), 33.8 (+, $CH(CH_3)_2$), 23.8 (+, $CH(CH_3)_2$); $C_{12}H_{16}O_3$: calcd C 69.21, H 7.74; found C 69.26, H 7.88.

1,1-Diethoxy-2-hydroxy-2-(4-isopropylphenyl)ethyldiphenylphosphine oxide (37) and 2-hydroxy-2-(4-isopropylphenyl) ethyl acetate (46): Aldehyde **27** (136 mg, 1.0 mmol) was used to prepare the title compound **37** (326 mg, 0.72 mmol, 72%) by the general procedure described above. Amorphous solid; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.83–7.62 (m, 4H, Ph), 7.50–7.10 (m, 8H, Ph), 6.90–6.80 (m, 3H, Ph), 6.90–6.86 (m, 2H, Ph), 5.58 (br, 1H, OH), 5.05 (d, J_{P-H} = 13.2 Hz, 1H, C*H*OH), 4.17–3.41 (m, 4H, $2OCH_2CH_3$), 2.73 (sep, J = 7.0 Hz, 1H, $CH(CH_3)_2$), 1.26, 1.13 (2t, J = 7.0 Hz, 6H, $2CH_3$), 1.13 (d, J = 7.0 Hz, 6H, $2CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.5–130.2 (o, Ph), 132.7–127.2 (+, Ph), 103.4 (o, d, J_{P-C} = 109.5 Hz, $C(OMe)_2$), 76.1 (+, d, J_{P-C} = 12.2 Hz, CHOH), 52.9, 50.5 (+, d, J_{P-C} = 3.9, 8.3 Hz, $PC(OCH_3)_2$).

Elimination and asymmetric dihydroxylation of **37** (1.0 mmol) according to the standard protocol afforded the title compound **46**[45] (196 mg, 0.88 mmol, 88%) after column chromatography (petroleum ether/ethyl acetate 20:1). The enantiomeric excess was determined by chiral GC: isothermal 115 °C, 105.39 min (2*S*), 97.65 min (2*R*); AD-mix α: $ee_{(S)}$ = 67.7%; AD-mix β: $ee_{(R)}$ = 80.3%; oil; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.35–7.19 (2dt, J = 8.4, 2.0 Hz, 4H, Ph), 5.12 (d, J = 6.0 Hz, 1H, C*H*OH), 4.28, 4.15 (dq, J = 7.0, 10.7 Hz, 2H, OCH_2CH_3), 3.46 (d, J = 6.0 Hz, 1H, OH), 2.90 (sep, J = 7.0 Hz, 1H, $CH(CH_3)_2$), 1.24 (d, J =

7.0 Hz, 6H, $CH(CH_3)_2$), 1.23 (t, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 173.8$ (o, C=O), 149.1, 135.5 (o, Ph), 126.7, 126.5 (+, Ph), 72.7 (+, CHOH), 62.1 (−, OCH_2CH_3), 33.8 (+, $CH(CH_3)_2$), 23.9 (+, $CH(CH_3)_2$), 14.0 (+, CH_3); $C_{13}H_{18}O_3$: calcd C 70.24, H 8.16; found C 69.96, H 8.34.

1,1-Diethoxy-2-hydroxy-2-(4-methoxyphenyl)ethyl-1-(diphenylphosphine oxide) (38), 4-methoxy mandelic acid ethyl ester (47), and 2-(4-methoxyphenyl)-2-oxoacetic acid ethyl ester (57): Aldehyde **28** (136 mg, 1.0 mmol) was used to prepare the title compound **38** (403 mg, 0.92 mmol, 92%) by the general procedure described above. Oil; ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.88 - 7.66$ (m, 4H, Ph), 7.48 – 7.34 (m, 6H, Ph), 7.30, 6.57 (2d, $J = 8.6$ Hz, Ph), 5.40 (d, $J = 6.6$ Hz, 1H, OH), 4.99 (dd, $J = 6.6$, 12.4 Hz, 1H, CHOH), 3.70 (s, 3H, OCH_3), 3.69 – 3.44 (m, 4H, $2OCH_2CH_3$), 1.19, 1.14 (2t, $J = 7.0$ Hz, 6H, $2CH_3$).

