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The Ester Dienolate [2,3]-Wittig Rearrangement. Diastereoselective Synthesis of 2,3-Dialkenyl-Substituted 2-Hydroxy-γ-Lactones

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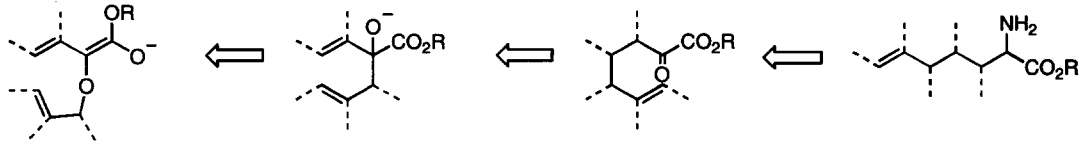
Abstract: The ester dienolate [2,3]-Wittig rearrangement proceeds with high yield and *anti/syn* diastereoselection to afford 3-alkoxycarbonyl-3-hydroxy-substituted 1,5-hexadienes. No donor solvent or metal salt additive was necessary to trigger the rearrangement. The rearrangement product was transformed to diastereomerically pure 2,3-dialkenyl-substituted γ-lactones. A transition state picture was proposed based on previously reported transition state models for enolate [2,3]-Wittig rearrangements.

We have recently initiated a research program toward the stereoselective synthesis of non-natural amino acids *via* the reductive amination of α-keto carboxylic acid derivatives (**2**→**1**).[1] We have identified a sequence of two sigmatropic rearrangements in order to gain access to a structurally diverse number of α-keto carboxylic acid derivatives in a stereoselective way. We envision that a 3-oxy-Cope rearrangement of a 3-alkoxycarbonyl-3-hydroxy-substituted 1,5-hexadiene should afford the desired α-keto ester (**3**→**2**).[2] The starting material for the oxy-Cope rearrangement should be accessible *via* a dienolate [2,3]-Wittig rearrangement of an α-allyloxy-substituted ester dienolate (**4**→**3**).



4 **3** **2** **1**

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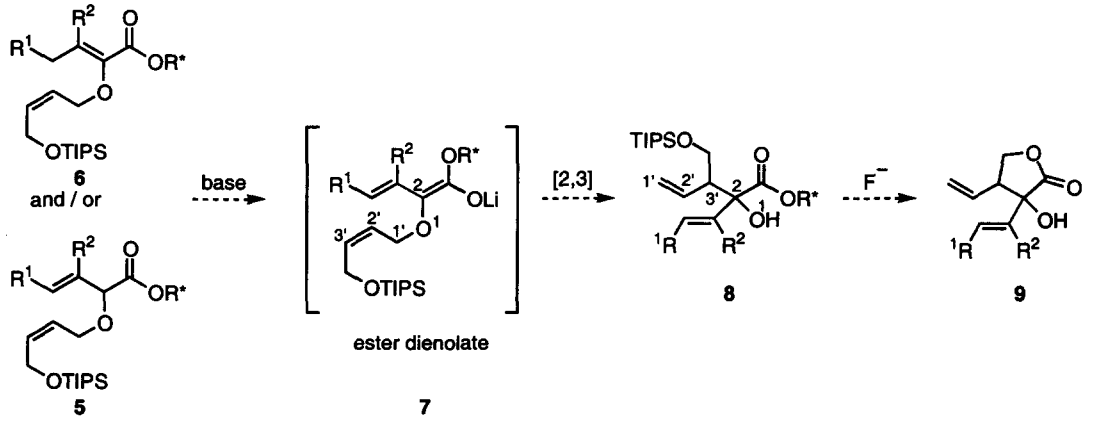
Surprisingly, based on the extensive literature data available from a number of review articles, we were unable to identify an example for a *di*enolate [2,3]-Wittig rearrangement.[3] The enolate [2,3]-Wittig rearrangement has been extensively studied since 1980 by Nakai, Katsuki and others. Powerful asymmetric versions were developed.[4],[5],[6] Nakai has shown that the ester enolate [2,3]-Wittig rearrangement proceeds with high diastereoselection if 8-phenylmenthol is utilized as a chiral auxiliary.[7] The major drawback of the ester enolate chemistry is the necessity of the presence of a donor solvent or a metal salt to trigger the rearrangement due to the low reactivity of a lithium ester enolate.[8] Nakai has also shown that the [2,3]-Wittig rearrangement of an α-substituted unsymmetrical diallyl ether afforded the corresponding tertiary alcohol as a mixture of stereoisomers.[9] Unfortunately, the rearrangement proceeded not regioselectively due to the competitive deprotonation in both α-positions.

We envisioned that combining the advantages of the ester enolate [2,3]-Wittig rearrangement (regioselective deprotonation, stereocontrol *via* a chiral auxiliary) and the [2,3]-Wittig rearrangement of diallyl ethers (reactivity, 3-hydroxy-1,5-hexadiene product framework) should enable us to get access to the desired 3-alkoxycarbonyl-3-hydroxy-substituted 1,5-hexadienes with a variable substitution pattern in a stereocontrolled fashion. The general strategy is outlined in Scheme 1. Enolization of the regioisomeric esters **5** and/or **6** should give an α-allyloxy-substituted ester dienolate **7**. A successful rearrangement (**7**→**8**) followed by desilylation and lactonization would afford a 2,3-dialkenyl-substituted 2-hydroxy-γ-lactone **9**. A NOESY experiment with the lactone **9** should give us the opportunity to establish the relative configuration of the newly created chirality centers.

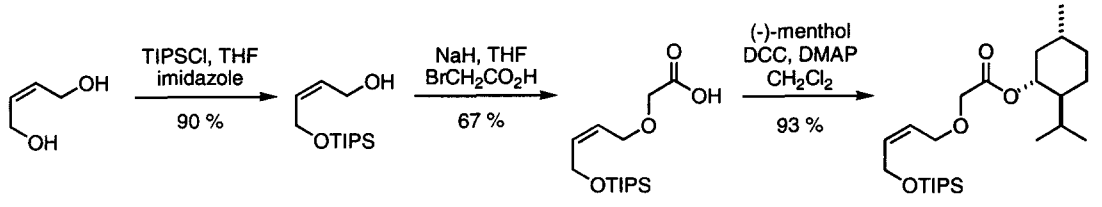
Scheme 1



The synthesis of the starting material for the rearrangement was realized as depicted in Scheme 2 and 3. Monosilylation of (*Z*)-2-butene-1,4-diol **10** afforded the silyl ether **11** which was transformed to the acid **12**. We utilized (-)-menthol as a cheap commercially available

chiral alcohol for our preliminary studies.[10] Esterification with (-)-menthol was performed with the DCC/DMAP method (**12**→**13**).[11]

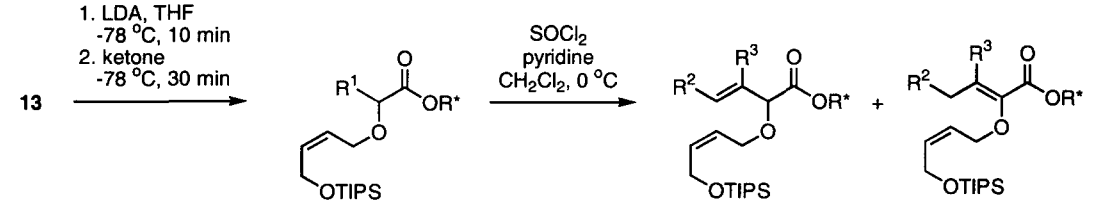
Scheme 2



10 **11** **12** **13**

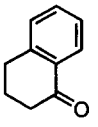
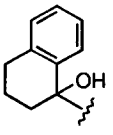
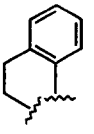
The (-)-menthyl ester **13** was deprotonated with LDA and the aldol addition with acetone or cyclopentanone afforded the desired product (**14a,b**) in high yield and as a 2:1 diastereomeric mixture (Scheme 3, Table 1).[12] The configuration of the newly created chirality center was not assigned. The elimination was successfully realized with thionyl chloride in pyridine and dichloromethane.[13] The elimination afforded two regioisomers (**5a,b** and **6a,b**) which can be separated by flash chromatography (Scheme 3, Table 1). For convenience, we isolated the regioisomers as a mixture since both compounds are transformed to the desired dienolate.

