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VIP

Radical Cyclization of α-Bromo Aluminum Acetals onto Alkenes and Alkynes (Radic[Al] Process): A Simple Access to γ-Lactols and 4-Methylene-γ-Lactols

Anne Boussonnière, Romain Bénéteau, Nicolas Zimmermann, Jacques Lebreton,* and Fabrice Dénès*[a]

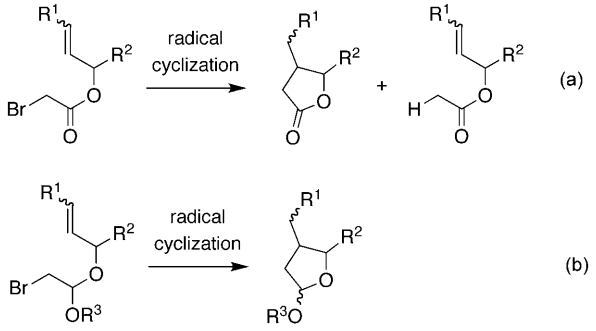
Abstract: An efficient preparation of γ-lactols and methylene-γ-lactols is described. Highly acid-sensitive lactols are prepared in a concise manner by using a radical cyclization of aluminum acetals. The precursors for the radical reactions are readily prepared from allyl or propargyl alcohols and α-bromo acids. Functionalization of the resulting γ-lactols and methylene-γ-lactols can be achieved following isolation, leading to synthetically useful building blocks, such as 1,4-diols, 1,4-dienes, γ-lactones, and polysubstituted tetrahydrofurans.

Keywords: aluminum acetals · bond-forming reactions · cyclization · lactols · radical reactions

Introduction

γ-Lactols represent versatile intermediates that can be easily converted into the corresponding lactones. They can be regarded as masked aldehydes and thus transformations involving the reactivity of the carbonyl group (e.g., Wittig olefination, nucleophilic addition, etc.) can be achieved, leading to the corresponding ring-opening products. Moreover, substitution of the hydroxyl group can be conveniently achieved by using various nucleophiles (e.g., allylsilanes, silicon hydrides, thiols or selenols, etc.), thus delivering the corresponding tetrahydrofuran derivatives and giving an entry to sugar and nucleoside chemistry. The versatility of saturated γ-lactols has been extensively exploited in the past, whereas the functionalization of related 4-methylene-γ-lactols has not been, thus far, the subject of intensive studies. The absence of general methods allowing an easy access to this highly acid-sensitive class of compounds might be responsible for this apparent lack of interest. We report herein a new access to γ-lactols and 4-methylene-γ-lactols based on a one-pot sequence involving the radical cyclization of thermally labile α-bromo aluminum acetals.

Radical reactions have been intensively investigated during the last three decades.[1] The new synthetic methods that arose from this work are characterized by their mildness and their complementarity to ionic processes. In particular, radical cyclizations have proven very successful for the preparation of five-membered rings. However, as a result of conformational constraints the radical cyclization of *O*-allyl- and *O*-propargyl α-haloesters under reducing conditions to form γ-lactones and methylene-γ-lactones, respectively, is not an efficient process. Although some isolated examples have been reported,[2] no general method is available to achieve the radical cyclization of α-haloesters, especially when the reaction has to be carried out at a low temperature and under reducing conditions (Scheme 1a). The cyclization of



Scheme 1. Radical cyclization of α-bromo esters (a) and α-bromo acetals (b).

α-haloacetals (the Ueno–Stork reaction),[3] developed independently by Ueno[4] and Stork[5] in the 1980s, has become a very popular approach to solve the problems encountered in the cyclization of related α-bromo esters under reductive conditions (Scheme 1b).[6] The resulting cyclic acetals have proven to be useful precursors for the corresponding lactols and lactones, though these transformations imply the use of Brönsted or Lewis acidic conditions, which constitutes a lim-

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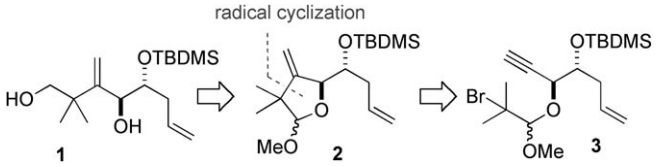
itation for this approach in the case of substrates possessing highly acid-sensitive functionalities.[7]