Elimination and asymmetric dihydroxylation of **38** (0.92 mmol) according to the standard protocol afforded the title compounds **47**[46] (120 mg, 0.57 mmol, 57%) and **57** (47 mg, 0.226 mmol, 23%) after column chromatography (petroleum ether/ethyl acetate 3:1). When the reaction time was limited to 3 h, the yield for **47** was improved to 71%.

1st fraction **57**: oil; ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.01$ and 6.98 (2d, 4H, $J = 8.8$ Hz, Ph), 4.44 (q, $J = 7.2$ Hz, 2H, OCH_2CH_3), 3.90 (s, 3H, OCH_3), 1.42 (t, $J = 7.2$ Hz, 3H, OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 184.8$ (o, C=O), 164.5 (o, CO_2), 164.1 (o, C-*para*), 132.5, 114.2 (+, Ph), 125.5 (o, C-*ipso*), 62.1 (−, OCH_2CH_3), 55.6 (+, OCH_3), 14.1 (+, CH_3); LRMS (DCI): *m/z* (%): 226.0 (100) $[M+NH_4]^+$.

2nd fraction **47**: The enantiomeric excess of **47** was determined by chiral GC: isothermal 131 °C, 52.1 min (2*S*), 47.9 min (2*R*); AD-mix α: $ee_{(S)} = 86.1\%$, $[\alpha]$ $\Theta_{238.8\,nm} = 16901°$, $\Theta_{253.8\,nm} = 755°$, $\Theta_{274.6\,nm} = 2114°$, $\Theta_{287.6\,nm} = 1456°$, $\Theta_{280.6\,nm} = 1742°$ ($c = 0.580$ mM, MeOH, 26 °C); AD-mix β: $ee_{(R)} = 88.0\%$, $[\alpha]$ $\Theta_{206.8\,nm} = -6470°$, $\Theta_{216.0\,nm} = -219°$, $\Theta_{232.0\,nm} = -26100°$, $\Theta_{255.0\,nm} = -1030°$, $\Theta_{273.8\,nm} = -2430°$, $\Theta_{277.8\,nm} = -1730°$, $\Theta_{280.6\,nm} = -1880°$ ($c = 0.286$ mM, MeOH, 26.5 °C); oil; ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.34$, 6.90 (2 d, $J = 8.8$ Hz, 4H, Ph), 5.11 (d, $J = 5.8$ Hz, 1H, CHOH), 4.28, 4.17 (dq, $J = 7.2$, 10.6 Hz, 2H, OCH_2CH_3), 3.81 (s, 3H, OCH_3), 3.39 (d, $J = 5.8$ Hz, 1H, OH), 1.24 (t, $J = 7.2$ Hz, 3H, OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 173.8$ (o, C=O), 159.6, 130.8 (o, Ph), 127.8, 114.9 (+, Ph), 72.4 (+, CHOH), 62.1 (−, OCH_2CH_3), 55.2 (+, OCH_3), 14.0 (+, CH_3).

1,1-Diethoxy-2-hydroxy-4-phenyl-but-3-enyl-1-(diphenylphosphine oxide) (39) and (*E*)-2-hydroxy-4-phenylbut-3-enoic acid ethyl ester (48): Aldehyde **11** (132 mg, 1.0 mmol) was used to prepare the title compound **39** (294 mg, 0.72 mmol, 72%) by the general procedure described above. Amorphous solid; ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.92 - 7.26$ (m, 9H, Ph), 7.22 – 6.95 (m, 6H, Ph), 6.61 (dd, $J = 1.3$, 15.6 Hz, 1H, =CH−Ph), 6.12 (dd, $J = 5.4$, 15.6 Hz, 1H, −CH=CHPh), 5.30 (br, 1H, OH), 4.97 (ddd, $J = 1.2$, 5.4, 5.6 Hz, 1H, CHOH), 3.90 – 3.42 (m, 4H, $2OCH_2CH_3$), 1.18, 1.12 (2t, $J = 7.0$ Hz, 6H, $2CH_3$); $C_{26}H_{29}O_4P$: calcd C 71.54, H 6.70; found C 71.66, H 6.74.