Scheme 3



14a-c **5a-c** **6a-c**

Table 1. Aldol addition and elimination.

ketone	compound	R^1=	yield (%), d.r.[a]	compound	R^2, R^3=	yield (%)
			18a-c			ratio **5a-c**[b]:**6a-b**
	**14a**		90 2:1	**5a, 6a**	R^2= H R^3= CH_3	74 1:1
	**14b**		92 2:1	**5b, 6b**		89 2:1
	**14c**		61 35:18:5:3	**5c**		26[c] 1:0

(a) Diastereomeric ratio determined from ^{1}H NMR spectra, configuration not assigned. (b) Diastereomeric ratio= 2:1, determined from ^{1}H NMR spectra, configuration not assigned. (c) The chloride substitution product was isolated (43 %).

The aldol addition with tetralone was less efficient and the aldol adduct **14c** was isolated in moderate yield as a mixture of diastereomers. The $SOCl_2$-mediated elimination gave a separable mixture of the desired olefin **5c** and the substitution product (Scheme 3, Table 1).
The ester dienolate [2,3]-Wittig rearrangement was performed with the mixture of the regioisomeric olefins **5** and **6** (Scheme 4, Table 2). Treatment of the esters **5** and **6** with LDA at -78 °C for 10 minutes led to a yellow colored enolate solution. The rearrangement proceeded when the dry ice bath was exchanged for an ice bath to afford the rearrangement product in high yield as a mixture of the two *anti* diastereomers **8a-c** (and the C-2, C-3 epimer, not depicted). It is worth mentioning that no additive is necessary and that the overall reaction time is extremely short compared to the ester enolate [2,3]-Wittig rearrangement.[8] The one-pot desilylation and lactonization sequence afforded the γ-lactones **9a-c** as single diastereomers. This result indicated that the rearrangement proceeds with complete *anti/syn* diastereoselection. As expected, the induced diastereoselection of the rearrangement is low due to the weak diastereoface differentiating capability of menthol. As we had envisioned, the results of NOESY experiments with all three γ-lactones are in agreement with the suggested *syn* configuration of the alkenyl-substituents.[14]

Scheme 4

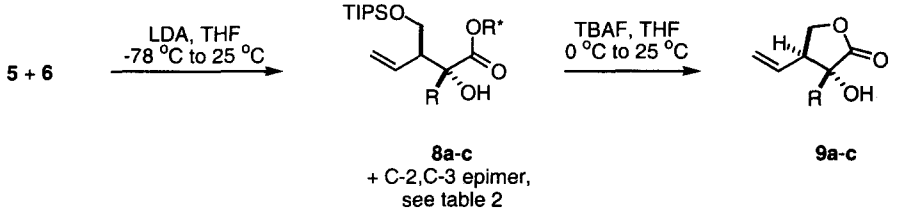
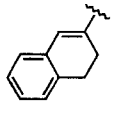


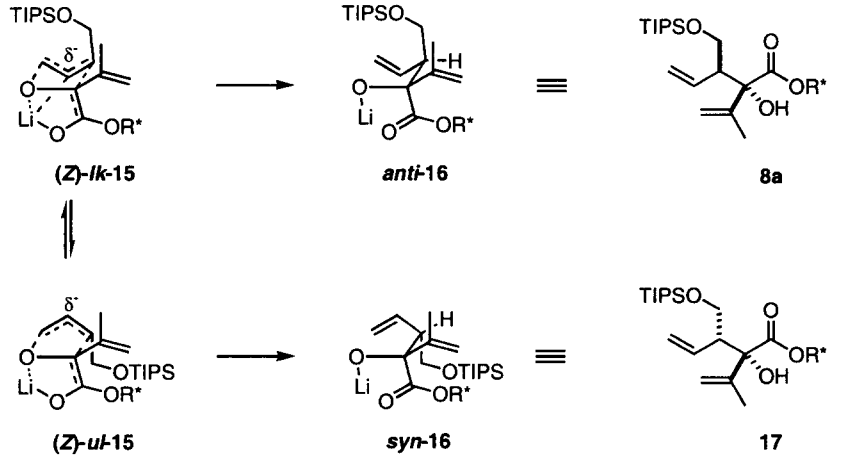
Table 2. Diastereoselection of the ester dienolate [2,3]-Wittig rearrangement.

starting material	R=	product	yield (%)[a] **8a-c**	*anti*:*syn*[b],[c] **8a-c**	product	yield (%)[a],[d] **9a-c**	d.r.[b] **9a-c**
5a+6a		**8a**	92	>95 (2 : 1) : 5	**9a**	78	single diastereomer
5b+6b		**8b**	90	>95 (2 : 1) : 5	**9b**	59	single diastereomer
5c		**8c**	71	>95 (1.2 : 1) : 5	**9c**	87	single diastereomer

(a) Isolated yield after chromatographic purification. (b) Diastereomeric ratio determined from ^1H NMR spectra. (c) In parentheses: Diastereomeric ratio of the two *anti* diastereomers with respect to R*, configuration not assigned. (d) (-)-Menthol was isolated in 70-90 % yield.

Based on the suggested relative configuration, the diastereoselection can be qualitatively explained in terms of the previously reported transition state models for the enolate [2,3]-Wittig rearrangement.[15] As depicted in Scheme 5, based on a chelated (*Z*)-configurated enolate, the five-membered transition state for the concerted [2,3]-Wittig rearrangement leads to a pseudo bicyclo[3.3.0]octane framework for the transition state. In the *like* transition state **(*Z*)-*lk*-15**, the triisopropylsiloxymethyl substituent is directed toward the convex face of the bicyclic transition state framework. This leads to the *anti* configurated product ***anti*-16**. In the unlike transition state **(*Z*)-*ul*-15**, the triisopropylsiloxymethyl substituent is directed toward the more crowded concave face of the transition state. Consequently, it is reasonable to assume that the *like* transition state **(*Z*)-*lk*-15** is preferred for steric reasons. A rearrangement *via* the transition state **(*Z*)-*lk*-15** affords the *anti* configurated product ***anti*-16** what was experimentally verified by our study.

Scheme 5



Furthermore, the *like* transition state could be favored due to the stabilization of a partially negative charge which develops on the central atom (*C*-2') of the allyl ether moiety as depicted in Scheme 5. A recent computational analysis has identified this interaction as stabilizing for the transition state of the carboxylic acid dianion [2,3]-Wittig rearrangement.[16] This interaction should be less efficient for the *unlike* transition state **(*Z*)-*ul*-15** because *C*-2' is directed toward the convex face of the bicyclo[3.3.0]octane framework.

The "*Z* to *anti*" relationship between the configuration of the allylic ether double bond and the relative configuration of the newly formed chirality centers is in accordance with the previously reported rules for enolate [2,3]-Wittig rearrangements.

In summary, we have reported first examples for the ester dienolate [2,3]-Wittig rearrangement which proceeds with high yield and under complete control of the *anti*:*syn* (>95:5) diastereoselection. No donor solvents or metal salt additives are necessary to trigger

the rearrangement. The rearrangement allows the stereoselective access to 3-hydroxy-3-alkoxycarbonyl-substituted hexadienes which should be valuable intermediates for further stereoselective transformations. The 3-oxy-Cope rearrangements to α-keto-esters is currently under investigation in our laboratory. Further work in order to study the relationship between substrate structure, reactivity and stereoselection as well as the aza-version of the dienolate [2,3]-Wittig rearrangement is currently under way and will be reported in due course.

