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Asymmetric Dihydroxylation of β,γ-Unsaturated Carboxylic Esters with Trisubstituted C=C Bonds – Enantioselective Syntheses of Trisubstituted γ-Butyrolactones

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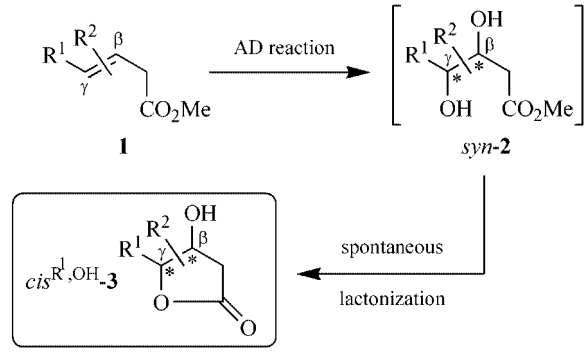
β,γ-Unsaturated esters with stereodefined trisubstitued C=C double bonds were prepared by the Arndt–Eistert homologation of α,β-unsaturated carboxyl halides, by two-step methoxycarbonylation of allylbarium reagents, by deconjugation of α,β-unsaturated esters, and by Horner–Wadsworth–Emmons variants of the Stobbe condensation. Sharpless asymmetric dihydroxylation of the β,γ-unsaturated esters, followed by spontaneous cyclization, afforded β-hydroxy-γ-lactones in moderate to good yields and with enantiomeric excesses of up to 97 %. Similarly, tetrahydroxy-γ-lactones were obtained from diunsaturated esters; these lactones were converted into a bislactone and an unsaturated β-hydroxy γ-lactone.

Introduction

γ-Lactones are a commonly encountered structural motif in nature[1] and synthesis (both as targets and synthetic intermediates). This is particularly true if these γ-lactones are enantiomerically pure. Accordingly, a considerable body of methods for synthesizing such lactones with saturated ("butanolides"[2]) or α,β-unsaturated rings ("Δ^3-butenolides"[3]) has been developed over the years. They include a straightforward asymmetric synthesis by our group, based on Sharpless' asymmetric dihydroxylation ("AD reaction")[4] of β,γ-unsaturated carboxylic esters **1** (Scheme 1).[5] This approach provides γ-lactones **3** with *ee*s of typically 94–98 %, in good yields and a single step.[5–7]

In all previous studies by this group[5b,6,7] (with a single exception;[8] vide infra) and by others[5a,9] the AD reaction has been performed upon β,γ-unsaturated carboxylic esters **1** containing disubstituted $C^{\beta}=C^{\gamma}$ double bonds (Scheme 1: R^2 = H), resulting in the formation of γ-*mono*alkyl- or γ-*mono*aryl-β-hydroxy-γ-lactones **3** (R^2 = H). A logical extension of this concept appeared to be analogous AD reactions of β,γ-unsaturated carboxylic esters **1** containing *tri*substituted $C^{\beta}=C^{\gamma}$ double bonds (Scheme 1: $R^2 \neq$ H). They should provide β,γ-dialkyl- and γ,γ-dialkyl-β-hydroxy-γ-lactones **3** ($R^2 \neq$ H) as well as their aryl-containing congeners. This paper describes how this concept was put into practice.

A prerequisite for this study was the acquisition of model esters for the AD reaction as pure stereoisomers with respect to their $C^{\beta}=C^{\gamma}$ double bonds; otherwise AD reactions of these esters would give mixtures of lactone diastereomers. Stereodefined β,γ-unsaturated esters were obtained by the following approaches: Arndt–Eistert homologation of α,β-unsaturated acids [**7**–**10**, (*E*)- and (*Z*)-**14**], carboxylation of allyl barium compounds [(*E*)- and (*Z*)-**18**], Horner–Wadsworth–Emmons reactions ("HWE reactions") [(*E*)-**31**–**34**, (*Z*)-**31**, (*Z*)-**33** and -**34**], and deprotonation/reprotonation of α,β-unsaturated carboxylic esters (**24**, **25**).



1 *syn*-**2** *cis*$^{R^1,OH}$-**3**

Scheme 1. Dihydroxylation strategy for the asymmetric synthesis of γ-lactones.

Results and Discussion

Preparation of the AD Precursors

The majority of our syntheses of stereochemically pure β,γ-unsaturated carboxylic esters were achieved by Arndt–Eistert homologation of analogously substituted α,β-unsat-

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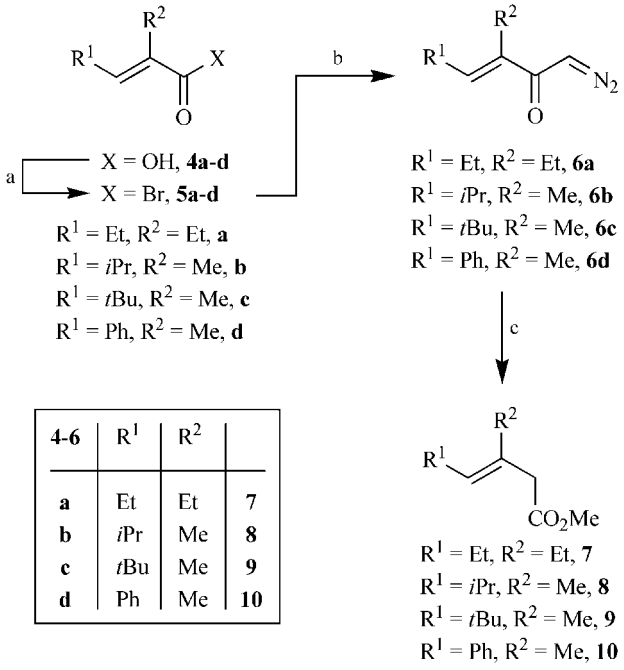
urated carboxylic acids.[10] This approach worked well when starting from the α,β-dialkylated α,β-unsaturated acids **4a**–**d** (Scheme 2) and the β,β-dialkylated α,β-unsaturated acids (*E*)- and (*Z*)-**11** (Scheme 3). Acids **4a** and **4b** were obtained by alkaline hydrolyses of the corresponding (*E*)-configured α,β-unsaturated esters (not shown), these in turn being obtained by Wittig reactions.[11] Acid **4c** was synthesized as described,[36] whilst acid **4d** is commercially available. Acids (*E*)- and (*Z*)-**11** were produced through *cis*-selective carbocuprations of appropriately substituted alkynoic acids.[12]

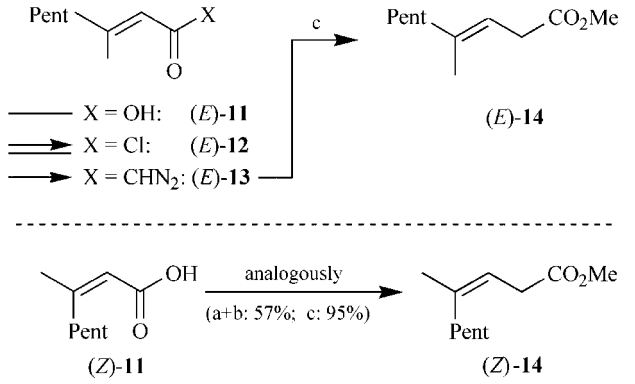


4-6	R^1	R^2	
a	Et	Et	**7**
b	*i*Pr	Me	**8**
c	*t*Bu	Me	**9**
d	Ph	Me	**10**

Scheme 2. Arndt–Eistert homologation of α,β-dialkyl α,β-unsaturated carboxyl bromides. Reagents and conditions: (a) For **5a**–**c**: $(COBr)_2$ (1.01 equiv.), no solvent, –15 °C, overnight; for **5d**: 1-bromo-2-(dimethylamino)-2-methyl-1-propene (1.0 equiv.), CH_2Cl_2, 0 °C → room temp., 1 h. (b) CH_2N_2 (1.0 equiv.), *i*Pr_2NEt (1.1 equiv.), Et_2O, 0 °C → room temp., 2 h; **6a**: 28% over the two steps; **6b**: 83% over the two steps; **6c**: 81% over the two steps; **6d**: 52% over the two steps. (c) AgOBz, NEt_3, MeOH, room temp., 5 h; **7** (*E*:*Z* = 100:0): 76%; **8** (*E*:*Z* = 100:0): 77%; **9** (*E*:*Z* = 100:0): 87%; **10** (*E*:*Z* = 100:0): 86%.

It is known that the acylation of diazomethane with activated α,β-unsaturated carboxylic acids may be accompanied by pyrazoline formation through a 1,3-dipolar cycloaddition of diazomethane to the electron-deficient $C^{\alpha}=C^{\beta}$ bond.[13] This competition was detrimental to formation of the desired diazo ketones **6a**–**d** from the acid chlorides obtained from the α,β-dialkylated α,β-unsaturated acids **4a**–**d** (Scheme 2). In contrast, pyrazoline formation was insignificant in diazomethane treatment of acid chlorides (*E*)- and (*Z*)-**12** [→ diazo ketones (*E*)- and (*Z*)-**13**, respectively; Scheme 3]. With use of the α,β-unsaturated acid bromides **5a**–**d** – rather than the analogous chlorides – as acylating agents, however, diazo ketones **6a**–**d** were also generated successfully (Scheme 2).

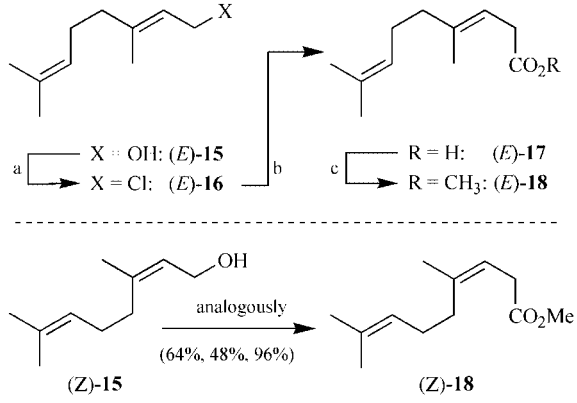
Silver benzoate-induced Wolff rearrangements[14] of diazo ketones **6a**–**d**, (*E*)-**13**, and (*Z*)-**13** in methanol furnished



Scheme 3.[8] Arndt–Eistert homologation of β,β-dialkyl α,β-unsaturated carboxylic acid chlorides. Reagents and conditions: (a) $SOCl_2$ (1.0 equiv.), DMF (cat.), CH_2Cl_2, 0 °C → room temp., 3 h. (b) CH_2N_2 (2.0 equiv.), *i*Pr_2NEt (1.0 equiv.), Et_2O, 0 °C → room temp., 1 h: 55% over the two steps. (c) AgOBz (0.3 equiv.), NEt_3 (4.7 equiv.), MeOH, room temp., 5 h; 88% (*E*:*Z* = 100:0). (*Z*)-**14**: *Z*:*E* = 100:0.

the desired β,γ-unsaturated methyl esters **7**–**10**, (*E*)-**13**, and (*Z*)-**13**, respectively. These were produced with complete retention of the C=C double bond configuration.

Geraniol [(*E*)-**15**] and nerol [(*Z*)-**15**] were converted into the analogous chlorides (*E*)- and (*Z*)-**15**, respectively, through treatment with mesyl chloride and triethylamine[15] (Scheme 4). The corresponding barium derivatives – obtained by treatment with Rieke barium (from anhydrous barium iodide and lithium biphenylide) – were C_1-extended through addition to carbon dioxide. This afforded the β,γ-unsaturated carboxylic acids (*E*)- and (*Z*)-**17** stereospecifically, as reported by Yamamoto et al.[16] Methyl ester formation with (trimethylsilyl)diazomethane[17] in benzene/methanol gave the desired β,γ-unsaturated esters (*E*)- and (*Z*)-**18** in 96% yield and diastereomerically pure within the limits of ^1H NMR detection.

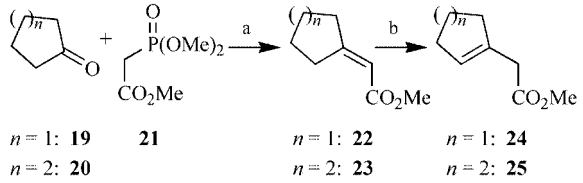


Scheme 4. Methoxycarbonylation of allylbarium reagents. Reagents and conditions: (a) $MeSO_2Cl$ (1.5 equiv.), pentane, –5 °C, 30 min; pyridine (2.0 equiv.), pentane, room temp., 14 h; 83% (ref.[15] 74%). (b) BaI_2 (2.2 equiv.), Li biphenylide (4.4 equiv.), THF, –78 °C, 30 min; CO_2 (gaseous), 30 min; 61% (ref.[16] 87%). (c) Me_3SiCHN_2 (1.3 equiv.), MeOH/benzene (1:3.6), room temp., 1 h; 96% (*E*:*Z* = 100:0). (*Z*)-**18**: *Z*:*E* = 100:0.

We found the syntheses of ester (*E*)-**18** shown in Scheme 4 superior to carboxymethylation of either allyl

chloride (*E*)-**16** or the analogous allyl phosphate with CO/methanol in the presence of $Pd_2(dba)_3$/NaOMe.[18] This kind of reaction was poorly stereoselective in our hands; chloride (*E*)-**16**, for example, gave (*E*)-**18**:(*Z*)-**18** = 73:27 (74%).

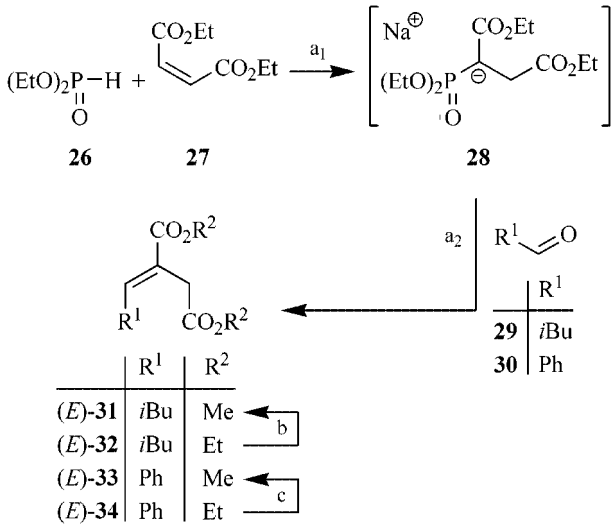
β,γ-Unsaturated esters **24**[19] and **25**[20] contain endocyclic $C^{\beta}=C^{\gamma}$ bonds: namely, a cyclopentenyl and a cyclohexenyl moiety, respectively (Scheme 5). These compounds were obtained by deconjugation of the isomeric α,β-unsaturated esters **22**[19] and **23**,[20] respectively, these in turn being obtained by HWE reactions between the appropriate cycloalkanones and phosphonate **21**.[21] Deconjugation was achieved by subsequent deprotonation with LDA followed by reprotonation with aqueous NH_4Cl and glacial acetic acid, respectively.



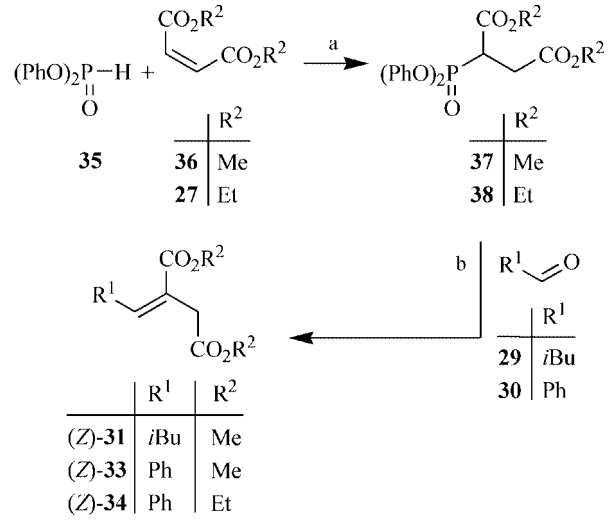
Scheme 5. Formation and deconjugation of α,β-unsaturated esters. Reagents and conditions: (a) NaOMe (1.2 equiv.), methanol, room temp., 12 h, **22**: 93% (as a 90:10 mixture with **24**), **23**: 98%. (b) LDA (1.1 equiv.), THF, –78 °C, 1 h; NH_4Cl (for **24**) or HOAc (for **25**); **24**: 76%, **25**: 78%.

