The Dienolate [2,3]-Wittig Rearrangement – Diastereoselective Synthesis of Highly Functionalized Tertiary Alcohols

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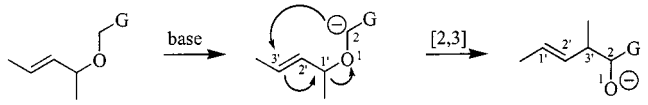
The [2,3]-Wittig rearrangement of dienolates generated from α-allyloxy-substituted α,β- and/or β,γ-unsaturated esters **4/5a–g** has been investigated. The rearrangement proceeds with high yield and diastereoselectivity to afford 3-hydroxy-3-alkyloxycarbonyl-substituted 1,5-hexadienes **6a–e**. The influence of the reaction conditions and of various substituents on the rearrangement has been studied. A transition state structure is suggested in order to explain the simple diastereoselectivity observed. The starting material for the rearrangement was prepared utilizing an aldol condensation strategy. The α-allyloxy-substituted esters **2a–c** were deprotonated and treated with various ketones to chemoselectively afford the alcohols **3a–g**. Thionyl chloride mediated elimination provided the desired unsaturated esters **4/5a–g** as starting materials for the rearrangement. The difference in reactivity between an enolate and a dienolate is explained on the basis of a DFT quantum chemical calculation of the HOMO/LUMO energy gap.

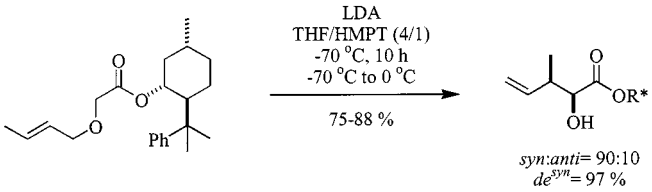
The [2,3]-Wittig rearrangement has been developed as a powerful tool for the stereoselective synthesis of homoallylic alcohols starting from allylic ethers (Scheme 1).[2] The reaction conditions used and the stereochemical outcome of the [2,3]-Wittig rearrangement are strongly dependent on the nature of the group G.



Scheme 1. The [2,3]-Wittig rearrangement

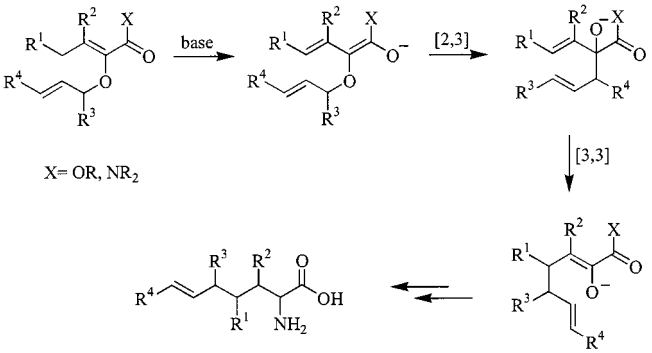
A useful version of the [2,3]-Wittig rearrangement utilizes the carbonyl group or a related functional group as G in order to stabilize the α-allyloxy carbanion. The resulting enolate [2,3]-Wittig rearrangement offers potential advantages over the [2,3]-Wittig rearrangement of diallyl ethers, e.g. regioselective deprotonation under milder conditions, and the possibility of introducing a covalently-bonded chiral auxiliary. Consequently, a number of stereoselective enolate and aza-enolate [2,3]-Wittig rearrangements have been developed.[3–5] For example, Nakai reported the diastereoselective ester enolate [2,3]-Wittig rearrangement utilizing 8-phenylmenthol as chiral auxiliary, lithium diisopropylamide (LDA) as the base, and a mixture of THF and hexamethylphosphoric triamide (HMPT) as the solvent (Scheme 2).[6] However, the utility of the enolate [2,3]-Wittig rearrangement is limited by the fact that it has to be performed in the presence of a donor solvent or a metal salt additive in order to obtain a sufficient chemical yield and stereoselectivity.[7]

Our interest in the [2,3]-Wittig rearrangement is as part of a research project aimed at exploiting highly substituted



Scheme 2. Diastereoselective enolate [2,3]-Wittig rearrangement[6]

α-keto carboxylic acid derivatives as precursors for the synthesis of non-natural amino acids through reductive amination.[8] For this purpose, we have identified a sequence of sigmatropic rearrangements allowing stereocontrolled access to a variety of substituted α-keto carboxylic acid derivatives.[9] As depicted in Scheme 3, the dienolate [2,3]-Wittig rearrangement[10] of an α-allyloxy-substituted ester dienolate should give access to a 3-oxy-3-alkyloxycarbonyl-substituted 1,5-hexadiene, the appropriate starting material for a 3-oxy-Cope rearrangement, which would provide the desired α-keto ester.[11]



Scheme 3. Non-natural amino acids via sequential sigmatropic rearrangements

We have recently reported the synthesis of 2,3-dialkenyl-substituted γ-lactones utilizing the dienolate [2,3]-Wittig rearrangement as the key step for the diastereoselective C–C

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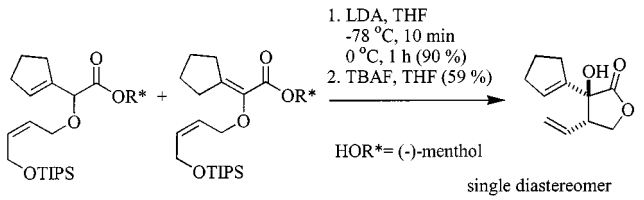
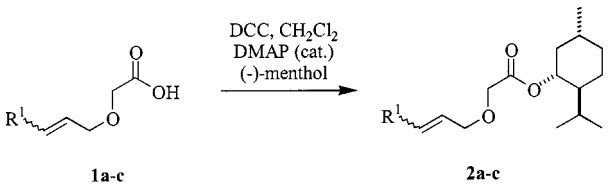
bond formation (Scheme 4).[12] We initiated further studies to elucidate the relationship between substrate structure, reactivity, and stereochemical outcome of this useful rearrangement. In this account, we report our results concerning the influence of the allylic ether double bond configuration on the reactivity and stereoselectivity. A number of different substitution patterns were investigated in order to study the scope and limitations of the rearrangement.



Scheme 4. Diastereoselective dienolate [2,3]-Wittig rearrangement[12]

Results and Discussion

The starting material for the dienolate [2,3]-Wittig rearrangement was prepared following an aldol condensation strategy. Three different α-allyloxy-substituted esters **2a**–**c** were synthesized starting from the corresponding acids **1a**–**c** and (−)-menthol (Scheme 5, Table 1).[13]



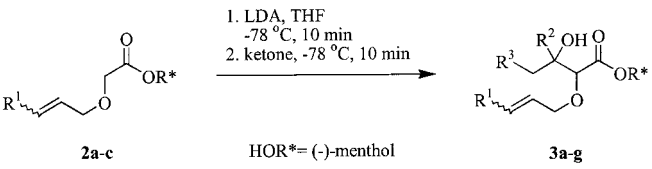
Scheme 5. Ester formation

Table 1. Ester formation with DCC/DMAP

Product	R^1	Configuration	Yield [%]
2a	Ph	(*E*)	62
2b	*n*Pr	(*E*)	91
2c	*n*Pr	(*Z*)	85

The appropriate α-allyloxy-substituted (−)-menthyl acetate **2a**–**c** was deprotonated with LDA and treated with various ketones to afford the tertiary alcohols **3a**–**g** (Scheme 6, Table 2). Carrying out the deprotonation in a short time at low temperature suppressed the enolate [2,3]-Wittig rearrangement and led to the chemoselective formation of the aldol adduct **3a**–**g**.[14][15]

The elimination was conveniently accomplished by treating the alcohol **3a**–**g** with freshly distilled thionyl chloride and pyridine to afford a mixture of the regioisomeric elimination products **4a**–**g** and **5a**–**g** (Scheme 7 and Table 3).[16] The regioisomers **4a**–**g** could be separated by carefully performed column chromatography. For convenience, we isolated the double bond regioisomers **4a**–**g** as a mixture since these should give the same dienolate upon exposure to a base.

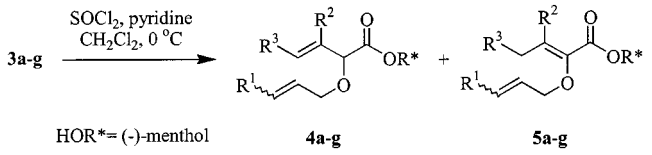


Scheme 6. Chemoselective aldol addition of **2** to **3**

Table 2. Aldol addition of **2** to **3**

Substrate	Ketone	Product	R^1	R^2, R^3	Yield [%] [a]
2a		**3a**	(*E*)-Ph	R^2= CH_3, R^3= H	64
2a		**3b**	(*E*)-Ph		64
2b		**3c**	(*E*)-*n*-Pr	R^2= CH_3, R^3= H	74
2b		**3d**	(*E*)-*n*-Pr		81
2b		**3e**	(*E*)-*n*-Pr		81 [b]
2c		**3f**	(*Z*)-*n*-Pr	R^2= CH_3, R^3= H	78
2c		**3g**	(*Z*)-*n*-Pr		92

[a] Isolated as a 2:1 mixture of diastereomers. Ratio determined from ^{1}H-NMR data, configuration not assigned. – [b] Only two diastereomers were isolated.



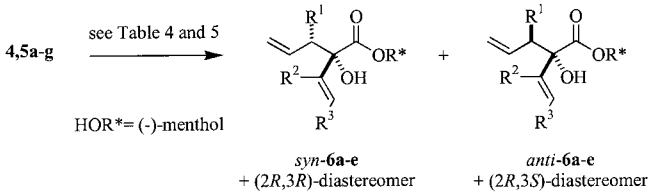
Scheme 7. Elimination to the α,β- and β,γ-unsaturated esters **5** and **4**

Table 3. The dehydration of **3** to **4** and **5**

alcohol	product	R^1	R^2,R^3	yield [%] of **4**+**5**	ratio[a] **4**:**5**
3a	**4a, 5a**	(*E*)-Ph	R^2= CH_3, R^3= H	81	1.5:1
3b	**4b, 5b**	(*E*)-Ph		44	5.5:1
3c	**4c, 5c**	(*E*)-*n*-Pr	R^2= CH_3, R^3= H	82	1.4:1
3d	**4d, 5d**	(*E*)-*n*-Pr		88	2.4:1
3e	**4e**	(*E*)-*n*-Pr		20	1:0
3f	**4f, 5f**	(*Z*)-*n*-Pr	R^2= CH_3, R^3= H	77	1.5:1
3g	**4g, 5g**	(*Z*)-*n*-Pr		69	5.1:1

[a] **4a**–**g** isolated as a 2:1 mixture of diastereomers, configuration not assigned. Ratio determined by ^{1}H-NMR analysis.

The dienolate [2,3]-Wittig rearrangement was studied under a variety of reaction conditions (Scheme 8, the second *syn* or *anti* diastereomer with respect to *R** is not depicted). The results for the optimized conditions are summarized in Table 4.



Scheme 8. The dienolate [2,3]-Wittig rearrangement

Table 4. The dienolate [2,3]-Wittig rearrangement (optimized reaction conditions: 1.2 equiv. LDA, THF, temperature and reaction time see table)

entry	ester	Product	R^1	R^2,R^3	T [°C] t	yield [%] [a]	d.r. [b]	*syn*:*anti*
1	**4a**,**5a**	**6a**	Ph	R^2= CH_3 R^3= H	-78, 12 h	72	57:14:16:13	71:29
2	**4b**,**5b**	**6b**	Ph		-78, 12 h	69	39:21:29:11	60:40
3	**4c**,**5c**	**6c**	(*E*)-*n*-Pr	R^2= CH_3 R^3= H	-78, 12 h	90	66:27:5:2	93:7
4	**4d**,**5d**	**6d**	(*E*)-*n*-Pr		-78, 12 h	80	62:31:5:2	93:7
5	**4d**	**6d**	(*E*)-*n*-Pr		-78, 12 h	90	61:30:6:3	91:9
6	**4e**	**6e**	(*E*)-*n*-Pr		-78, 12 h	80	47:40:9:5	87:13
7	**4f**,**5f**	**6c**	(*Z*)-*n*-Pr	R^2= CH_3 R^3= H	1. -78, 10 min 2. 0, 1 h	78	4:2:33:61	6:94
8	**4g**,**5g**	**6d**	(*Z*)-*n*-Pr		1. -78, 10 min 2. 0, 1 h	91	4:3:34:59	7:93

[a] Isolated yield after chromatographic purification. – [b] Diastereomeric ratio, determined from ^{1}H-NMR spectra. Absolute configuration not assigned.