Experimental Section

General. All reaction were performed in oven dried and septum sealed glassware under an atmosphere of argon. Reagents were transferred with a syringe or cannula. THF was distilled from potassium. CH_2Cl_2 was distilled from CaH_2. The titration of the commercial *n*-BuLi solution in hexanes was realized following the procedure of Kofron.[17] NaH was used without further purificaton. Silica gel (230-400 mesh) was used for column chromatography. ^1H and ^{13}C spectra were recorded on a Bruker AC 300 or DRX 500 in $CDCl_3$. For diastereomeric mixtures, the term n+nH refers to nH for each diastereomer. IR spectra were recorded on a Nicolet 205 FT-IR spectrometer. Elemental analyses were obtained with Carlo Erba CHN-S-Analyzer. Melting points are uncorrected.

(Z)-4-(Triisoproylsiloxy)-2-butene-1-ol (11).[18] To a stirred solution of (Z)-2-butene-1,4-diol (14.8 mL, 180 mmol) and imidazole (1.36 g, 20 mmol) in THF (50 mL) at 0 °C was added triisopropylsilyl chloride over a period of 30 min. The reaction mixture was allowed to warm to room temperature and stirred for additional 8 h. The reaction mixture was quenched with water (50 mL), the phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2×50 mL). The combined organic phases were dried with $MgSO_4$ and concentrated. Chromatographic purification (heptane/ethyl acetate 6/1) afforded the monosilylated diol (4.39 g, 90 %) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 1.02-1.12 (m, 21 H), 4.21-4.31 (m, 2H), 4.31-4.34 (m, 2H), 5.68-5.72 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.9, 17.9, 58.9, 59.8, 129.9, 131.4; IR 3326, 1464 cm^{-1}; Anal. Calcd. for $C_{13}H_{28}O_2Si$: C, 63.87; H, 11.55. Found: C, 63.39; H, 11.97.

(Z)-4-(Triisoproylsiloxy)-2-butenyloxy acetic acid (12). To a stirred suspension of NaH (164 mg, powder, moistened with oil 60 %, 4.1 mmol) in THF (10 mL) was added a solution of the alcohol **11** (1 g, 4.1 mmol) in THF (3 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 90 min. The orange solution was cooled to 0 °C and NaH (164 mg, powder, moistened with oil 60 %, 4.1 mmol) was added followed by a solution of bromo-acetic acid (568 mg, 4.1 mmol) in THF (5 mL). The reaction mixture was stirred 2 h at 25 °C and refluxed for 1 h. The reaction was quenched with an 1 N aqueous KOH solution (50 mL). The phases were separated and the organic layer was extracted with an 1 N aqueous KOH solution (3×50 mL). The combined aqueous phases were acidified with a 3 N HCl solution. The acidic solution was extracted with $CHCl_3$ (5×100 mL). The combined organic layers were dried and concentrated. The crude product oil was purified by kugelrohr distillation to give the desired acid **12** (832 mg, 67 %) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 1.02-1.10 (m, 21 H), 4.12 (s, 2H), 4.22 (mc, 2H); 4.33 (mc, 2H), 5.60 (ttd, J = 11.3, 6.5, 1.6

Hz, 1H), 5.80 (ttd, J = 11.3, 5.7, 1.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.0, 18.0, 59.8, 66.8, 67.3, 125.1, 134.4, 173.9.

(Z)-4-(Triisoproylsiloxy)-2-butenyloxy acetic acid (-)-menthyl ester (13). To a stirred solution of the acid **12** (2.5 g, 8.27 mmol) in CH_2Cl_2 (70 mL) at 0 °C was subsequently added DMAP (101 mg, 0.827 mmol), DCC (1.88 g, 9.09 mmol) and (-)-menthol (1.29 g, 8.27 mmol). The reaction mixture was stirred at 0 °C until TLC indicated that the acid was consumed. The precipitate was removed by filtration and washed with ethyl acetate. The filtrate was concentrated, diluted with ethyl acetate and filtrated again. The solvent was removed and the crude product was purified by flash chromatography to yield the ester **13** (3.41 g, 93 %) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02-1.10 (m, 21H), 0.97-1.15 (m, 21H), 1.19-2.05 (series of m, 9H), 4.04 (s, 2H), 4.17 (d, J = 5.8 Hz, 2H), 4.32 (d, J = 5.8 Hz, 2H), 4.83 (td, J = 10.9, 4.6 Hz, 1H), 5.55-5.66 (m, 1H), 5.71-5.82 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.0, 16.4, 18.0, 20.7, 21.9, 23.5, 26.4, 31.4, 34.2, 40.9, 47.1, 59.8, 67.2, 67.5, 74.9, 125.7, 133.8, 169.9; IR 1751, 1463 cm^{-1}; Anal. Calcd. for $C_{25}H_{48}O_4Si$: C, 68.13; H, 10.98. Found: C, 68.37; H, 10.89.

General procedure for the aldol reaction (13→14a-c). To a solution of diisopropylamine in THF at 0 °C was added *n*-BuLi. After being stirred for 30 min at 0 °C, the reaction mixture was cooled to –78 °C and a cooled solution (-78 °C) of the ester **13** in THF was added with a syringe. After being stirred for 10 min at –78 °C, the ketone was added undiluted in one portion. The reaction mixture was stirred for 30 min and quenched wil saturated aqueous NH_4Cl solution at –78 °C. The reaction mixture was warmed to room temperature and diluted with water (20 mL) and CH_2Cl_2 (30 mL). The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2×50 mL). The combined organic layers were dried and concentrated. Chromatographic purification (heptane/ethyl acetate) afforded the desired alcohol.

General procedure for the elimination (14a-c→5a-c,6a-b). To a solution of freshly distilled $SOCl_2$ in CH_2Cl_2 at 0 °C was slowly added a solution of the alcohol **14a-c** in pyridine. The reaction mixture was stirred at 0 °C until TLC indicated that the starting material was consumed. The reaction was quenched with saturated aqueous $NaHCO_3$ solution (50 mL). The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3×50 mL). The combined organic phases were dried, concentrated and the pyridine was removed at room temperature under reduced pressure (0.05 mbar). Chromatographic purification (heptane/ethyl acetate) afforded the desired ester.

General procedure for the dienolate [2,3]-Wittig rearrangement (5a-c,6a-b→8a-c). To a stirred solution of diisopropylamine in THF was added *n*-BuLi at 0 °C. After being stirred for 30 min at 0 °C, the solution was cooled to –78 °C. To this mixture was added a cool (-78 °C) solution of the esters **5a-c** and **6a-b** in THF with a syringe. The slightly yellow reaction mixture was stirred at –78 °C for 10 min, then warmed to 0 °C and stirred for 1 h and finally warmed to room temperature and stirred for 15 min. The reaction was quenched with saturated aqueous NH_4Cl solution (20 mL), diluted with water (5 mL) and CH_2Cl_2 (50 ml). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2×50 mL). The combined organic phases were dried and concentrated to give a slightly yellow crude product

which was purified by chromatography (heptane/ethyl acetate) to afford the desired alcohol **8a-c** as a colorless oil.

(2*R*)- and (2*S*)-3-Hydroxy-3-methyl-2-[(*Z*)-(4-triisopropylsiloxy)-but-2-enyloxy]-butyric acid (-)-menthyl ester (14a). Following the general procedure for the aldol reaction, diisopropylamine (507 mg, 5.01 mmol) in THF (8 mL) was treated with *n*-BuLi (1.93 mL of a 2.4 M solution in hexanes, 4.63 mmol), the ester **13** (1.7 g, 3.86 mmol) in THF (10 mL) and acetone (0.57 mL, 7.72 mmol). Chromatographic purification (heptane/ethyl acetate 5/1) afforded the desired alcohol **14a** (1.72 g, 90 %) as a colorless oil and as a 2:1 mixture of diastereomers. Spectral data reported for the mixture of diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.76 (d, J = 6.8 Hz, $3H^{minor}$), 0.77 (d, J = 6.8 Hz, $3H^{major}$), 0.88-0.94 (series of 4 d, 6H), 0.98-1.15 (m, 24+24H), 1.24 (s, 3+3H), 1.27 (s, 3+3H), 1.36-1.62 (m, 2+2H), 1.65-1.77 (m, 2+2H), 1.84-1.97 (m, 2+2H), 1.97-2.09 (m, 2+2H), 2.86 (s, 1+2H), 3.67 (s, $1H^{minor}$), 3.69 (s, $1H^{major}$), 3.97-4.08 (m, 2+2H), 4.17-4.26 (m, 2+2H), 4.31 (d, J = 5.8 Hz, 2+2H), 4.79 (dt, J = 11.3, 4.3 Hz, $1H^{minor}$), 4.82 (td, J = 10.9 Hz, 4.4 Hz, $1H^{major}$), 5.53-5.65 (m, 1+1H), 5.70-5.81 (m, 1+1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.9, 15.6, 16.0, 18.0, 20.7, 20.8, 21.9, 22.8, 23.2, 25.4, 25.55, 25.6, 25.9, 31.4, 34.1, 34.9, 40.7, 40.8, 46.7, 46.9, 59.8, 66.8, 66.9, 71.6, 71.7, 75.3, 75.7, 85.0, 85.1, 125.4, 125.5, 133.7, 133.9, 170.7, 171.0 ; IR 3488, 1741, 1463 cm^{-1}; Anal. Calcd. for $C_{28}H_{54}O_5Si$: C, 67.42; H, 10.91. Found: C, 67.38; H, 11.10.