The second largest number of β,γ-unsaturated ester syntheses in this study was obtained by HWE variants of the Stobbe condensation (Scheme 6, Scheme 7). These reactions furnished diethyl diesters (*E*)-**32**, (*E*)-**34**, and (*Z*)-**34** and dimethyl diesters (*Z*)-**31** and (*Z*)-**33**. Subsequent transesterifications of diethyl diesters (*E*)-**32** and (*E*)-**34** with sodium methoxide also gave the dimethyl diesters (*E*)-**31** and (*E*)-**33**.

We tried to establish the $C^{\beta}=C^{\gamma}$ bonds in the described "Stobbe condensation products" stereoselectively by varying the phosphonate moieties in the employed HWE reagents: with a $(EtO)_2P(=O)$ moiety in HWE reagent **28** (Scheme 6) as opposed to a $(PhO)_2P(=O)$ moiety in the HWE reagents **37** and **38**[22] in Scheme 7. The presence of the $(EtO)_2P(=O)$ moiety in HWE reagent **28** made the olefinations of the aliphatic aldehyde **29** and of benzaldehyde (**30**) (*E*)-selective to extents of 82:18 (**32**) and 93:7 (**34**), respectively (Scheme 6). The $(PhO)_2P(=O)$-containing HWE reagents **37** and **38**[22] olefinated the same aldehydes with *Z*:*E* selectivities between 81:19 (→**34**) and 67:33 (→**31**; Scheme 7);[23] to the best of our knowledge, these last reagents have been used for (*Z*)-selective succinylidenations for the first time. In all instances, the major unsaturated ester isomer could be obtained isomerically pure by flash chromatography[24] on silica gel.



Scheme 6. (*E*)-selective Horner–Wadsworth–Emmons variant of the Stobbe condensation. Reagents and conditions: (a_1) **26**, NaH (1.0 equiv.), EtOH, 0 °C → room temp., 30 min; addition of **27** (1.0 equiv.), 1 h (→ **28**; not isolated). (a_2) Crude **28**, **29** (1.0 equiv.) or **30** (1.0 equiv.), 4 h [for preparation of (*E*)-**32**] or overnight [for preparation of (*E*)-**34**]; (*E*)-**32**: 61% (*E*:*Z* = 82:18); (*E*)-**34**: 48% (*E*:*Z* = 93:7). (b) NaH (2.0 equiv.), MeOH, room temp., 2 d; 87% (*E*:*Z* = 81:19); (c) same as b), 3 d; 81% (*E*:*Z* = 92:8).



Scheme 7. (*Z*)-selective Horner–Wadsworth–Emmons variant of the Stobbe condensation. Reagents and conditions: (a) **35**, NaH (1.0 equiv.), THF, 0 °C → room temp., 30 min, addition of **36** (1.0 equiv.), 3 h; 69% **37**; **38**.[22] (b) **37** or **38**, NaH (1.0 equiv.), **29** (1.0 equiv.) or **30** (1.0 equiv.), THF, 0 °C → room temp., 3 h [for preparation of (*Z*)-**31** and (*Z*)-**33**] or 1 h [for preparation of (*Z*)-**34**]; (*Z*)-**31**: 86% (*Z*:*E* = 80:20); (*Z*)-**33**: 48% (*Z*:*E* = 67:33); (*Z*)-**34**: 79% (*Z*:*E* = 81:19).

AD Reactions

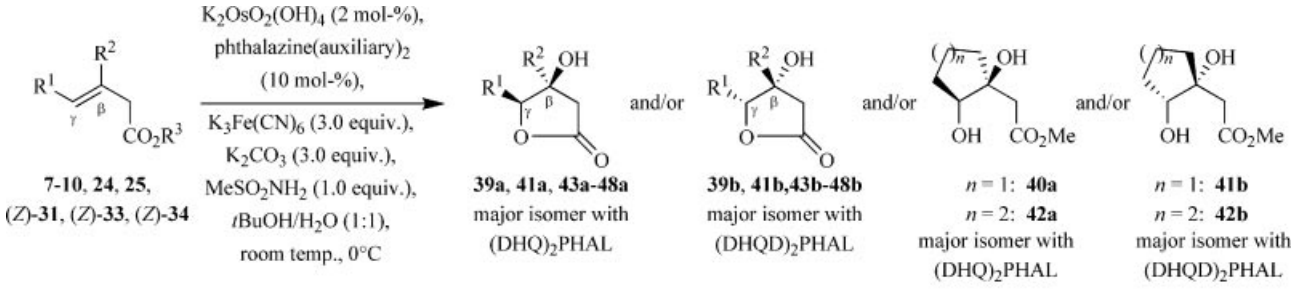
Having made the selected β,γ-unsaturated model esters accessible as single stereoisomers, we proceeded to examine magnitudes of stereocontrol during their AD reactions. In order to collect a fairly comprehensive set of data, all AD reactions were performed separately in the presence of the chiral auxiliaries contained in AD mix® α [i.e., $(DHQ)_2$-PHAL] and AD mix® β [$(DHQD)_2$PHAL], routinely using the so-called "improved"[25] conditions and only occasionally oxidant and auxiliary stoichiometries approaching "standard AD conditions".[26]

All AD results are shown in Table 1, Table 2, and Table 3. Table 1 relates to β,γ-disubstituted esters containing (*E*)-configured R^1–C=C–CH_2–CO_2R^3 moieties as substrates, Table 2 to AD reactions of β,γ-disubstituted esters with (*Z*)-configured R^1–C=C–CH_2–CO_2R^3 moieties, and Table 3 to the behavior of pairs of *E*,*Z*-isomeric γ-disubstituted β,γ-unsaturated esters under AD conditions.

The AD reactions of β,γ-disubstituted esters with (*E*)-configured (cf. footnote [a] of Table 1) R^1–C=C–CH_2–CO_2R^3 moieties were reasonably high-yielding (Table 1), the yields for 18 reactions averaging 69% and the peak yield being 87% (Entries 3, 7). The lowest yields, not unexpectedly, resulted from AD reactions with benzylidene succinates (*Z*)-**33** and (*Z*)-**34** (38%, 47%, 49%; Entries 15–17) and with ester **9**, which contains a *tert*-butylated C=C bond (55%, 56%; Entries 9, 10). This appears to reflect an electronic and a steric effect, respectively.

An unusual chemoselectivity of two pairs of AD reactions in Table 1 deserves mention (Entries 3–6). β,γ-Dihydroxy ester **40a** (or its enantiomer **40b**) obtained from cyclopentene **24** did not lactonize at all (Entries 3, 4). Similarly (Entries 5, 6), only ca. 25% of the β,γ-dihydroxy ester **42a** (or its enantiomer **42b**) obtained from cyclohexene **25** cyclized to give γ-lactone **41a** (or its enantiomer **41b**). These observations contrast with the spontaneous and complete lactonization of *all* β,γ-dihydroxy esters previously obtained under AD conditions (Scheme 1). The decreased driving force for lactonization in the cases under scrutiny must be due to the extra strain expected for *trans*-fused *bicyclic* γ-lactones.

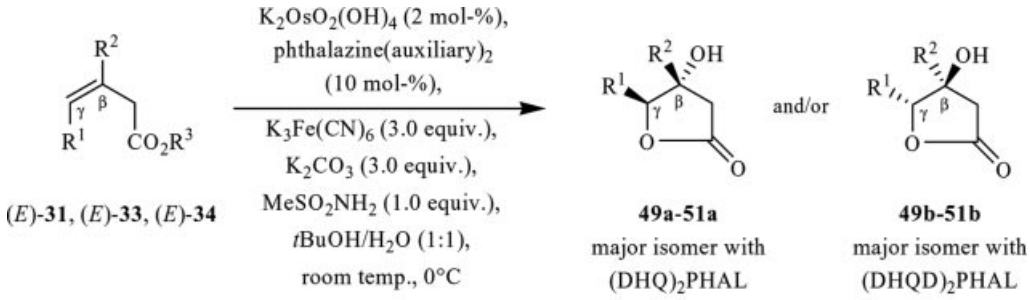
Table 1. AD reactions[25] of β,γ-unsaturated β,γ-disubstituted esters containing (*E*)-configured[a] R^1-C=C–CH^2–CO_2R^3 moieties.



Entry	R^1	R^2	R^3	Auxiliary	Substrate (isomer ratio >99:1)	Product(s)[b]	*ee* [%][c]	Yield [%]
1	Et	Et	Me	DHQ	**7**	**39a**	68	65
2				DHQD		**39b**	72	84
3	–$(CH_2)_3$–		Me	DHQ	**24**	**40a**	66[d]	87
4				DHQD		**40b**	79[d]	83
5	–$(CH_2)_4$–		Me	DHQ	**25**	**41a** + **42a** (24:76)	23	77
6				DHQD		**41b** + **42b** (27:73)	44	85
7	*i*Pr	Me	Me	DHQ	**8**	**43a**	58	87
8				DHQD		**43b**	69	66
9	*t*Bu	Me	Me	DHQ	**9**	**44a**	59	55
10				DHQD		**44b**	65	56
11	Ph	Me	Me	DHQ	**10**	**45a**	83	75
12				DHQD		**45b**	85	69
13	*i*Bu	CO_2Me	Me	DHQ	(*Z*)-**31**	**46a**	30	73
14				DHQD		**46b**	41	71
15	Ph	CO_2Me	Me	DHQ	(*Z*)-**33**	**47a**	72	47
16				DHQD		**47b**	61	38
17	Ph	CO_2Et	Et	DHQ	(*Z*)-**34**	**48a**	50	49
18				DHQD		**48b**	44	66

[a] This classification is also true for the substrates of Entries 9–14 although their C=C configurations are "(*Z*)" by the Cahn–Ingold–Prelog priority rules. [b] Absolute configurations were not proven but were assigned in accordance with "Sharpless' mnemonic" (ref.[4c,4g]). [c] Determined by chiral GC and HPLC (details: Experimental Part). [d] Determined after transformation into the corresponding acetonide (without formula number; for details see the Exp. Sect.).

Table 2. AD reactions[25] of β,γ-unsaturated β,γ-disubstituted esters containing (*Z*)-configured[a] R^1-C=C–CH^2–CO_2R^3 moieties.



(*E*)-**31**, (*E*)-**33**, (*E*)-**34**

49a-51a major isomer with $(DHQ)_2PHAL$

49b-51b major isomer with $(DHQD)_2PHAL$

Entry	R^1	R^2	R^3	Auxiliary	Substrate (isomer ratio >99:1)	Product[b]	*ee* [%][c]	Yield [%]
1	*i*Bu	CO_2Me	Me	DHQ	(*E*)-**31**	**49a**	63	89
2				DHQD		**49b**	78	88
3	Ph	CO_2Me	Me	DHQ	(*E*)-**33**	**50a**	82	70
4				DHQD		**50b**	87	77
5	Ph	CO_2Et	Et	DHQ	(*E*)-**34**	**51a**	84	76
6				DHQD		**51b**	90	83

[a] This classification is true for all substrates of this Table even if their C=C configuration is "(*E*)" by the Cahn–Ingold–Prelog priority rules. [b] Absolute configurations were not proven but were assigned in accordance with "Sharpless' mnemonic" (ref.[4c,4g]). [c] Determined by chiral GC and HPLC (for details see the Exp. Sect.).

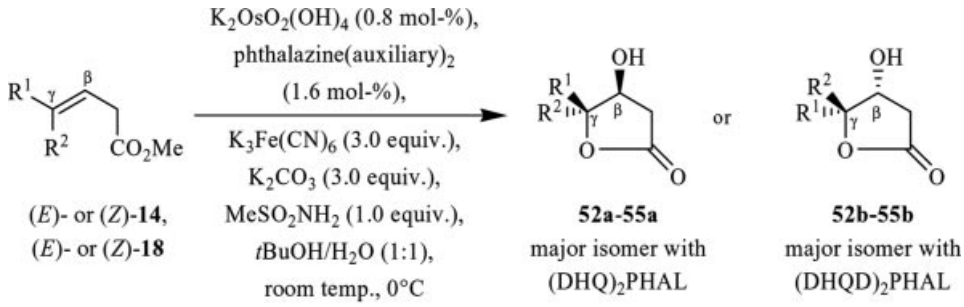
The enantiomeric excesses in the AD reactions in Table 1 span a range from 83–85% *ee* at best (for the γ-phenylated ester **10**; Entries 11, 12) to 23% *ee* at worst (for the cyclohexene-containing ester **25**; Entry 5). For most substrates, $(DHQD)_2PHAL$ is a more efficient chiral auxiliary than $(DHQ)_2PHAL$ (Entries 1–14), as usually observed in AD chemistry.[4] However, the AD reactions of benzylidene succinates (*Z*)-**33** and -**34** represent exceptions (Entries 15–18). Also noteworthy is that the AD reaction of cyclopent-annulated ester **24** proceeds with considerably more stereocontrol (66% and 79% *ee*s; Entries 3, 4) than that of the cyclohex-annulated analogue **25** (23% and 44% *ee*s; Entries 5, 6). The absolute configurations of the products depicted in Table 1 were not elucidated experimentally but were assigned on the basis of Sharpless' "mnemonic aid",[4c,4g] which is believed to predict correctly the C–OH bond orientations resulting from the *trans*-configured R^1-C=C–R^2 substructure of any AD substrate containing it.

The AD reactions of β,γ-disubstituted esters containing (*Z*)-configured (cf. footnote [a], Table 2) R^1–C=C–CH_2–CO_2R^3 moieties are summarized in Table 2. The configurations of the resulting γ-lactones were again not determined experimentally but assigned on the basis of Sharpless' "mnemonic aid".[4c,4g] The yields and *ee*s of the AD products in Table 2 were consistently higher than those observed on starting from the isomeric substrates (Table 1, Entries 13–18). As almost always,[4] $(DHQD)_2PHAL$ was more powerful than $(DHQ)_2PHAL$ as a chiral auxiliary. Consistently with this, the highest *ee* (90%) was observed in the $(DHQD)_2PHAL$-mediated AD of benzylidenesuccinate (*E*)-**34**.

AD reactions of two pairs of *E*,*Z*-isomeric γ,γ-disubstituted β,γ-unsaturated esters [(*E*)- and (*Z*)-**14**,[8] (*E*)- and (*Z*)-**18**] proceeded with yields around 75–90% (Table 3). Esters (*E*)- and (*Z*)-**18** underwent dihydroxylation at *both* C=C bonds, giving rise to the trihydroxy-γ-lactones **53** and **55**.