We were delighted to find that the ester dienolates underwent the desired rearrangement in the absence of a donor solvent or a metal salt additive. The rearrangement afforded a mixture of four diastereomers. Removal of the (–)-menthol group by diisobutylaluminium hydride (DIBAH) reduction enabled us to assign the *syn*/*anti* ratio (Scheme 9, Table 6).[17] The relative configurations of the rearrangement products **6a**–**e** were assigned on the basis of the previously established relationship between the configuration of the allylic ether double bond in the starting material and the relative configuration of the rearrangement product. As depicted in Scheme 4, we have recently found that the (*Z*)-ester affords exclusively the *anti* rearrangement product. This result is in agreement with the previously reported stereochemical rules ["(*E*) to *syn* and (*Z*) to *anti*"] for the enolate [2,3]-Wittig rearrangement.[2] Consequently, we assign the major diastereomer **6c**/**d**, formed by the rearrangement of the starting material with a (*Z*)-allylic ether double bond **4**/**5f**–**g**, as the *anti* diastereomer *anti*-**6c**/**d** (Table 4, entries 7 and 8).

Several noteworthy features can be established from Table 4. The *syn*/*anti* diastereoselectivity is of the order of 9:1 for the starting materials with an *n*-propyl-substituted allylic ether double bond **4**/**5c**–**g**, but is significantly decreased for the phenyl-substituted substrates **4**/**5a**–**b** (Table 4). The simple diastereoselectivity is reversed when the allylic ether double bond configuration is changed from (*E*) to (*Z*) (Table 4, entries 3, 7 and 4, 8). The (*E*)- and (*Z*)-configured starting materials show differing reactivities. The ester with a (*Z*)-allylic ether double bond does not rearrange at –78°C and mainly starting material is isolated. Nevertheless, at 0°C the rearrangement proceeds with high yield and diastereoselectivity. In certain cases, the reactivity of the pure regioisomers was investigated. Earlier studies had not shown a difference in reactivity between the 2,3- or 3,4-unsaturated esters.[18] In accordance with these results, no significant difference in yield or diastereoselectivity was observed using either a mixture of double bond regioisomers or a pure regioisomer as the starting material for the rearrangement (Table 4, entries 4 and 5). As expected, the auxiliary-induced diastereoselectivity was low due to the weak diastereofacial differentiation by the (–)-menthyl auxiliary.

Various bases and reaction conditions were employed in order to evaluate their influence on the rearrangement (Table 5). Lithium *N*-*tert*-butyltrimethylsilylamide

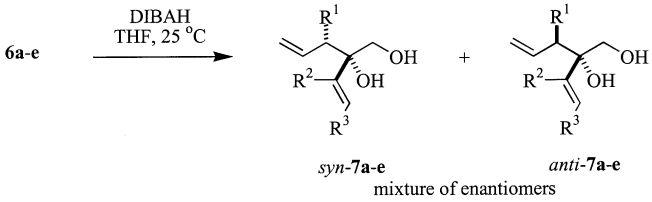
Table 5. The dienolate [2,3]-Wittig rearrangement (the influence of the base and the reaction conditions)

Entry	Ester	Product	Scale [mmol]	Base	*T* [°C]	*t*	Yield [%][a]	*syn*/*anti*[b]
1	**4c**,**5c**	**6c**	3.1	*t*Bu(TMS)NLi	–78	12 h	90	93:7
2	**4c**	**4c**/**5c**/**6c** = 2:1:1	1	LDA	–78	15 min	–	–
3	**4d**	**6d**	1.2	*t*Bu(TMS)NLi	(i) –78 (ii) 0	10 min 30 min	93	82:18
4	**4d**,**5d**	**6d**	1.4	LiTMP	–78	12 h	90	89:11
5	**4d**,**5d**	**6d**	3.1	LDA	–78	12 h	80	93:7

[a] Diastereomeric ratio, determined from ^{1}H-NMR spectra.

[*t*Bu(TMS)NLi] and LDA proved to be equally well suited for the generation of the dienolate (Table 5, entries 1 and 5). The use of lithium 2,2,6,6-tetramethylpiperidide (LiTMP) did not improve the chemical yield or the diastereoselectivity (Table 5, entry 4). Treating the ester **4c**, with an (*E*)-allylic double bond, with LDA at −78°C for 15 min afforded a mixture of the regioisomeric esters **4/5c** and the desired product **6c**, indicating that the rearrangement proceeds slowly at low temperature (Table 5, entry 2). Increasing the reaction temperature to 0°C forced the rearrangement to reach completion, but a concomitant decrease in diastereoselectivity was observed (Table 5, entry 3).

Finally, we investigated the possibility of removing the chiral alcohol (−)-menthol from the rearrangement product. A reductive method was employed in order to gain access to the 1,2-diols **7a**−**e** (Scheme 9). Treatment of the rearrangement products **6a**−**e** with DIBAH in THF afforded the desired diols **7a**−**e** in moderate to good yields (Table 6).



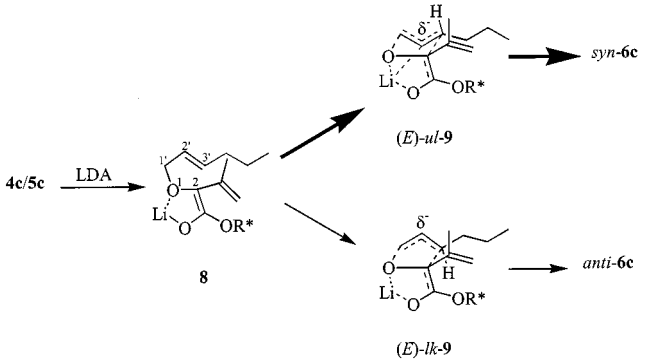
Scheme 9. Reduction to the tertiary alcohols **7a**−**e**

Table 6. Reduction of **6** to **7**

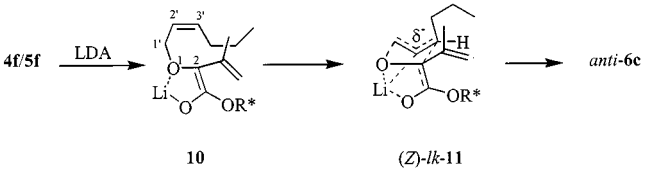
substrate	*syn*:*anti* [a] **6a-e**	product	R^1	$R^{2,3}$	yield [b] [%]	*syn*:*anti* [a],[c]
6a	71:29	**7a**	Ph	H	56	71:29
6b	60:40	**7b**	Ph		57	57:43
6c	93:7	**7c**	*n*-Pr	H	89	93:7
6d	93:7	**7d**	*n*-Pr		75	-[d]
6e	87:13	**7e**	*n*-Pr		57	86:14

[a] Diastereomeric ratio determined from ^{1}H-NMR spectra. The *ee* was not explicitly determined but should be the consequence of the observed de^{syn} and de^{anti} in Table 4. − [b] Not optimized. − [c] (−)-Menthol was isolated in yields exceeding 90%, see Experimental Section. − [d] Diastereomeric ratio was not determined due to overlapping NMR signals.

Experimental studies on the enolate [2,3]-Wittig rearrangement have revealed that simple 2-(*E*)-allyloxy-substituted ester enolates afford predominantly 2,3-*syn* products (see Scheme 2 for an example). The corresponding 2-(*Z*)-allyloxy-substituted ester enolates show a preference for the 2,3-*anti* product.[2] It is well accepted that the ester enolate [2,3]-Wittig rearrangement proceeds via a transition state structure with a bicyclo[3.3.0]octane framework based on a (*Z*)-configured chelated ester enolate.[2] A recent computational analysis of the carboxylic acid dianion [2,3]-Wittig rearrangement has revealed a stabilizing interaction between the lithium cation and a partial negative charge that develops on the central atom of the allylic ether moiety in the transition state.[19] Based on these arguments, we suggest the following transition state structure for the dienolate [2,3]-Wittig rearrangement in order to explain the observed diastereoselectivity and the reactivity of the ester dienolates (Schemes 10 and 11).



Scheme 10. Possible transition state structures



Scheme 11. Possible transition state structures

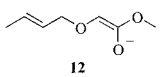
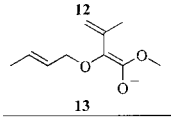
The deprotonation of a mixture of the regioisomeric esters (e.g. **4c/5c**) with an (*E*)-allylic ether double bond leads to a dienolate **8**, which could rearrange via (*E*)-*lk*-**9** to *anti*-**6c** or via (*E*)-*ul*-**9** to *syn*-**6c** (Scheme 9).[20] The (*E*)-*lk*-**9** transition state can be expected to be destabilized by a pseudo-*eclipsed* arrangement between the sp^2-hybridized carbon atoms C-2 and C-3′, which approach each other in the C−C bond-forming step. (*E*)-*ul*-**9** would lead to a less destabilizing pseudo-*gauche* interaction between C-2 and C-3′ and an unfavorable pseudo-1,3-diaxial interaction between the H-atom on C-2′ and the ester enolate unit. On the other hand, (*E*)-*ul*-**9** should be significantly more stabilized by the electrostatic stabilization of the partial negative charge on C-2′ due to the shorter distance between the lithium cation and the allylic ether moiety compared to the situation in (*E*)-*lk*-**9**. Thus, a combination of steric and electrostatic interactions could favor (*E*)-*ul*-**9** and the formation of *syn*-**6a**−**e** in the rearrangements of starting materials with an (*E*) allylic ether double bond **4/5a**−**e**. As previously stated for a related substrate,[12] we suggest that the rearrangement of the ester dienolate **10** with a (*Z*) allylic ether double bond proceeds preferentially via (*Z*)-*lk*-**11** to give the *anti* diastereomer *anti*-**6** (Scheme 11).

The (*Z*)-*lk*-**11** transition state structure is characterized by the suggested electrostatic stabilization and an *exo* arrangement of the double bond *n*-propyl substituent with respect to the bicyclo[3.3.0]octane framework. This pseudo-axial position of the double bond *n*-propyl substituent might be responsible for the diminished reactivity of the (*Z*)

starting materials **4/5f−g** compared to ester dienolates with an (*E*)-allylic ether double bond.

The reason for the increased reactivity of an ester dienolate as compared to an ester enolate in the [2,3]-Wittig rearrangement can be explained in terms of the frontier orbital theory. The energy difference between the HOMO and the LUMO of the enolate **12** and the dienolate **13** was calculated (Table 7). The results of a quantum chemical geometry optimization by density functional theory (DFT) indicate that the energy gap between the HOMO and the LUMO for dienolate **13** is 6.3 kcal/mol smaller than the HOMO−LUMO gap of enolate **12**. A more pronounced difference of 16.7 kcal/mol was found by a Hartree−Fock (HF) single-point calculation. The calculated results for the model systems **12** and **13** nicely explain the experimentally observed difference in reactivity between the dienolate **8** and the enolate generated from the ester **2b**.[21]

Table 7. Calculated energy differences of the HF[a] and DFT[b] frontier orbitals

compound	ε_{HOMO} [kcal/mol]		ε_{LUMO} [kcal/mol]		$\Delta\varepsilon$ [kcal/mol]	
	HF	DFT	HF	DFT	HF	DFT
 **12**	-165.085	-101.330	4.800	-22.132	169.886	79.198
 **13**	-148.783	-96.580	4.361	-23.695	153.144	72.885

[a] HF/6-31+G* single point calculations based on DFT optimum geometry. − [b] Energy differences obtained by B3LYP/6-31+G* geometry optimization.