Elimination and asymmetric dihydroxylation of **39** (204 mg, 0.5 mmol) according to the standard protocol afforded the title compound **48**[47] (71 mg, 0.37 mmol, 73%) after column chromatography (petroleum ether/ethyl acetate 12:1). The enantiomeric excess of **48** was determined by chiral GC: isothermal 107 °C, 42.83 min (2*S*), 41.20 min (2*R*); AD-mix α: $ee_{(S)} = 95.7\%$; AD-mix β: $ee_{(R)} = 93.5\%$; oil; ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.43 - 7.25$ (m, 5H, Ph), 6.82 (dd, $J = 1.2$, 15.6 Hz, PhCH=), 6.25 (dd, $J = 5.4$, 15.6 Hz, 1H, PhCH=CH), 4.83 (ddd, $J = 1.2$, 5.4, 5.6 Hz, 1H, CHOH), 4.32, 4.27 (2dq, $J = 7.0$, 10.6 Hz, 2H, OCH_2CH_3), 3.08 (d, $J = 5.6$ Hz, 1H, OH), 1.32 (t, $J = 7.0$ Hz, 3H, OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 177.2$ (o, C=O), 152.7 (+, C-4), 139.0 – 128.2 (o and +, Ph), 122.4 (+, C-3), 73.5 (+, CHOH), 62.9 (−, OCH_2CH_3), 15.8 (+, CH_3).

1,1-Dimethoxy-2-hydroxy-4-phenylbutyl-1-(diphenylphosphine oxide) (40) and 2-hydroxy-4-phenylbutyric acid methyl ester (49): Aldehyde **29** (134 mg, 1.0 mmol) was used to prepare the title compound **40** (293 mg, 0.71 mmol, 71%) by the general procedure described above. Colorless crystals, m.p. 132 °C; ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.1 - 7.85$ (m, 4H, Ph), 7.60 – 7.35 (m, 6H, Ph), 7.30 – 6.95 (m, 5H, Ph), 4.05 – 3.84 (m, 2H, CHOH), 3.39, 3.29 (2s, 6H, $2OCH_3$), 2.84 (ddd, $J = 4.8$, 9.4, 14.0 Hz, 1H, PhCH), 2.52 (ddd, $J = 7.7$, 8.7, 14.0 Hz, 1H, PhCH′), 1.96 – 1.56 (m, 2H, $PhCH_2CH_2$); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 141.7$ (o, Ph), 132.9, 131.1 (o, d, $J_{P-C} = 9.2$, 11.7 Hz, Ph), 132.4 – 125.5 (+, Ph), 103.9 (o, d, $J_{P-C} = 111.3$ Hz, $C(OMe)_2$), 74.0 (+, d, $J_{P-C} = 12.2$ Hz, CHOH), 52.0, 51.5 (+, d, $J_{P-C} = 5.8$, 7.3 Hz, $PC(OCH_3)_2$), 34.0, 32.4 (−, $PhCH_2CH_2$); $C_{24}H_{27}O_4P$: calcd C 70.23, H 6.63; found C 70.28, H 6.60.

Elimination and asymmetric dihydroxylation of **40** (1.0 mmol) according to the standard protocol afforded the title compound **49**[48] (66 mg, 0.34 mmol, 34%) after column chromatography (petroleum ether/ethyl acetate 9:1). The enantiomeric excess of **49** was determined by chiral GC: isothermal 130 °C, 31.10 min (2*S*), $[\alpha]_D^{23} = +10.8°$ ($c = 0.88$, $CHCl_3$); 27.94 min (2*R*), $[\alpha]_D^{23} = -12.0°$ ($c = 0.5$, $CHCl_3$); AD-mix α: $ee_{(S)} = 93.0\%$; AD-mix β: $ee_{(R)} = 94.0\%$; oil; ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.35 - 7.14$ (m, 5H, Ph), 4.19 (dd, $J = 4.1$, 7.8 Hz, CHOH), 3.75 (s, 1H, OCH_3), 2.74 (m, 3H, CHOH, $PhCH_2$), 2.13 (ddt, $J = 4.1$, 8.3, 14.0 Hz, 1H, $PhCH_2H'CH$), 1.98 (ddt, $J = 6.7$, 7.8, 14.0 Hz, 1H, $PhCH_2H'CH$); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 175.6$ (o, C=O), 141.0 (o, Ph), 128.5 – 126.0 (+, Ph), 69.6 (+, CHOH), 52.5 (+, CO_2CH_3), 35.8, 31.0 (−, $PhCH_2CH_2$).