Half of the *ee*s of the AD reactions summarized in Table 3 were in the nineties (Entries 1, 2, 7, 8), half in the eighties (Entries 3–6). Of the monounsaturated substrate isomers (*E*)- and (*Z*)-**14**, the former (Entries 1, 2) reacted with higher enantioselectivity than the latter (Entries 5, 6): (*E*)-**14** → 97% *ee* in the presence of $(DHQD)_2PHAL$ vs. (*Z*)-**14** → 85% *ee*; (*E*)-**14** → 91% *ee* in the presence of $(DHQ)_2PHAL$ vs. (*Z*)-**14** → 80% *ee*. For the diunsaturated isomeric substrates (*E*)- and (*Z*)-**18**, this order was reversed, with the (*E*) isomer (Entries 3, 4) reacting less enantioselectively than the (*Z*) isomer (Entries 7, 8): (*E*)-**18** → 82% *ee* in the presence of $(DHQD)_2PHAL$ vs. (*Z*)-**18** → 93% *ee*; (*E*)-**18** → 83% *ee* in the presence of $(DHQ)_2PHAL$ vs. (*Z*)-**18** → 90% *ee*. These juxtapositions imply the following: (*i*) the Me_2C=CH–CH_2 moiety in the di-unsaturated substrate **18** is dihydroxylated as rapidly as – or even more rapidly than – the C^{γ}=C^{β}H–CH_2–CO_2Me moiety, and (*ii*) the resulting Me_2C(OH)–CH(OH)–CH_2 moiety exerts some substrate control over stereoselectivity during the (remainder) of the dihydroxylation of the C^{γ}=C^{β}H–CH_2–CO_2Me moiety, opposing reagent control for the (*E*)-olefin ("mis-

Table 3. AD reactions ("compromise stoichiometry" between the quantities of ref.[26] and ref.[25]) of β,γ-unsaturated γ-disubstituted esters [pairs of (*E*)- and (*Z*) isomers].



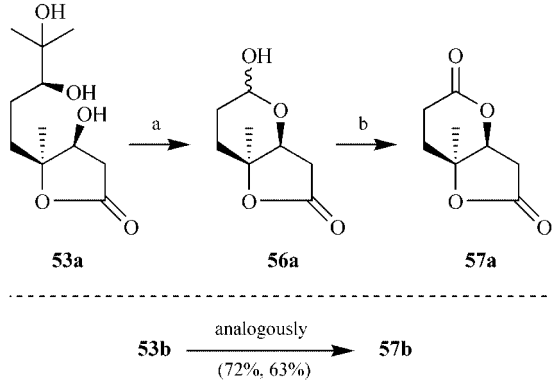
Entry	R^1	R^2	Auxiliary	Substrate (isomer ratio >99:1)	Product[a]	*ee* [%][b]	Yield [%]
1[8]	Pent	Me	DHQ	(*E*)-**14**	**52a**	91	83
2[8]			DHQD		**52b**	97	82
3	Prenyl-CH_2-[c]	Me	DHQ	(*E*)-**18**	**53a**	83[d,e]	62
4			DHQD		**53b**	82[d,e]	75
5[8]	Me	Pent	DHQ	(*Z*)-**14**	**54a**	80	92
6[8]			DHQD		**54b**	85	85
7	Me	Prenyl-CH_2-[c]	DHQ	(*Z*)-**18**	**55a**	90[d,f]	77
8			DHQD		**55b**	93[d,f]	84

[a] Absolute configurations were assigned by "Sharpless' mnemonic" (ref.[4c,4g]); moreover, they are consistent with the independently assigned absolute configurations of the β-hydroxy-γ-methyl-γ-pentyl-γ-butyrolactone stereoisomers obtained by analogous AD reactions (ref.[8]). [b] Determined by chiral GC; for details see Experimental Part. [c] This moiety was also dihydroxylated during the AD reaction. [d] Twice as much of each reagent was used as indicated in the equation. [e] Determined after transformation into **57a** and **57b**, respectively (Scheme 8). [f] Determined after transformation into **59a** and **59b**, respectively (Scheme 9).

matched case") and reinforcing it for the (*Z*)-olefin ("matched case").

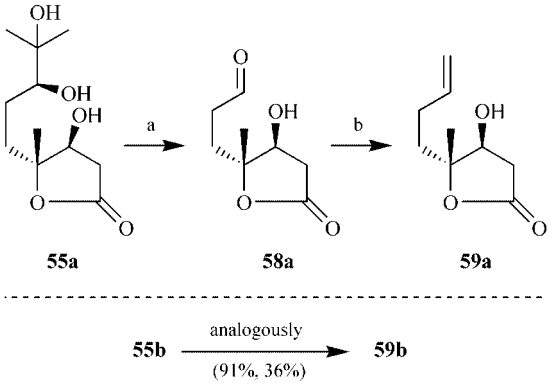
The monohydroxy lactone **54a** (80% *ee*; Table 3, Entry 5) and its enantiomer **54b** (85% *ee*, Entry 1) had been employed previously for elucidation of the 3D structure of a butenolide from the moss *Plagiomnium undulatum* by synthesis.[8] The trihydroxy lactones **53** and **55** were carried on as summarized in Scheme 8 and Scheme 9, respectively. These transformations served two purposes: (*i*) determination of the stereochemical purity of the lactone moiety, and (*ii*) preparation of nonracemic β-hydroxy-γ-lactones containing an additional functional group in one γ-substituent.

Trihydroxy lactone **53a** and its enantiomer **53b** – both derived from methyl geranylcarboxylate – were consecutively subjected to glycol cleavage[27] and PCC oxidation of the resulting lactols[28] (Scheme 8), affording bislactone **57a** and its enantiomer **57b**, respectively. We needed these compounds chiefly for analytical purposes – namely, *ee* determination (83 and 82%, respectively) – though their syntheses also represent a straightforward enantioselective route to a structural motif that might otherwise be difficult to obtain.



Scheme 8. Bislactone synthesis from butyrolactone **53a** and its enantiomer. Reagents and conditions: (a) $NaIO_4$ (1.1 equiv.), THF, H_2O, room temp., 2 h; 64%, *dr* 79:21. (b) PCC (2.0 equiv.), CH_2Cl_2, room temp., 12 h; 57%.

Trihydroxy lactone **55a** and its enantiomer **55b** – both derived from methyl nerylcarboxylate – rendered the lactone-containing hydroxyaldehydes **58** when subjected to glycol cleavage[27] (Scheme 9). Obviously, lactol formation



Scheme 9. Unsaturated lactone synthesis from butyrolactone **55a** and its enantiomer. Reagents and conditions: (a) $NaIO_4$ (1.1 equiv.), EtOAc, H_2O, room temp., 30 min; 94%. (b) $Ph_3P{=}CH_2$ (1.6 equiv.), THF, –5 °C → room temp., 1.5 h; 31%.

was hampered by the arising of ring-strain. Wittig methylenation[11,29] of the aldehyde group furnished the unsaturated γ-lactone **59a** (90% *ee*) and its enantiomer **59b** (93% *ee*).

Conclusions

We have studied the asymmetric dihydroxylation of β,γ-unsaturated carboxylic esters with *tri*substituted double bonds. Except in those esters in which the $C^{\gamma}{=}C^{\beta}$ bond was part of a five-membered (namely compound **24**) or a six-membered ring (namely compound **25**), each substrate was smoothly converted into the corresponding trisubstituted γ-lactone (Table 1-Table 3). Lactone yields were good to excellent (up to 92%, Table 3, Entry 5). Enantiocontrol strongly depended on the substrate, lactone *ee* values spanning a range from 97% (Table 3, Entry 2) to 23% (Table 1, Entry 5), though half of our AD reactions proceeded with *ee*s >80%. This shows that our strategy for the construction of enantioenriched γ-lactones through the AD reactions of β,γ-unsaturated carboxylic esters is not limited to the production of disubstituted γ-lactones but is also useful for the synthesis of trisubstituted γ-lactones.

Experimental Section

All reactions were performed in oven-dried (110 °C) glassware under N_2. THF was freshly distilled from K, CH_2Cl_2 was distilled from CaH_2. Diazomethane was prepared as an ethanol-free diethyl ether solution as described in the literature[30] with the aid of an ALDRICH Diazald® Kit; the diazomethane concentrations were determined[30] prior to use. Products were purified by flash chromatography[24] on Merck silica gel 60 and were isolated as liquids or oils unless stated differently (only for one enantiomer). Yields refer to analytically pure samples. ^1H [$CHCl_3$ (δ = 7.26 ppm) as internal standard in $CDCl_3$. C_6HD_5 (δ = 7.15 ppm) as internal standard in C_6D_6]: Varian Mercury VX 300, Bruker AM 400, and Bruker DRX 500. Integrals are in accordance with assignments; coupling constants are in Hz. The assignments of ^1H NMR resonances refer to the IUPAC nomenclature except within substituents where primed numbers are used. Combustion analyses: E. Hickl, Institut für Organische Chemie und Biochemie, University of Freiburg. MS: Dr. J. Wörth and C. Warth, Institut für Organische Chemie und Biochemie, University of Freiburg. IR spectra: Perkin–Elmer Paragon 1000. Optical rotations were measured with a Perkin–Elmer polarimeter 341 at 589 nm and 20 °C and were calculated by the Drude equation $\{[\alpha]_D = (\alpha_{exp} \times 100)/(c \times d)\}$; rotational values are the average of five measurements of α_{exp} in a given solution of the respective sample. Melting points were measured on a Dr. Tottoli apparatus (Büchi) and are uncorrected. The *ee* values were determined by chiral GC with a Carlo Erba Instruments HRC 5160 Mega series apparatus with a Varian CP7502 (β-cyclodextrin/dimethylpolysiloxane) column (isothermal analysis) or by chiral HPLC with a Chiralpak AD (Daicel Chemical Ind. Ltd.) column.

(*E*)-2-Ethylpent-2-enoic Acid (4a):[31] a) Propionaldehyde (131 mg, 2.25 mmol, 1.3 equiv.) was added to a solution of ethyl 2-(triphenylphosphanylidene)butanoate[32] (636 mg, 1.69 mmol) in benzene (5 mL). After having been heated at 70 °C for 3.5 h, the mixture was allowed to reach room temperature and stirred overnight. After evaporation in vacuo the residue was purified by flash chromatography (cyclohexane/EtOAc, 60:1) to afford ethyl (*E*)-2-ethylpent-2-enoate[31] (225 mg, 96%, *E*:*Z* = 96:4): ^1H NMR (300 MHz, $CDCl_3$): δ = 1.00 (t, $J_{2',1'}$ = 7.5 Hz, 2′-H_3)*, 1.05 (t, $J_{5,4}$ = 7.5 Hz, 5-H_3)*, 1.29 [t, J_{vic} = 7.1 Hz, $CO_2CH_2CH_3$; (*E*) isomer], superimposed by 1.30 [t, J_{vic} = 7.2 Hz, $CO_2CH_2CH_3$; (*Z*) isomer], 2.19 (dq, $J_{4,3} = J_{4,5}$ = 7.5, 4-H_2), 2.31 (q, $J_{1',2'}$ = 7.5 Hz, 1′-H_2), 4.19 (q, J_{vic} = 7.1 Hz, $CO_2CH_2CH_3$), 5.81 [m_c, 3-H; (*Z*) isomer], 6.70 [t, $J_{3,4}$ = 7.5 Hz, 3-H; (*E*) isomer] ppm; * = assignments interchangeable.

b) A solution of $LiOH{\cdot}H_2O$ (6.64 g, 0.158 mol, 10 equiv.) in H_2O (40 mL) was added to a solution of ethyl (*E*)-2-ethylpent-2-enoate (2.472 g, 15.82 mmol) in MeOH (165 mL). The mixture was heated at 45 °C for 7.5 h and stirred overnight at room temperature. After removal of MeOH in vacuo, the mixture was acidified with HCl (2 M) and extracted with EtOAc (3 × 70 mL). The combined organic extracts were dried with $MgSO_4$ and the solvents were evaporated in vacuo. The residue was purified by flash chromatography (cyclohexane/EtOAc, 15:1) to afford the title compound (1.604 g, 79%): ^1H NMR (300 MHz, $CDCl_3$): δ = 1.03 (t, $J_{5,4}$ = 7.5 Hz, 5-H_3)*, 1.07 (t, $J_{2',1'}$ = 7.5 Hz, 2′-H_3)*, 2.23 (dq, $J_{4,3} = J_{4,5}$ = 7.4 Hz, 4-H_2), partly superimposed by 2.32 (q, $J_{1',2'}$ = 7.4 Hz, 1′-H_2), 6.87 (t, $J_{3,4}$ = 7.5 Hz, 3-H), 11.70 (br. s, CO_2H) ppm; * = assignments interchangeable.

(*E*)-2,4-Dimethylpent-2-enoic Acid (4b):[33] a) Isobutyraldehyde (3.732 g, 51.75 mmol, 1.7 equiv.) was added to a solution of ethyl 2-(triphenylphosphanylidene)propionate[34] (10.84 g, 30.00 mmol) in benzene (30 mL). After having been heated at 70 °C overnight, the mixture was allowed to reach room temperature and the solvents were evaporated in vacuo. The residue was purified by flash chromatography (cyclohexane/EtOAc, 60:1) to afford ethyl (*E*)-2,4-dimethylpent-2-enoate[35] (4.241 g, 90%, *E*:*Z* = 96:4): ^1H NMR (300 MHz, $CDCl_3$): δ = 0.98 [d, $J_{4\text{-Me},4} = J_{5,4}$ = 6.7 Hz, 4-CH_3, 5-H_3; (*Z*) isomer], 1.02 [d, $J_{4\text{-Me},4} = J_{5,4}$ = 6.6 Hz, 4-CH_3, 5-H_3; (*E*) isomer], 1.29 (t, J_{vic} = 7.1 Hz, $CO_2CH_2CH_3$), 1.83 [d, J_{allyl} = 1.2 Hz, 2-CH_3, (*E*) isomer], 1.87 [d, J_{allyl} = 1.2 Hz, 2-CH_3, (*Z*) isomer], 2.63 [dqq, $J_{4,3}$ = 9.9, $J_{4,4\text{-Me}} = J_{4,5}$ = 6.6 Hz, 4-H; (*E*) isomer], 3.20 [m_c, 4-H, (*Z*) isomer], 4.16 (q, J_{vic} = 7.1 Hz, $CO_2CH_2CH_3$), 5.68 [incompletely resolved dq, $J_{3,4}$ = 9.7, J_{allyl} = 1.3 Hz, 3-H; (*Z*) isomer], 6.56 [incompletely resolved dq, $J_{3,4}$ = 9.7, J_{allyl} = 1.3 Hz, 3-H; (*E*) isomer] ppm.

b) The title compound (**4b**; 1.153 g, 71%, *E*:*Z* = 94:6) was prepared from ethyl (*E*)-2,4-dimethylpent-2-enoate (1.976 g, 12.65 mmol, *E*:*Z* = 96:4) in a manner analogous to that specified for **4a**, part b):

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99 [d, $J_{4\text{-Me},4} = J_{5,4}$ = 6.6 Hz, 4-CH_3, 5-H$_3$; (*Z*) isomer], 1.04 [d, $J_{4\text{-Me},4} = J_{5,4}$ = 6.7 Hz, 4-CH_3, 5-H$_3$; (*E*) isomer], 1.85 [d, J_{allyl} = 1.3 Hz, 2-CH_3; (*E*) isomer], 1.89 [d, J_{allyl} = 1.3 Hz, 2-CH_3; (*Z*) isomer], 2.67 [dqq, $J_{4,3}$ = 10.0, $J_{4,4\text{-Me}} = J_{4,5}$ = 6.6 Hz, 4-H; (*E*) isomer], 3.35 [dqq, $J_{4,3}$ = 9.9, $J_{4,4\text{-Me}} = J_{4,5}$ = 6.6 Hz, 4-H; (*Z*) isomer], 5.86 [incompletely resolved dq, $J_{3,4}$ = 9.9, J_{allyl} = 1.4 Hz, 3-H; (*Z*) isomer], 6.72 [dq, $J_{3,4}$ = 9.8, J_{allyl} = 1.3 Hz, 3-H; (*E*) isomer], 12.05 (br. s, CO_2H) ppm.