(2*R*)- and (2*S*)-3-Methyl-2-[(*Z*)-(4-triisopropylsiloxy)-but-2-enyloxy]-but-3-enoic acid (-)-menthyl ester (5a), 3-methyl-2-[(*Z*)-(4-triisopropylsilyloxy)-but-2-enyloxy]-but-2-enoic acid (-)-menthyl ester (6a). Following the general procedure for the elimination, $SOCl_2$ (0.69 mL, 9.54 mmol) in CH_2Cl_2 (22 mL) was treated with the alcohol **14a** (1.57 g, 3.18 mmol) in pyridine (9 mL). The crude product oil was subjected to flash chromatography (heptane/ethyl acetate 20/1). The ester **6a** was isolated as a 2:1 mixture with the ester **5a** in 34 % yield. The ester **5a** was isolated as a mixture with the ester **6a** and as pure compound in combined 41 % yield and as a 2:1 mixture of diastereomers. The isolated compounds were not feasible for combustion analysis due to sulfur impurities. Ester **5a**, spectral data reported from a mixture of diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.72 (d, J = 6.8 Hz, $3H^{minor}$), 0.77 (d, J = 6.8 Hz, $3H^{major}$), 0.86-0.93 (series of 4 d, 6+6H), 1.01-1-17 (m, 24+24H), 1.35-2.08 (series of m, 6+6H), 1.75 (d, J = 1 Hz, 3+3H), 4.08 (d, J = 6.2 Hz, 2+2H), 4.30 (s, $1H^{major}$), 4.31 (s, $1H^{minor}$), 4.73 (td, J = 10.8, 4.1 Hz, $1H^{minor}$), 4.77 (td, J = 10.9, 4.2 Hz, $1H^{major}$), 5.06 (q, J = 1 Hz, 1+1H), 5.13 (s, 1+1H), 5.55-5.66 (m, 1+1H), 5.69-5.78 (m, 1+1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.9, 15.9, 16.2, 17.8, 18.1, 20.7, 22.0, 23.1, 23.4, 25.9, 26.2, 31.3, 31.4, 34.2, 40.4, 40.8, 46.8, 46.9, 59.8, 64.8, 64.9, 74.9, 75.1, 82.0, 82.1, 115.8, 116.2, 125.8, 133.48, 133.52, 140.2, 140.4, 169.96, 169.99. Ester **6a**: diagnostic spectroscopic data reported from the mixture: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.85 (s, 3H), 2.04 (s, 3H), 4.16-4.28 (m, 2H), 4.79 (td, J = 10.8, 4.3 Hz), 5.64-5.78 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.0, 16.1, 18.0, 19.8, 20.1, 20.8, 23.3, 26.1, 31.5, 34.2, 41.0, 47.1, 59.7, 67.7, 74.9, 125.7, 133.2, 135.7, 164.2.

(2*R*,3*R*)- and (2*S*,3*S*)-2-Hydroxy-2-isopropenyl-3-triisopropylsiloxymethyl-pent-4-enoic acid (-)-menthyl ester (8a). Following the general procedure, diisopropylamine (151 mg, 1.5 mmol) in THF (3.3 mL) was treated with *n*-BuLi (0.63 mL of a 2.4 M solution in hexanes, 1.5 mmol) and the esters **5a** and **6a** (514 mg, 1.07 mmol) in THF (5 mL). Chromatographic purification (heptane/ethyl acetate 20/1) afforded the desired alcohol **8a**

(473 mg, 92 %) as a colorless oil. The NMR data indicated a 2:1 diastereomeric mixture. Spectroscopic data reported from the mixture, assignment is based on COSY and HSQC experiments: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.69 (d, J = 6.8 Hz, 3+3H, menthyl-CH_3), 0.84-0.92 (series of 4 d and 1 m, 7+7H, menthyl-CH_3 and menthyl-H-4), 0.99-1.12 (m, 23+23H, TIPS-H, menthyl-H-3, -H-6), 1.37-1.51 (m, 2+2H, menthyl-H-2, -H-5), 1.62-1.72 (m, 2+2H, menthyl-H-3, -H-4), 1.74-1.99 (m, 2+2H, menthyl-isopropyl-H, -H-6), 1.87 (s, 3+3H, isopropenyl-(C**H**$_3$)C=CH$_2$), 2.88-2.98 (m, 1+1H, H-3), 3.77-3.88 (m, 2+2H, -C**H**$_2$OTIPS), 4.09 (s, 1H^{major}, OH), 4.19 (s, 1H^{minor}, OH), 4.70 (td, J = 11.1, 3.9 Hz, 1H^{minor}, menthyl-H-1), 4.74 (td, J = 11.0, 4.4 Hz, 1H^{major}, menthyl-H-1), 5.08 (s, 1+1H, isopropenyl-(CH$_3$)C=C**H**$_2$), 5.13-5.24 (m, 2+2H, H-5), 5.36 (s, 1H^{major}, isopropenyl-(CH$_3$)C=C**H**$_2$), 5.40 (s, 1H^{minor}, isopropenyl-(CH$_3$)C=C**H**$_2$), 5.86-6.07 (m, 1+1H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.8 (TIPS), 15.7, 15.8 (menthyl-CH_3), 18.0 (TIPS), 19.4, 19.5 (isopropenyl-(**C**H$_3$)C=CH$_2$), 20.7, 20.8 (menthyl-CH_3), 21.96, 21.98 (menthyl-CH_3), 22.9, 23.0 (menthyl-CH_2), 25.5, 25.6 (menthyl-isopropyl-C), 31.4, 31.8 (menthyl-C-5), 34.10, 34.12 (menthyl-CH_2), 40.4, 40.5 (menthyl-CH_2), 46.8, 47.0 (menthyl-C-2), 49.4, 50.2 (C-3), 63.7, 64.2 (**C**H$_2$OTIPS), 76.0, 76.2 (menthyl-C-1), 81.5, 82.1 (C-2), 114.4 (isopropenyl-(CH$_3$)**C**=CH$_2$), 118.6, 119.0 (C-5), 135.3, 135.4 (C-4), 143.9, 144.0 (isopropenyl-(CH$_3$)**C**=CH$_2$), 172.8 (C-1); IR 3500, 1717, 1461 cm^{-1}; Anal. Calcd. for $C_{28}H_{52}O_4Si$: C, 69.94; H, 10.90. Found: C, 69.41; H, 11.01.