1,1-Dimethoxy-2-hydroxyundecyl-1-(diphenylphosphine oxide) (41), 1-hydroxydecyl-1-(diphenylphosphine oxide) (53), and 2-hydroxyundecanoic acid methyl ester (50): Aldehyde **30** (156 mg, 1.0 mmol) was used to prepare the title compound **41** (352 mg, 0.81 mmol, 81%) and **53** (63 mg, 0.17 mmol, 17%) by the general procedure described above.

1st fraction **41**: colorless crystals; m.p. 78 °C; ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.1 - 7.85$ (m, 4H, Ph), 7.60 – 7.35 (m, 6H, Ph), 3.98 – 3.73 (m, 2H, CHOH), 3.43, 3.32 (2s, 6H, $2OCH_3$), 1.61 – 0.98 (m, 16H, $(CH_2)_8$), 0.95 – 0.79 (m, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 133.8 - 131.0$ (o, Ph), 132.5 – 128.1 (+, Ph), 103.9 (o, d, $J_{P-C} = 111.3$ Hz, $C(OMe)_2$), 74.9 (+, d, $J_{P-C} = 12.2$ Hz, CHO), 52.0, 51.3 (+, d, $J_{P-C} = 5.4$, 7.8 Hz, $C(OCH_3)_2$), 32.9 (−, d, $J_{P-C} = 1.5$ Hz, C-3), 31.8 – 22.6 (−, C-4 – C-10), 14.2 (+, C-11); $C_{25}H_{37}O_4P$: calcd C 69.42, H 8.62; found C 69.38, H 8.82.

2nd fraction **53**: colorless crystals; m.p. 100 °C; ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.95 - 7.72$ (m, 4H, Ph), 7.60 – 7.37 (m, 6H, Ph), 4.39 (d, $J = 9.2$ Hz, 1H, PCHOH), 3.62 (br, 1H, OH), 1.79 – 1.15 (m, 16H, $(CH_2)_8$), 0.92 – 0.80 (m, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 132.0 - 128.3$ (+, Ph), 130.2, 129.4 (o, Ph), 70.6 (+, d, $J_{P-C} = 83.6$ Hz, PCHOH), 31.8 – 22.6 (−, C-3 – C-9), 30.5 (−, d, $J_{P-C} = 2.9$ Hz, C-2), 14.1 (+, C-10); $C_{22}H_{31}OP$: calcd C 73.72, H 8.72; found C 73.88, H 8.69.

Elimination and asymmetric dihydroxylation of **41** (433 mg, 1.0 mmol) according to the standard protocol afforded the title compound **50**[49] (152 mg, 0.7 mmol, 70%) after column chromatography (petroleum ether/ethyl acetate 10:1). The enantiomeric excess of **50** was determined by chiral GC: isothermal 108 °C, 29.36 min (2*S*), $[\alpha]_D^{23} = +7.2°$ (*c* 1.0, $CHCl_3$); 27.88 min (2*R*); $[\alpha]_D^{21} = -10.2°$ (*c* 1.0, $CHCl_3$); AD-mix α: $ee_{(S)} = 92.0\%$; AD-mix β: $ee_{(R)} = 98.0\%$; oil; ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 4.19$ (ddd, $J = 4.2$, 5.6, 6.8 Hz, 1H, CHOH), 3.79 (s, 3H, OCH_3), 2.70 (d, $J = 5.6$ Hz, 1H, OH), 1.84 – 1.20 (m, 16H, $(CH_2)_8$), 0.93 – 0.83 (m, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 175.9$ (o, C=O), 70.4 (+, CHOH), 52.5 (+, OCH_3), 34.4 – 22.7 (−, $(CH_2)_8$), 14.1 (+, CH_3). $C_{12}H_{24}O_3$: calcd C 66.63, H 11.18; found C 66.66, H 11. 36.