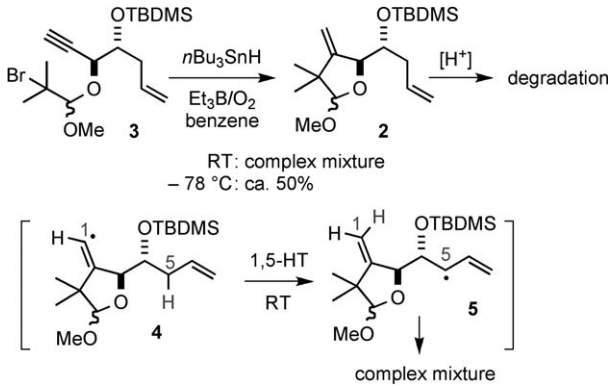
Results and Discussion

During the course of our research on the synthesis of biologically relevant macrocyclic compounds from marine sources, we were in need for diol **1** as a key intermediate. The desired diol **1** was expected to be obtained from cyclic acetal **2** by hydrolysis into the corresponding γ-lactol, followed by ring-opening in the presence of a metal hydride. We decided to then investigate the cyclization of bromo acetal **3** under Ueno–Stork conditions to form the cyclic acetal **2** (Scheme 2).



Scheme 2. Retrosynthetic analysis for the preparation of key-intermediate **1**.

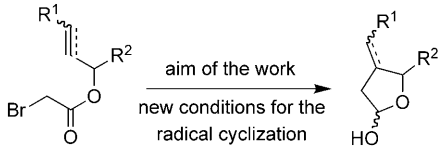
Attempts at cyclizing α-bromo acetal **3** (Scheme 3) at room temperature in toluene, in the presence of nBu$_3$SnH and by using Et$_3$B/O$_2$ as a radical initiator, led to a complex mixture the origin of which was attributed to the formation of a highly reactive vinyl radical intermediate **4**. Indeed,



Scheme 3. Radical cyclization of α-bromo acetal **3** under classical Ueno–Stork conditions.

such vinyl radicals are known to undergo 1,5-hydrogen transfer,[8] a rearrangement facilitated in the case of **4** by both a geminal effect of the substituents[9] and by the stabilization of the resulting radical species **5**. Although 1,5-hydrogen transfer in vinyl radicals is usually favored at higher temperatures, examples of translocation at room temperature have also been reported.[10]

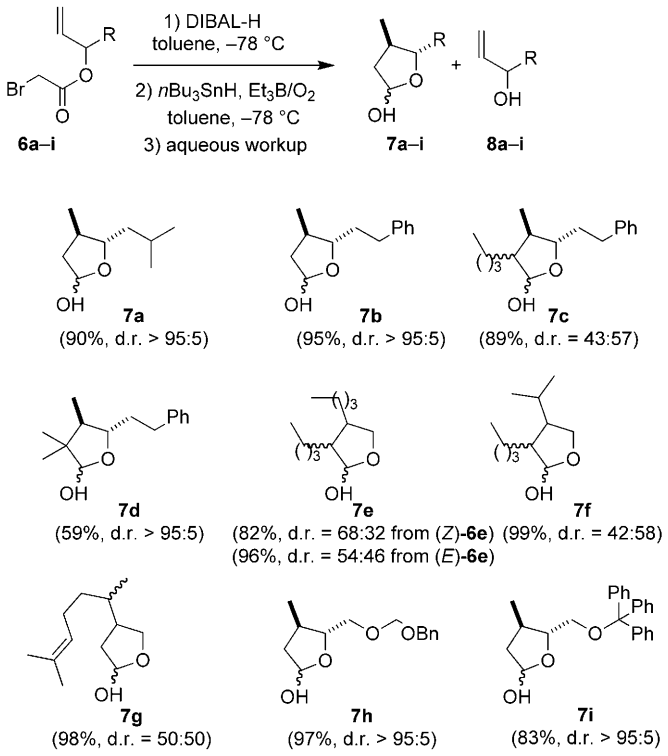
Accordingly, by performing the radical cyclization at −78 °C, the competitive process could be suppressed and the desired cyclic acetal **2** was obtained in 50% yield (unoptimized). Unfortunately, the hydrolysis of acetal **2** into the corresponding γ-lactols proved to be, in our hands, unsuccessful. These observations clearly indicate that, even at relatively high concentrations in tin hydride (initially 10^{-1} mol L^{-1} in our case), side reactions are to be expected when conducting the radical cyclization of α-bromo acetals or α-bromo esters onto carbon–carbon triple bonds at temperatures allowing the vinyl radical intermediate to undergo rearrangements. Moreover, the presence of acid-sensitive functionalities on the substrate (a *O*-TBDMS (TBDMS = *tert*-butyldimethylsilyl) silyl ether in compound **2**) severely limits the reaction conditions to choose from to access γ-lactols from cyclic acetals and calls for a new synthetic method. Ideally, the latter should allow one to perform the radical cyclization at low temperature from simple precursors and would deliver the desired γ-lactols without the need for an additional step. These observations prompted us to develop a more practical approach to γ-lactols, starting from α-bromo esters the preparation of which under classical esterification conditions is well documented, by using a one-pot reaction involving the formation of an α-bromo aluminum acetal and its cyclization under reductive radical conditions at low temperature (Scheme 4).[11]