(2*SR*,3*SR*)-3-Hydroxy-3-isopropenyl-4-vinyl-dihydro-furan-2-one (9a). To a solution of the ester **8a** (410 mg, 0.85 mmol) in THF (5 mL) was added TBAF (0.93 mL of an 1 M solution in THF, 0.93 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 10 h at 25 °C. The reaction was quenched with water (20 mL) and diluted with CH_2Cl_2 (20 mL). The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2×30 mL). The combined organic phases were dried and concentrated. The crude product was purified by chromatography (heptane/ethyl acetate 5/1) to yield menthol (121 mg, 91 %) and the desired lactone (112 mg, 78 %) as a white solid and as a single diastereomer. Assignment is based on COSY, HSQC and NOESY experiments: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.81 (s, 3H, isopropenyl-CH_3), 3.28 (mc, 1H, 4H), 3.44-3.49 (m, 1H, OH), 4.01 (dd, J = 10.4, 9.0 Hz, 1H, 5-H), 4.42 (dd, J = 8.3, 9.0 Hz, 1H, 5-H), 4.94 (s, 1H, isopropenyl-H), 5.13 (s, 1H, isopropenyl-H), 5.24 (d, J = 10.1 Hz, 1H, vinyl-H), 5.27 (d, J = 17.2 Hz, 1H, vinyl-H), 5.64 (ddd, J = 17.2, 8.4, 10.1 Hz, 1H, vinyl-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.2 (isopropenyl-CH_3), 51.5 (C-4), 68.1 (C-5), 113.9 (ispropenyl-CH_2), 120.0 (vinyl-CH_2), 131.1 (vinyl-CH), 141.1 (isopropenyl-C), 178.1 (carbonyl-C); IR 3423, 1757 cm^{-1}; mp 76 °C; Anal. Calcd. for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.29; H, 7.65.

(2*R*)- and (2*S*)-(1-Hydroxy-cyclopentyl)-[(*Z*)-4-triisopropylsiloxy-but-2-enyloxy]-acetic acid (-)-menthyl ester (14b). Following the general procedure for the aldol reaction, diisopropylamine (439 mg, 4.34 mmol) in THF (7 mL) was treated with *n*-BuLi (1.89 mL of a 2.3 M solution in hexanes, 4.34 mmol), the ester **13** (1.47 g, 3.34 mmol) in THF (10 mL) and cyclopentanone (0.59 mL, 6.68 mmol). Chromatographic purification (heptane/ethyl acetate 10/1) afforded the desired alcohol **14b** (1.61 g, 92 %) as a colorless oil and as a 2:1 mixture of diastereomers. Spectral data reported for the mixture of diastereomers: ^{1}H NMR

(300 MHz, $CDCl_3$) δ 0.75 (d, J = 6.8 Hz, $3H^{minor}$), 0.76 (d, J = 6.8 Hz, $3H^{major}$), 0.86-0.93 (series of 4 d, 6+6H), 1.36-2.08 (series of m, 24+24H), 2.14 (s, broad, 1+1H), 3.77 (s, $1H^{minor}$), 3.79 (s, $1H^{major}$), 3.96-4.07 (m, 1+1H), 4.16-4.26 (m, 1+1H), 4.29 (mc, 2+2H), 4.78 (td, J = 10.9, 4.3 Hz, $1H^{minor}$), 4.81 (td, J = 10.9, 4.4 Hz, $1H^{major}$), 5.52-5.64 (m, 1+1H), 5.69-5.79 (m, 1+1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.0, 15.7, 16.1, 18.0, 20.7, 20.9, 23.0, 23.4, 23.9, 23.93, 24.2, 26.0, 26.3, 31.5, 34.21, 34,24, 36.4, 36.5, 37.3, 37.7, 40.87, 40.91, 46.9, 47.0, 59.8, 66.7, 66.9, 75.3, 75.6, 82.7, 82.9, 83.6, 125.6, 125.7, 133.7, 133.9, 170.8, 171.2; IR 3508, 1741, 1463 cm^{-1}; Anal. Calcd. for $C_{30}H_{56}O_5Si$: C, 68.65; H, 10.75. Found: C, 68.51; H, 11.21.

(2*R*)- and (2*S*)-Cyclopent-1-enyl-[(*Z*)-4-triisopropylsiloxy-but-2-enyloxy]-acetic acid (-)-menthyl ester (5b), cyclopentylidene-[(*Z*)-4-triisopropylsiloxy-but-2-enyloxy]-acetic acid (-)-menthyl ester (6b). Following the general procedure for the elimination, $SOCl_2$ (0.60 mL, 8.2 mmol) in CH_2Cl_2 (22 mL) was treated with the alcohol **14a** (1.44 g, 2.73 mmol) in pyridine (6 mL). The crude product oil was subjected to flash chromatography (heptane/ethyl acetate 50/1). The ester **6b** was isolated in pure form (283 mg, 21 %) and as a 1:1 mixture with the ester **5b** (125 mg, 9 %) yield. The ester **5b** was isolated as a mixture with the ester **6b** and as a pure compound in combined 59 % yield and as a 2:1 mixture of diastereomers. The isolated compounds were not feasible for combustion analysis due to sulfur impurities. Ester **6b**: ^1H NMR (300 MHz, $CDCl_3$) δ 0.76 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.5 Hz, 3H), 0.99-1.13 (m, 24H), 1.38-1.77 (series of m, 6H), 1.85-1.98 (m, 1H), 1.99-2.09 (m, 1H), 2.50 (t, broad, J = 7 Hz, 2H), 2.66 (dt, J = 7.0, 1.6 Hz, 2H), 4.28-4.34 (m, 4H), 4.79 (td, J = 10.8, 4.4 Hz, 1H), 5.70 (mc, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.0, 16.2, 18.0, 20.9, 22.0, 23.4, 25.5, 26.3, 27.1, 31.5, 31.8, 32.0, 34.3, 41.3, 47.3, 59.8, 67.5, 74.3, 126.2, 133.1, 137.9, 149.7, 164.0. Ester **5b**, spectroscopic data reported from a mixture of diastereomers: ^1H NMR (300 MHz, $CDCl_3$) δ 0.70 (d, J = 7.1 Hz, $3H^{minor}$), 0.75 (d, J = 6.8 Hz, $3H^{major}$), 0.83-0.92 (series of d, 6+6H), 0.96-1.13 (m, 24+24H), 1.32-2.07 (series of m, 8+8H), 2.18-2.42 (m, 4+4H), 4.07 (mc, 2+2H), 4.29 (mc, 2+2H), 4.49 (s, $1H^{major}$), 4.52 (s, $1H^{minor}$), 4.71 (td, J = 11.0, 4.2 Hz, $1H^{minor}$), 4.77 (dt, J = 10.8, 4.1 Hz, $1H^{major}$), 5.53-5.64 (m, 1+1H), 5.67-5.76 (m, 1+1H), 5.78 (s, broad, 1+1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.0, 16.0, 16.3, 18.0, 20.7, 20.73, 22.0, 23.1, 23.2, 23.3, 23.4, 26.0, 26.3, 31.4, 31.6, 32.0, 32.4, 34.3, 40.6, 40.9, 59.9, 65.1, 65.3, 75.0, 75.1, 77.5, 77.9, 126.0, 130.2, 131.0, 133.5, 139.3, 139.4, 170.2; IR 1745, 1463 cm^{-1}.

(2*R*,3*R*)- and (2*S*,3*S*)-2-Cyclopent-1-enyl-2-hydroxy-3-triisopropylsiloxymethyl-pent-4-enoic acid (-)-menthyl ester (8b). Following the general procedure, diisopropylamine (232 mg, 2.29 mmol) in THF (5 mL) was treated with *n*-BuLi (0.89 mL of a 2.4 M solution in hexanes, 2.13 mmol) and the esters **5b** and **6b** (830 mg, 1.64 mmol) in THF (5 mL). Chromatographic purification (heptane/ethyl acetate 13/1) afforded the desired alcohol **8b** (769 mg, 93 %) as a colorless oil. The NMR data indicated a 2:1 diastereomeric mixture. Spectroscopic data reported from the mixture, assignment is based on COSY and HSQC experiments: ^1H NMR (300 MHz, $CDCl_3$) δ 0.68 (d, J = 6.8 Hz, $3H^{major}$, menthyl-CH_3), 0.69 (d, J = 6.8 Hz, $3H^{minor}$, menthyl-CH_3), 0.80-0.91 (series of 4 d and 1 m, 7+7H, menthyl-CH_3 and menthyl-H-4), 0.96-1.11 (m, 23+23H, TIPS-H, menthyl-H-6, -H-3), 1.35-1.53 (series of m, 2+2H, menthyl-H-2, -H-5), 1.60-1.97 (series of m, 6+6H, menthyl-H-3, -H-4, -isopropyl-