(*E*)-2-Ethylpent-2-enoyl Bromide (5a): Oxalyl bromide (2.96 mL, 6.80 g, 31.5 mmol, 1.01 equiv.) and DMF (cat.) were added at –15 °C to (*E*)-2-ethylpent-2-enoic acid (**4a**; 4.00 g, 31.2 mmol). After stirring overnight, the crude product was converted into **6a** without further purification.

(*E*)-2,4-Dimethylpent-2-enoyl Bromide (5b): This compound was prepared from (*E*)-2,4-dimethylpent-2-enoic acid (**4b**; 920 mg, 7.18 mmol) in a manner analogous to that specified for **5a** and was also used without purification.

(*E*)-2,4,4-Trimethylpent-2-enoyl Bromide (5c): This compound was prepared from (*E*)-2,4,4-trimethylpent-2-enoic acid (**4c**;[36] 1.20 g, 8.45 mmol) in a manner analogous to that specified for **5a** and was also used without purification.

(*E*)-2-Methyl-3-phenylpropenoyl Bromide (5d): 1-Bromo-2-(dimethylamino)-2-methylpropene[37] (1.00 M in CH_2Cl_2, 1.43 mL, 1.43 mmol, 1.0 equiv.) was added at 0 °C to a solution of α-methylcinnamic acid (211 mg, 1.30 mmol) in CH_2Cl_2 (1.5 mL). After warming to room temperature and stirring for 1 h, the solution was used directly for the preparation of **6d**.

(*E*)-1-Diazo-3-ethylhex-3-en-2-one (6a): The crude acid bromide **5a** was added at 0 °C to a solution of CH_2N_2 (0.37 M in diethyl ether, 84 mL, 31 mmol, 1.0 equiv.) and *i*Pr_2NEt (5.99 mL, 4.43 g, 34.3 mmol, 1.1 equiv.). The mixture was allowed to reach room temperature and stirred for 2 h. After filtration and evaporation in vacuo, the residue was purified by flash chromatography (petroleum ether/diethyl ether 20:1 → 10:1) to afford the title compound (1.334 g, 28% over two steps) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.99 (t, $J_{6,5}$ = 7.5 Hz, 6-H$_3$)*, 1.05 (t, $J_{2',1'}$ = 7.5 Hz, 2′-H$_3$)*, 2.21 (dq, $J_{5,4} = J_{5,6}$ = 7.5 Hz, 5-H$_2$), 2.32 (q, $J_{1',2'}$ = 7.5 Hz, 1′-H$_2$), 5.54 (s, 1-H)**, 6.16 (t, $J_{4,5}$ = 7.4 Hz, 4-H)** ppm; * = assignments interchangeable, ** = distinguishable by a C,H correlation spectrum. IR (film): $\tilde{\nu}$ = 3125, 3090, 2970, 2935, 2875, 2100, 1640, 1605, 1460, 1390, 1365, 1345, 1300, 1225, 1200, 1155, 1115, 1100, 1065 cm^{-1}. HRMS (EI = 70 eV) $C_8H_{12}N_2O$: calcd. 152.0950; found 152.0949.

(*E*)-1-Diazo-3,5-dimethylhex-3-en-2-one (6b): Compound **6b** (126 mg, 83% over two steps) was prepared from crude **5b** in a manner analogous to that specified for **6a**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.02 (d, $J_{5\text{-Me},5} = J_{6,5}$ = 6.6 Hz, 5-CH_3, 6-H$_3$), 1.83 (d, J_{allyl} = 1.4 Hz, 3-CH_3), 2.66 (dqq, $J_{5,4}$ = 9.4, $J_{5,5\text{-Me}} = J_{5,6}$ = 6.7 Hz, 5-H), 5.54 (s, 1-H), 6.07 (dq, $J_{4,5}$ = 9.4, J_{allyl} = 1.4 Hz, 4-H) ppm. IR (film): $\tilde{\nu}$ = 3090, 2965, 2930, 2870, 2360, 2335, 2105, 1740, 1700, 1645, 1605, 1560, 1540, 1515, 1460, 1395, 1345, 1245, 1155, 1060 cm^{-1}. HRMS (EI = 70 eV) $C_8H_{12}N_2O$: calcd. 152.0950; found 152.0949.

(*E*)-1-Diazo-3,5,5-trimethylhex-3-en-2-one (6c): Compound **6c** (94 mg, 81% over two steps) was prepared from crude **5c** in a manner analogous to that specified for **6a**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.17 (s, 2×5-CH_3, 6-H$_3$), 1.94 (d, J_{allyl} = 1.4 Hz, 3-CH_3), 5.52 (s, 1-H), 6.23 (q, J_{allyl} = 1.4 Hz, 4-H) ppm. IR (film): $\tilde{\nu}$ = 3090, 2960, 2910, 2870, 2100, 1735, 1635, 1610, 1465, 1405, 1360, 1345, 1230, 1185, 1145, 1100, 1060, 1030, 1005, 990, 925, 855, 720, 700 cm^{-1}; elemental analysis calcd. (%) for $C_9H_{14}N_2O$ (166.2): C 65.03, H 8.49, N 16.85; found: C 64.95, H 8.27, N 16.59.

(*E*)-1-Diazo-3-methyl-4-phenylbut-3-en-2-one (6d):[10b] This compound (127 mg, 52%) was prepared from a crude solution of **5d** in a manner analogous to that specified for **6a**: yellow solid (m.p. 85 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.11 (d, J_{allyl} = 1.3 Hz, 3-CH_3), 5.70 (s, 1-H), 7.24 (incompletely resolved q, J_{allyl} = 1.0 Hz, 4-H), 7.29–7.45 (m, 5× Ar-H) ppm; elemental analysis calcd. (%) for $C_{11}H_{10}N_2O$ (186.2): C 70.95, H 5.41, N 15.04; found C 70.73, H 5.69, N 14.78.

Methyl (*E*)-3-Ethylhex-3-enoate (7): Under exclusion of light, a solution of silver(I) benzoate (400 mg, 1.75 mmol, 0.2 equiv.) in triethylamine (4 mL) was added dropwise to a solution of **6a** (1.334 g, 8.771 mmol) in methanol (15 mL). After the mixture had been stirred for 5 h at room temperature, the solvent was evaporated in vacuo and the residue was purified by flash chromatography (petroleum ether/diethyl ether 40:1) to afford the title compound (1.044 g, 76%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, $J_{6,5} = J_{2',1'}$ = 7.5 Hz, 6-H$_3$, 2′-H$_3$), 2.04 (dq, $J_{5,4} = J_{5,6}$ = 7.8 Hz, 5-H$_2$), superimposed in part by 2.11 (q, $J_{1',2'}$ = 7.8 Hz, 1′-H$_2$), 2.99 (br. s, 2-H$_2$), 3.67 (s, CO_2CH_3), 5.24 (t, $J_{4,5}$ = 7.2 Hz, 4-H) ppm. IR (film): $\tilde{\nu}$ = 2965, 2935, 2875, 1740, 1560, 1540, 1505, 1460, 1435, 1375, 1335, 1300, 1255, 1195, 1155, 1015 cm^{-1}. HRMS (EI = 70 eV) $C_9H_{16}O_2$: calcd. 156.1150; found 156.1146.

Methyl (*E*)-3,5-Dimethylhex-3-enoate (8): This compound (497 mg, 77%) was prepared from **6b** in a manner analogous to that specified for **7**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (d, $J_{5\text{-Me},5} = J_{6,5}$ = 6.7 Hz, 5-CH_3, 6-H$_3$), 1.67 (d, J_{allyl} = 1.4 Hz, 3-CH_3), 2.52 (dqq, $J_{5,4}$ = 9.1, $J_{5,5\text{-Me}} = J_{5,6}$ = 6.7 Hz, 5-H), 2.96 (m_c, 2-H$_2$), 3.67 (s, CO_2CH_3), 5.10 (dm_c, $J_{4,5}$ = 9.1 Hz, 4-H) ppm. IR (film): $\tilde{\nu}$ = 2960, 2870, 1745, 1465, 1435, 1415, 1390, 1360, 1335, 1300, 1260, 1225, 1190, 1160, 1040, 1005 cm^{-1}; elemental analysis calcd. (%) for $C_9H_{16}O_2$ (156.2): C 69.25, H 10.25; found: C 69.08, H 10.36.

Methyl (*E*)-3,5,5-Trimethylhex-3-enoate (9): This compound (637 mg, 87%) was prepared from **6c** in a manner analogous to that specified for **7**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.10 (s, 2×5-CH_3, 6-H$_3$), 1.78 (d, J_{allyl} = 1.4 Hz, 3-CH_3), 2.92 (d, $J_{2,4}$ = 0.9 Hz, 2-H$_2$), 3.66 (s, CO_2CH_3), 5.28–5.29 (m, 4-H) ppm. IR (film): $\tilde{\nu}$ = 2955, 2905, 2870, 1745, 1465, 1435, 1365, 1335, 1285, 1250, 1195, 1150, 1040, 1030, 1010, 890, 845, 820, 760, 710 cm^{-1}. HRMS (EI = 70 eV) $C_{10}H_{18}O_2$: calcd. 170.1307; found 170.1305.

Methyl (*E*)-3-Methyl-4-phenylbut-3-enoate (10):[10b] The title compound (102 mg, 86%) was prepared from **6d** in a manner analogous to that specified for **7**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.94 (d, J_{allyl} = 1.4 Hz, 3-CH_3), 3.19 (d, $J_{2,4}$ = 1.1 Hz, 2-H$_2$), 3.72 (s, CO_2CH_3), 6.39 (br. s, 4-H), 7.19–7.23 and 7.24–7.27 (C_6H_5) ppm; elemental analysis calcd. (%) for $C_{12}H_{14}O_2$ (190.2): C 75.76, H 7.42; found: C 75.52, H 7.51.

Compounds (*E*)- and (*Z*)-11, -12, -13, and -14: These compounds were synthesized as described in ref.[8]

Methyl (*E*)-4,8-Dimethylnona-3,7-dienoate [(*E*)-18]:[16] (Trimethylsilyl)diazomethane (2.0 M in hexane, 0.83 mL, 1.66 mmol, 1.3 equiv.) was added to a solution of (*E*)-4,8-dimethylnona-3,7-dienoic acid [(*E*)-**17**;[16] 235 mg, 1.28 mmol] in methanol (2.5 mL) and benzene (9 mL). After the mixture had been stirred for 1 h, the solvent was evaporated in vacuo and the residue was purified by flash chromatography (cyclohexane/EtOAc, 50:1) to afford the title compound (240 mg, 96%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60, 1.63, and 1.68 (3×s, 4-CH_3, 8-CH_3, 9-H$_3$), 2.01–2.11 (m, 5-H$_2$, 6-H$_2$), 3.05 (br. d, $J_{2,3}$ = 7.2 Hz, 2-H$_2$),

3.68 (s, CO_2CH_3), 5.09 (m_c, 7-H), 5.33 (br. t, $J_{3,2}$ = 7.5 Hz, 3-H) ppm.

Methyl (*Z*)-4,8-Dimethylnona-3,7-dienoate [(*Z*)-18]:[16] This compound (244 mg, 96%) was prepared from (*Z*)-**17**[16] (239 mg, 1.30 mmol) in a manner analogous to that specified for (*E*)-**18**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.61, 1.68, and 1.74 (3×s, 4-CH_3, 8-CH_3, 9-H_3), 2.04 (m_c, 5-H_2, 6-H_2), 3.04 (dm_c, $J_{2,3}$ = 7.2 Hz, 2-H_2), 3.67 (s, CO_2CH_3), 5.06–5.12 (m, 7-H), 5.32 (tm_c, $J_{3,2}$ = 7.5 Hz, 3-H) ppm.

Methyl Cyclopentylideneacetate [(22),[19] **90:10 Mixture with Methyl (Cyclopent-1-enyl)acetate (24)]:** Methyl (dimethoxyphosphonyl)acetate (**21**,[21] 10.0 mL, 11.3 g, 61.8 mmol, 1.0 equiv.) was added to NaH (1.78 g, 74.1 mmol, 1.2 equiv.) in methanol (48 mL). After the mixture had been stirred for 40 min, cyclopentanone (5.47 mL, 5.20 g, 61.8 mmol) was added and the mixture was stirred overnight. Aq. NH_4Cl (100 mL) was added and the mixture was extracted with EtOAc (4×100 mL). The combined organic extracts were dried with $MgSO_4$ and the solvents were evaporated in vacuo. The residue was purified by vacuum distillation (140–145 °C/2.0 kPa) to afford a 90:10 mixture of **22/24** (8.06 g, 93%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.66 (dddd, $J_{4',3'\text{-H}(1)}$ = $J_{4',3'\text{-H}(2)}$ = $J_{4',5'\text{-H}(1)}$ = $J_{4',5'\text{-H}(2)}$ = 6.8 Hz, 4′-H_2; **22**), 1.76 (dddd, $J_{3',2'\text{-H}(1)}$ = $J_{3',2'\text{-H}(2)}$ = $J_{3',4'\text{-H}(1)}$ = $J_{3',4'\text{-H}(2)}$ = 6.8 Hz, 3′-H_2; **22**), 1.85–1.95 (m, 4′-H_2; **24**), 2.31–2.37 (m, 3′-H_2, 5′-H_2; **24**), 2.44 (br. t, $J_{5',4'\text{-H}(1)}$ = $J_{5',4'\text{-H}(2)}$ = 7.0 Hz, 5′-H_2, **22**), 2.78 (tm_c, $J_{2',3'\text{-H}(1)}$ = $J_{2',3'\text{-H}(2)}$ = 6.7 Hz, 2′-H_2; **22**), 3.13 (br. s, 2-H_2; **24**), 3.69 (s, CO_2CH_3; **22**, **24**), 5.54 (m_c, 2′-H; **24**), 5.81 (m_c, 2-H; **22**) ppm.

Methyl Cyclohexylideneacetate (23):[20] The title compound (6.114 g, 98%) was prepared from cyclohexanone (4.20 mL, 3.97 g, 40.5 mmol) in a manner analogous to that specified for **22**, but the purification was carried out by flash chromatography (cyclohexane/EtOAc, 8:1): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.56–1.67 (m, 3′-H_2, 4′-H_2, 5′-H_2), 2.19 (br. t, $J_{6',5'\text{-H}(1)}$ = $J_{6',5'\text{-H}(2)}$ = 6.2 Hz, 6′-H_2)*, 2.82 (br. t, $J_{2',3'\text{-H}(1)}$ = $J_{2',3'\text{-H}(2)}$ = 5.8 Hz, 2′-H_2)*, 3.68 (s, CO_2CH_3), 5.60 (m_c, 2-H) ppm; * = assignments interchangeable.

Methyl (Cyclopent-1-enyl)acetate (24):[19] *n*-BuLi (2.6 M in hexane, 6.47 mL, 16.8 mmol, 1.1 equiv.) was added at –78 °C to a solution of diisopropylamine (2.61 mL, 1.87 g, 18.5 mmol, 1.2 equiv.) in THF (16 mL). After the mixture had been stirred for 1 h, a solution of **22** (2.14 g, 15.3 mmol; 90:10 mixture with **24**) in THF (7 mL) was added over 1 h and the mixture was stirred for 1 h. Aq. NH_4Cl (10 mL) was added and the mixture was allowed to reach room temperature. After extraction with EtOAc (4×40 mL), the combined organic extracts were washed with aq. NaCl (2×40 mL) and dried with $MgSO_4$. Evaporation in vacuo followed by flash chromatography (cyclohexane/EtOAc, 50:1) afforded the title compound (1.637 g, 76%): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.90 (dddd, $J_{4',3'\text{-H}(1)}$ = $J_{4',3'\text{-H}(2)}$ = $J_{4',5'\text{-H}(1)}$ = $J_{4',5'\text{-H}(2)}$ = 7.5 Hz, 4′-H_2), 2.33 (m_c, 3′-H_2, 5′-H_2), 3.13 (br. s, 2-H_2), 3.69 (s, CO_2Me), 5.54 (m_c, 2′-H) ppm.