1,1-Diethoxy-2-hydroxy-(2-furyl)ethyl-1-(diphenylphosphine oxide) (55) and furan-2-yloxoacetic acid ethyl ester (56): Aldehyde **54** (282 mg, 3.0 mmol) was used to prepare the title compound **55** (466 mg, 1.26 mmol, 42%) by the general procedure described above. Oil; ^1H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.88 - 7.67$ (m, 3H, Ph), 7.49 – 7.16 (m, 7H, Ph), 7.03 (d, $J = 2.5$ Hz, 1H, OCHCHCH), 6.14 (d, $J = 3.4$ Hz, 1H, OCHCH), 5.92 (dd, $J = 2.5$, 3.4 Hz, 1H, OCHCH), 5.18 (br, 1H, CHOH), 5.04 (d, $J = 11.0$ Hz, 1H, CHOH), 4.16 – 3.44 (m, 4H, $2OCH_2CH_3$), 1.09, 1.04 (2t, $J = 7.0$ Hz, 6H, $2CH_3$).

Elimination and asymmetric dihydroxylation of **55** (400 mg, 1.0 mmol) according to the standard protocol with AD-mix α afforded the title compound **56**[50] (42 mg, 0.25 mmol, 25%) after column chromatography (petroleum ether/ethyl acetate 19:1 and trace of NEt_3). Oil; ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.01$, (d, $J = 7.5$ Hz, 1H, OCH), 7.67 (d, $J = 7.5$ Hz, 1H, OCHCHCH), 7.52 (t, $J = 7.5$ Hz, 1H, OCHCHCH), 4.45 (q, $J = 7.0$ Hz, 2H, OCH_2CH_3), 1.43 (t, $J = 7.0$ Hz, 3H, OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 184.1$ (o, C=O), 165.6 (o, CO_2Et), 151,5 (+, OCH), 142.1 (o, OCHCHCH), 111.0 (+, OCHCHCH), 108.9 (+, OCHCH), 62.2 (−, OCH_2CH_3), 14.9 (+, CH_3).

(2*RS*,3*R*)-1,1-Dimethoxy-2-hydroxy-3-phenylbutyl-1-(diphenylphosphine oxide) (66) and (2*RS*,3*R*)-2-Hydroxy-3-phenylbutyric acid methyl ester (61a,b): Aldehyde **60** (402 mg, 3.0 mmol) was used to prepare the title compound **66** (902 mg, 2.2 mmol, 73%) by the general procedure described

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above. Compound **66** was obtained as 10:1 mixture of which the major isomer was isolated after column chromatography in pure form. Colorless crystals; m.p. 127 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.18 - 7.98$ (m, 4H, Ph), 7.58 – 7.38 (m, 6H, Ph), 7.16 – 7.05 (m, 3H, Ph), 6.73 – 6.67 (m, 2H, Ph), 4.10 (ddd, $J = 3.5, 5.1, 9.5$ Hz, 1H, C*H*OH), 3.41, 3.37 (2s, 6H, $2OCH_3$), 3.45 – 3.24 (m, 1H, PhCH), 3.28 (d, $J = 9.5$ Hz, 1H, OH), 1.32 (d, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 146.2 - 132.3$ (o, Ph), 132.5 – 125.7 (+, Ph), 104.1 (o, d, $J_{P-C} = 111.3$ Hz, *C*$(OMe)_2$), 78.4 (+, d, $J_{P-C} = 17.0$ Hz, CHO), 52.5, 52.1 (+, d, $J_{P-C} = 5.3, 8.8$ Hz, $C(OCH_3)_2$), 40.1 (+, d, $J_{P-C} = 1.5$ Hz, C-3), 14.4 (+, CH_3).

Elimination and asymmetric dihydroxylation of **66** (410 mg, 1.0 mmol) according to the standard protocol afforded the title compound **61a,b**[51] (151 mg, 0.78 mmol, 78 %) after column chromatography (petroleum ether/ethyl acetate 10:1). The diastereomeric excess of **61a,b*** was determined by chiral GC: isothermal 122 °C, 27.42 min (2*S*, 3*R*); 20.59 min (2*R*, 3*R*); AD-mix α: $de_{(2S)} = 91.0$ %; AD-mix β: $de_{(2R)} = 77.8$ %; oil; ^{1}H NMR (200 MHz, $CDCl_3$, TMS): $\delta = 7.35 - 7.16$ (m, 5H, Ph), 4.37 (m, 1H, C*H*OH), 3.76, 3.69* (s, 3H, CO_2CH_3), 3.33 – 3.17 (m, 1H, PhC*H*), 2.76, 2.57* (d, $J = 6.2, 7.0$* Hz, OH), 1.29, 1.15* (d, $J = 6.8, 6.8$* Hz, 3H, PhCHCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 174.6, 174.2$* (o, C=O), 142.5, 140.5* (o, Ph), 128.5 – 126.8 (+, Ph), 75.0, 74.9 (+, *C*HOH), 52.5, 52.2* (+, CO_2CH_3), 43.4*, 43.3 (+, Ph*C*H), 17.5*, 14.4 (+, PhCH*C*H_3); $C_{11}H_{14}O_3$: calcd C 68.02, H 7.27; found C 66.68, H 7.16.