Conclusion

Several examples of the ester dienolate [2,3]-Wittig rearrangement have been investigated in order to gain insight into the factors that determine the stereochemical outcome of the rearrangement. The α-allyloxy-substituted dienolate was conveniently generated by treatment of an α,β- or β,γ-unsaturated α-allyloxy-substituted ester **4/5a−g** with LDA in THF at low temperature (Scheme 8, Tables 4 and 5). The rearrangement proceeds at −78 °C or 0 °C depending on the configuration of the allylic ether double bond. No donor solvents or metal salt additives were necessary to promote the rearrangement. The *di*enolate with an (*E*) allylic ether double bond (e.g. **8**) proved to be significantly more reactive than the corresponding enolate. This experimental observation was rationalized by a quantum chemical calculation on model systems, which indicated the HOMO−LUMO gap of the dienolate to be significantly smaller compared to that for the corresponding enolate. The rearrangement establishes the diastereoselective access to substituted 3-hydroxy-3-alkyloxycarbonyl-substituted 1,5-hexadienes **6a−d**, which should be valuable starting materials for further transformations. High simple diastereoselectivities along with very good chemical yields have been achieved. The diastereoselectivity was in the region of 9:1 for the substrates **4/5c−g** bearing an *n*-propyl-substituted allylic ether double bond. The diastereomeric excess and the chemical yield were unaffected by the allylic ether double bond configuration of the starting material. The observed simple diastereoselectivity follows the general trend that an (*E*)-configured starting material **4/5a−e** rearranges preferentially via a transition state structure with an *unlike* topicity to give the *syn* product. The (*Z*)-configured starting material **4/5f−g** prefers a "(*Z*) via *lk* to *anti*" behavior.

Further work aimed at utilizing the dienolate [2,3]-Wittig rearrangement in natural product syntheses and studying the dienolate aza-[2,3]-Wittig rearrangement as well as the domino dienolate [2,3]-Wittig/3-oxy-Cope rearrangement is currently underway.

Experimental Section

General Remarks: All reactions were performed in flame-dried and septum-sealed flasks under an atmosphere of argon. Solvents and reagents were transferred by means of syringes. THF was distilled from potassium; CH_2Cl_2 was distilled from CaH_2. All reagents were used as purchased unless otherwise noted. Commercial *n*BuLi solution in hexanes was titrated following the procedure of Kofron.[22] NaH was used without further purification. Silica gel (230−400 mesh) was used for column chromatography. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker AC 300 or DRX 500 in $CDCl_3$. For diastereomeric mixtures, the term $n + n$ H refers to n H for each diastereomer. The terms H^{minor} and H^{major} are used to indicate a separated proton resonance for the major or the minor diastereomer. IR spectra were recorded on a Nicolet 205 FT-IR spectrometer. Elemental analyses were obtained on a Carlo Erba CHN-S analyzer.

Computational Details: DFT quantum chemical calculations were performed using the 1994 release of the GAUSSIAN suite of programs.[23] The functional used throughout this study consists of a non-local hybrid HF/DF exchange functional as defined by Becke's three-parameter equation[24] in conjunction with the non-local Lee−Yang−Parr correlation functional[25] (abbreviated as B3LYP). The ground state geometry was obtained by full geometry optimization. The optimum structures were confirmed by the Hessian matrices. For the sake of comparison, HF[26] single-point calculations were also performed at the DFT optimum geometry. All calculations were carried out using the valence double-ξ basis set 6-31G augmented by a set of polarization functions and a set of diffuse functions at the non-hydrogen atoms.

General Procedure A for Ester Formation: To a stirred solution of the acid **1a−c** (1 equiv.) in CH_2Cl_2 at 0 °C were successively added DMAP (0.05−0.1 equiv.), DCC (1 equiv.), and (−)-menthol (1 equiv.). The reaction mixture was stirred at 0 °C until TLC indicated that the acid had been consumed. The precipitate was then removed by filtration and washed with ethyl acetate. The filtrate was concentrated, diluted with ethyl acetate, and filtered once more. The solvent was then removed and the crude product was purified by kugelrohr distillation or flash chromatography (heptane/ethyl acetate, 10−20:1) to yield the ester **2a−c** as a colorless oil.

Ester 2a: Following general procedure A, acid **1a** (4.7 g, 24 mmol) in CH_2Cl_2 (50 mL) was treated with DMAP (300 mg, 2.4 mmol), DCC (5.01 g, 24 mmol), and (−)-menthol (3.75 g, 24 mmol). The crude product was purified by chromatography (heptane/ethyl acet-

ate, 10:1) to yield the ester **2a** (4.9 g, 62%) as a colorless oil. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.76 (d, *J* = 7.5 Hz, 3 H), 0.88 (d, *J* = 16.8 Hz, 3 H), 0.89 (d, *J* = 6.5 Hz, 3 H), 0.98 (m_c, 2 H), 1.05 (m_c, 1 H), 1.25–1.4 (m, 1 H), 1.4–1.65 (m, 1 H), 1.6–1.7 (m, 2 H), 1.83 (m_c, 1 H), 2.0 (m_c, 1 H), 4.1 (d, *J* = 2 Hz, 2 H), 4.3 (dd, *J* = 6, 1 Hz, 2 H), 4.8 (td, *J* = 6.5, 4 Hz, 1 H), 6.3 (dt, *J* = 16, 6 Hz, 1 H), 6.62 (d, *J* = 16 Hz, 1 H), 7.22–7.4 (m, 5 H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.3, 20.7, 21.9, 23.5, 26.4, 31.4, 34.2, 40.9, 47.0, 67.3, 72.0, 74.9, 125.1, 126.6, 127.8, 128.4, 128.5, 133.5, 136.5, 170.0. – IR (neat): $\tilde{\nu}$ = 1731 cm^{-1}. – $C_{21}H_{30}O_3$ (330.5): calcd. C 76.33, H 9.14; found C 75.99, H 9.02.

Ester 2b: Following general procedure A, acid **1b** (3.45 g, 19 mmol) in CH_2Cl_2 (50 mL) was treated with DMAP (232 mg, 1.9 mmol), DCC (3.91 g, 19 mmol), and (–)-menthol (2.97 g, 19 mmol) at 0°C. The crude product was purified by kugelrohr distillation to yield the ester **2b** (4.58 g, 91%) as a colorless oil. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.77 (d, *J* = 6.8 Hz, 3 H), 0.86–0.95 (series of 3 d, 9 H), 0.86–1.15 (m, 3 H), 1.33–2.09 (series of m, 10 H), 4.00–4.07 (m, 4 H), 4.79 (td, *J* = 10.9, 4.3 Hz, 1 H), 5.51–5.62 (m, 1 H), 5.66–5.78 (m, 1 H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 16.3, 20.7, 22.0, 22.1, 23.5, 26.4, 31.4, 34.2, 34.3, 40.9, 47.0, 67.0, 72.1, 74.8, 125.5, 135.9, 170.1. – IR (neat): $\tilde{\nu}$ = 1730 cm^{-1}. – $C_{18}H_{32}O_3$ (296.5): calcd. C 73.51, H 10.42; found C 72.93, H 10.87.

Ester 2c: Following general procedure A, acid **1c** (2.90 g, 18.3 mmol) in CH_2Cl_2 (70 mL) was treated with DMAP (224 mg, 1.83 mmol), DCC (4.54 g, 22 mmol), and (–)-menthol (2.86 g, 18.3 mmol). The crude product was purified by chromatography (heptane/ethyl acetate, 20:1) to afford the ester **2c** (4.63 g, 85%) as a colorless oil. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (d, *J* = 6.8 Hz, 3 H), 0.86–0.94 (m, 9 H), 0.94–1.13 (m, 2 H), 1.22 (series of m, 5 H), 1.63–2.10 (series of m, 6 H), 4.04 (s, 2 H), 4.16 (d, *J* = 6.2 Hz, 2 H), 4.80 (td, *J* = 10.9, 4.4 Hz, 1 H), 5.60 (m_c, 2 H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 16.2, 20.7, 21.9, 22.6, 23.3, 26.2, 29.5, 31.3, 31.8, 40.8, 46.9, 66.6, 67.0, 74.7, 125.1, 134.7, 170.1. – IR (neat): $\tilde{\nu}$ = 1730 cm^{-1}. – $C_{18}H_{32}O_3$ (296.5): calcd. C 72.92, H 10.87; found C 73.49, H 11.23.

General Procedure B for the Aldol Addition: Lithium diisopropylamide was prepared by the addition of *n*-butyllithium (1.2 equiv.) to a solution of diisopropylamine (1.3 equiv.) in THF (2–2.5 mL/mmol of ester) at 0°C. The reaction mixture was stirred for 30 min at 0°C and then cooled to –78°C. To this mixture was added a precooled (–78°C) solution of the ester **2a–c** (1 equiv.) in THF. After stirring for 5–10 min, the ketone (2 equiv.) was rapidly added either neat or as a solution in THF (tetralone). The resulting mixture was stirred for 30 min and then quenched at –78°C by the addition of saturated aqueous NH_4Cl solution. The mixture was allowed to warm to room temperature and then diluted with water and CH_2Cl_2. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2×). The combined organic layers were dried ($MgSO_4$) and concentrated. Chromatographic purification (heptane/ethyl acetate, 5:1) afforded the desired alcohols **3a–g** as colorless oils.

Alcohol 3a: Following general procedure B, a solution of LDA (prepared in situ from 8.3 mmol diisopropylamine and 7.6 mmol *n*-butyllithium) in THF (13 mL) was treated with the ester **2a** (2.1 g, 6.4 mmol) and acetone (743 mg, 12.8 mmol) in THF (5 mL) to afford the alcohol **3a** (1.6 g, 64%) as a colorless oil. Spectral data are reported for a 2:1 mixture of diastereomers. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.75 (d, *J* = 7.1 Hz, 3 H^{major}), 0.84–0.92 (series of d, m, 7 H^{major} + 10 H^{minor}), 0.94–1.12 (m, 2 + 2 H), 1.25 (s, 3 + 3 H), 1.29 (s, 3 + 3 H), 1.37 (m, 2 + 2 H), 1.63–1.74 (m, 2 + 2 H), 1.83–2.04 (series of m, 2 + 2 H), 2.86 (br. s, 1 + 1 H), 3.76 (s, 1 H^{minor}), 3.79 (s, 1 H^{major}), 4.08 (ddd, *J* = 12.5, 6.7, 1.1 Hz, 1 H^{major}), 4.14 (ddd, *J* = 12.3, 6.6, 1.2 Hz, 1 H^{minor}), 4.31 (ddd, *J* = 11.1, 5.9, 1.4 Hz, 1 H^{major}), 4.34 (ddd, *J* = 12.4, 5.8, 1.4 Hz, 1 H^{minor}), 4.77 (td, *J* = 10.7, 4.8 Hz, 1 H^{minor}), 4.82 (td, *J* = 10.9, 4.6 Hz, 1 H^{major}), 6.27 (dt, *J* = 16.0, 6.5 Hz, 1 + 1 H), 6.57 (d, *J* = 16.0 Hz, 1 H^{major}), 6.58 (d, *J* = 16.0 Hz, 1 H^{minor}), 7.21–7.40 (m, 5 + 5 H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.6, 16.1, 20.7, 20.9, 21.9, 22.0, 22.8, 23.2, 25.5, 25.6, 25.7, 25.9, 26.1, 26.2, 31.4, 34.10, 34.13, 40.7, 40.8, 46.7, 46.9, 71.6, 71.7, 71.8, 72.0, 75.3, 75.7, 84.3, 84.9, 124.8, 124.9, 126.5, 128.0, 128.5, 133.67, 133.72, 136.31, 136.34, 171.1. – IR (KBr): $\tilde{\nu}$ = 3487, 1737 cm^{-1}. – $C_{24}H_{36}O_4$ (388.5): calcd. C 74.19, H 9.33; found C 73.58, H 9.96.