Scheme 4. Aim of the work.

Aluminum acetals are well-known intermediates commonly obtained from carboxylic acid esters by reduction with aluminum hydrides. When di-*iso*-butylaluminum hydride (DIBAL-H) is used as a reducing agent, the aluminum acetal intermediates have proven to be stable at low temperature, thus allowing the selective reduction of carboxylic acid esters into the corresponding aldehydes with limited over-reduction into the alcohols.[12,13] Since the 1980s, aluminum acetals have found some applications in organic synthesis. In particular, they have been trapped with electrophiles, such as silyl triflates and silyl imidazole or acetic anhydride and acid fluorides to give the corresponding monosilyl acetals[14–16] and α-acetoxy acetals,[17,18] respectively. The latter were found to be very efficient for the generation of oxacarbenium ions, which could engage further in Prins[19] and oxonia-Cope[20] rearrangements or could be trapped by various nucleophiles.[21,22] Despite the aforementioned applications of aluminum acetals in ionic processes, their use as intermediates in radical reactions was unknown until very recently, since our group reported a convenient radical cyclization of *O*-allyl-α-bromo esters leading to γ-lactols.[11]

Cyclization of *O*-allyl-α-bromo esters: α-Bromo esters **6a–i** were easily prepared in high yields from allylic alcohols **8a–i** and α-bromo acids by using standard procedures for esterification (see the Supporting Information for details). We started a feasibility study in which various α-bromo aluminum acetals were generated by DIBAL-H reduction of the parent α-bromo esters and subsequently subjected to radical cyclization conditions according to (Scheme 5).

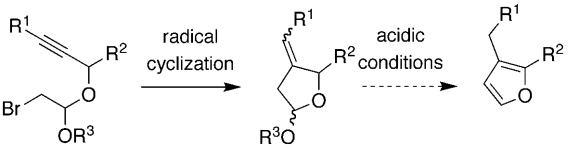


Scheme 5. Preparation of γ-lactols by sequential one-pot reduction–cyclization of α-bromo esters (Radic[Al] process).

α-Bromo ester **6a**, which has a substituent at the allylic position, was converted into the corresponding aluminum acetal by reduction with DIBAL-H in toluene at −78 °C. After complete disappearance of the starting material (ca. 15–30 min, TLC monitoring indicates formation of alcohol **8a**), tri-*n*-butyltin hydride (1.1–1.3 equiv) and Et_3B (0.3-1 equiv, 1 M in hexane) were simultaneously introduced at −78 °C, followed by air (ca. 1 mL). The conversion was monitored by TLC analysis, which allowed the disappearance of alcohol **8a** to be observed. Gratifyingly, the desired γ-lactol **7a** was obtained in 90% yield, following aqueous workup and purification by flash chromatography over silica gel (Scheme 5). Similarly, substrate **6b** led to the desired γ-lactol **7b** in 95% yield. Substituents at the carboxylic acid moiety were also tolerated, as illustrated by the cyclization to **7c–f**. In most cases, only trace amounts of over-reduction products **8a–i** could be detected but for **6d**, which gave the expected γ-lactol **7d** in somewhat lower yield (59%) together with a significant amount (ca. 40%) of recovered alcohol **8d**. Mono- and disusbtitution at the terminal position of the alkene also led to the γ-lactols in high yields (82–99%). As illustrated by the cyclization of esters **6h** and **6i**, which both contain labile protecting groups, such as benzyloxy methyl (BOM) or trityl (Tr), the method tolerates acid-sensitive functionalities, the corresponding γ-lactols **7h** and **7i** being isolated in good to high yields.