(2*S*,3*R*,4*S*)-5-*tert*-Butyldiphenylsiloxy-2-hydroxy-4-methyl-5-tetrahydropyranyloxypentanoic acid methyl ester (63): Aldehyde **62** (two isomers 3:1; 440 mg, 1.0 mmol) and lithiated diphenylphosphine oxide **31** (3.0 mmol) were used to prepare the corresponding intermediate phosphine oxide (350 mg, 0.49 mmol, 49 %), which was directly converted into the title compound **63** (two isomers 3:1*; 160 mg, 0.32 mmol, 65 %) by applying the general procedure described above, with AD-mix α. Oil; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.78$– 7.61 (m, 4H, Ph), 7.50 – 7.31 (m, 6H, Ph), 4.66 (dd, $J = 2.8, 3.8$ Hz, 1H, OCHO (THP, tetrahydropuran)), 4.58 (dd, $J = 2.2, 4.2$ Hz, 1H, C*H*OH), 5.53* [dd, 1H, OCHO (THP)), 4.12* (dd, $J = 2.6, 4.6$ Hz, 1H, C*H*OH), 4.01 – 3.50 (m, 5H, CHOTHP, $SiOCH_2$, CH_2O (THP)), 3.81 (s, 3H, OCH_3), 3.78* (s, 3H, OCH_3), 2.79* (dq, 1H, C*H*CH_3), 2.55 (dq, $J = 2.0, 7.0$ Hz, 1H, C*H*CH_3), 1.89 – 1.25 (m, 6H, THP), 1.07 (s, 9H, *t*Bu), 0.78 (d, $J = 7.0$ Hz, 3H, CHCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 175.3$ (o, C=O), 133.5, 133.4 (o, Ph), 135.8 – 127.5 (+, Ph), 100.8 (+, OCO (THP)), 81.2, 71.1 (+, C-2, C-3), 64.6, 62.5 (–, C-5, CH_2O (THP)), 52.4 (+, OCH_3), 37.6, (+, C-4), 30.8, 25.3, 19.6 (–, 3 CH_2 (THP)), 26.8 (+, *t*Bu), 19.3 (o, *t*Bu), 10.3 (+, CH_3); $C_{28}H_{40}O_6Si$: calcd C 67.17, H 8.05; found C 67.15, H 8.24.

(2*R*,4*R*)-4-(*tert*-Butyldiphenylsiloxy)-2-hydroxypentanoic acid ethyl ester (65): Aldehyde **64** (259 mg, 0.726 mmol) and lithiated diphenylphosphine oxide **32** (3.0 mmol) were used to prepare the corresponding intermediate phosphine oxide (oil: 293 mg, 0.46 mmol, 64 %; 2:3 diastereomeric ratio), of which 155 mg, 0.246 mmol were directly converted into the title compound **65** (92 mg, 0.23 mmol, 94 %) by applying the general procedure with AD-mix β. Purification was achieved by after column chromatography (petroleum ether/ethyl acetate 1:1). The diastereomeric excess of **65** was determined by NMR spectroscopy. Oil; $[\alpha]_D^{24} = +4.1°$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.74 - 7.69$ (m, 4H, Ph), 7.46 – 7.36 (m, 6H, Ph), 4.36 – 4.14 (m, 4H, OCH_2CH_3, 2-H, 4-H), 2.99 (br, 1H, OH), 1.97 (ddd, 1H, $J = 4.0, 6.4, 13.8$ Hz, 1H, 3-H), 1.85 (ddd, $J = 5.6, 8.8, 13.8$ Hz, 1H, 3-H′), 1.29 (t, $J = 7.2$ Hz, 3H, OCH_2CH_3), 1.14 (d, $J = 6.0$ Hz, 1H, 5-H), 1.08 (s, 9H, *t*Bu); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 175.0$ (o, C=O), 134.4, 134.2 (o, Ph), 135.8 – 127.5 (+, Ph), 68.7, 67.9 (+, C-2, C-4), 61.1 (–, OCH_2CH_3), 43.5 (–, C-3), 26.9 (+, *t*Bu), 23.0 (+, C-5), 19.2 (o, *t*Bu), 14.1 (+, OCH_2CH_3); $C_{23}H_{32}O_4Si$: calcd C 68.96, H 8.05; found C 68.81, H 7.89.