H, -H-6, cyclopentenyl-=CHCH$_2$C**H$_2$**CH$_2$C=), 2.23-2.58 (series of m, 4+4H, cyclopentenyl-=CHC**H$_2$**CH$_2$C**H$_2$**C=), 2.79-2.91 (m, 1+1H, H-3), 3.76-3.87 (m, 2+2H, -C**H$_2$**OTIPS), 4.69 (td, J = 10.7, 4 Hz, 1H^{minor}, menthyl-H-1), 4.73 (td, J = 10.9, 4.4 Hz, 1H^{major}, menthyl-H-1), 5.10-5.22 (m, 2+2H, H-5), 5.84-6.07 (m, 2+2H, H-4, cyclopentenyl-=C**H**CH$_2$CH$_2$CH$_2$C=); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.81, 11.84 (TIPS), 15.7, 15.8 (menthyl-CH_3), 18.0 (TIPS), 20.8, 20.9 (menthyl-CH_3), 22.0 (menthyl-CH_3), 22.7, 22.9 (cyclopentenyl-=CHCH$_2$**C**H$_2$CH$_2$C=), 23.7, 24.1, (menthyl-CH_2), 25.6 (menthyl-isopropyl-H), 31.5 (menthyl-CH), 32.2, 32.4, 32.47, 32.52 (cyclopentenyl-=CH**C**H$_2$CH$_2$**C**H$_2$C=), 34.10, 34.14 (menthyl-4-CH_2), 40.6, 40.7 (menthyl-6-CH_2), 47.0, 47.3 (menthyl-CH), 50.2, 51.2 (C-3), 63.8, 64.3 (-**C**H$_2$OTIPS), 76.0, 76.1 (menthyl-C-1), 79.6, 80.5 (C-2), 118.5, 118.8 (C-5), 128.9, 129.0 (cyclopentenyl-=**C**HCH$_2$CH$_2$CH$_2$C=), 135.3 (C-4), 144.0, 144.2 (cyclopentenyl-=CHCH$_2$CH$_2$CH$_2$**C**=), 172.4, 173.0 (C-1); IR 3505, 1720, 1465 cm^{-1}; Anal. Calcd. for $C_{30}H_{54}O_4Si$: C, 71.09; H, 10.74. Found: C, 71.10; H, 10.82.

(2*SR*,3*SR*)-3-Cyclopent-1-enyl-3-hydroxy-4-vinyl-dihydro-furan-2-one (9b). To a solution of the ester **8b** (733 mg, 1.45 mmol) in THF (14.5 mL) was added TBAF (1.59 mL of an 1 M solution in THF, 1.59 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 10 h at 25 °C. The reaction was quenched with water (20 mL) and diluted with CH_2Cl_2 (30 mL). The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2×30 mL). The combined organic phases were dried and concentrated. The crude product was purified by chromatography (heptane/ethyl acetate 6/1) to yield menthol (200 mg, 88 %) and the desired lacton **9b** (166 mg, 59 %) as a white waxy solid and as a single diastereomer. Assignment is based on COSY, HSQC and NOESY experiments: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.79-2.01 (m, 2H, cyclopentenyl-=CHCH$_2$C**H$_2$**CH$_2$C=), 2.25-2.50 (m, 4H, cyclopentenyl-=CHC**H$_2$**CH$_2$C**H$_2$**C=), 3.08 (m, 1H, OH), 3.23-3.45 (m, 1H, 4-H), 4.02 (dd, J = 10.7, 9.1 Hz, 1H, 5-H), 4.41 (dd, J = 9.1, 8.1 Hz, 1H, 5-H), 5.19-5.23 (m, 1H, vinyl-H), 5.23-5.29 (m, 1H, vinyl-H), 5.67-5.68 (m, 1H, vinyl-H), 5.69-5.75 (m, 1H, cyclopentenyl-=C**H**CH$_2$CH$_2$CH$_2$C=); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.2 (cyclopentenyl-=CHCH$_2$**C**H$_2$CH$_2$C=), 32.3, 32.4 (cyclopentenyl-=CH**C**H$_2$CH$_2$**C**H$_2$C=), 52.3 (C-4), 68.2 (C-5), 78.1 (C-3), 119.8 (vinyl-CH_2), 129.3 (cyclopentenyl-=**C**HCH$_2$CH$_2$CH$_2$C=), 131.2 (vinyl-**C**H), 139.9 (cyclopentenyl-=CH**C**H$_2$CH$_2$CH$_2$**C**=), 178.1 (carbonyl-C); IR 3428, 1768 cm^{-1}; Anal. Calcd. for $C_{11}H_{14}O_3Si$: C, 68.02; H, 7.27. Found: C, 67.68; H, 7.44.

(2*R*) and (2*S*)-(1-Hydroxy-1,2,3,4-tetrahydro-naphthalen-1-yl)-[(*Z*)-4-triisopropylsiloxy-but-2-enyloxy]-acetic acid (-)-menthyl ester (14c). Following the general procedure for the aldol reaction, diisopropylamine (463 mg, 4.57 mmol) in THF (7 mL) was treated with *n*-BuLi (1.76 mL of a 2.4 M solution in hexanes, 4.22 mmol), the ester **13** (1.55 g, 3.52 mmol) in THF (5 mL) and tetralone (0.94 mL, 7.04 mmol) in THF (2 mL). Chromatographic purification (hexanes/ethyl acetate 5/1) afforded the desired alcohol **14c** (1.39 g, 61 %) as a colorless oil and as a 35:18:5:3 mixture of diastereomers. Spectral data reported for the mixture of the two major diastereomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.37 (dd, J = 23.0, 12.0 Hz, 1H^{major}), 0.47 (d, J = 6.8 Hz, 3H^{minor}), 0.62 (d, J = 7.1 Hz, 3H^{minor}), 0.67 (d, J = 6.8 Hz, 3H^{major}), 0.79 (d, J = 6.5 Hz, 3H^{major}), 0.81 (d, J = 6.8 Hz, 3H^{major}), 0.85 (d, J = 6.5 Hz,

$3H^{minor}$), 0.76-0.97 (m, $2H^{major}$+$3H^{minor}$), 0.98-1.14 (m, 24+24H), 1.22-2.19 (series of m, 10+10H), 2.54-2.68 (m, 1+1H), 2.70-2.83 (m, 1+1H), 4.00-4.11 (m, 1+1H), 4.18-4.33 (m, 4+4H), 4.53 (td, J = 10.6, 4.2 Hz, $1H^{major}$), 4.56 (td, J = 10.0, 4.6 Hz, $1H^{minor}$), 5.54-5.65 (m, 1+1H), 5.70-5.81 (m, 1+1H), 7.02-7.08 (m, 1+1H), 7.13-7.20 (m, 2+2H), 7.53-7.59 (m, 1+1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.0, 15.3, 16.1, 18.0, 19.2, 20.7, 21.0, 21.8, 21.9, 22.6, 23.3, 24.8, 26.2, 30.0, 30.1, 31.2, 31.4, 33.0, 33.2, 34.1, 40.0, 40.7, 46.5, 46.6, 59.8, 67.0, 67.1, 73.0, 73.3, 74.9, 75.4, 84.9, 85.1, 125.5, 125.7, 125.8, 127.6, 127.7, 128.2, 128.3, 128.7, 128.86, 128.89, 133.9, 134.0, 136.5, 137.1, 138.0, 138.2, 169.7, 170.0; IR 3507, 1736, 1459 cm^{-1}; Anal. Calcd. for $C_{35}H_{58}O_5Si$: C, 71.62; H, 9.96. Found: C, 71.22; H, 10.18.