Methyl (Cyclohex-1-enyl)acetate (25):[20] *n*-BuLi (2.07 M in hexane, 18.8 mL, 38.9 mmol, 1.05 equiv.) was added at –78 °C to a solution of diisopropylamine (5.50 mL, 3.94 g, 38.9 mmol, 1.05 equiv.) in THF (40 mL). After the mixture had been stirred for 1 h, a solution of **23** (5.71 g, 37.0 mmol) in THF (50 mL) was added and the mixture was stirred for a further 1 h. HOAc (6.4 mL, 6.7 g, 0.11 mol, 3.0 equiv.) was added and the mixture was stirred for 15 min. After addition of $KHSO_4$ (1.0 M in H_2O, 62 mL) the mixture was allowed to reach room temperature. After extraction with EtOAc (3×100 mL) the combined organic extracts were washed with aq. $NaHCO_3$ (2×50 mL) and aq. NaCl (50 mL) and dried with $MgSO_4$. Evaporation in vacuo and vacuum distillation (98–102 °C/3.0 kPa) afforded the title compound (4.443 g, 78%): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.53–1.68 (m, 4′-H_2, 5′-H_2), 2.00–2.05 (m, 3′-H_2, 6′-H_2), 2.95 (br. s, 2-H_2), 3.68 (s, CO_2CH_3), 5.56 (m_c, 2′-H) ppm.

Dimethyl (*E*)-2-(3-Methylbutylidene)succinoate [(*E*)-31,[38] **81:19 Mixture with (*Z*)-31]:** A solution of (*E*)-**32** (500 mg, 2.06 mmol, *E*:*Z* = 82:18) in methanol (5 mL) was added to NaH (99 mg, 4.1 mmol, 2.0 equiv.) in methanol (5 mL). After the mixture had been stirred for 2 d at room temperature, aq. NH_4Cl (10 mL) was added. The mixture was extracted with EtOAc (5×20 mL) and the combined organic extracts were dried with $MgSO_4$. After evaporation in vacuo, the residue was purified by flash chromatography (cyclohexane/EtOAc, 20:1 → 15:1) to afford **31** (386 mg, 87%, *E*:*Z* = 81:19). Isomerically pure (*E*)-**31** for the next step could be obtained by more meticulously performed flash chromatography: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.77 (qqt, $J_{3',3'\text{-Me}}$ = $J_{3',4'}$ = $J_{3',2'}$ = 6.7 Hz, 3′-H), 2.07 (t, $J_{2',1'}$ = $J_{2',3'}$ = 7.3 Hz, 2′-H_2), 3.35 (s, 3-H_2), 3.67 (s, $^4CO_2CH_3$)*, 3.74 (s, $^1CO_2CH_3$)*, 6.99 (t, $J_{1',2'}$ = 7.6 Hz, 1′-H) ppm; * = interchangeable.

Dimethyl (*Z*)-2-(3-Methylbutylidene)succinoate [(*Z*)-31,[39] **80:20 Mixture with (*E*)-31]:** A solution of **37** (2.00 g, 5.30 mmol) in THF (10 mL) was added at 0 °C to a suspension of NaH (127 mg, 5.29 mmol, 1.0 equiv.) in THF (10 mL). The mixture was allowed to reach room temperature and stirred for 30 min. After the mixture had been cooled to 0 °C, a solution of isovaleraldehyde (**29**; 456 mg, 5.30 mmol, 1.0 equiv.) in THF (10 mL) was added. The mixture was allowed to reach room temperature and stirred for 3 h. After addition of aq. NH_4Cl (55 mL), the mixture was extracted with EtOAc (4×50 mL) and dried with $MgSO_4$. Evaporation in vacuo and flash chromatography (cyclohexane/EtOAc, 25:1) afforded **31** (977 mg, 86%, *Z*:*E* = 80:20). Isomerically pure (*Z*)-**31** for the next step could be obtained by more meticulously performed flash chromatography: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (d, $J_{3'\text{-Me},3'}$ = $J_{4',3'}$ = 6.6 Hz, 3′-CH_3, 4′-H_3), 1.72 (qqt, $J_{3',3'\text{-Me}}$ = $J_{3',4'}$ = $J_{3',2'}$ = 6.7 Hz, 3′-H), 2.47 (br. t, $J_{2',1'}$ = $J_{2',3'}$ = 7.2 Hz, 2′-H_2), 3.68 and 3.73 (2×s, 2×CO_2CH_3), 6.08 (br. t, $J_{1',2'}$ = 7.5 Hz, 1′-H) ppm.

Diethyl (*E*)-2-(3-Methylbutylidene)succinoate [(*E*)-32,[40] **82:18 Mixture with (*Z*)-32]:** NaH (168 mg, 7.00 mmol, 1.0 equiv.) was added at 0 °C to a solution of diethyl phosphite (**26**; 967 mg, 7.00 mmol) in EtOH (35 mL). The mixture was allowed to reach room temperature and stirred for 30 min. After addition of diethyl maleate (**27**, 1.21 g, 7.00 mmol, 1.0 equiv.) stirring was continued for 1 h. Isovaleraldehyde (**29**; 603 mg, 7.00 mmol, 1.0 equiv.) was added and the mixture was stirred for 4 h. After addition of aq. NH_4Cl (25 mL), the mixture was extracted with EtOAc (4×30 mL). The combined organic extracts were dried with $MgSO_4$. After evaporation in vacuo the residue was purified by flash chromatography (cyclohexane/EtOAc, 15:1 → 10:1) to afford **32** (1.034 g, 61%, *E*:*Z* = 82:18): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (d, J_{vic} = 6.7 Hz, 3′-CH_3, 4′-H_3), 1.24 (t, J_{vic} = 7.2 Hz, $^4CO_2CH_2CH_3$)*, 1.28 (t, J_{vic} = 7.1 Hz, $^1CO_2CH_2CH_3$)*, 1.72 [qqt, $J_{3',3'\text{-Me}}$ = $J_{3',4'}$ = $J_{3',2'}$ = 6.8 Hz, 3′-H; (*Z*)-**32**], superimposed in part by 1.78 [qqt, $J_{3',3'\text{-Me}}$ = $J_{3',4'}$ = $J_{3',2'}$ = 6.6 Hz, 3′-H; (*E*)-**32**], 2.08 [t, $J_{2',1'}$ = $J_{2',3'}$ = 7.3 Hz, 2′-H_2; (*E*)-**32**], 2.47 [t, $J_{2',1'}$ = $J_{2',3'}$ = 7.3 Hz, 2′-H_2; (*Z*)-**32**], 3.26 [br. s, 3-H_2; (*Z*)-**32**], 3.33 [br. s, 3-H_2; (*E*)-**32**], 4.15 (q, J_{vic} = 7.0 Hz, $^4CO_2CH_2CH_3$)**, 4.20 (q, J_{vic} = 7.0 Hz, $^1CO_2CH_2CH_3$)**, 6.06 [t, $J_{1',2'}$ = 7.5 Hz, 1′-H; (*Z*)-**32**], 6.97 [t, $J_{1',2'}$ = 7.7 Hz, 1′-H; (*E*)-**32**] ppm; *,** = interchangeable; elemental analysis calcd. (%) for $C_{13}H_{22}O_4$ (242.3): C 64.45, H 9.15; found: C 64.65, H 9.29.

Dimethyl (*E*)-2-Benzylidenesuccinoate [(*E*)-33,[41] **92:8 Mixture with (*Z*)-33]:** A solution of (*E*)-**34** (1.92 g, 7.33 mmol, *E*:*Z* = 92:8) in

methanol (20 mL) was added to NaH (352 mg, 14.7 mmol, 2.0 equiv.) in methanol (70 mL). After the mixture had been stirred for 3 d at room temperature, aq. NH_4Cl (50 mL) was added. The mixture was extracted with EtOAc (4 × 50 mL) and the combined organic extracts were dried with $MgSO_4$. After evaporation in vacuo, the residue was purified by flash chromatography (cyclohexane/EtOAc, 5:1 → 3:1) to afford **33** (1.383 g, 81%, *E*:*Z* = 92:8). Isomerically pure (*E*)-**33** for the next step could be obtained by more meticulously performed flash chromatography: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.54 (s, 3-H_2), 3.73 and 3.83 (2 × s, 2 × CO_2CH_3), 7.33–7.43 (m, C_6H_5), 7.90 (s, 1′-H) ppm.

Dimethyl (*Z*)-2-Benzylidenesuccinoate [(*Z*)-33,[42] 67:33 Mixture with (*E*)-33]: The title compound (795 mg, 48%, *Z*:*E* = 67:33) was prepared from benzaldehyde (**30**; 757 mg, 7.13 mmol, 1.0 equiv.) in a manner analogous to that specified for (*Z*)-**31**. Isomerically pure (*Z*)-**33** for the next step could be obtained by more meticulously performed flash chromatography: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.48 (s, 3-H_2), 3.64 and 3.72 (2 s, 2 CO_2CH_3), 6.88 (s, 1′-H), 7.26–7.35 (m, C_6H_5) ppm.

Diethyl (*E*)-2-Benzylidenesuccinoate [(*E*)-34,[43] 93:7 Mixture with (*Z*)-34]: NaH (42 mg, 1.8 mmol, 1.0 equiv.) was added at 0 °C to a solution of diethyl phosphite (**26**; 242 mg, 1.75 mmol) in EtOH (9 mL). The mixture was allowed to reach room temperature and stirred for 30 min. After addition of diethyl maleate (**27**; 301 mg, 1.75 mmol, 1.0 equiv.) stirring was continued for 3 h. Benzaldehyde (**30**; 0.18 mL, 0.19 g, 1.75 mmol, 1.0 equiv.) was added and the mixture was stirred overnight. After addition of aq. NH_4Cl (20 mL), the mixture was extracted with EtOAc (4 × 20 mL). The combined organic extracts were dried with $MgSO_4$. After evaporation in vacuo the residue was purified by flash chromatography (cyclohexane/EtOAc, 15:1) to afford **34** (220 mg, 48%, *E*:*Z* = 93:7). Isomerically pure (*E*)-**34** for the next step could be obtained by more meticulously performed flash chromatography: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, J_{vic} = 7.2 Hz, $^4CO_2CH_2CH_3$)*, 1.34 (t, J_{vic} = 7.1 Hz, $^1CO_2CH_2CH_3$)*, 3.53 (s, 3-H_2), 4.19 (q, J_{vic} = 7.1 Hz, $^4CO_2CH_2CH_3$)**, 4.28 (q, J_{vic} = 7.1 Hz, $^1CO_2CH_2CH_3$)**, 7.30–7.43 (m_c, C_6H_5), 7.89 (s, 1′-H) ppm; *, ** = interchangeable.

Diethyl (*Z*)-2-Benzylidenesuccinoate [(*Z*)-34,[43] 81:19 Mixture with (*E*)-34]: The title compound (207 mg, 79%, *Z*:*E* = 81:19) was prepared from **38**[22] (406 mg, 1.00 mmol) and benzaldehyde (**30**; 106 mg, 1.00 mmol, 1.0 equiv.) in a manner analogous to that specified for (*Z*)-**31** but with stirring for only 1 h after the addition of the aldehyde. Isomerically pure (*Z*)-**34** for the next step could be obtained by more meticulously performed flash chromatography: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.09 (t, J_{vic} = 7.1 Hz, $^1CO_2CH_2CH_3$)*, 1.27 (t, J_{vic} = 7.2 Hz, $^4CO_2CH_2CH_3$)*, 3.46 (d, $J_{3,1'}$ = 1.2 Hz, 3-H_2), 4.11 (q, J_{vic} = 7.2 Hz, $^4CO_2CH_2CH_3$)**, 4.18 (q, J_{vic} = 7.1 Hz, $^1CO_2CH_2CH_3$)**, 6.88 (br. s, 1′-H), 7.27–7.33 (m, C_6H_5) ppm; *, ** = interchangeable.

Dimethyl 2-(Diphenoxyphosphonyl)succinate (37): Diphenyl phosphite (**35**; 3.83 mL, 4.68 g, 20.0 mmol) was added at 0 °C to a suspension of NaH (480 mg, 20.0 mmol, 1.0 equiv.) in THF (20 mL). The mixture was allowed to reach room temperature and stirred for 30 min. Dimethyl maleate (**36**, 2.50 mL, 2.88 g, 20.0 mmol, 1.0 equiv.) was added and the mixture was stirred for 3 h. After addition of H_2O (10 mL), the mixture was extracted with EtOAc (4 × 25 mL) and dried with $MgSO_4$. After evaporation in vacuo, the residue was purified by flash chromatography (cyclohexane/EtOAc, 7:1) to afford the title compound (5.184 g, 69%): ^{1}H NMR (300 MHz, $CDCl_3$): δ = AB signal (δ_A = 3.03, δ_B = 3.27, J_{AB} = 17.5, A part additionally split by $J_{A,^{31}P}$ = 10.0, $J_{A,2}$ = 3.4, B part additionally split by $J_{B,2}$ = 11.4, $J_{B,^{31}P}$ = 7.7 Hz, 3-H_2), 3.71 (s, CO_2CH_3), 3.82 (ddd, $J_{2,^{31}P}$ = 24.8, $J_{2,3\text{-H(B)}}$ = 11.4, $J_{2,3\text{-H(A)}}$ = 3.4 Hz, 2-H), superimposed by 3.81 (s, CO_2CH_3), 7.16–7.21 and 7.30–7.35 (2 m, 2 Ph) ppm. IR (film): $\tilde{\nu}$ = 3070, 3005, 2955, 1740, 1590, 1490, 1455, 1440, 1410, 1365, 1325, 1280, 1210, 1185, 1160, 1070, 1025, 1010, 945, 905, 860, 840, 770, 690 cm^{-1}; elemental analysis calcd. (%) for $C_{18}H_{19}O_7P$ (378.3): C 57.16, H 5.06; found: C 57.00, H 5.28.

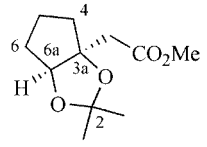
(4*S*,5*S*)-4,5-Diethyl-4-hydroxy-4,5-dihydro-3*H*-furan-2-one (39a): $(DHQ)_2PHAL$ (78 mg, 0.10 mmol, 10 mol-%), $K_3Fe(CN)_6$ (988 mg, 3.00 mmol, 3.0 equiv.), K_2CO_2 (415 mg, 3.00 mmol, 3.0 equiv.), $MeSO_2NH_2$ (95 mg, 1.0 mmol, 1.0 equiv.), and $K_2OsO_2(OH)_4$ (7.4 mg, 20 μmol, 2 mol-%) were dissolved in *t*BuOH (5 mL) and H_2O (5 mL). After the mixture had been cooled to 0 °C, **7** (156 mg, 1.00 mmol) was added. After the mixture had been stirred overnight at 0 °C, aq. Na_2SO_3 (5 mL) was added, the mixture was stirred for 1 h at room temperature and extracted with EtOAc (4 × 20 mL), and the combined organic extracts were dried with $MgSO_4$. After evaporation in vacuo the residue was purified by flash chromatography (cyclohexane/EtOAc, 2:1) to afford the title compound (103 mg, 65%): $[\alpha]_D$ = –69.6 (*c* = 0.3 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.01 (t, $J_{2',1'}$ = 7.5 Hz, 2′-H_3)*, 1.09 (t, $J_{2'',1''}$ = 7.4 Hz, 2′′-H_3)*, AB signal (δ_A = 1.61, δ_B = 1.73, J_{AB} = 14.8, A part additionally split by $J_{A,2'}$ = 7.2, B part additionally split by $J_{B,2'}$ = 7.2 Hz, 1′-H_2), superimposed by AB signal (δ_A = 1.67, δ_B = 1.79, J_{AB} = 14.6, A part additionally split by $J_{A,2''}$ = 7.1, $J_{A,5}$ = 3.2, B part additionally split by $J_{B,5}$ = 9.8, $J_{B,2''}$ = 7.3 Hz, 1′′-H_2), 2.12 (br. s, 4-OH), AB signal (δ_A = 2.54, δ_B = 2.60, J_{AB} = 17.5 Hz, 3-H_2), 4.11 (dd, $J_{5,1''\text{-H(B)}}$ = 9.8, $J_{5,1''\text{-H(A)}}$ = 3.2 Hz, 5-H) ppm; * = interchangeable. IR (film): $\tilde{\nu}$ = 3445, 2975, 2940, 2885, 1780, 1770, 1760, 1755, 1465, 1405, 1380, 1355, 1310, 1265, 1230, 1170, 1140, 1120, 1085, 1050, 1020, 1000, 970, 935, 825 cm^{-1}; t_r(4*S*,5*S*) = 29.96 min, t_r(4*R*,5*R*) = 25.79 min (*n*-heptane/propan-2-ol, 96:4); 68% *ee*; elemental analysis calcd. (%) for $C_8H_{14}O_3$ (158.2): C 60.74, H 8.92; found: C 60.94, H 9.12.