Alcohol 3b: Following general procedure B, a solution of LDA (prepared in situ from 7.9 mmol diisopropylamine and 7.3 mmol *n*-butyllithium) in THF (12 mL) was treated with the ester **2a** (2.0 g, 6.05 mmol) and cyclopentanone (1.02 g, 12.1 mmol) in THF (7 mL) to afford the alcohol **3b** (1.6 g, 64%) as a colorless oil. Spectral data are reported for a 2:1 mixture of diastereomers. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.76 (d, *J* = 7 Hz, 3 H^{minor}), 0.77 (d, *J* = 7 Hz, 3 H^{major}), 0.9–1.1 (series of m, 9 + 9 H), 1.4–2.0 (series of m, 14 + 14 H), 2.6 (br. s, 1 + 1 H), 3.7 (s, 1 H^{minor}), 3.9 (s, 1 H^{major}), 4.08 (ddd, *J* = 12.6, 7.1, 1.1 Hz, 1 H^{major}), 4.13 (ddd, *J* = 12.7, 6.5, 1.3 Hz, 1 H^{minor}), 4.3 (ddd, *J* = 11, 5.9, 1.4 Hz, 1 H^{minor}), 4.37 (ddd, *J* = 12.5, 5.7, 1.3 Hz, 1 H^{major}), 4.77 (td, *J* = 11, 4 Hz, 1 H^{minor}), 4.83 (td, *J* = 11, 4 Hz, 1 H^{major}), 6.21–6.33 (m, 1 + 1 H), 6.6 (d, *J* = 16 Hz, 1 H^{minor}), 6.6 (d, *J* = 16 Hz, 1 H^{major}), 7.2–7.4 (m, 5 + 5 H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.6, 16.1, 20.7, 20.8, 21.9, 22.9, 23.3, 23.8, 23.9, 24.1, 25.9, 26.2, 31.4, 34.2, 34.1, 36.3, 36.5, 37.3, 37.7, 40.78, 40.8, 46.8, 49.9, 71.4, 71.8, 75.2, 75.6, 82.8, 82.9, 83.0, 83.4, 125.0, 125.1, 126.5, 127.3, 128.5, 133.47, 133.50, 136.4, 170.6, 171.1. – IR (neat): $\tilde{\nu}$ = 3431, 1730 cm^{-1}. – $C_{26}H_{38}O_4$ (415.6): calcd. C 75.15, H 9.22; found C 75.63, H 9.47.

Alcohol 3c: Following a modified general procedure B, a solution of LDA (prepared in situ from 12 mmol diisopropylamine and 12 mmol *n*-butyllithium) in THF (20 mL) was treated with the ester **2b** (2.97 g, 10 mmol) and acetone (1.16 g, 20 mmol) to afford the alcohol **3c** (2.61 g, 74%) as a 2:1 mixture of diastereomers. Spectral data are reported for this mixture of diastereomers. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.76 (d, *J* = 6.8 Hz, 3 H^{minor}), 0.78 (d, *J* = 6.8 Hz, 3 H^{major}), 0.88–0.96 (m, 9 + 9 H), 0.88–1.15 (m, 3 + 3 H), 1.23 (s, 3 + 3 H), 1.27 (s, 3 + 3 H), 1.34–1.58 (m, 4 + 4 H), 1.65–1.76 (m, 2 + 2 H), 1.85–2.09 (m, 4 + 4 H), 2.65 (br. s, 1 + 1 H), 3.71 (s, 1 H^{minor}), 3.74 (s, 1 H^{major}), 3.89 (dd, *J* = 12.0, 7.0 Hz, 1 H^{minor}), 3.85 (dd, *J* = 11.8, 7.1 Hz, 1 H^{major}), 4.11 (dd, *J* = 12.0, 5.7 Hz, 1 H^{minor}), 4.16 (dd, *J* = 11.8, 5.8 Hz, 1 H^{major}), 4.78 (td, *J* = 10.9, 4.2 Hz, 1 H^{minor}), 4.82 (td, *J* = 10.9, 4.2 Hz, 1 H^{major}), 5.47–5.59 (m, 1 + 1 H), 5.62–5.75 (m, 1 + 1 H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 15.6, 16.1, 20.7, 20.8, 21.9, 22.1, 22.9, 23.2, 25.5, 25.6, 25.7, 25.9, 26.0, 26.2, 31.4, 34.16, 34.19, 40.77, 40.84, 46.7, 46.9, 71.57, 71.6, 71.7, 72.0, 75.2, 75.5, 83.9, 84.5, 125.4, 125.5, 135.85, 135.89, 170.7, 171.2 – IR (neat): $\tilde{\nu}$ = 3507, 1741 cm^{-1}. – $C_{21}H_{38}O_4$ (354.5): calcd. C 71.14, H 10.80; found C 71.03, H 11.09.

Alcohol 3d: Following general procedure B, a solution of LDA (prepared in situ from 13 mmol diisopropylamine and 12 mmol *n*-butyllithium) in THF (20 mL) was treated with the ester **2b** (2.97 g, 10 mmol) and cyclopentanone (1.68 g, 20 mmol) to afford the alcohol **3d** (3.81 g, 81%) as a 2:1 mixture of diastereomers. Spectral data are reported for this mixture of diastereomers. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.76 (d, *J* = 6.8 Hz, 3 H^{minor}), 0.78 (d, *J* = 6.8 Hz, 3 H^{major}), 0.84–0.94 (m, 9 + 9 H), 0.95–1.11 (m, 2 +

2 H), 1.33−2.08 (series of m, 19 + 19 H), 2.62 (s, 1 H^{major}), 2.66 (s, 1 H^{minor}), 3.79−3.93 (m, 2 + 2 H), 4.09−4.22 (m, 1 + 1 H), 4.78 (td, J = 11.5, 4.3 Hz, 1 H^{minor}), 4.82 (td, J = 11.1, 4.3 Hz, 1 H^{major}), 5.46−5.59 (m, 1 + 1 H), 5.61−5.74 (m, 1 + 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 15.7, 16.1, 20.7, 20.8, 21.9, 22.1, 22.9, 23.3, 23.8, 23.9, 24.1, 25.9, 26.2, 31.4, 34.2, 34.3, 36.3, 36.4, 37.3, 37.7, 40.8, 40.9, 46.8, 47.0, 71.4, 71.8, 75.1, 75.5, 82.4, 82.7, 82.8, 82.9, 125.5, 125.6, 135.8, 170.8, 171.3. − IR (neat): ṽ = 3504, 1742 cm^{-1}. − $C_{23}H_{40}O_4$ (380.6): calcd. C 72.59, H 10.59; found C 72.16, H 10.59.

Alcohol 3e: Following a modified general procedure B, a solution of LDA (prepared in situ from 13 mmol diisopropylamine and 12 mmol *n*-butyllithium) in THF (26 mL) was treated with the ester **2b** (3.0 g, 10 mmol) and a solution of tetralone (1.9 g, 13 mmol) in THF (3 mL) to afford the alcohol **3e** (3.81 g, 81%) as a colorless oil. Spectral data are reported for a 2:1 mixture of diastereomers. − ^1H NMR (300 MHz, $CDCl_3$): δ = 0.35 (m_c, 1 + 1 H), 0.49 (d, J = 6.8 Hz, 3 H^{minor}), 0.64 (d, J = 6.8 Hz, 3 H^{major}), 0.68 (d, J = 6.8 Hz, 3 H^{major}), 0.78−1.09 (series of m, 11 + 11 H), 1.28−2.16 (series of m, 12 + 12 H), 2.55−2.68 (m, 1 + 1 H), 2.71−2.83 (m, 1 + 1 H), 3.12 (s, 1 H^{major}), 3.17 (s, 1 H^{minor}), 3.90 (dd, J = 12, 7.3 Hz, 1 H^{major}), 3.94 (dd, J = 12, 7.1 Hz, 1 H^{minor}), 4.14 (ddd, J = 12, 5.8, 1 Hz, 1 H^{minor}), 4.18 (ddd, J = 12, 5.6, 1 Hz, 1 H^{major}), 4.31 (s, 1 H^{major}), 4.34 (s, 1 H^{minor}), 4.53 (td, J = 10.6, 4.3, 1 H^{major}), 4.62 (td, J = 11.0, 4.3 Hz, 1 H^{minor}), 5.47−5.60 (m, 1 + 1 H), 5.62−5.76 (m, 1 + 1 H), 7.02−7.09 (m, 1 + 1 H), 7.13−7.22 (m, 2 + 2 H), 7.53−7.61 (m, 1 + 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 15.3, 16.2, 19.2, 20.6, 20.9, 21.8, 21.9, 22.1, 22.6, 23.2, 24.8, 26.2, 30.0, 30.1, 31.1, 31.4, 33.1, 33.2, 34.05, 34.1, 34.27, 34.3, 39.9, 40.7, 46.4, 46.6, 71.8, 71.9, 73.0, 73.2, 74.6, 75.1, 83.9, 84.1, 125.45, 125.5, 125.6, 125.7, 127.4, 127.6, 128.3, 128.4, 128.6, 128.7, 135.8, 135.9, 136.7, 137.3, 137.9, 138.1, 169.8, 170.0. − IR (neat): ṽ = 3508, 1736 cm^{-1}. − $C_{28}H_{42}O_4$ (442.6): calcd. C 75.98, H 9.56; found C 75.54, H 9.78.

Alcohol 3f: Following general procedure B, a solution of LDA (prepared in situ from 6.6 mmol diisopropylamine and 6.1 mmol *n*-butyllithium) in THF (10 mL) was treated with the ester **2c** (1.5 g, 5.1 mmol) and acetone (640 mg, 11 mmol) to afford the alcohol **3f** (1.4 g, 78%) as a 2:1 mixture of diastereomers. Spectral data are reported for this mixture of diastereomers. − ^1H NMR (300 MHz, $CDCl_3$): δ = 0.77 (d, J = 6.8 Hz, 3 H^{minor}), 0.78 (d, J = 7.1 Hz, 3 H^{major}), 0.87−0.93 (m, 10 + 10 H), 0.96−1.14 (m, 2 + 2 H), 1.23 (s, 3 + 3 H), 1.27 (s, 3 + 3 H), 1.32−1.59 (m, 4 + 4 H), 1.65−1.77 (m, 2 + 2 H), 1.86−2.08 (m, 4 + 4 H), 2.86 (s, 1 H^{major}), 2.90 (s, 1 H^{minor}), 3.71 (s, 1 + 1 H), 4.03 (m_c, 1 + 1 H), 4.18 (d, J = 6.2 Hz, 1 H^{major}), 4.22 (d, J = 5.8 Hz, 1 H^{minor}), 4.80 (td, J = 11.1, 4.3 Hz, 1 H^{minor}), 4.83 (td, J = 11.0, 4.2 Hz, 1 H^{major}), 5.48−5.69 (m, 1 + 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 15.6, 16.0, 20.7, 20.9, 22.0, 22.6, 22.8, 23.1, 25.4, 25.6, 25.9, 26.0, 26.1, 29.5, 31.4, 34.11, 34.14, 40.7, 40.8, 46.7, 46.9, 66.2, 66.4, 71.60, 71.64, 71.2, 75.6, 84.4, 84.6, 125.1, 134.7, 134.8, 170.8, 171.2. − IR (neat): ṽ = 3507, 1747 cm^{-1}. − $C_{21}H_{38}O_4$ (354.5): calcd. C 71.14, H 10.80; found C 71.61, H 11.16.

Alcohol 3g: Following general procedure B, a solution of LDA (prepared in situ from 5.7 mmol diisopropylamine and 5.27 mmol *n*-butyllithium) in THF (10 mL) was treated with the ester **2c** (1.3 g, 4.4 mmol) and cyclopentanone (740 mg, 8.8 mmol) to afford the alcohol **3g** (1.53 g, 92%) as a 2:1 mixture of diastereomers. Spectral data are reported for this mixture of diastereomers. − ^1H NMR (300 MHz, $CDCl_3$): δ = 0.74 (d, J = 6.8 Hz, 3 H^{minor}), 0.75 (d, J = 6.8 Hz, 3 H^{major}), 0.82−0.92 (series of m, 10 + 10 H), 0.93−1.12 (m, 2 + 2 H), 1.29−2.06 (series of m, 16 + 16 H), 2.60 (s, 1 H^{major}), 2.66 (s, 1 H^{minor}), 3.77 (s, 1 H^{minor}), 3.78 (s, 1 H^{major}), 3.94−4.07 (m, 2 + 2 H), 4.13−4.23 (m, 1 + 1 H), 4.71−4.86 (m, 1 + 1 H), 5.44−5.66 (m, 2 + 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 15.6, 16.0, 20.8, 20.9, 22.0, 22.6, 22.8, 23.1, 23.8, 23.9, 24.14, 24.17, 25.9, 26.1, 29.5, 31.4, 34.1, 34.2, 36.2, 37.3, 37.7, 40.79, 40.83, 46.7, 46.9, 66.0, 66.2, 75.1, 75.5, 82.7, 82.8, 82.9, 83.0, 125.1, 125.2, 134.6, 134.7, 170.9, 171.4. − IR (KBr): ṽ = 3503, 1742 cm^{-1}. − $C_{23}H_{40}O_4$ (380.6): calcd. C 72.59, H 10.59; found C 72.82, H 10.97.