(2*S*,2′*S*,3′*R*,4′*R*,5′*R*,6′*R*)-1,1-Dimethoxy-2-hydroxy-2-[2′(3′,4′,5′,6′-di-*O*-*iso*-propylidene)tetrahydropyranyl]ethyl-1-(diphenylphosphine oxide) (68), **(2*RS*,2′*S*,3′*R*,4′*R*,5′*R*,6′*R*)-2-hydroxy-2-[2′(3′,4′,5′,6′-di-*O*-isopropylidene)-tetrahydropyranyl]acetic acid methyl ester (69a,b), and (2′*S*,3′*R*,4′*R*,5′*R*,6′*R*)-2-[2′(3′,4′,5′,6′-di-*O*-isopropylidene)tetrahydropyranyl]acetic acid methyl ester (70)**: Aldehyde **67** (310 mg, 1.2 mmol) was used to prepare the title compound **68** (359 mg, 0.67 mmol, 56 %) by the general procedure described above. Colorless solid, m.p. 70 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 8.17 - 8.03$ (m, 4H, Ph), 7.5 – 7.32 (m, 6H, Ph), 5.54 (d, $J = 4.8$ Hz, 1H, 6′-H), 4.61 (brd, $J = 5.6$ Hz, 1H, 2′-H), 4.56 (dd, $J = 1.8, 6.0$ Hz, 1H, 4′-H), 4.51 (dd, $J = 1.0, 6.0$ Hz, 1H, 3′-H), 4.47 (dd, $J = 5.6$ Hz, $J_{P-C} = 12.4$ Hz, 1H, 2-H), 4.25 (dd, $J = 1.8, 4.8$ Hz 1H, 5′-H), 3.41, 3.37 (2s, 6H, $2OCH_3$), 2.76 (br, 1H, COH), 1.06, 1.40, 1.31, 1.30, 1.06 (4s, $2C(CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 134.5$ (o, d, $J_{P-C} = 19.9$ Hz, Ph), 132.7 (o, d, $J_{P-C} = 21.4$ Hz, Ph), 132.1 – 127.8 (+, Ph), 108.8, 108.7 (o, $2C(CH_3)_2$), 104.6 (o, d, $J_{P-C} = 114.2$ Hz, *C*$(OCH_3)_2$), 96.3 (+, C-6′), 73.0, 71.1, 70.8 (+, C-5′, C-4′, C-3′), 71.3 (+, d, $J_{P-C} = 12.2$ Hz, C-2′), 64.9 (+, d, $J_{P-C} = 2.9$ Hz, *C*HOH), 52.7, 51.4 (+, d, $J_{P-C} = 6.8$ Hz, $2OCH_3$), 26.0, 25.9, 25.0, 23.9 (+, $2C(CH_3)_2$).

Elimination and asymmetric dihydroxylation of **68** (536 mg, 1.0 mmol) by applying the standard protocol described above except that a threefold excess of the AD-mix α reagent was employed afforded the title compounds (2*S*)-**69a** (257 mg, 0.81 mmol, 81 %) and **70** (18.1 mg, 0.06 mmol, 6 %) after column chromatography (petroleum ether/ethyl acetate 10:1). The diastereomeric excess was determined by ^{1}H NMR spectroscopy of the crude product.