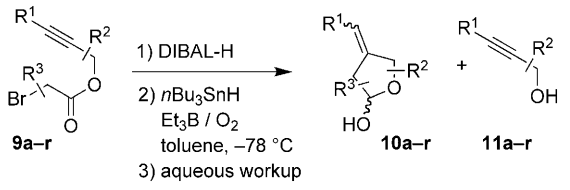
Disregarding the hemiacetal center, the stereoselectivity of the cyclization reaction leading to **7a–d** and **7h–i** (C_4–C_5 selectivity) was in all cases over 95:5. For clarity, the selectivity reported in Scheme 5 does not take into account the hemiacetal center.

Cyclization of *O*-propargyl-α-bromo esters: We then turned our attention to the more challenging formation of 4-methylene-γ-lactols. The radical cyclization of α-halo acetals onto the carbon–carbon triple bond has been found to be an efficient process since the early development of this methodology (Scheme 6).[23] Nevertheless, the hydrolysis of the cyclic acetal generally results in the aromatization into the furan derivatives instead of delivering the desired methylene-γ-lactols.[24–27]



Scheme 6. Radical cyclization of α-bromo acetals onto carbon–carbon triple bonds under classical Ueno–Stork conditions.

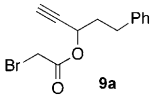
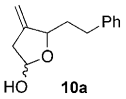
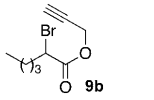
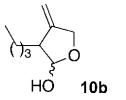
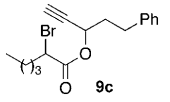
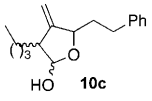
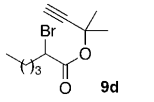
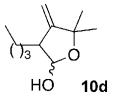
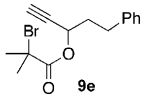
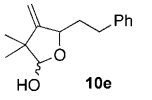
We envisioned that our strategy could be applicable to the cyclization of *O*-propargyl-α-bromo esters, allowing a more practical approach to highly acid-sensitive methylene-γ-lactols, by starting from easily available α-bromo esters. A series of representative α-bromo esters were prepared by using standard protocols for esterification and they engaged in the tandem Radic[Al] reaction, according to Scheme 7.



Scheme 7. Preparation of 4-methylene-γ-lactols by sequential one-pot reduction–cyclization of α-bromo esters (Radic[Al] process).

The reduction/cyclization sequence was examined first with α-bromo esters **9a–e** containing a terminal alkyne. The results are collected in Table 1. In most cases, the tandem reaction proved successful, with the acid-sensitive methylene-γ-lactols being isolated in good to high yields. For instance, cyclization of **9a** led to the corresponding methylene-γ-lactols **10a** in 67% yield (Table 1, entry 1). The latter,

Table 1. Synthesis of 4-methylene-γ-lactols by using the reduction–cyclization sequence.

Entry	Substrate[a]	Product[b]	Yield [%][c]
1	 **9a**	 **10a**	67
2	 **9b**	 **10b**	82
3	 **9c**	 **10c**	77[d]
4	 **9d**	 **10d**	79[e]
5	 **9e**	 **10e**	57[e]