General Procedure C for the Elimination with Thionyl Chloride: To a vigorously stirred solution of freshly distilled thionyl chloride (3 equiv.) in CH_2Cl_2 (7−8 mL/mmol of the alcohol) at 0°C was added a solution of the alcohol **3a−g** (1 equiv.) in pyridine. Stirring was continued for approximately 30 min, after which TLC indicated that the starting material had been fully consumed. The reaction was then carefully quenched with saturated aqueous $NaHCO_3$ solution. The mixture was diluted with CH_2Cl_2 and water, the phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2×). The combined organic phases were dried ($MgSO_4$) and concentrated. The pyridine was removed under high vacuum conditions at room temperature. Chromatographic purification (heptane/ethyl acetate, 20:1−30:1) afforded the desired esters **4a−g** and **5a−g**. The regioisomeric esters could be separated by carefully performed chromatography. The conjugated esters **4a−g** have higher R_f values and are UV-active at 254 nm upon TLC analysis. We were unable to obtain accurate elemental analysis data for the elimination products **4/5a−g** due to the presence of sulfur impurities.

Ester 4a: Following general procedure C, the alcohol **3a** (1.53 g, 3.94 mmol) was treated with $SOCl_2$ (1.6 g, 11.8 mmol) and pyridine (5 mL) in CH_2Cl_2 to afford a 1.5:1 mixture of the ester **4a** and **5a** (1.81 g, 81%). Spectral data for the ester **4a** are reported for a 2:1 mixture of diastereomers. − ^1H NMR (300 MHz, $CDCl_3$): δ = 0.65 (d, J = 7.1 Hz, 3 H^{minor}), 0.69 (d, J = 6.8 Hz, 3 H^{major}), 0.77−0.86 (series of 4 d, m, 7 + 7 H), 0.86−1.04 (m, 2 + 2 H), 1.27−1.48 (series of m, 2 + 2 H), 1.54−1.65 (m, 2 + 2 H), 1.71 (s, 3 + 3 H), 1.73−1.99 (series of m, 2 + 2 H), 4.11 (d, J = 6.2 Hz, 2 + 2 H), 4.31 (s, 1 H^{minor}), 4.32 (s, 1 H^{major}), 4.66 (td, J = 10.9, 4.3 Hz, 1 H^{minor}), 4.71 (td, J = 10.9, 4.4 Hz, 1 H^{major}), 5.01 (q, J = 1.5 Hz, 1 + 1 H), 5.07 (s, 1 H^{minor}), 5.08 (s, 1 H^{major}), 6.22 (dt, J = 15.9, 6.2 Hz, 1 + 1 H), 6.52 (d, J = 15.9 Hz, 1 + 1 H), 7.13−7.33 (m, 5 + 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.9, 16.2, 18.0, 18.2, 20.7, 22.0, 23.1, 23.4, 25.9, 26.2, 31.3, 31.4, 34.2, 40.5, 40.8, 46.8, 46.9, 69.7, 74.9, 75.2, 81.6, 82.0, 115.8, 116.3, 126.6, 127.8, 128.5, 133.2, 136.5, 140.3, 140.4, 170.07, 170.1.

Ester 4b: Following general procedure C, the alcohol **3b** (1.44 g, 3.47 mmol) was treated with $SOCl_2$ (1.4 g, 10.4 mmol) and pyridine (5 mL) in CH_2Cl_2 to afford a 5.5:1 mixture of the esters **4b** and **5b** (600 mg, 44%) as a colorless oil. Spectral data are reported for a 2:1 mixture of diastereomers of the ester **4b**. − ^1H NMR (300 MHz, $CDCl_3$): δ = 0.71 (d, J = 7.1 Hz, 3 H^{minor}), 0.76 (d, J = 6.8 Hz, 3 H^{major}), 0.85−1.10 (series of m, 12 + 12 H), 1.32−1.56 (m, 2 + 2 H), 1.59−1.74 (m, 2 + 2 H), 1.75−2.02 (m, 4 + 4 H), 2.30−2.44 (m, 4 + 4 H), 4.10−4.27 (m, 2 + 2 H), 4.59 (s, 1 H^{major}), 4.60 (s, 1 H^{minor}), 4.71 (td, J = 10.6, 4.2 Hz, 1 H^{minor}), 4.79 (td, J = 10.9, 4.6 Hz), 5.82 (br. s, 1 + 1 H), 6.27 (t, J = 6.2 Hz, 1 H^{minor}), 6.32 (t, J = 6.2 Hz, 1 H^{major}), 6.58 (d, J = 15.9 Hz, 1 + 1 H), 7.21−7.40 (m, 5 + 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.9, 16.2, 20.66, 20.72, 21.9, 22.0, 23.1, 23.2, 23.4, 31.4, 31.7, 32.0, 32.4, 34.2, 40.6, 40.8, 46.9, 47.1, 70.02, 70.05, 75.0, 75.1, 77.5, 125.5, 126.5, 127.7, 128.5, 130.1, 131.0, 133.1, 133.2, 136.6, 139.3, 170.25, 170.30.

Ester 4c: Following general procedure C, the alcohol **3c** (2.6 g, 7.4 mmol) was treated with $SOCl_2$ (2.64 g, 22.2 mmol) and pyridine (8 mL) in CH_2Cl_2 to afford a 1.4:1 mixture of the esters **4c** and **5c** (2.03 g, 82%). Spectral data of the ester **4c** are reported for a 2:1 mixture of diastereomers. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.72 (d, *J* = 6.8 Hz, 3 H^{minor}), 0.77 (d, *J* = 6.8 Hz, 3 H^{major}), 0.86–0.94 (m, 9 + 9 H), 0.86–0.94 (m, 3 + 3 H), 1.34–1.58 (m, 4 + 4 H), 1.62–1.73 (m, 4 + 4 H), 1.75 (s, 3 + 3 H), 1.79–2.09 (series of m, 4 + 4 H), 3.89–4.03 (m, 2 + 2 H), 4.32 (s, 1 H^{minor}), 4.33 (s, 1 H^{major}), 4.73 (td, *J* = 10.8, 3.7 Hz, 1 H^{minor}), 4.77 (td, *J* = 10.8, 4.2 Hz, 1 H^{major}), 5.03–5.07 (m, 1 + 1 H), 5.11 (s, 1 + 1 H), 5.50–5.61 (m, 1 + 1 H), 5.62–5.74 (m, 1 + 1 H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 15.9, 16.3, 18.0, 18.2, 20.7, 22.0, 22.2, 23.2, 23.5, 25.9, 26.3, 31.3, 31.4, 34.2, 34.3, 40.5, 40.8, 46.9, 47.0, 69.9, 74.8, 75.1, 81.2, 81.7, 115.4, 115.8, 125.7, 125.8, 140.5, 170.2.

Ester 4d: Following general procedure C, the alcohol **3d** (3.0 g, 7.9 mmol) was treated with $SOCl_2$ (2.81 g, 23.7 mmol) and pyridine (8 mL) in CH_2Cl_2 to afford a 2.4:1 mixture of the esters **4d** and **5d** (2.53 g, 88%) as a colorless oil. Spectral data of the ester **4d** are reported from a 2:1 mixture of diastereomers. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.72 (d, *J* = 6.8 Hz, 3 H^{minor}), 0.77 (d, *J* = 6.8 Hz, 3 H^{major}), 0.86–0.93 (m, 9 + 9 H), 1.34–1.59 (m, 4 + 4 H), 1.62–1.73 (m, 2 + 2 H), 1.76–2.08 (series of m, 4 + 4 H), 2.20–2.41 (m, 4 + 4 H), 3.88–4.07 (m, 2 + 2 H), 4.53 (s, 1 H^{major}), 4.55 (s, 1 H^{minor}), 4.72 (td, *J* = 10.9, 4.4 Hz, 1 H^{minor}), 4.78 (td, *J* = 10.9, 4.3 Hz, 1 H^{major}), 5.62 (m$_c$, 2 + 2 H), 5.79 (s, 1 + 1 H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 15.9, 16.2, 20.66, 20.72, 21.9, 22.1, 23.1, 23.2, 23.4, 25.9, 26.2, 31.4, 31.7, 32.0, 32.4, 34.2, 34.3, 40.6, 40.9, 46.9, 47.1, 74.8, 75.0, 77.0, 77.1, 129.8, 135.3, 135.4, 139.4, 139.5, 170.4.

Ester 4e: Following general procedure C, the alcohol **3e** (2.5 g, 5.65 mmol) was treated with $SOCl_2$ (2.02 g, 16.9 mmol) and pyridine (6 mL) in CH_2Cl_2 to afford a 2:1 diastereomeric mixture of the ester **4e** (778 mg, 33%) as a colorless oil and the starting material (493 mg, 20%). Spectral data are reported for a 2:1 mixture of diastereomers. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.33 (d, *J* = 6.8 Hz, 3 H^{minor}), 0.62 (d, *J* = 6.8 Hz, 3 H^{minor}), 0.68 (d, *J* = 6.8 Hz, 3 H^{major}), 0.80–0.95 (m, 9 H^{major} + 6 H^{minor}), 0.89–0.93 (m, 2 + 2 H), 1.17–1.85 (series of m, 9 + 9 H), 1.98–2.09 (m, 2 + 2 H), 2.27–2.37 (m, 2 + 2 H), 2.68–2.78 (m, 2 H), 4.00–4.13 (m, 2 + 2 H), 4.62 (dt, *J* = 10.9, 4.4 Hz, 1 H^{minor}), 4.71 (dt, *J* = 11.0, 4.4 Hz, 1 H^{major}), 4.77 (s, 1 H^{minor}), 4.86 (s, 1 H^{major}), 5.65 (m$_c$, 1 + 1 H), 6.19 (t, *J* = 4.6 Hz, 1 H^{minor}), 6.23 (t, *J* = 4.7 Hz, 1 H^{major}), 7.08–7.19 (m, 3 + 3 H), 7.44–7.49 (m, 1 H^{major}), 7.53–7.57 (m, 1 H^{minor}). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 15.3, 16.2, 20.6, 20.7, 21.9, 21.94, 22.1, 22.8, 23.0, 23.1, 23.4, 25.4, 26.2, 27.86, 27.92, 31.3, 34.2, 34.3, 40.2, 40.8, 46.9, 47.1, 69.8, 70.1, 74.9, 75.0, 78.5, 79.1, 123.6, 124.0, 125.8, 125.9, 126.3, 126.4, 127.0, 127.1, 127.3, 127.4, 129.8, 131.1, 132.70, 132.74, 133.0, 133.1, 135.5, 135.6, 136.3, 136.4, 170.6.

Ester 4f: Following general procedure C, the alcohol **3f** (1.35 g, 3.81 mmol) was treated with $SOCl_2$ (1.36 g, 11.42 mmol) and pyridine (4 mL) in CH_2Cl_2 to afford a 1.5:1 mixture of the esters **4f** and **5f** (986 mg, 77%). Spectral data for the ester **4f** are reported for a 2:1 mixture of diastereomers. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.72 (d, *J* = 6.8 Hz, 3 H^{minor}), 0.77 (d, *J* = 6.8 Hz, 3 H^{major}), 0.86–0.93 (m, 10 + 10 H), 0.93–1.13 (m, partially overlapped, 2 + 2 H), 1.31–1.58 (series of m, 4 + 4 H), 1.61–1.73 (m, 2 + 2 H), 1.76 (s, 3 + 3 H), 1.81–2.09 (series of m, 4 + 4 H), 4.00–4.13 (m, 2 + 2 H), 4.31 (s, 1 H^{major}), 4.32 (s, 1 H^{minor}), 4.68–4.84 (m, 1 + 1 H), 5.05 (br. s, 1 + 1 H), 5.12 (br. s, 1 + 1 H), 5.50–5.66 (m, 2 + 2 H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 15.9, 16.2, 17.9, 18.2, 20.7, 22.0, 22.7, 23.1, 23.3, 25.9, 26.2, 29.6, 31.3, 34.2, 40.4, 40.8, 46.8, 46.9, 64.5, 64.6, 74.8, 75.0, 81.6, 81.7, 115.5, 116.0, 125.45, 125.5, 134.17, 134.21, 140.4, 140.6, 170.2.