1st fraction **70**: Oil; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 5.49$ (d, $J = 5.0$ Hz, 1H, 6′-H), 4.63 (dd, $J = 2.3, 7.8$ Hz, 1H, 4′-H), 4.31 (dd, $J = 2.3, 5.0$ Hz, 1H, 5′-H), 4.34 – 4.19 (m, 2H, 2′-H, 3′-H), 3.71 (s, 3H, OCH_3), 2.71 (dd, $J = 7.4, 16.2$ Hz, 1H, C*H*CO_2CH_3), 2.61 (dd, $J = 5.8, 16.2$ Hz, 1H, C*H*′CO_2CH_3), 1.59, 1.46 (2s, 6H, $C(CH_3)_2$), 1.34 (s, 6H, $2C(CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 171.5$ (o, C=O), 109.3, 108.8 (o, $2C(CH_3)_2$), 96.3 (+, C-6′), 72.3, 70.8, 70.4, 64.7 (+, C-5′, C-4′, C-3′, C-2′), 51.8 (+, OCH_3), 35.4 (–, $CH_2CO_2CH_3$), 25.9, 25.8, 25.0, 24.4 (+, $2C(CH_3)_2$); $C_{14}H_{22}O_7$: calcd C 55.62, H 7.33; found C 55.64, H 7.55.

2nd fraction: **69a**: Oil; $[\alpha]_D^{24} = -45.3°$ ($c = 1$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 5.57$ (d, $J = 5.0$ Hz, 1H, 6′-H), 4.64 (dd, $J = 2.4, 8.0$ Hz, 1H, 4′-H), 4.56 (dd, $J = 2.3, 3.2$ Hz, 1H, C*H*OH), 4.48 (dd, $J = 1.8, 8.0$ Hz, 1H, 3′-H), 4.33 (dd, $J = 2.4, 5.0$ Hz, 1H, 5′-H), 4.19 (dd, $J = 1.8, 3.2$ Hz, 1H, 2′-H), 3.82 (s, 3H, OCH_3), 3.73 (d, $J = 2.3$ Hz, 1H, OH), 1.54, 1.49, 1.46, 1.33 (4s, 12H, $2C(CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 171.3$ (o, C=O), 110.0, 109.0 (o, $2C(CH_3)_2$), 96.4 (+, C-6′), 72.9, 72.0, 71.0, 70.6, 67.2 (+, C-5′, C-4′, C-3′, C-2′, CHOH), 52.6 (+, OCH_3), 25.9, 25.7, 25.0, 24.0 (+, $2C(CH_3)_2$).

Accordingly, a threefold excess of AD-mix β afforded (2*R*)-**69b** (248 mg, 0.78 mmol, 78 %) starting from aldehyde **67** (536 mg, 1.0 mmol). Colorless crystals, m.p. 152 °C; $[\alpha]_D^{23} = -65.4°$ ($c = 0.5$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 5.56$ (d, $J = 5.0$ Hz, 1H, 6′-H), 4.64 (dd, $J = 2.5, 8.0$ Hz, 1H, 4′-H), 4.43 (dd, $J = 1.8, 7.0$ Hz, 1H, 3′-H), 4.43 (dd, $J = 7.2, 9.0$ Hz, 1H, C*H*OH), 4.34 (dd, $J = 2.5, 5.0$ Hz, 1H, 5′-H), 3.96 (dd, $J = 1.7, 7.2$ Hz, 1H, 2′-H), 3.82 (s, 3H, OCH_3), 3.24 (d, $J = 9.0$ Hz, 1H, OH), 1.53, 1.49, 1.36, 1.33 (4s, 12H, $2C(CH_3)_2$); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 173.3$ (o, C=O), 109.8, 108.9 (o, $2C(CH_3)_2$), 96.4 (+, C-6′), 71.1, 71.1, 71.0, 71.0, 67.7 (+, C-5′, C-4′, C-3′, C-2′, CHOH), 52.6 (+, OCH_3), 26.0, 25.8, 24.9, 24.2 (+, $2C(CH_3)_2$); $C_{14}H_{22}O_8$: calcd C 52.82, H 6.97; found C 52.80, H 7.16.

Asymmetric dihydroxylation of *O*,*S*-ketene acetal **71** (118 mg, 0.3 mmol) with the AD-mix α afforded the title compounds **69a,b** (9 mg, 0.028 mmol, 9 %) as a 2:1 diastereomeric mixture. In analogy, sulfoxide **72** (315 mg, 0.77 mmol) gave **69a,b** (76 mg, 0.24 mmol, 31 %) as a 1:1 mixture after use of the AD-mix β under the standard conditions. In both cases, the analytical data were in accordance with those described above.

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