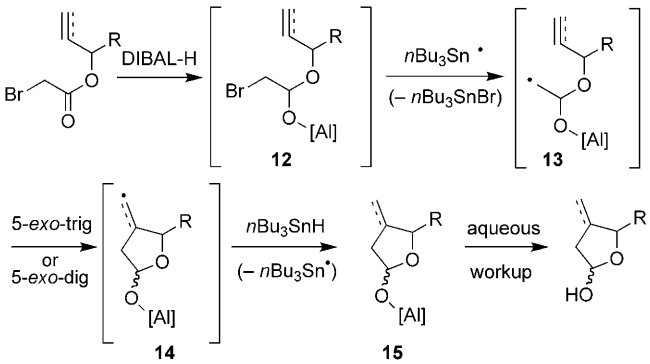
[a] All reactions were carried out with α-bromo esters (2 mmol) in toluene (see the Supporting Information for details), by using DIBAL-H (1.1 equiv) at −78 °C, then nBu$_3$SnH (1.1 equiv) and Et$_3$B (0.3–1.1 equiv), unless otherwise stated. [b] Lactols were isolated as mixture of diastereoisomers. [c] Yields of isolated products. [d] Diastereoselectivity C_3–C_5: d.r. = 62:38. [e] Two equivalents of DIBAL-H were used for the reduction.

however, was found to be particularly unstable and could not be stored for a prolonged period of time. Similar results were obtained with **9b** and **9c**, which afforded **10b** and **10c** in 82 and 77% yields, respectively (Table 1, entries 2 and 3). α-Bromo esters **9d** presenting a *gem*-disubstituted position, which could prevent aromatization into the corresponding furans, led to the expected methylene-γ-lactols **10d** in 79% yield (Table 1, entry 4). It is worthy of note that the reduction of **9d** required the use of two equivalents of DIBAL-H to reach complete conversion. Similarly, reduction of the more hindered α-bromo esters **9e** also required the use of an excess of DIBAL-H. In this case, the radical cyclization led to the expected lactol **10e** in only 57% yield (Table 1, entry 5).

With these promising results in hands, we then turned our attention to the preparation of alkylidene- and arylidene-γ-lactols. The results are presented in Table 2. Under the same reaction conditions, α-bromo ester **9f** gave the corresponding alkylidene-γ-lactol **10f** in 78% yield and with a moderate *E*/*Z* selectivity in favor of the *E* isomer (*E*/*Z* 71:29, Table 2, entry 1). The diastereoselectivity could be slightly increased by using a bulkier alkyl substituent (vide infra, Table 2, entry 4). Cyclization of **9g**, containing a *gem*-disubstitution at the propargylic position, led to **10g** in excellent yield (Table 2, entry 2). On the other hand, *gem*-disubstituted α-bromo ester **9h** was converted into lactol **10h** in moderate yield (Table 2, entry 3). Alkylidene-γ-lactol **10i** was obtained in 74% yield from **9i** as a 82:18 mixture of *E*/*Z* isomers (Table 2, entry 4). The reduction/cyclization sequence carried out with **9j**, which presents a TMS-substituted alkynyl moiety, gave the corresponding lactol **10j** in 94% yield (*E*/*Z* 31:69, Table 2, entry 5). Arylidene-γ-lactols **10k** and **10l** were obtained in 88 and 91% yields, respectively, from esters **9k** and **9l**, which both present a phenyl-substituted alkynyl side chain (Table 2, entries 6 and 7). It is worthy of note that under our reaction conditions (−78 °C, initial concentration of nBu$_3$SnH of 1.1×10^{-1} mol.L^{-1}) compound **10l** could be isolated in high yield without any traces of bicyclic products resulting from a 6-*exo*-trig cyclization onto the pendant alkenyl side chain. Accordingly, the cyclization of **9m** and **9n** led to **10m** and **10n** in moderate to high yields (Table 2, entries 8 and 9) with high levels of diastereoselectivity (*E*/*Z* > 95:5 and *E*/*Z* = 5:95, respectively). As previously observed for **9e** and **9h**, the reduction of the sterically demanding α-bromo ester **9m** was better achieved in the presence of two equivalents of DIBAL-H.