Ester 4g: Following general procedure C, the alcohol **3g** (1.3 g, 3.42 mmol) was treated with $SOCl_2$ (1.22 g, 10.3 mmol) and pyridine (4 mL) in CH_2Cl_2 to afford a 5.1:1 mixture of the esters **4g** and **5g** (850 mg, 69%) as a colorless oil. Spectral data reported for a 2:1 mixture of diastereomers of the ester **4g**. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.53 (d, *J* = 7.1 Hz, 3 H^{minor}), 0.58 (d, *J* = 6.8 Hz, 3 H^{major}), 0.65–0.75 (series of m, 10 + 10 H), 0.77–0.95 (m, 2 + 2 H), 1.13–1.89 (series of m, 13 + 13 H), 2.10–2.23 (m, 3 + 3 H), 3.81–3.97 (m, 2 + 2 H), 4.32 (s, 1 H^{major}), 4.36 (s, 1 H^{minor}), 4.55 (td, *J* = 11.2, 5.3 Hz, 1 H^{minor}), 4.60 (td, *J* = 10.9, 4.6 Hz, 1 H^{major}), 5.31–5.47 (m, 2 + 2 H), 6.00 (s, 1 + 1 H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 15.9, 16.1, 20.7, 20.8, 22.0, 22.7, 23.0, 23.1, 23.2, 25.8, 26.1, 29.6, 31.35, 31.38, 31.6, 32.0, 32.4, 34.2, 40.6, 40.8, 46.8, 47.0, 64.7, 64.9, 74.8, 75.0, 77.05, 77.4, 125.53, 125.57, 130.0, 130.9, 134.17, 134.21, 139.3, 139.4, 170.44, 170.48.

General Procedure D for the Dienolate [2,3]-Wittig Rearrangement: Lithium diisopropylamide was prepared by the addition of *n*-butyllithium (1.2 equiv.) to a solution of diisopropylamine (1.3 equiv.) in THF (2.2 mL/mmol of ester) at 0°C. The reaction mixture was stirred for 30 min at 0°C and then cooled to −78°C. To this mixture was added a precooled (−78°C) solution of the ester (1 equiv.) in THF (4–5 mL/mmol of ester). Starting from the (*E*)-esters **4**/**5a**–**e**, the reaction mixture was stirred at −78°C for 12 h. The reaction was then quenched by the addition of saturated aqueous NH_4Cl solution at −78°C. Starting from the (*Z*)-esters **4**/**5f**,**g**, the reaction mixture was stirred at −78°C for 10 min, the dry ice bath was then replaced by an ice bath and stirring was continued for 1 h at 0°C. The reaction was subsequently quenched by the addition of saturated aqueous NH_4Cl solution at 0°C. The mixture was allowed to warm to room temperature and diluted with water and CH_2Cl_2. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2×). The combined organic phases were dried ($MgSO_4$) and concentrated. Chromatographic purification (heptane/ethyl acetate, 10–20:1) gave the desired alcohol **6a**–**g** as a colorless oil.

(2*SR*,3*SR*)-Ester 6a: Following a modified general procedure C, a solution of LDA (generated from 3.42 mmol diisopropylamine and 3.42 mmol *n*BuLi) in THF (6.3 mL) was treated with the ester **4**/**5a** (1.06 g, 2.86 mmol) in THF (5 mL) to afford the hexadiene **6a** (700 mg, 72%) as a colorless oil. Spectral data are reported for a mixture of four diastereomers (57:16:14:13). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.50 (d, *J* = 6.8 Hz, 3 H), 0.55 (d, *J* = 7.1 Hz, 3 H), 0.69–0.98 (series of d, m, 10 + 10 + 7 + 7 H), 0.98–1.16 (m, 4 × 2 H), 1.23–2.05 (series of m, 4 × 6 H), 1.68 (s, 3 H), 1.70 (s, 3 H, 57%), 1.94 (s, 3 H), 1.96 (s, 3 H), 3.60 (s, 1 H, 13%), 3.67 (s, 1 H, 14%), 3.74 (s, 1 H, 16%), 3.81 (s, 1 H, 57%), 4.01–4.08 (m, 4 × 1 H), 4.47–4.60 (m, 2 × 1 H), 4.71–4.90 (series of m, 2 + 2 + 1 + 1 H), 4.97–5.16 (series of m, 4 × 2 H), 5.23 (s, 1 + 1 H), 5.44 (s, 1 H), 5.45 (s, 1 H), 6.03–6.28 (m, 4 × 1 H), 7.15–7.47 (m, 4 × 5 H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.6, 15.66, 15.71, 15.77, 19.57, 19.62, 19.69, 20.82, 20.85, 21.0, 21.86, 21.89, 21.95, 22.0, 22.84, 22.87, 22.9, 25.4, 25.6, 25.8, 31.26, 31.3, 31.4, 34.0, 34.1, 40.0, 40.29, 40.3, 40.6, 46.8, 47.07, 47.12, 47.3, 53.4, 53.5, 54.5, 54.8, 76.8, 81.96, 82.0, 114.4, 114.8, 115.0, 117.0, 117.1, 117.19, 117.22, 126.5, 126.6, 126.8, 127.0, 127.9, 128.0, 128.1, 129.45, 129.49, 129.5, 129.9, 136.8, 136.9, 137.6, 137.7, 139.7, 139.8, 139.98, 140.03, 143.77, 143.83, 143.88, 143.97, 172.5, 172.6, 172.85, 172.92. – IR (KBr): $\tilde{\nu}$ = 3494, 1716 cm^{-1}. – $C_{24}H_{34}O_3$ (370.5): calcd. C 77.80, H 9.25; found C 77.11, H 9.39.

(2*SR*,3*SR*)-Ester 6b: Following a modified general procedure D, a solution of LDA (generated from 1.46 mmol diisopropylamine and 1.46 mmol *n*BuLi) in THF (3.2 mL) was treated with the ester **4/5b** (478 mg, 1.2 mmol) in THF (5 mL) to afford the hexadiene **6b** (330 mg, 69%) as a colorless oil. Spectral data are reported for a mixture of four diastereomers (39:29:11:21). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.49 (d, *J* = 6.8 Hz, 3 H), 0.58 (d, *J* = 6.8 Hz, 3 H), 0.68−1.12 (series of m, 12 + 12 + 9 + 9 H), 1.23−2.63 (m, 4 × 12 H), 3.59 (s, 1 H, 21%), 3.65 (s, 1 H, 11%), 3.72 (s, 1 H, 29%), 3.79 (s, 1 H, 39%), 3.91−4.00 (m, 4 × 1 H), 4.51 (td, *J* = 10.7, 4.2 Hz, 1 H), 4.54 (td, *J* = 10.8, 4.3 Hz, 1 H), 4.75 (td, *J* = 11.4, 4.7 Hz, 1 H), 4.81 (td, *J* = 10.9, 4.4 Hz, 1 H), 4.93−5.15 (series of m, 4 × 2 H), 5.68−5.74 (m, 1 + 1 H), 5.96−6.00 (m, 1 + 1 H), 6.04−6.27 (m, 4 × 1 H), 7.13−7.27 (m, 4 × 3 H), 7.33−7.43 (m, 4 × 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.5, 15.66, 15.7, 15.78, 20.8, 20.91, 20.94, 20.99, 21.9, 21.97, 22.0, 23.5, 23.7, 23.9, 24.2, 25.4, 25.5, 25.66, 25.73, 31.26, 31.32, 31.4, 31.9, 32.0, 32.2, 32.3, 32.4, 32.51, 32.54, 32.6, 34.0, 34.08, 34.11, 40.2, 40.4, 40.5, 40.7, 46.8, 47.1, 47.3, 47.4, 54.0, 54.2, 55.2, 55.5, 76.7, 76.9, 77.17, 77.2, 79.8, 80.2, 80.5, 116.8, 117.1, 117.2, 126.4, 126.8, 127.0, 127.8, 127.9, 128.0, 128.1, 129.0, 129.2, 129.32, 129.36, 129.39, 129.45, 129.54, 129.7, 137.1, 137.2, 137.3, 139.7, 139.8, 139.86, 139.9, 143.5, 143.6, 143.8, 143.9, 173.3, 174.1. − IR (KBr): $\tilde{\nu}$ = 3490, 1717 cm^{-1}. − $C_{26}H_{36}O_3$ (396.6): calcd. C 78.74, H 9.15; found C 77.06, H 9.39; we were unable to obtain an accurate combustion analysis for this compound.

(2*S*,3*S*)- and (2*R*,3*R*)-Ester *syn*-6c: Following a modified general procedure D, a solution of LDA (generated from 1.43 mmol diisopropylamine and 1.43 mmol *n*BuLi) in THF (3.2 mL) was treated with the ester **4/5c** (400 mg, 1.19 mmol) in THF (4 mL) to afford the hexadiene *syn*-**6c** (360 mg, 90%) as a colorless oil. Spectral data for the two *syn* diastereomers are reported from a mixture of four diastereomers (66:27:5:2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.67−0.80 (series of 2 d, 3 + 3 H), 0.81−0.95 (m, 10 + 10 H), 0.96−1.20 (m, 3 + 3 H), 1.33−2.05 (series of m, 9 + 9 H), 1.81 (s, 3 + 3 H), 2.57−2.76 (m, 1 + 1 H), 3.47 (s, 1 H, 66%), 3.50 (s, 1 H, 27%), 3.56 (s, 1 H, 2%), 3.60 (s, 1 H, 5%), 4.69−4.87 (m, 1 + 1 H), 4.92−5.15 (m, 3 + 3 H), 5.24−5.35 (m, 1 + 1 H), 5.51−5.69 (m, 1 + 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 14.0, 15.68, 15.72, 19.2, 19.3, 20.4, 20.7, 20.8, 21.87, 21.90, 22.86, 22.92, 25.8, 31.99, 31.43, 31.82, 34.07, 34.13, 40.3, 40.6, 47.0, 47.2, 48.2, 48.6, 81.9, 82.2, 113.7, 113.8, 116.7, 117.0, 136.7, 136.8, 144.4, 174.2, 174.3. − IR (neat): $\tilde{\nu}$ = 3513, 1716 cm^{-1}. − $C_{21}H_{36}O_3$ (336.5): calcd. C 74.95, H 10.78; found C 74.88, H 10.75.