(2*R*)- and (2*S*)-(3,4-Dihydro-naphthalen-1-yl)-[(*Z*)-4-triisopropylsilanyloxy-but-2-enyloxy]-acetic acid (-)-menthyl ester (5c). Following the general procedure for the elimination, $SOCl_2$ (0.36 mL, 5.02 mmol) in CH_2Cl_2 (12 mL) was treated with the alcohol **14c** (0.98 g, 1.67 mmol) in pyridine (6 mL). The crude product oil was subjected to flash chromatography (heptane/ethyl acetate 20/1). The ester **5c** (242 mg, 26 %) was isolated as a colorless oil and as a 2:1 mixture of diastereomers. The isolated compound was not feasible for combustion analysis due to sulfur impurities. ^1H NMR (300 MHz, $CDCl_3$) δ 0.30 (d, J = 6.8 Hz, $3H^{minor}$), 0.60 (d, J = 6.8 Hz, $3H^{minor}$), 0.67 (d, J = 6.8 Hz, 3 H^{major}), 0.72-0.95 (series of m, 8+8H), 0.95-1.13 (series of m, 22+22H), 1.16-1.83 (series of m, 6+6H), 2.27-2.38 (m, 2+2H), 2.68-2.79 (m, 2+2H), 4.13-4.20 (m, 2+2H), 4.24-4.30 (m, 2+2H), 4.55-4.75 (m, 1+1H), 4.72 (s, $1H^{minor}$), 4.80 (s, $1H^{major}$), 5.89-5.80 (m, 2+2H), 6.19 (t, J = 4.7 Hz, $1H^{minor}$), 6.23 (t, J = 4.7 Hz, $1H^{major}$), 7.09-7.18 (m, 3+3H), 7.44-7.49 (m, $1H^{major}$), 7.52-7.57 (m, $1H^{minor}$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.9, 15.2, 16.1, 18.0, 20.7, 21.9, 22.0, 23.05, 23.1, 23.3, 25.3, 26.1, 27.8, 27.9, 31.3, 31.4, 34.1, 40.2, 40.8, 46.8, 59.8, 64.7, 65.0, 75.0, 75.1, 79.6, 79.9, 123.6, 124.1, 125.8, 126.4, 126.5, 127.1, 127.2, 127.36, 127.42, 130.2, 131.6, 132.5, 132.8, 133.7, 136.2, 136.3, 170.4, 170.5.

(2*R*,3*R*)- and (2*S*,3*S*)-2-(3,4-Dihydro-naphthalen-1-yl)-2-hydroxy-3-triisopropylsiloxy methyl -pent-4-enoic acid (-)-menthyl ester (8c). Following the general procedure, diisopropylamine (75 mg, 0.74 mmol) in THF (5 mL) was treated with *n*-BuLi (0.32 mL of a 2.3 M solution in hexanes, 0.73 mmol) and the ester **5c** (300 mg, 0.56 mmol) in THF (7 mL). Chromatographic purification (heptane/ethyl acetate 13/1) afforded the desired alcohol **8c** (213 mg, 71 %) as a colorless oil. The NMR data indicated a 1.2:1 diastereomeric mixture. Spectroscopic data reported from the mixture, assignment is based on COSY and HSQC experiments: ^1H NMR (300 MHz, $CDCl_3$) δ 0.33 (d, J = 6.8 Hz, 3H, menthyl-CH_3), 0.51 (d, J = 7.1 Hz, 3H, menthyl-CH_3), 0.62 (d, J = 0.62 Hz, 3H, menthyl-CH_3), 0.75 (d, J = 6.8 Hz, 3H, menthyl-CH_3), 0.83 (d, J = 6.5 Hz, 3H, menthyl-CH_3), 0.88 (d, J = 6.5 Hz, 3H, menthyl-CH_3), 0.73-0.97 (m, 3+3H, menthyl-3-CH_2, -4-CH_2, -6-CH_2), 0.97-1.08 (m, 21+21H, TIPS-H), 1.30-1.47 (m, 3+2H, menthyl-*iso*-propyl-H, -H-2, -H-5), 1.51-1.67 (m, 2+2H, menthyl-3-CH_2, -4-CH_2), 1.70-1.79 (m, 1H, menthyl-isopropenyl-H), 1.82-1.90 (m, 1H, 6-CH_2), 1.93-2.02 (m, 1H, 6-CH_2), 2.12-2.37 (m, 2+2H, -ArC=CHC**H**$_2$C**H**$_2$Ar), 2.56-2.73 (m, 2+2H, -ArC=CHC**H**$_2$C**H**$_2$Ar), 3.15 (mc, 1H, 3-H), 3.27 (mc, 1H, 3-H), 3.85 (dd, J = 10, 6.5 Hz, -C**H**$_2$OTIPS), 3.90 (d, J = 4.6 Hz, 2H, -C**H**$_2$OTIPS), 4.07 (dd, J = 10, 3.7 Hz, -C**H**$_2$OTIPS), 4.32 (s, 1H, -OH), 4.57-4.68 (m, 1+1H, menthyl-H-1), 4.69 (s, 1H, -OH), 5.10-5.22 (m, 2+2H, 5-H), 5.88-6.03 (m, 1H, 4-H), 6.07-6.21 (m, 1H, 4-H), 6.46 (t, J = 4.9 Hz, 1H, -ArC=C**H**CH$_2$CH$_2$Ar), 6.58 (t, J = 4.9 Hz, 1H, -ArC=CHCH$_2$CH$_2$Ar), 7.05-7.16 (m, 3+3H,

Ar-H), 7.61-7.67 (m, 1H, Ar-H), 7.67-7.72 (m, 1H, Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.7, 11.8 (TIPS), 15.3, 15.5 (menthyl-CH_3), 17.89, 17.94 (TIPS), 20.71, 20.75 (menthyl-CH_3), 21.9, 22.0 (menthyl-CH_3), 22.7, 22.8 (menthyl-CH_2), 23.3, 23.5 (-ArC=CH**C**H_2CH_2Ar), 25.2, 25.4 (menthyl-*iso*-propyl-C), 28.5, 28.7 (-ArC=CHCH_2**C**H_2Ar), 31.3, 31.4 (menthyl-CH), 34.08, 34.1 (menthyl-CH_2), 40.2, 40.8 (menthyl-6-CH_2), 46.7, 47.0 (menthyl-CH), 49.8, 51.7 (C-3), 64.7, 65.9 (-**C**H_2OTIPS), 76.0, 76.3 (menthyl-C-1), 118.0, 118.8 (C-5), 125.1, 125.4, 126.08, 126.12, 126.49, 126.52 (Aryl-C), 129.3, 129.6 (-ArC=**C**HCH_2CH_2Ar), 132.9, 133.0 (C-4), 135.4, 135.5, (Aryl-C), 135.9, 136.7, 137.3, 137.5 (Aryl-C, -Ar**C**=CHCH_2CH_2Ar); Anal. Calcd. for $C_{35}H_{56}O_4Si$: C, 73.89; H, 9.92. Found: C, 73.50; H, 10.20.

(2*SR*,3*SR*)-3-(3,4-Dihydro-naphthalen-1-yl)-3-hydroxy-4-vinyl-dihydro-furan-2-one (9c). To a solution of the ester **8c** (156 mg, 0.274 mmol) in THF (10 mL) was added TBAF (0.28 mL of an 1 M solution in THF, 0.28 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 10 h at 25 °C. The reaction was quenched with water (20 mL) and diluted with CH_2Cl_2 (30 mL). The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2×30 mL). The combined organic phases were dried and concentrated. The crude product was purified by chromatography (heptane/ethyl acetate 5/1) to yield (-)-menthol (31 mg, 72 %) and the desired lacton **9c** (61 mg, 87 %) as a white solid and as a single diastereomer. Assignment is based on COSY, HSQC and NOESY experiments: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.25-2.36 (m, 2H, -ArC=CHC**H**$_2$CH_2Ar), 2.60-2.84 (m, 2H, -ArC=CHCH_2C**H**$_2$Ar), 3.46 (dd, J = 16.9, 9 Hz, 4-H), 3.95 (pseudo-t, J = 9.4 Hz, 5-H), 4.41 (dd, J = 9.1, 7.8 Hz, 5-H), 5.01 (dd, J = 10, 1.6 Hz, vinyl-CH=C**H**$_2$), 5.21 (dd, J = 17, 1.6 Hz, 1H, vinyl-CH=C**H**$_2$), 5.35-5.49 (m, 1H, vinyl-C**H**=CH$_2$), 6.02 (t, J = 6.0 Hz, 1H, -ArC=C**H**CH$_2$CH_2Ar), 7.12-7.17 (m, 3H, Aryl-H), 7.76-7.82 (m, 1H, Aryl-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.0 (-ArC=CH**C**H_2CH_2Ar), 28.0 (-ArC=CHCH_2**C**H_2Ar), 52.6 (C-4), 68.4 (C-5), 119.5 (vinyl-CH=**C**H_2), 125.8, 127.3, 127.56, 127.6 (Aryl-C), 129.2 (-ArC=**C**HCH_2CH_2Ar), 131.5, 132.5 (vinyl-CH=**C**H_2), 132.9, 137.1, 178.4 (C-2); mp 95 °C; Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 75.16; H, 6.49.