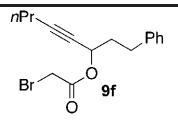
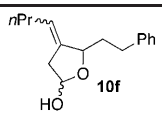
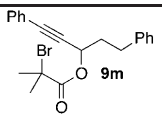
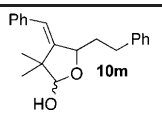
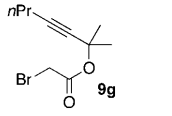
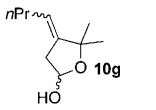
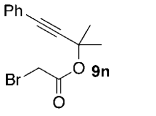
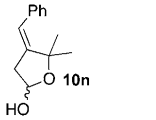
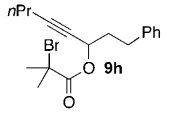
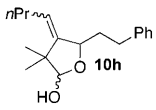
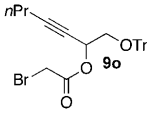
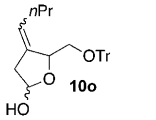
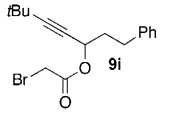
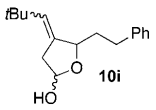
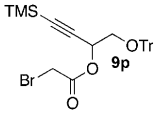
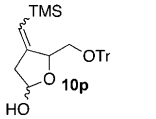
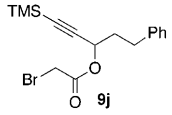
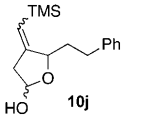
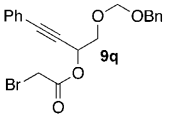
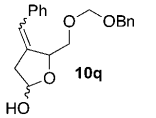
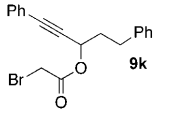
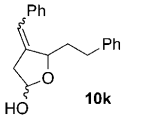
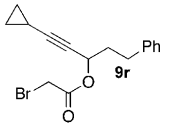
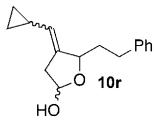
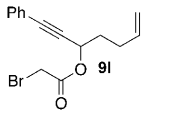
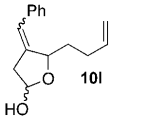
As illustrated by the cyclization of some representative substrates and/or lactols presented in Table 2, the method tolerates the presence of acid-sensitive functionalities. For instance, under the previously described reaction conditions, α-bromo esters **9o** and **9p** afforded the corresponding lactols **10o** and **10p** in satisfactory yields (72 and 74%, respectively) without cleavage of the *O*-trityl bond (Table 2, entries 10 and 11). Similarly, the *O*-benzyloxymethyl-protected arylidene-γ-lactol **10q** could be obtained in 69% yield from **9q** (Table 2, entry 12). Under the same reaction conditions, the cyclization of **9r** led to methylene-γ-lactol **10r** in 78% yield, without ring-opening of the cyclopropylvinyl radical intermediate (Table 2, entry 13).[28]

Mechanistic considerations: The following mechanistic rational can be proposed to account for the results obtained in both series (*O*-allyl- and *O*-propargyl esters). Aluminum acetal **12**, obtained by reduction of the α-bromo ester with DIBAL-H, undergoes halogen abstraction by the tin-centered radical, generated from nBu$_3$SnH in the presence of Et$_3$B/O$_2$ as a radical initiator, to form the corresponding carbon-centered radical **13**, which undergoes a 5-*exo*-trig or 5-*exo*-dig radical cyclization to give **14** (Scheme 8). Hydrogen-atom abstraction from the tin hydride reagent by the cyclized carbon-centered radical **14** gives the cyclic aluminum



Scheme 8. Mechanistic proposal for the cyclization of α-bromo esters by using the Radic[Al] process.

Table 2. Synthesis of alkylidene- and arylidene-γ-lactols by using the reduction–cyclization sequence (Radic[Al] process).

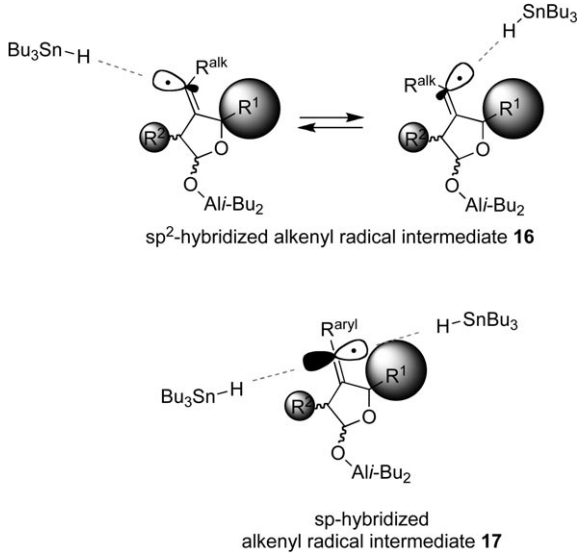
Entry	α-Bromo ester[a]	Product[b]	d.r.[c]	Yield [%][d]	Entry	α-Bromo ester[a]	Product[b]	d.r.[c]	Yield [%][d]
1			71:29	78	8			>95:5	58[e]
2			63:37	99[e]	9			5:95	94[e]
3			62:38	50[e]	10			37:63	72
4			82:18	74	11			17:83	74
5			31:69	94	12			26:74	69
6			26:74	88	13			52:48	78
7			22:78	91					