(2*S*,3*R*)- and (2*R*,3*S*)-Ester *anti*-6c: Following the general procedure D, a solution of LDA (generated from 2.62 mmol diisopropylamine and 2.42 mmol *n*BuLi) in THF (4.5 mL) was treated with the ester **4/5f** (678 mg, 2.02 mmol) in THF (8 mL) to afford the hexadiene *anti*-**6c** (527 mg, 78%) as a colorless oil. Spectral data for the two *anti* diastereomers are reported from a mixture of four diastereomers (61:33:2:4). The assignment is based on COSY and HSQC experiments. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.69 (d, *J* = 6.8 Hz, 3 H^{major}, menthyl-isopropyl-CH_3), 0.70 (d, *J* = 6.8 Hz, 3 H^{minor}, menthyl-isopropyl-CH_3), 0.85−0.93 (series of m, 10 + 10 H, 2 × menthyl-CH_3, -$CH_2CH_2CH_3$, menthyl 3/4-H), 0.93−1.07 (m, 2 + 2 H, menthyl 6-H, 4/3-H), 1.07−1.24 (m, 1 + 1 H, -$CH_2CH_2CH_3$), 1.24−1.52 (m, 5 + 5 H, -$CH_2CH_2CH_3$, menthyl 5-H, 2-H), 1.63−1.79 (series of m, 3 H^{major}, 2 H^{minor}, menthyl 3-H, 4-H, menthyl-isopropyl-H^{major}), 1.85 [s, 3 + 3 H, -C(CH_3)=CH_2], 1.88−2.05 (m, 1 H^{major}, 2 H^{minor}, menthyl 6-H, menthyl-isopropyl-H^{minor}), 2.60−2.67 (m, 1 + 1 H, 3-H), 3.48 (s, 1 H, 4%, OH), 3.50 (s, 1 H, 2%, OH), 3.57 (s, 1 H, 33%, OH), 3.61 (s, 1 H, 61%, OH), 4.66 (td, *J* = 11.0, 4.3 Hz, 1H^{minor}, menthyl 1-H), 4.74 (td, *J* = 11.0, 4.4 Hz, 1 H^{major}, menthyl 1-H), 4.99−5.12 [series of m, 3 + 3 H, 5-H, -C(CH_3)=CH_2], 5.31 [s, 1 H^{major}, -C(CH_3)=CH_2], 5.34 [s, 1 H^{minor}, -C(CH_3)=CH_2], 5.57−5.77 (m, 1 + 1 H, 4-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (-$CH_2CH_2CH_3$), 15.66, 15.7 (menthyl-isopropyl-CH_3), 19.6 [-C(CH_3)=CH_2], 20.3, 20.4 (-$CH_2CH_2CH_3$), 20.8, 20.9, 21.9, 22.0 (menthyl-CH_3), 22.8 (menthyl-C-3/4), 25.5, 25.7 (menthyl-isopropyl-C), 29.60, 29.63 ($CH_2CH_2CH_3$), 31.34, 31.35 (menthyl-C-5/2), 34.1 (menthyl-C-4/3), 40.2, 40.6 (menthyl-C-6), 47.0, 47.3 (menthyl-C-5/2), 47.8, 48.1 (-C-3), 76.5, 76.8 (menthyl-C-1), 81.4, 82.1 (C-2), 114.5 [-C(CH_3)=CH_2], 117.7, 118.1 (C-5), 137.09, 137.14 (C-4), 143.8, 143.9 [-C(CH_3)=CH_2], 174.0, 174.1 (C-1). − IR (KBr): $\tilde{\nu}$ = 3504, 1715 cm^{-1}. − $C_{21}H_{36}O_3$ (336.5): calcd. C 74.95, H 10.78; found C 75.18, H 11.00.

(2*S*,3*S*)- and (2*R*,3*R*)-Ester *syn*-6d: Following a modified general procedure D, a solution of LDA (generated from 3.06 mmol diisopropylamine and 3.06 mmol *n*BuLi) in THF (3.2 mL) was treated with the ester **4/5d** (1.05 g, 2.9 mmol) in THF (7 mL) to afford the hexadiene *syn*-**6d** (840 mg, 80%) as a colorless oil. Spectral data for the *syn* diastereomers are reported from a mixture of four diastereomers (62:31:5:2). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.72 (d, *J* = 7.1 Hz, 3 H^{major}), 0.76 (d, *J* = 6.8 Hz, 3 H^{minor}), 0.82−0.95 (m, 10 + 11 H), 0.96−1.22 (m, 3 + 2 H), 1.27−1.52 (m, 5 + 5 H), 1.62−2.03 (m, 6 + 6 H), 2.23−2.43 (m, 3 + 3 H), 2.54−2.69 (m, 1 + 1 H), 3.47 (s, 1 H, 31%), 3.51 (s, 1 H, 62%), 3.35 (s, 1 H, 2%), 3.62 (s, 1 H, 5%), 4.69−4.85 (m, 1 + 1 H), 4.96−5.13 (m, 2 + 2 H), 5.53−5.71 (m, 1 + 1 H), 5.79−5.85 (m, 1 + 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8, 13.9, 15.6, 15.7, 20.3, 20.7, 20.9, 21.90, 21.93, 22.9, 23.7, 24.1, 25.8, 25.9, 31.1, 31.38, 31.41, 31.5, 32.1, 32.17, 32.24, 34.08, 34.14, 40.5, 40.6, 47.1, 47.3, 48.9, 49.3, 76.3, 76.6, 80.0, 116.8, 117.0, 128.1, 128.4, 137.0, 137.1, 144.3, 144.5, 174.3, 174.4. − IR (neat): $\tilde{\nu}$ = 3512, 1719 cm^{-1}. − $C_{23}H_{38}O_3$ (362.6): calcd. C 76.20, H 10.56; found C 75.71, H 11.04.

(2*S*,3*R*)- and (2*R*,3*S*)-Ester *anti*-6d: Following the general procedure D, a solution of LDA (generated from 1.43 mmol diisopropylamine and 1.32 mmol *n*BuLi) in THF (2.5 mL) was treated with the ester **4/5g** (400 mg, 1.1 mmol) in THF (5 mL) to afford the hexadiene *anti*-**6d** (367 mg, 91%) as a colorless oil. Spectral data for the two *anti* diastereomers are reported from a mixture of four diastereomers (59:34:4:3). The assignment is based on COSY and HSQC experiments. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.67 (d, *J* = 6.8 Hz, 3 H^{major}, menthyl-isopropyl-CH_3), 0.69 (d, *J* = 6.5 Hz, 3 H^{minor}, menthyl-isopropyl-CH_3), 0.83−0.92 (series of m, 10 H^{major}, 11 H^{minor}, 3-*n*-propyl-CH_3, 2 × menthyl-CH_3, menthyl 3/4-H, 6-H^{minor}), 0.94−1.19 (m, 3 H^{major}, 2 H^{minor}, -$CH_2CH_2CH_3$, menthyl 3/4-H, menthyl 6-H^{major}), 1.27−1.52 (m, 5 + 5 H, menthyl 2-H, 5-H, -$CH_2CH_2CH_3$), 1.61−1.74 (m, 3 H^{major}, 2 H^{minor}, menthyl-isopropyl-H^{major}, menthyl 4/3-H, 3/4-H), 1.77−2.02 (m, 3 H^{major}, 4 H^{minor}, =$CHCH_2CH_2CH_2C$, menthyl 6-H, -isopropyl H^{minor}), 2.16−2.38 (m, 3 + 3 H, =$CHCH_2CH_2CH_2C$), 2.40−2.59 (m, 2 + 2 H, =$CHCH_2CH_2CH_2C$, 3-H), 3.47 (s, 1 H, 3%, OH), 3.50 (s, 1 H, 4%, OH), 3.53 (s, 1 H, 34%, OH), 3.61 (s, 1 H, 59%, OH), 4.64 (td, *J* = 11.0, 4.3 Hz, 1 H^{minor}, menthyl-H-1), 4.73 (td, *J* = 11.0, 4.4 Hz, 1 H^{major}, menthyl 1-H), 5.00 (dd, *J* = 17.4, 2.1 Hz, 1 H^{minor}, 5-H), 5.02 (dd, *J* = 17.4, 2.1 Hz, 1 H^{major}, 5-H), 5.06 (d, *J* = 2.1 Hz, 1 H^{major}, 5-H), 5.09 (d, *J* = 2.1 Hz, 1 H^{minor}, 5-H), 5.55−5.75 (m, 1 + 1 H, 4-H), 5.86 (t, *J* = 2.1 Hz, 1 H^{major}, = $CHCH_2CH_2CH_2C$), 5.88 (t, *J* = 2.1 Hz, 1 H^{minor}, = $CHCH_2CH_2CH_2C$). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 14.1 (-$CH_2CH_2CH_3$), 15.6, 15.7 (menthyl-isopropyl-CH_3), 20.3, 20.4 (-$CH_2CH_2CH_3$), 20.8, 21.0, 21.96, 22.0 (menthyl-CH_3), 22.7, 22.8 (menthyl C-3/4), 23.6, 24.1 (=$CHCH_2CH_2CH_2C$), 25.5, 25.6 (menthyl-isopropyl C), 29.8 (-$CH_2CH_2CH_3$), 31.4 (menthyl C-2/5),

32.2, 32.3, 32.46, 32.51 (=CH*C*H$_2$CH$_2$*C*H$_2$C), 34.1 (menthyl C-3/4), 40.3, 40.6 (menthyl C-6), 47.0, 47.4 (menthyl C-2/5), 48.9, 49.3 (C-3), 76.2, 76.8 (menthyl C-2), 79.7, 80.5 (C-2), 117.6, 118.1 (C-5), 128.97, 129.0 (=*C*HCH$_2$CH$_2$CH$_2$C), 136.93, 136.97 (C-4), 143.8, 144.0 (=CHCH$_2$CH$_2$CH$_2$*C*), 174.1, 174.4 (C-4). − IR (KBr): $\tilde{\nu}$ = 3508, 1718 cm^{-1}. − $C_{23}H_{38}O_3$ (362.6): calcd. C 76.20, H 10.56; found C 75.98, H 10.96.

(2*S*,3*S*)- and (2*R*,3*R*)-Ester *syn*-6e: Following a modified general procedure D, a solution of LDA (generated from 1.91 mmol diisopropylamine and 1.91 mmol *n*BuLi) in THF (4.2 mL) was treated with the ester **4e** (705 mg, 1.59 mmol) in THF (5 mL) to afford the hexadiene *syn*-**6e** (565 mg, 80%) as a colorless oil. Spectral data for the two *syn* diastereomers are reported from a mixture of four diastereomers (47:40:9:4). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.33 (d, *J* = 6.8 Hz, 3 H), 0.62 (d, *J* = 6.8 Hz, 3 H), 0.68 (d, *J* = 6.8 Hz, 3 H), 0.78−1.04 (series of m, 10 + 10 H), 1.08−1.71 (series of m, 10 + 10 H), 1.78−1.90 (m, 1 H), 2.00−2.09 (m, 1 + 1 H), 2.16−2.27 (m, 2 + 2 H), 2.57−2.67 (m, 2 + 2 H), 2.86−2.99 (1 + 1 H), 3.44 (s, 1 H, 40%), 3.54 (s, 1 H, 47%), 3.57 (s, 1 H, 4%), 3.66 (s, 1 H, 9%), 4.56−4.74 (m, 1 + 1 H), 4.91−5.22 (series of m, 2 + 2 H), 5.59−5.77 (m, 1 + 1 H), 6.36−6.44 (m, 1 + 1 H), 7.05−7.14 (m, 3 + 3 H), 7.63−7.70 (m, 2 + 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8, 13.9, 15.4, 15.6, 20.5, 20.69, 20.72, 20.8, 21.8, 21.9, 22.8, 23.3, 23.5, 25.3, 25.8, 28.5, 28.7, 31.3, 31.4, 31.6, 31.8, 34.1, 34.11, 40.1, 40.6, 46.9, 49.7, 49.8, 76.58, 76.1, 80.4, 81.0, 117.8, 118.2, 125.17, 125.23, 125.9, 126.1, 126.35, 126.4, 127.2, 129.6, 130.2, 133.4, 133.5, 135.8, 136.7, 137.36, 137.39, 137.5, 137.7, 174.5. − IR (neat): $\tilde{\nu}$ = 3505, 1716 cm^{-1}. − $C_{28}H_{40}O_3$ (424.6): calcd. C 79.20, H 9.50; found C 78.93, H 10.43.

General Procedure E for the DIBAL Reduction to the Alcohol: To a solution of diisobutylaluminium hydride (DIBAL, 5 equiv.) in THF (10 mL/mmol of the ester) was added a solution of the ester **6** (1 equiv.) in THF (2 mL/mmol of the ester) at 0 °C. The mixture was stirred at room temperature until TLC indicated that the starting material had been consumed. The reaction was then carefully quenched by the dropwise addition of water at 0 °C until the excess DIBAL had been hydrolyzed. $MgSO_4$ was then added, the mixture was diluted with CH_2Cl_2 and stirred for 30 min at room temperature. The solid was removed by filtration, the filtrate was concentrated, and the crude product oil was purified by chromatography (heptane/ethyl acetate, 2:1−4:1) to afford the desired diol **8** and (−)-menthol.