(4*R*,5*R*)-4,5-Diethyl-4-hydroxy-4,5-dihydro-3*H*-furan-2-one (39b): This compound (74 mg, 84%) was prepared from **7** (87 mg, 0.56 mmol) in a manner analogous to that specified for **39a** but with $(DHQD)_2PHAL$ as a ligand: $[\alpha]_D$ = +72.2 (*c* = 0.5 in $CHCl_3$); t_r(4*R*,5*R*) = 25.28 min, t_r(4*S*,5*S*) = 29.37 min (*n*-heptane/propan-2-ol, 96:4); 72% *ee*.

Methyl [(1*S*,2*S*)-1,2-Dihydroxycyclopentyl]acetate (40a): This compound (968 mg, 87%) was prepared from **24** (894 mg, 6.38 mmol) in a manner analogous to that specified for **39a**: $[\alpha]_D$ = +1.8 (*c* = 0.6 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.49 (ddddd, J_{gem} = 12.4, $J_{4'\text{-H(1)},5'\text{-H(1)}}$ = 9.1, $J_{4'\text{-H(1)},5'\text{-H(2)}}$ = 8.9, $J_{4'\text{-H(1)},3'\text{-H(1)}}$ = 6.9, $J_{4'\text{-H(1)},3'\text{-H(2)}}$ = 4.7 Hz, 4′-H^1), 1.60 (ddd, J_{gem} = 13.3, $J_{5'\text{-H(1)},4'\text{-H(1)}}$ = 9.3, $J_{5'\text{-H(1)},\ 4'\text{-H(2)}}$ = 6.7 Hz, 5′-H^1), 1.69 (dddd, J_{gem} = 13.1, $J_{3'\text{-H(1)},\ 4'\text{-H(2)}}$ = 9.7, $J_{3'\text{-H(1)},4'\text{-H(1)}}$ = $J_{3'\text{-H(1)},2'}$ = 7.0 Hz, 3′-H^1), 1.82 (ddddd, J_{gem} = 12.3, $J_{4'\text{-H(2)},3'\text{-H(1)}}$ = 9.6, $J_{4'\text{-H(2)},3'\text{-H(2)}}$ = 9.2, $J_{4'\text{-H(2)},5'\text{-H(1)}}$ = 6.7, $J_{4'\text{-H(2)},5'\text{-H(2)}}$ = 4.7 Hz, 4′-H^2), 1.91 (ddd, J_{gem} = 13.3, $J_{5'\text{-H(2)},4'\text{-H(1)}}$ = 8.8, $J_{5'\text{-H(2)},4'\text{-H(2)}}$ = 4.5 Hz, 5′-H^2), 1.99 (dddd, J_{gem} = 13.0, $J_{3'\text{-H(2)},4'\text{-H(2)}}$ = 8.4, $J_{3'\text{-H(2)},2'}$ = 7.8, $J_{3'\text{-H(2)},4'\text{-H(1)}}$ = 4.6 Hz, 3′-H^2), AB signal (δ_A = 2.56, δ_B = 2.65, J_{AB} = 15.9 Hz, 2-H_2), 3.16 (m_c, 2′-OH), 3.57 (s, 1′-OH), 3.71 (s, CO_2CH_3), 3.86 (ddd, $J_{2',3'\text{-H(1)}}$ = $J_{2',3'\text{-H(2)}}$ = 7.5, $J_{2',2'\text{-OH}}$ = 5.4 Hz, 2′-H) ppm. IR (film): $\tilde{\nu}$ = 3440, 2955, 2875, 1730, 1440, 1410, 1340, 1285, 1255, 1205, 1170, 1105, 1050, 1010, 975, 920, 855, 785, 725, 665, 585, 555 cm^{-1}.

The enantiomeric excess of **40a** was determined after transformation into its acetonide by the following procedure: *p*TsOH·H_2O (cat.) was added to a solution of **40a** (159 mg, 0.913 mmol) in 2,2-dimethoxypropane (10 mL). After the mixture had been stirred for 12 h, aq. $NaHCO_3$ (15 mL) was added. The mixture was extracted

with EtOAc (4 × 50 mL) and dried with $MgSO_4$. After evaporation in vacuo the residue was purified by flash chromatography (cyclohexane/EtOAc, 5:1) to afford the acetonide (= methyl {2,2-dimethyl-4,5,6,6a-tetrahydro-2*H*-cyclopent[1,3]dioxolan-3a-yl}-acetate) of compound **40a** (177 mg, 90%).



$[a]_D$ = +5.4 (*c* = 0.9 in $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.35 and 1.43 (2 s, 2× 2′′-CH_3), 1.53–1.66 and 1.79–1.97 (2 m, 3′-H_2, 4′-H_2, 5′-H_2), AB signal (δ_A = 2.74, δ_B = 2.87, J_{AB} = 14.9 Hz, 2-H_2), 3.69 (s, CO_2CH_3), 4.54 (dm_c, $J_{2',3'\text{-H}(1)}$ = 4.5 Hz, 2′-H) ppm. IR (film): $\tilde{\nu}$ = 2985, 2960, 2940, 2880, 2850, 1740, 1460, 1440, 1380, 1370, 1350, 1305, 1290, 1250, 1210, 1175, 1140, 1100, 1045, 1010, 910, 885, 810, 515 cm^{-1}; t_r(1′*S*,2′*S*) = 53.75 min, t_r(1′*R*,2′*R*) = 52.38 min (85 °C, 130 kPa); 66% *ee*; elemental analysis calcd. (%) for $C_{11}H_{18}O_4$ (214.3): C 61.66, H 8.47; found: C 61.62, H 8.34.

Methyl [(1*R*,2*R*)-1,2-Dihydroxycyclopentyl]acetate (40b): This compound (414 mg, 83%) was prepared from **24** (400 mg, 2.85 mmol) in a manner analogous to that specified for **39a** but with $(DHQD)_2PHAL$ as a ligand: $[a]_D$ = –2.9 (*c* = 1.4 in $CHCl_3$); elemental analysis calcd. (%) for $C_8H_{14}O_4$ (174.2): C 55.16, H 8.10; found: C 55.08, H 8.15.

The enantiomeric excess was determined after transformation of **40b** (150 mg, 0.861 mmol) into its acetonide (174 mg, 94%) by a procedure analogous to that described for **40a**: $[a]_D$ = –5.6 (*c* = 1.0 in $CHCl_3$); t_r(1′*R*,2′*R*) = 52.25 min, t_r(1′*S*,2′*S*) = 53.79 min (85 °C, 130 kPa); 79% *ee*.

(3a*S*,7a*S*)-3a-Hydroxy-3a,4,5,6,7,7a-hexahydrobenzo4,5-dihydro-3*H*-furan-2-one (41a),[44] as a 24:76 Mixture with [(1*S*,2*S*)-1,2-Dihydroxycyclohexyl]acetate (42a): A mixture (135 mg) of the title compounds (**41a**: 28 mg, 18%; **42a**: 107 mg, 59%) was prepared from **25** (150 mg, 0.973 mmol) in a manner analogous to that specified for **39a**: **41a**: $[a]_D$ = –27.4 (*c* = 1.0 in $CHCl_3$); t_r(3a*S*,7a*S*) = 53.66 min, t_r(3a*R*,7a*R*) = 53.79 min (120 °C, 100 kPa); 23% *ee*; elemental analysis calcd. (%) for $C_8H_{12}O_3$ (156.2): C 61.52, H 7.74; found: C 61.48, H 7.83.

(3a*R*,7a*R*)-3a-Hydroxy-3a,4,5,6,7,7a-hexahydrobenzo4,5-dihydro-3*H*-furan-2-one (41b), as a 27:73 Mixture with [(1*R*,2*R*)-1,2-Dihydroxycyclohexyl]acetate (42b): A mixture (150 mg) of the title compounds (**41b**: 35 mg, 23%; **42b**: 115 mg, 62%) was prepared from **25** (150 mg, 0.973 mmol) in a manner analogous to that specified for **39a** but with $(DHQD)_2PHAL$ as a ligand: **41b**: $[a]_D$ = +40.2 (*c* = 0.8 in $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.32–1.42 and 1.52–1.76 and 1.86–2.01 (3 m, 4-H_2, 5-H_2, 6-H_2, 7-H_2), 2.12 (m_c, 3a-OH), AB signal (δ_A = 2.51, δ_B = 2.54, J_{AB} = 16.4 Hz, 3-H_2), 4.01 (dd, $J_{7a,7\text{-H}(1)}$ = 11.4, $J_{7a,7\text{-H}(2)}$ = 5.0 Hz, 7a-H) ppm; t_r(3a*R*,7a*R*) = 51.12 min, t_r(3a*S*,7a*S*) = 53.14 min (120 °C, 100 kPa); 44% *ee*.

(4*S*,5*S*)-4-Hydroxy-5-isopropyl-4-methyl-4,5-dihydro-3*H*-furan-2-one (43a): This compound (138 mg, 87%) was prepared from **8** (156 mg, 1.00 mmol) in a manner analogous to that specified for **39a**: colorless solid (m.p. 47 °C). $[a]_D$ = –50.7 (*c* = 0.8 in $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.05 (d, $J_{1'\text{-Me},1'}$ = 6.8 Hz, 1′-CH_3)*, 1.10 (d, $J_{2',1'}$ = 6.6 Hz, 2′-H_3)*, 1.50 (s, 4-CH_3), 2.16 (dqq, $J_{1',5}$ = 8.6, $J_{1',1'\text{-Me}}$ = $J_{1',2'}$ = 6.7 Hz, 1′-H), 2.23 (br. s, 4-OH), AB signal (δ_A = 2.62, δ_B = 2.65, J_{AB} = 17.5 Hz, 3-H_2), 3.85 (d, $J_{5,1'}$ = 8.6 Hz, 5-H) ppm; * = interchangeable. IR (film): $\tilde{\nu}$ = 3450, 2965, 2935, 2880, 1765, 1745, 1480, 1465, 1390, 1370, 1340, 1275, 1240, 1170, 1145, 1120, 1110, 1095, 1010, 985, 950, 810 cm^{-1}; t_r(4*S*,5*S*) = 55.98 min, t_r(4*R*,5*R*) = 55.23 min (90 °C, 30 min, 2 °C/min, 140 °C, 100 kPa); 58% *ee*.

(4*R*,5*R*)-4-Hydroxy-5-isopropyl-4-methyl-4,5-dihydro-3*H*-furan-2-one (43b): This compound (104 mg, 66%) was prepared from **8** (156 mg, 1.00 mmol) in a manner analogous to that specified for **39a** but with $(DHQD)_2PHAL$ as a ligand: $[a]_D$ = +51.1 (*c* = 0.4 in $CHCl_3$); t_r(4*R*,5*R*) = 5.75 min, t_r(4*S*,5*S*) = 6.14 min (85 °C, 130 kPa); 69% *ee*; elemental analysis calcd. (%) for $C_8H_{14}O_3$ (158.1): C 60.74, H 8.92; found: C 60.81, H 9.00.

(4*S*,5*S*)-5-*tert*-Butyl-4-hydroxy-4-methyl-4,5-dihydro-3*H*-furan-2-one (44a): This compound (95 mg, 55%) was prepared from **9** (170 mg, 1.00 mmol) in a manner analogous to that specified for **39a**: $[a]_D$ = –21.6 (*c* = 1.0 in $CHCl_3$); t_r(4*S*,5*S*) = 18.43 min, t_r(4*R*,5*R*) = 23.46 min (*n*-heptane/propan-2-ol, 95:5); 59% *ee*.

(4*R*,5*R*)-5-*tert*-Butyl-4-hydroxy-4-methyl-4,5-dihydro-3*H*-furan-2-one (44b): This compound (96 mg, 56%) was prepared from **9** (170 mg, 1.00 mmol) in a manner analogous to that specified for **39a** but with $(DHQD)_2PHAL$ as a ligand: colorless solid (m.p. 86 °C). $[a]_D$ = +23.2 (*c* = 1.2 in $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.13 (s, 2× 1′-CH_3, 2′-H_3), 1.55 (s, 4-CH_3), AB signal (δ_A = 2.61, δ_B = 2.65, J_{AB} = 17.5 Hz, 3-H_2), 3.90 (s, 5-H) ppm. IR (film): $\tilde{\nu}$ = 3605, 3445, 3035, 3000, 2965, 2910, 2875, 1770, 1485, 1470, 1410, 1400, 1385, 1365, 1330, 1245, 1195, 1155, 1110, 1040, 1005, 940 cm^{-1}; t_r(4*R*,5*R*) = 22.65 min, t_r(4*S*,5*S*) = 18.51 min (*n*-heptane/propan-2-ol, 95:5); 65% *ee*; elemental analysis calcd. (%) for $C_9H_{16}O_3$ (172.1): C 62.77, H 9.36; found: C 62.54, H 9.37.

(4*S*,5*S*)-4-Hydroxy-4-methyl-5-phenyl-4,5-dihydro-3*H*-furan-2-one (45a): This compound (52 mg, 75%) was prepared from **10** (69 mg, 0.36 mmol) in a manner analogous to that specified for **39a**: $[a]_D$ = +10.1 (*c* = 0.8 in $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.22 (d, $^4J_{4\text{-OH},3\text{-H}(A)}$ = 2.0 Hz, 4-OH), 1.45 (s, 4-CH_3), AB signal (δ_A = 2.71, δ_B = 2.78, J_{AB} = 17.1, A part additionally split by $J_{A,4\text{-OH}}$ = 2.0 Hz, 3-H_2), 5.26 (s, 5-H), 7.36–7.46 (m, C_6H_5) ppm. IR (KBr): $\tilde{\nu}$ = 3520, 3455, 3065, 3035, 2975, 2935, 1790, 1780, 1770, 1760, 1755, 1500, 1455, 1385, 1275, 1235, 1200, 1105, 1015, 955, 945, 910, 875, 820, 750, 700 cm^{-1}; t_r(4*S*,5*S*) = 24.91 min, t_r(4*R*,5*R*) = 22.22 min (150 °C, 100 kPa); 83% *ee*.