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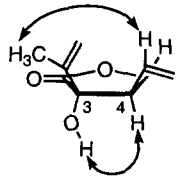
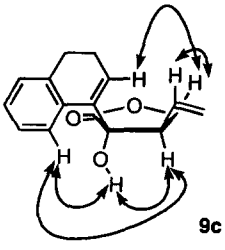
[1] Matsumoto, K.; Harada, K. *J. Org. Chem.* **1966**, *31*, 1956.
[2] For an example of the oxy-Cope rearrangement of a 3-hydroxy-3-(*N,N*-diethylaminocarbonyl)-substituted 1,5 hexadiene, see Koft, E. R., Williams, M. D. *Tetrahedron Lett.* **1986**, *27*, 2227.
[3] (a) Kallmerten, J. in Houben-Weyl, Methods of Organic Chemistry; Eds.: Helmchen, G.; Hoffmann, R. W.; Mulzer, J.; Schaumann, E.; Thieme Verlag Stuttgart **1995**, Vol. E 21d, 3757. (b) Nakai, T.; Mikami, K. *Org. React.* **1994**, *46*, 105. (c) Brückner,R. in Comprehensive Organic Synthesis; Eds: Trost, B. M.; Flemming, I.; Winterfeldt, E.; Pergamon Press Oxford **1991**, Vol. 6, 873. (d) Marshall, J. A. in Comprehensive Organic Synthesis; Eds: Trost, B. M.; Flemming, I.; Pergamon Press Oxford **1991**, Vol. 3, 975. (e) Brückner, R. *Nachr. Chem. Tech. Lab.* **1990**, *38*, 1506. (f) Mikami, K.; Nakai, T. *Synthesis* **1991**, 594. (h) Nakai, T.; Mikami, K. *Chem. Rev.* **1986**, *86*, 885. (g) Schöllkopf, U. *Angew. Chem. Int. Engl. Ed.* **1970**, *9*, 763.
[4] For asymmetric amide enolate [2,3]-Wittig rearrangements, see (a) Mikami, K.; Takahashi, O.; Kasuga, T.; Nakai, T *Chem. Lett.* **1985**, 1729. (b) Uchikawa, M.; Hanamoto, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 4577. (c) Kress, M. H.; Yang, C.; Yasuda, N.; Grabowski, E. J. J. *Tetrahedron Lett.* **1997**, *38*, 2633.
[5] For asymmetric oxazoline azaenolate [2,3]-Wittig rearrangements, see (a) Mikami, K.; Fujimoto, K.; Kasuga, T.; Nakai, T. *Tetrahedron Lett.* **1984**, *25*, 6011. (b) Mikami, K.; Kasuga, T.; Fujimoto, K.; Nakai, T. *Tetrahedron Lett.* **1986**, *27*, 4185.
[6]For an asymmetric hydrazone azaenolate [2,3]-Wittig rearrangement, see Enders, D.; Backhaus, D.; Runsink, J. *Angew. Chem. Int. Engl. Ed.* **1994**, *33*, 2098.
[7] Takhashi, O.; Mikami, K.; Nakai, T. *Chem. Lett.* **1987**, 69.
[8] (a) Takahashi, O.; Maeda, T.; Mikami, K.; Nakai, T. *Chem. Lett.* **1986**, 1355. (b) Takahashi, O.; Saka, T.; Mikami, K.; Nakai, T. *Chem. Lett.* **1986**, 1599. (c) Uchikawa, M.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 4581. (d) Kuroda, S.; Katsuki, T. Yamaguchi, M. *Tetrahedron Lett.* **1987**, *28*, 803. (e) Kuroda, S.; Sakaguchi, S.; Ikegami, S.; Hanamoto, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1988**, *29*, 4763. (f) Brückner, R. *Chem. Ber.* **1989**, *122*, 703. (g) Mikami, K.; Takahashi, O.; Fujimoto, K.; Nakai, T. *Synlett* **1991**, 629. (h) Oh, T.; Wrobel, Z.; Rubenstein, S. M. *Tetrahedron Lett.* **1991**, *32*, 4647. Marshall, J. A.; Wang, X. *J. Org. Chem.* **1991**, *56*, 4913. (i) Okamura, H.; Kuroda, S.; Ikegami, S.; Tomita, K.; Sugimoto, Y.; Sakaguchi, S.; Ito, Y.; Katsuki, T.; Yamaguchi, M. *Tetrahedron* **1993**, 49, 10531. (j) Fujimoto, K.; Nakai, T. *Tetrahedron Lett.* **1994**, *35*, 5019. (k) Reetz, M. T.; Griebenow, N.; Goddard, R. *J. Chem. Soc. Chem. Commun.* **1995**, 1605. (l) Konno, T.; Umetani, H.; Kitazume, T. *J. Org. Chem.* **1997**, *62*, 137.
[9] Nakai, T.; Mikami, K.; Taya, S. *J. Am. Chem. Soc.* **1981**, *105*, 6492.
[10] We are aware of the lack of diastereoface differentiating ability of menthol which is well documented. Nevertheless, (-)-menthol provides a cheap commercially available mimic for the more expensive 8-phenylmenthol which can serve as a powerful chiral auxiliary and will be utilized in further studies. For a review concerning cyclohexyl-based chiral auxiliaries, see Whitesell, J. K. *Chem. Rev.* **1992**, *92*, 953.
[11] (a) Höfle, G.; Steglich, W.; Vorbrüggen, H. *Angew. Chem. Int. Engl. Ed.* **1978**, *17*, 569. (b) Neises, B.; Steglich, W. *Angew. Chem. Int. Engl. Ed.* **1978**, *17*, 552.
[12] An example for the chemoselective aldol addition of a 2-allyloxy-substituted ester enolate without obtaining the possible [2,3]-Wittig rearrangement product has been reported, see Nakahara, Y.; Shimizu, M.; Yoshioka, H. *Tetrahedron Lett.* **1988**, *29*, 2325.
[13] Touzin, A. M. *Tetrahedron Lett.* **1975**, *18*, 1477.
[14] NOESY experiments with the lactones **9a-c** indicating a *syn* configuration of the 3-OH and the 4-H. Selected NOEs are depicted in the following scheme:



9a



9c

[15] (a) Wu, Y.-D.; Houk, K. N.; Marshall, J. A. *J. Org. Chem.* **1990**, *55*, 1421. (b) Mikami, K.; Kimura, Y.; Kishi, N; Nakai, T *J. Org. Chem.* **1983**, *48*, 281. (c) Tsai, D. J.-S.; Midland, M. M. *J. Org. Chem.* **1984**, *49*, 1842. (d) Rautenstrauch, V. *J. Chem. Soc., Chem. Commun.* **1970**, 4.
[16] Okajima, T.; Fukuzawa, Y. *Chem. Lett.* **1997**, 81. The same effect was found to stabilize the calculated transition state of the [2,3]-Wittig rearrangement of a crotyloxy acetaldehyde enolate, see Mikami, K.; Uchida, T.; Hirano, T.; Wu, Y.; Houk, K. N. *Tetrahedron* **1994**, 50, 5917.
[17] Kofron, W. G., Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.
[18] For the preparation of (*Z*)-4-(*tert*-butyldimethylsiloxy)-2-butene-1-ol, see Sodeoka, M.; Yamada, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1990**, *112*, 4906.