(2*S,3*S**)- and (2*S**,3*R**)-Diol 7a:** Following general procedure E, a solution of the ester **6a** (650 mg, 1.75 mmol) in THF (20 mL) was treated with DIBAL (8.75 mmol) to afford the diol **7a** (214 mg, 56%) as a colorless oil. Spectral data are reported for a 71:29 mixture of diastereomers. The assignment is based on COSY and HSQC experiments. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.61 [s, 3 H^{major}, -C(C*H*$_3$)=CH$_2$], 1.77 [s, 3 H^{minor}, -C(C*H*$_3$)=CH$_2$], 1.93 (br. s, 1 H^{minor}), 2.24 (br. s, 1 H^{major}), 2.66 (s, 1 H^{minor}), 2.76 (s, 1 H^{major}), 3.20 (d, *J* = 11.4 Hz, 1 H^{minor}, 1-H), 3.42 (d, *J* = 9.4 Hz, 1 H^{major}, 3-H), 3.47 (d, *J* = 8.4 Hz, 1 H^{minor}, 3-H), 3.55 (d, *J* = 11.4 Hz, 1 H^{minor}, 1-H), 3.67 (s, 2 H^{major}, 1-H), 4.83 [s, 1 H^{major}, -C(CH$_3$)=C*H*$_2$], 4.86 [s, 1 H^{minor}, -C(CH$_3$)=C*H*$_2$], 4.96 [s, 1 H^{minor}, -C(CH$_3$)=C*H*$_2$], 5.02 [s, 1 H^{minor}, -C(CH$_3$)=C*H*$_2$], 5.05−5.23 (m, 2 + 2 H, 5-H), 6.17−6.36 (m, 1 + 1 H, 4-H), 7.13−7.32 (m, 5 + 5 H, aryl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.8, 19.9 [-C(*C*H$_3$)=CH$_2$], 54.2, 55.2 (C-3), 66.3, 66.4 (C-1), 79.4, 79.5 (C-2), 113.9, 114.1 [-C(CH$_3$)=*C*H$_2$], 116.8, 116.9 (C-5), 126.5, 126.8, 127.9, 128.2, 128.9, 129.5 (aryl-C), 136.8, 137.7 (C-4), 139.8, 140.1, 145.5 [aryl-C, -*C*(CH$_3$)=CH$_2$]. − IR (KBr): $\tilde{\nu}$ = 3442 cm^{-1}. − $C_{14}H_{18}O_2$ (218.3): calcd. C 77.03, H 8.31; found C 76.53, H 8.67.

(2*S,3*S**)- and (2*S**,3*R**)-Diol 7b:** Following general procedure E, a solution of the ester **6b** (260 mg, 0.66 mmol) in THF (20 mL) was treated with DIBAL (2.62 mmol) to afford the diol **7b** (181 mg, 57%) as a colorless oil. Spectral data are reported for a 57:43 mixture of diastereomers. The assignment is based on COSY and HSQC experiments. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.63−1.94 (series of m, 2 + 2 H, =CHCH$_2$C*H*$_2$CH$_2$C=), 2.06−2.41 (series of m, 4 + 4 H, =CHC*H*$_2$CH$_2$C*H***2**C=), 2.51 (br. s, 1 H^{major}), 2.57 (br. s, 1 H^{minor}), 3.30 (d, *J* = 11 Hz, 1/2 AB system, 1 H^{major}), 3.46 (d, *J* = 3.6 Hz, 1 H, 3-H), 3.49 (d, *J* = 2.3 Hz, 1 H, 3-H), 3.52 (d, *J* = 11 Hz, 1/2 AB system, 1 H^{major}), 3.59 (d, *J* = 11.4 Hz, 1/2 AB system, 1 H^{minor}), 3.67 (d, *J* = 11.4 Hz, 1/2 AB system, 1 H^{minor}), 4.97−5.18 (series of m, 2 + 2 H, 5-H), 5.36−5.40 (m, 1 H^{minor}, = C*H*CH$_2$CH$_2$CH$_2$C=), 5.67−5.72 (m, 1 H^{major}, = C*H*CH$_2$CH$_2$CH$_2$C=), 6.12−6.39 (m, 1 + 1 H, 4-H), 7.14−7.31 (m, 5 + 5 H, aryl-H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.6, 23.8 (=CHCH$_2$*C*H$_2$CH$_2$C=), 32.2, 32.3, 32.7, 32.9 (=*C*HCH$_2$CH$_2$*C*H$_2$C=), 55.2, 55.8 (C-3), 66.6 (C-1), 77.8, 78.1 (C-2), 116.9, 117.3 (C-5), 126.5, 126.8, 127.9, 128.1, 128.2, 128.3, 128.46, 128.52, 128.8, 129.2, 129.4 (aryl-C, =*C*HCH$_2$CH$_2$CH$_2$C=), 137.1, 137.3 (C-4), 139.8, 140.2, 145.6, 145.4. − IR (neat): $\tilde{\nu}$ = 3434 cm^{-1}. − $C_{16}H_{20}O_2$ (244.3): calcd. C 78.65, H 8.25; found C 78.38, H 8.87.

(2*S,3*S**)-Diol *syn*-7c:** Following general procedure E, a solution of the ester *syn*-**6c** (446 mg, 1.27 mmol) in THF (20 mL) was treated with DIBAL (4.1 mmol) to afford the diol *syn*-**7c** (209 mg, 89%) as a colorless oil and (−)-menthol (196 mg, 99%) as a white solid. Spectral data for the *syn* diastereomer are reported from a mixture of two diastereomers (*syn*/*anti* = 93:7). The assignment is based on COSY and HSQC experiments. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.76−0.88 (t, *J* = 7 Hz, 3 H, -CH$_2$CH$_2$C*H*$_3$), 1.03−1.57 (series of m, 4 H, -C*H*$_2$C*H*$_2$CH$_3$), 1.76 (s, 3 H, isopropenyl-CH$_3$), 2.14−2.29 (m, 2 H, 3-H, -OH), 2.61 (s, 1 H, -OH), 3.62 (d, *J* = 11, 7 Hz, 2 H, 1-H), 3.70 (d, *J* = 11, 5 Hz, 1 H, 1-H), 4.97−5.13 [m, 3 H, 5-H, -C(CH$_3$)=C*H*$_2$], 5.61 (ddd, *J* = 17, 10, 10 Hz, 1 H, 4-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9 (-CH$_2$CH$_2$*C*H$_3$), 20.0 (isopropenyl-CH$_3$), 20.8 (-CH$_2$*C*H$_2$CH$_3$), 30.1 (-*C*H$_2$CH$_2$CH$_3$), 49.8 (C-3), 66.0 (C-1), 79.1 (C-2), 113.2 [-C(CH$_3$)=*C*H$_2$], 117.1 (C-5), 137.9 (C-4), 146.2 [-*C*(CH$_3$)=CH$_2$]. − IR (neat): $\tilde{\nu}$ = 3427 cm^{-1}. − $C_{11}H_{20}O_2$ (184.2778): calcd. C 71.69, H 10.94; found C 71.58, H 11.18.

(2*S,3*S**)-Diol *syn*-7d:** Following general procedure E, a solution of the ester *syn*-**6d** (761 mg, 2.1 mmol) in THF (10 mL) was treated with DIBAL (10.5 mmol) to afford the diol *syn*-**7d** (331 mg, 75%) as a colorless oil and (−)-menthol (328 mg, 100%) as a white solid. Spectral data for the (2*S**,3*S**)-diastereomer are reported from a mixture of two diastereomers. The assignment is based on COSY and HSQC experiments. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.1 Hz, 3 H, -CH$_2$CH$_2$C*H*$_3$), 1.05−1.42 (series of m, 3 H, -C*H*$_2$C*H*$_2$CH$_3$), 1.57−1.73 (m, 1 H, -C*H*$_2$CH$_2$CH$_3$), 1.73 (br. s, 2 H, OH), 1.82−1.94 (m, 2 H, =CHCH$_2$C*H*$_2$CH$_2$CH=), 2.16−2.26 (m, 1 H, 3-H), 2.26−2.44 (m, 4 H, =CHC*H*$_2$CH$_2$C*H*$_2$CH=), 3.55−3.70 (m, 2 H, 1-H), 5.02−5.14 (m, 2 H, 5-H), 5.53−5.64 (m, 1 H, 4-H), 5.64−5.68 (m, 1 H, =CHCH$_2$CH$_2$CH$_2$C*H*=). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9 (-CH$_2$CH$_2$*C*H$_3$), 20.7 (-CH$_2$*C*H$_2$CH$_3$), 23.7 (=CHCH$_2$*C*H$_2$CH$_2$CH=), 30.3 (-CH$_2$*C*H$_2$CH$_3$), 32.2 and 32.9 (=CH*C*H$_2$CH$_2$*C*H$_2$CH=), 50.8 (C-3), 66.7 (C-1), 77.2 (C-2), 117.1 (C-5), 127.2 (=CHCH$_2$CH$_2$CH$_2$*C*H=), 138.3 (C-3). − IR (neat): $\tilde{\nu}$ = 3420 cm^{-1}. − $C_{13}H_{22}O_2$ (210.3): calcd. C 74.24, H 10.54; found C 73.60, H 8.02; we were unable to obtain an accurate combustion analysis for this compound.

(2*S,3*S**)- and (2*S**,3*R**)-Diol 7e:** Following the general procedure E, a solution of the ester **6e** (520 mg, 1.17 mmol) in THF (10 mL)

was treated with DIBAL (7.05 mmol) to afford the diol **7e** (181 mg, 57%) as a colorless oil and (−)-menthol (175 mg, 96%) as a white solid. Spectral data are reported for a mixture of two diastereomers (86:14). The assignment is based on COSY and HSQC experiments. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.73 (t, *J* = 7.1 Hz, 3 H^{major}, -$CH_2CH_2CH_3$), 0.73 (t, hidden signal, 3 H^{minor}), 0.90−1.05 (m, 1 + 1 H, -$CH_2CH_2CH_3$), 1.18−1.44 (m, 3 + 3 H, -$CH_2CH_2CH_3$), 1.81 (br. s, 2 H^{minor}, OH), 2.16 (br. s, 2 H^{major}, OH), 2.20−2.30 (m, 2 + 2 H, ArCH_2CH_2CH=CAr-), 2.60−2.84 (m, 3 + 3 H, -ArCH_2CH_2CH=CAr-, 3-H), 3.71 (d, *J* = 11.4 Hz, 1 H^{major}, 1-H), 4.02 (d, *J* = 11.4 Hz, 1 H^{major}, 1-H), 5.04 (dd, *J* = 17, 2 Hz, 1 H^{major}, 5-H), 5.13 (dd, *J* = 10, 2 Hz, 1 H^{minor}, 5-H), 5.17 (dd, *J* = 10, 2 Hz, 1 H^{major}, 5-H), 5.68 (ddd, *J* = 10, 10, 17 Hz, 1 H^{major}, 4-H), 5.80 (ddd, *J* = 10, 10, 17 Hz, 1 H^{minor}, 4-H), 6.24 (t, *J* = 5 Hz, 1 H^{major}, ArCH_2CH_2CH=CAr-), 6.41 (t, *J* = 5 Hz, 1 H^{minor} ArCH_2CH_2CH=CAr-), 7.08−7.21 (m, 3 + 3 H, aryl-H), 7.51−7.56 (m, 1 H^{minor}, aryl-H), 7.88 (d, *J* = 7.5 Hz, 1 H^{major}, aryl-H). − Major diastereomer: ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.7 (-$CH_2CH_2CH_3$), 20.9 (-$CH_2CH_2CH_3$), 23.2 (-$CH_2CH_2CH_3$), 28.98 (-ArCH_2CH_2CH=CAr-), 30.8 (-ArCH_2CH_2CH=CAr-), 49.8 (C-3), 65.6 (C-1), 79.1 (C-2), 118.5 (C-5), 125.8 (aryl-C), 125.9 (aryl-C), 126.5 (aryl-C), 127.7 (aryl-C), 129.1 (-ArCH_2CH_2CH=CAr-), 133.4, 137.0, 138.1, 138.2 (C-4). − Minor diastereomer: ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.6, 20.2, 23.2, 29.1, 30.1, 49.6, 67.4, 79.2, 117.1, 124.7, 125.9, 126.6, 127.9, 129.2, 133.1, 137.2, 139.1. − IR (neat): $\tilde{\nu}$ = 3405 cm^{-1}. − $C_{18}H_{24}O_2$ (272.4): calcd. C 79.37, H 8.88; found C 79.45, H 9.15.

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