(4*R*,5*R*)-4-Hydroxy-4-methyl-5-phenyl-4,5-dihydro-3*H*-furan-2-one (45b): This compound (28 mg, 69%) was prepared from **10** (40 mg, 0.21 mmol) in a manner analogous to that specified for **39a** but with $(DHQD)_2PHAL$ as a ligand: colorless solid (m.p. 106 °C). $[a]_D$ = –10.8 (*c* = 1.0 in $CHCl_3$); t_r(4*R*,5*R*) = 21.66 min, t_r(4*S*,5*S*) = 24.82 min (150 °C, 100 kPa); 85% *ee*; elemental analysis calcd. (%) for $C_{11}H_{12}O_3$ (192.2): C 68.75, H 6.29; found: C 68.65, H 6.41.

(4*S*,5*S*)-4-Hydroxy-5-isobutyl-4-methoxycarbonyl-4,5-dihydro-3*H*-furan-2-one (46a): This compound (74 mg, 73%) was prepared from (*Z*)-**31** (100 mg, 0.467 mmol) in a manner analogous to that specified for **39a**: $[a]_D$ = –27.9 (*c* = 1.1 in $CHCl_3$); t_r(4*S*,5*S*) = 40.93 min, t_r(4*R*,5*R*) = 42.18 min (126 °C, 100 kPa); 30% *ee*; elemental analysis calcd. (%) for $C_{10}H_{16}O_5$ (216.2): C 55.56, H 7.46; found: C 55.31, H 7.35.

(4*R*,5*R*)-4-Hydroxy-5-isobutyl-4-methoxycarbonyl-4,5-dihydro-3*H*-furan-2-one (46b): This compound (72 mg, 71%) was prepared from (*Z*)-**31** (100 mg, 0.467 mmol) in a manner analogous to that specified for **39a** but with $(DHQD)_2PHAL$ as a ligand: $[a]_D$ = +32.2 (*c* = 1.2 in $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.92 (d, $J_{2'\text{-Me},2'}$ = 6.6 Hz, 2′-CH_3)*, 0.94 (d, $J_{3',2'}$ = 6.6 Hz, 3′-H_3)*, 1.31–1.37 (m, 1′-H^1), 1.70–1.81 (m, 1′-H^2, 2′-H), AB signal (δ_A = 2.69, δ_B = 3.15, J_{AB} = 17.4, B part additionally split by $^4J_{B,4\text{-OH}}$ = 1.1 Hz,

3-H_2), 3.44 (br. d, $^4J_{4\text{-OH},3\text{-H(B)}}$ = 1.1 Hz, 4-OH), 3.88 (s, CO_2CH_3), 4.64 (dd, $J_{5,1'\text{-H(2)}}$ = 9.1, $J_{5,1'\text{-H(1)}}$ = 4.0 Hz, 5-H) ppm; * = interchangeable. IR (film): $\tilde{\nu}$ = 3470, 2960, 2875, 1790, 1745, 1470, 1440, 1410, 1390, 1370, 1355, 1300, 1265, 1220, 1195, 1135, 1105, 1065, 1035, 985, 955 cm^{-1}; t_r(4*R*,5*R*) = 42.53 min, t_r(4*S*,5*S*) = 41.52 min (125 °C, 100 kPa); 41% *ee*.

(4*S*,5*S*)-4-Hydroxy-4-methoxycarbonyl-5-phenyl-4,5-dihydro-3*H*-furan-2-one (47a): This compound (95 mg, 47%) was prepared from (*Z*)-**33** (200 mg, 0.854 mmol) in a manner analogous to that specified for **39a**: $[\alpha]_D$ = –36.5 (*c* = 1.0 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.59 (d, $^4J_{4\text{-OH},3\text{-H(B)}}$ = 2.0 Hz, 4-OH), AB signal (δ_A = 2.89, δ_B = 3.37, J_{AB} = 17.3, B part additionally split by $J_{B,4\text{-OH}}$ = 2.0 Hz, 3-H_2), 3.92 (s, CO_2CH_3), 5.68 (s, 5-H), 7.23–7.27 and 7.39–7.43 (2 × m, C_6H_5) ppm. IR (KBr): $\tilde{\nu}$ = 3480, 3065, 3015, 2955, 1795, 1725, 1455, 1435, 1410, 1330, 1320, 1295, 1260, 1220, 1195, 1155, 1110, 1085, 1015, 770, 700, 500 cm^{-1}; t_r(4*S*,5*S*) = 25.33 min, t_r(4*R*,5*R*) = 23.89 min (160 °C, 100 kPa); 72% *ee*; elemental analysis calcd. (%) for $C_{12}H_{12}O_5$ (236.2): C 61.01, H 5.12; found C 60.88, H 5.28.

(4*R*,5*R*)-4-Hydroxy-4-methoxycarbonyl-5-phenyl-4,5-dihydro-3*H*-furan-2-one (47b): This compound (77 mg, 38%; mp. 79 °C) was prepared from (*Z*)-**33** (200 mg, 0.854 mmol) in a manner analogous to that specified for **39a** but with $(DHQD)_2PHAL$ as a ligand: colorless solid (m.p. 79 °C). $[\alpha]_D$ = +16.3 (*c* = 1.0 in $CHCl_3$); t_r(4*R*,5*R*) = 23.93 min, t_r(4*S*,5*S*) = 25.40 min (160 °C, 100 kPa); 61% *ee*.

(4*S*,5*S*)-4-Ethoxycarbonyl-4-hydroxy-5-phenyl-4,5-dihydro-3*H*-furan-2-one (48a): This compound (46 mg, 49%) was prepared from (*Z*)-**34** (98 mg, 0.37 mmol) in a manner analogous to that specified for **39a**: $[\alpha]_D$ = –25.4 (*c* = 0.8 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (tm_c, J_{vic} = 7.2 Hz, $CO_2CH_2CH_3$), AB signal (δ_A = 2.88, δ_B = 3.37, J_{AB} = 17.2 Hz, 3-H_2), 4.37 (m_c, $CO_2CH_2CH_3$), 5.67 (s, 5-H), 7.24–7.27 and 7.38–7.43 (2 m, C_6H_5) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3545, 3035, 3030, 3015, 2990, 2940, 1795, 1740, 1455, 1405, 1370, 1316, 1270, 1220, 1180, 1105, 1085, 1035, 1020, 875, 860, 795 cm^{-1}; t_r(4*S*,5*S*) = 48.35 min, t_r(4*R*,5*R*) = 46.04 min (160 °C, 100 kPa); 50% *ee*; elemental analysis calcd. (%) for $C_{13}H_{14}O_5$ (250.2): C 62.39, H 5.64; found: C 62.33, H 5.74.

(4*R*,5*R*)-4-Ethoxycarbonyl-4-hydroxy-5-phenyl-4,5-dihydro-3*H*-furan-2-one (48b): This compound (39 mg, 66%; mp. 79 °C) was prepared from (*Z*)-**34** (62 mg, 0.24 mmol) in a manner analogous to that specified for **39a** but with $(DHQD)_2PHAL$ as a ligand: colorless solid (m.p. 79 °C). $[\alpha]_D$ = +16.3 (*c* = 1.0 in $CHCl_3$); t_r(4*R*,5*R*) = 45.73 min, t_r(4*S*,5*S*) = 48.17 min (150 °C, 100 kPa); 44% *ee*.

(4*R*,5*S*)-4-Hydroxy-5-isobutyl-4-methoxycarbonyl-4,5-dihydro-3*H*-furan-2-one (49a): This compound (81 mg, 89%) was prepared from (*E*)-**31** (90 mg, 0.42 mmol) in a manner analogous to that specified for **39a**: colorless solid (m.p. 62 °C). $[\alpha]_D$ = –93.9 (*c* = 1.0 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (d, $J_{2'\text{-Me},2'}$ = 6.6 Hz 2′-CH_3)*, 0.95 (d, $J_{3',2'}$ = 6.6 Hz, 3′-H_3)*, AB signal (δ_A = 1.30, δ_B = 1.38, J_{AB} = 14.1 Hz, A part additionally split by $J_{A,2'}$ = 8.6, $J_{A,5}$ = 3.0, B part additionally split by $J_{B,5}$ = 10.2, $J_{B,2'}$ = 5.4 Hz, 1′-H_2), 1.82 (m_c, 2′-H), AB signal (δ_A = 2.84, δ_B = 2.95, J_{AB} = 17.4 Hz, 3-H_2), 3.65 (s, 4-OH), 3.87 (s, CO_2CH_3), 4.40 (dd, $J_{5,1'\text{-H(B)}}$ = 10.5 Hz, $J_{5,1'\text{-H(A)}}$ = 3.1 Hz, 5-H) ppm; * = interchangeable. IR ($CHCl_3$): $\tilde{\nu}$ = 3530, 3355, 3035, 3010, 2960, 2940, 2910, 2875, 1785, 1740, 1470, 1440, 1415, 1295, 1245, 1175, 1140, 1100, 990 cm^{-1}; t_r(4*R*,5*S*) = 12.94 min, t_r(4*S*,5*R*) = 14.60 min (135 °C, 100 kPa); 63% *ee*, elemental analysis calcd. (%) for $C_{10}H_{16}O_5$ (216.2): C 55.56, H 7.46; found: C 55.53, H 7.59.

(4*S*,5*R*)-4-Hydroxy-5-isobutyl-4-methoxycarbonyl-4,5-dihydro-3*H*-furan-2-one (49b): This compound (89 mg, 88%) was prepared from (*E*)-**31** (100 mg, 0.47 mmol) in a manner analogous to that specified for **39a** but with $(DHQD)_2PHAL$ as a ligand: $[\alpha]_D$ = +120.8 (*c* = 0.9 in $CHCl_3$); t_r(4*S*,5*R*) = 14.15 min, t_r(4*R*,5*S*) = 12.71 min (135 °C, 100 kPa); 78% *ee*.

(4*R*,5*S*)-4-Hydroxy-4-methoxycarbonyl-5-phenyl-4,5-dihydro-3*H*-furan-2-one (50a): This compound (71 mg, 70%) was prepared from (*E*)-**33** (100 mg, 0.427 mmol) in a manner analogous to that specified for **39a**: $[\alpha]_D$ = –52.2 (*c* = 0.6 in $CHCl_3$); t_r(4*R*,5*S*) = 18.37 min, t_r(4*S*,5*R*) = 17.48 min (160 °C, 100 kPa); 82% *ee*.

(4*S*,5*R*)-4-Hydroxy-4-methoxycarbonyl-5-phenyl-4,5-dihydro-3*H*-furan-2-one (50b): This compound (78 mg, 77%) was prepared from (*E*)-**33** (100 mg, 0.427 mmol) in a manner analogous to that specified for **39a** but with $(DHQD)_2PHAL$ as a ligand: colorless solid (m.p. 86 °C). $[\alpha]_D$ = +58.7 (*c* = 1.0 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = AB signal (δ_A = 3.02, δ_B = 3.11, J_{AB} = 17.5 Hz, 3-H_2), 3.47 (s, CO_2CH_3), 3.90 (s, 4-OH), 5.47 (s, 5-H), 7.30–7.35 (m, C_6H_5) ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3505, 3395, 3005, 2955, 2930, 1795, 1750, 1495, 1455, 1440, 1275, 1240, 1225, 1215, 1175, 1150, 1080, 1040, 1025, 975, 860, 750, 700, 630, 550 cm^{-1}; t_r(4*S*,5*R*) = 17.50 min, t_r(4*R*,5*S*) = 18.45 min (160 °C, 100 kPa); 87% *ee*; elemental analysis calcd. (%) for $C_{12}H_{12}O_5$ (236.2): C 61.01, H 5.12; found: C 60.87, H 5.18.

(4*R*,5*S*)-4-Ethoxycarbonyl-4-hydroxy-5-phenyl-4,5-dihydro-3*H*-furan-2-one (51a): This compound (72 mg, 76%) was prepared from (*E*)-**34** (100 mg, 0.38 mmol) in a manner analogous to that specified for **39a**: colorless solid (m.p. 108 °C). $[\alpha]_D$ = –40.3 (*c* = 1.1 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02 (t, J_{vic} = 7.2 Hz, $CO_2CH_2CH_3$), AB signal (δ_A = 3.01, δ_B = 3.10, J_{AB} = 17.3 Hz, 3-H_2), 3.81 (dq, J_{gem} = 10.6 Hz, J_{vic} = 7.2 Hz, 1′-H^1), 3.96 (dq, J_{gem} = 10.7 Hz, J_{vic} = 7.1 Hz, 1′-H^2), superimposed by 3.97 (s, 4-OH), 5.49 (s, 5-H), 7.32–7.37 (m, Ph-H) ppm. IR (KBr): $\tilde{\nu}$ = 3570, 3515, 3090, 3065, 3035, 3025, 3020, 3010, 2985, 2940, 2910, 1800, 1735, 1455, 1415, 1320, 1270, 1240, 1165, 1135, 1040, 1025, 860, 780 cm^{-1}; t_r(4*R*,5*S*) = 32.83 min, t_r(4*S*,5*R*) = 31.97 min (150 °C, 100 kPa); 84% *ee*; elemental analysis calcd. (%) for $C_{13}H_{14}O_5$ (250.2): C 62.41, H 5.64; found: C 62.20, H 5.64.

(4*S*,5*R*)-4-Ethoxycarbonyl-4-hydroxy-5-phenyl-4,5-dihydro-3*H*-furan-2-one (51b): This compound (79 mg, 83%) was prepared from (*E*)-**34** (100 mg, 0.38 mmol) in a manner analogous to that specified for **39a** but with $(DHQD)_2PHAL$ as a ligand: $[\alpha]_D$ = +43.9 (*c* = 1.0 in $CHCl_3$); t_r(4*S*,5*R*) = 30.98 min, t_r(4*R*,5*S*) = 32.58 min (150 °C, 100 kPa); 90% *ee*.

Compounds 52a and 52b: These compounds were obtained as described in ref.[8]

(4*S*,5*S*)-5-[(3*S*)-3,4-Dihydroxy-4-methylpentyl]-4-hydroxy-5-methyl-4,5-dihydro-3*H*-furan-2-one (53a): This compound (146 mg, 62%) was prepared from (*E*)-**18** (200 mg, 1.02 mmol) in a manner analogous to that specified for **39a**, but twice as much of each reagent was used: ^{1}H NMR (300 MHz, D_2O): δ = 1.24 (s, 4′-CH_3, 5′-H_3), 1.37–1.51 (m, 2′-H^1)*, superimposed by 1.44 (s, 5-CH_3), 1.76–1.88 (m, 1′-H^1, 2′-H^2)*, 2.10–2.20 (m, 1′-H^2)*, 2.61 (dd, J_{gem} = 18.5 Hz, $J_{3\text{-H}(1),4}$ = 2.1 Hz, 3-H^1), 3.30 (dd, J_{gem} = 18.5 Hz, $J_{3\text{-H}(2),4}$ = 6.2 Hz, 3-H^2), 3.43 (dd, $J_{3',2'\text{-H}(1)}$ = 10.6 Hz, $J_{3',2'\text{-H}(2)}$ = 1.6 Hz, 3′-H), 4.41 (dd, $J_{4,3\text{-H}(2)}$ = 6.2 Hz, $J_{4,3\text{-H}(1)}$ = 2.2 Hz, 4-H) ppm; * = assignments interchangeable. IR (KBr): $\tilde{\nu}$ = 3410, 2980, 2940, 2880, 1775, 1740, 1460, 1450, 1440, 1415, 1390, 1295, 1215, 1185, 1165, 1090, 1070, 1020, 995, 950, 885, 795 cm^{-1}. This solid was too sparingly soluble for accurate determination of $[\alpha]_D$.

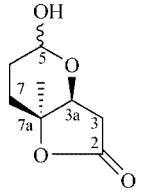
(4*R*,5*R*)-5-[(3*R*)-3,4-Dihydroxy-4-methylpentyl]-4-hydroxy-5-methyl-4,5-dihydro-3*H*-furan-2-one (53b): This compound (135 mg, 75%) was prepared from (*E*)-**18** (152 mg, 0.774 mmol) in a manner

analogous to that specified for **39a**, but twice as much of each reagent and $(DHQD)_2PHAL$ as a ligand was used: colorless solid (m.p. 128 °C); elemental analysis calcd. (%) for $C_{11}H_{20}O_5$ (232.2): C 56.89, H 8.68; found: C 56.70, H 8.76. This solid was too sparingly soluble for accurate determination of $[a]_D$.

Compounds 54a and 54b: These compounds were obtained as described in ref.[8]

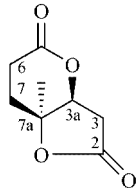
(4*S*,5*R*)-5-[(3*S*)-3,4-Dihydroxy-4-methylpentyl]-4-hydroxy-5-methyl-4,5-dihydro-3*H*-furan-2-one (55a): This compound (556 mg, 77%) was prepared from (*Z*)-**18** (609 mg, 3.10 mmol) in a manner analogous to that specified for **39a**, but twice as much of each reagent was used: ^{1}H NMR [500 MHz, D_2O, $(CD_3)_2CO$]: δ = 1.22 and 1.23 (2 s, 4′-CH_3, 5′-H_3), 1.43–1.51 (m, 2′-H^1)*, superimposed by 1.46 (s, 5-CH_3), 1.76–1.79 (m, 1′-H^1, 2′-H^2), 1.92–1.99 (m, 1′-H^2)**, 2.63 (dd, J_{gem} = 18.5 Hz, $J_{3\text{-}H(1),4}$ = 3.4 Hz, 3-H^1), 3.22 (dd, J_{gem} = 18.5 Hz, $J_{3\text{-}H(2),4}$ = 6.7 Hz, 3-H^2), 3.38 (dd, $J_{3',2'\text{-}H(1)}$ = 10.6 Hz, $J_{3',2'\text{-}H(2)}$ = 1.4 Hz, 3′-H), 4.41 (dd, $J_{4,3\text{-}H(2)}$ = 6.7 Hz, $J_{4,3\text{-}H(1)}$ = 3.3 Hz, 4-H) ppm; *, ** = assignable by a C,H correlation spectrum. IR (KBr): $\tilde{\nu}$ = 3415, 2985, 2965, 2945, 2910, 2875, 2530, 2505, 2475, 1750, 1450, 1385, 1295, 1255, 1180, 1150, 1105, 1065, 1030, 1020, 945, 895, 810, 720, 630 cm^{-1}. This solid was too sparingly soluble for accurate determination of $[a]_D$.

(4*R*,5*S*)-5-[(3*R*)-3,4-Dihydroxy-4-methylpentyl]-4-hydroxy-5-methyl-4,5-dihydro-3*H*-furan-2-one (55b): This compound (300 mg, 84%) was prepared from (*Z*)-**18** (300 mg, 1.53 mmol) in a manner analogous to that specified for **39a**, but twice as much of each reagent and $(DHQD)_2PHAL$ as a ligand were used: colorless solid (m.p. 133 °C); elemental analysis calcd. (%) for $C_{11}H_{20}O_5$ (232.2): C 56.88, H 8.68; found: C 56.83, H 8.52. This solid was too sparingly soluble for accurate determination of $[a]_D$.



(3a*S*,7a*S*)-5-Hydroxy-7a-methyl-3,3a,5,6,7,7a-hexahydrofuro[3,2-*b*]-pyran-2-one (56a): $NaIO_4$ (370 mg, 1.73 mmol, 1.1 equiv.) was added to a solution of **53a** (365 mg, 1.57 mmol) in H_2O (18 mL) and THF (1.8 mL). After the mixture had been stirred for 2 h, aq. NH_4Cl (10 mL) was added. The mixture was extracted with CH_2Cl_2 (5×15 mL) and the combined organic extracts were dried with $MgSO_4$. Evaporation in vacuo and flash chromatography (cyclohexane/EtOAc, 1:3) afforded the title compound [174 mg, 64%; *dr* 79:21 (Dia-A:Dia-B)]: colorless solid (m.p. 132 °C). $[a]_D$ = –94.5 (c = 1.0 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.30 (s, 7a-CH_3; Dia-B), 1.32 (s, 7a-CH_3; Dia-A), 1.56–1.81, 1.88–1.95, 2.00–2.07, and 2.27–2.30 (4 m, 6-H_2 and 7-H_2; Dia-A and Dia-B), AB signal (δ_A = 2.43, δ_B = 2.88, J_{AB} = 17.7, B part additionally split by $J_{B,3a}$ = 4.8 Hz, 3-H_2; Dia-A), AB signal (δ_A = 2.57, δ_B = 2.88, J_{AB} = 17.6 Hz, B part additionally split by $J_{B,3a}$ = 4.5 Hz, 3-H_2; Dia-B), 3.03 (m_c, 5-OH; Dia-A), 3.34 (br. d, $J_{5\text{-}OH,5}$ = 7.4 Hz, 5-OH; Dia-B), 4.18 (d, $J_{3a,3\text{-}H(B)}$ = 4.5 Hz, 3a-H; Dia-B), 4.32 (d, $J_{3a,3\text{-}H(B)}$ = 4.8 Hz; Dia-A), 4.76 (m_c, presumably interpretable as ddd, $J_{5,6\text{-}H(1)}$ = 8.9 Hz, $J_{5,5\text{-}OH}$ = 7.2 Hz, $J_{5,6\text{-}H(2)}$ = 1.8 Hz, 5-H; Dia-B), 5.25 (q, $J_{5,5\text{-}OH}$ = $J_{5,6\text{-}H(1)}$ = $J_{5,6\text{-}H(2)}$ = 3.2 Hz, 5-H; Dia-A) ppm. IR (film): $\tilde{\nu}$ = 3425, 2990, 2970, 2965, 2950, 1745, 1725, 1445, 1430, 1385, 1340, 1320, 1275, 1195, 1120, 1090, 1045, 1000, 955, 940, 825, 790, 595 cm^{-1}; elemental analysis calcd. (%) for $C_8H_{12}O_4$ (172.1): C 55.81, H 7.03; found: C 55.70, H 6.92.

(3a*R*,7a*R*)-5-Hydroxy-7a-methyl-3,3a,5,6,7,7a-hexahydrofuro[3,2-*b*]-pyran-2-one (56b): This compound (120 mg, 72%; *dr* 79:21) was prepared from **53b** (224 mg, 0.964 mmol) in a manner analogous to that specified for **56a**: $[a]_D$ = +90.6 (c = 1.1 in $CHCl_3$).



(3a*S*,7a*S*)-7a-Methyl-3a,6,7,7a-tetrahydrofuro[3,2-*b*]pyran-2,5-(3*H*)-dione (57a): Pyridinium chlorochromate (571 mg, 2.65 mmol, 2.0 equiv.) was added to a solution of **56a** (228 mg, 1.32 mmol) in CH_2Cl_2 (10 mL). After stirring overnight, the mixture was filtered through Celite, evaporated in vacuo, and purified by flash chromatography (cyclohexane/EtOAc, 1:2) to afford the title compound (129 mg, 57%): colorless solid (m.p. 129 °C). $[a]_D$ = –19.2 (c = 1.1 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.51 (s, 7a-CH_3), AB signal (δ_A = 2.17, δ_B = 2.30, J_{AB} = 14.5 Hz, A part additionally split by $J_{A,6\text{-}H(B)}$ = 9.8 Hz, $J_{A,6\text{-}H(A)}$ = 4.8 Hz, B part additionally split by $J_{B,6\text{-}H(A)}$ = 7.3, $J_{B,6\text{-}H(B)}$ = 5.0 Hz, 7-H_2), AB signal (δ_A = 2.49, δ_B = 2.65, J_{AB} = 17.2, A part additionally split by $J_{A,7\text{-}H(B)}$ = 7.3 Hz, $J_{A,7\text{-}H(A)}$ = 4.8 Hz, B part additionally split by $J_{B,7\text{-}H(A)}$ = 9.8 Hz, $J_{B,7\text{-}H(B)}$ = 4.9 Hz, 6-H_2), AB signal (δ_A = 2.82, δ_B = 3.09, J_{AB} = 18.9 Hz, B part additionally split by $J_{B,3a}$ = 6.4 Hz, 3-H_2), 4.79 (dd, $J_{3a,3\text{-}H(B)}$ = 6.5 Hz, $J_{3a,3\text{-}H(A)}$ = 0.6 Hz, 3a-H) ppm. IR (film): $\tilde{\nu}$ = 2980, 2945, 2885, 1780, 1760, 1750, 1455, 1435, 1410, 1385, 1315, 1285, 1240, 1225, 1185, 1155, 1100, 1050, 985, 950, 880, 805, 695, 625, 565, 535 cm^{-1}; t_r(3a*S*,7a*S*) = 15.19 min, t_r(3a*R*,7a*R*) = 14.19 min (150 °C, 100 kPa); 83% *ee*; elemental analysis calcd. (%) for $C_8H_{10}O_4$ (170.2): C 56.47, H 5.92; found: C 56.53, H 5.79.

(3a*R*,7a*R*)-7a-Methyl-3a,6,7,7a-tetrahydrofuro[3,2-*b*]pyran-2,5-(3*H*)-dione (57b): This compound (63 mg, 63%) was prepared from **56b** (102 mg, 0.592 mmol) in a manner analogous to that specified for **57a**: $[a]_D$ = +20.1 (c = 0.7 in $CHCl_3$); t_r(3a*R*,7a*R*) = 13.66 min, t_r(3a*S*,7a*S*) = 14.76 min (150 °C, 100 kPa); 82% *ee*.

(4*S*,5*R*)-4-Hydroxy-5-methyl-5-(3-oxopropionyl)-4,5-dihydro-3*H*-furan-2-one (58a): H_2O (0.3 mL) was added to a suspension of **55a** (72 mg, 0.31 mmol), EtOAc (6 mL), and $NaIO_4$ (73 mg, 0.34 mmol, 1.1 equiv.). After 30 min, EtOAc (20 mL) was added. The mixture was dried with $MgSO_4$, evaporated in vacuo, and purified by flash chromatography (EtOAc) to afford the title compound (50 mg, 94%): $[a]_D$ = +8.0 (c = 1.0 in $CHCl_3$).

(4*R*,5*S*)-4-Hydroxy-5-methyl-5-(3-oxopropionyl)-4,5-dihydro-3*H*-furan-2-one (58b): This compound (197 mg, 91%) was prepared from **55b** (292 mg, 1.26 mmol) in a manner analogous to that specified for **58a**: $[a]_D$ = –8.8 (c = 1.0 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38 (s, 5-CH_3), AB signal (δ_A = 1.93, δ_B = 1.98, J_{AB} = 14.7 Hz, A part additionally split by $J_{A,2'\text{-}H(B)}$ = 8.4 Hz, $J_{A,2'\text{-}H(A)}$ = 6.4 Hz, B part additionally split by $J_{B,2'\text{-}H(A)}$ = 8.3 Hz, $J_{B,2'\text{-}H(B)}$ = 6.4 Hz, 1′-H_2), 2.29 (br. s, 4-OH), AB signal (δ_A = 2.58, δ_B = 2.93, J_{AB} = 18.0 Hz, A part additionally split by $J_{A,4}$ = 4.8 Hz, B part additionally split by $J_{B,4}$ = 6.9 Hz, 3-H_2), AB signal (δ_A = 2.66, δ_B = 2.70, J_{AB} = 18.7 Hz, A part additionally split by $J_{A,1'\text{-}H(B)}$ = 8.3 Hz, $J_{A,1'\text{-}H(A)}$ = 6.5 Hz, $J_{A,3'}$ = 0.9 Hz, B part additionally split by $J_{B,1'\text{-}H(A)}$ = 8.3 Hz, $J_{B,1'\text{-}H(B)}$ = 6.4 Hz, $J_{B,3'}$ = 0.8 Hz, 2′-H_2), 4.25 (br. dd, $J_{4,3\text{-}H(B)}$ = 6.8 Hz, $J_{4,3\text{-}H(A)}$ = 4.8 Hz, 4-H), 9.82 (m_c, 3′-H) ppm. IR (film): $\tilde{\nu}$ = 3430, 2985, 2940, 2845, 2735, 1770, 1725, 1440, 1415, 1385, 1300, 1260, 1195, 1170, 1110, 1095, 1075,

1045, 945, 800 cm^{-1}; elemental analysis calcd. (%) for $C_8H_{12}O_4$ (172.1): C 55.81, H 7.02; found: C 55.69, H 7.04.

(4*S*,5*R*)-5-But-3-enyl-4-hydroxy-5-methyl-4,5-dihydro-3*H*-furan-2-one (59a): *n*-BuLi (2.3 M hexane, 0.28 mL, 0.64 mmol, 1.4 equiv.) was added at –5 °C to a suspension of triphenylmethylphosphonium bromide (266 mg, 0.744 mmol, 1.6 equiv.) in THF (2 mL). The mixture was allowed to reach room temperature. After stirring for 1 h, the mixture was cooled to –5 °C and a solution of **58a** (80 mg, 0.47 mmol) in THF (2 mL) was added. The mixture was allowed to reach room temperature and stirred for 1.5 h. Aq. NH_4Cl (10 mL) was added and the mixture was extracted with EtOAc (4 × 20 mL) and dried with $MgSO_4$. Evaporation in vacuo and purification by flash chromatography (cyclohexane/EtOAc, 2:1) afforded the title compound (25 mg, 31%): $[\alpha]_D$ = +1.1 (*c* = 0.6 in $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.40 (s, 5-CH_3), 1.65–1.77 (m, 1′-H_2)*, 2.11–2.24 (m, 2′-H_2)*, AB signal (δ_A = 2.56, δ_B = 2.91, J_{AB} = 18.0 , A part additionally split by $J_{A,4}$ = 4.3 , B part additionally split by $J_{B,4}$ = 7.0 Hz, 3-H_2), A part superimposed 2.56 (br. s, 4-OH), 4.27 (dd, $J_{4,3\text{-}H(B)}$ = 6.9 , $J_{4,3\text{-}H(A)}$ = 4.3 Hz, 4-H), 4.99 (dm_c, 4′-H^1), 5.05 (dm_c, 4′-H^2), 5.79 (dddd, J_{trans} = 17.0 , J_{cis} = 10.4 , $J_{3',2'\text{-}H(1)} = J_{3',2'\text{-}H(2)}$ = 6.6 Hz, 3′-H) ppm; * = assignable by a C,H correlation spectrum. IR (film): $\tilde{\nu}$ = 3440, 3080, 2980, 2940, 2860, 1755, 1640, 1450, 1415, 1385, 1300, 1260, 1200, 1175, 1065, 1000, 950, 920, 795 cm^{-1}; t_r(4*S*,5*R*) = 13.25 min, t_r(4*R*,5*S*) = 14.32 min (135 °C, 100 kPa); 90% *ee*; elemental analysis calcd. (%) for $C_9H_{14}O_3$ (232.2): C 63.51, H 8.29; found: C 63.23, H 8.42.

(4*R*,5*S*)-5-(But-3-enyl)-4-hydroxy-5-methyl-4,5-dihydro-3*H*-furan-2-one (59b): This compound (49 mg, 36%) was prepared from **58b** (139 mg, 0.807 mmol) in a manner analogous to that specified for **59a**: $[\alpha]_D$ = –1.2 (*c* = 1.1 in $CHCl_3$); t_r(4*R*,5*S*) = 14.16 min, t_r(4*S*,5*R*) = 13.28 min (150 °C, 100 kPa); 93% *ee*.

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