[a] Unless otherwise stated, all reactions were carried out with α-bromo esters (2 mmol) in toluene (see the Experimental Section for details), by using DIBAL-H (1.1 equiv) at −78 °C, then nBu$_3$SnH (1.1–1.3 equiv), Et$_3$B (0.3–1.1 equiv), and air (ca. 1 mL). [b] Major E/Z isomer shown. [c] E/Z selectivity determined by NMR spectroscopic analysis after reduction into the corresponding diols with NaBH$_4$ or LiAlH$_4$ (see below and the Supporting Information for details). For clarity reasons, the selectivity reported in Table 2 does not take into account the hemiacetal center. [d] Yields of isolated products. [e] Two equivalents of DIBAL-H were used for the reduction.

acetal **15**, which leads to the γ-lactol upon aqueous workup. To the best of our knowledge, this is the first report of a reaction involving a radical aluminum acetal species.

The cyclization of aluminum acetals onto internal alkynes led to a mixture of E and Z isomers. The nature of the substituent at the terminal position of the alkyne and the presence of side chains on the lactol ring showed a strong influence on the diastereoselectivity. The reverse E/Z selectivity observed for **10k** and **10l** relative to **10f** and **10i** (Table 2, entries 6 and 7, vs. entries 1 and 4) is in agreement with previous studies, which have demonstrated that sp-hybridized phenyl-substituted vinyl radicals, such as **17** (Scheme 9), are trapped under kinetic control from the less hindered side and thus lead to the less stable Z olefins, whereas sp^2-hybridized vinyl radicals, such as **16** (Scheme 9), preferentially abstract a hydrogen atom from the more hindered side (except for **10h**), leading to the more stable E olefin.[29–31] Accordingly, the cyclization of **9m** and **9n** into **10m** and **10n** (Table 2, entries 8 and 9) occurred with high levels of diastereoselectivity (E/Z > 95:5 and E/Z 5:95, respectively).

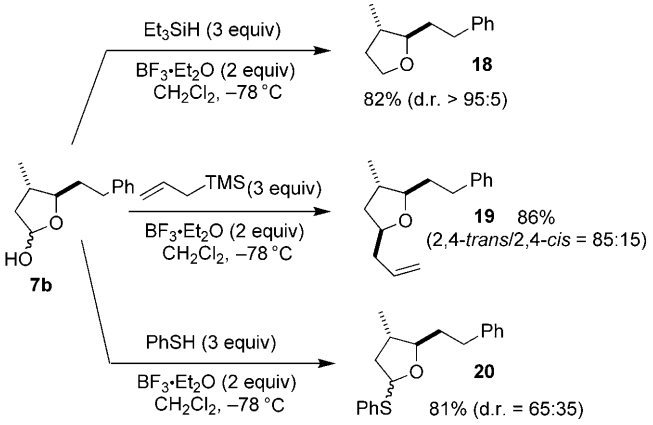
Interestingly, the radical cyclization onto 1-TMS-alkynes also led to the more sterically demanding Z olefin, thus sup-



Scheme 9. Hydrogen abstraction from nBu$_3$SnH by the alkenyl radical intermediate under kinetic control. Stereoselectivity outcome depending upon the nature of the alkenyl radical and the substituents.

porting previous reports in which alkenyl radicals substituted with a silyl group are believed to be sp-hybridized.[32] The nature of the protecting group of the hydroxyl functionality in **9o**, **9p**, and **9q** also played a role in the control of the carbon–carbon double bond configuration. Indeed, while no significant changes have been observed in the cyclization of aryl-substituted alkynes **9k**, **9l**, and **9q**, the *E*/*Z* selectivity was either reversed (71:29 and 37:63, for **10f** and **10o**, respectively), or increased (from 31:69 to 17:83 for **10j** and **10p**, respectively) by using a bulky triphenylmethyl protecting group.

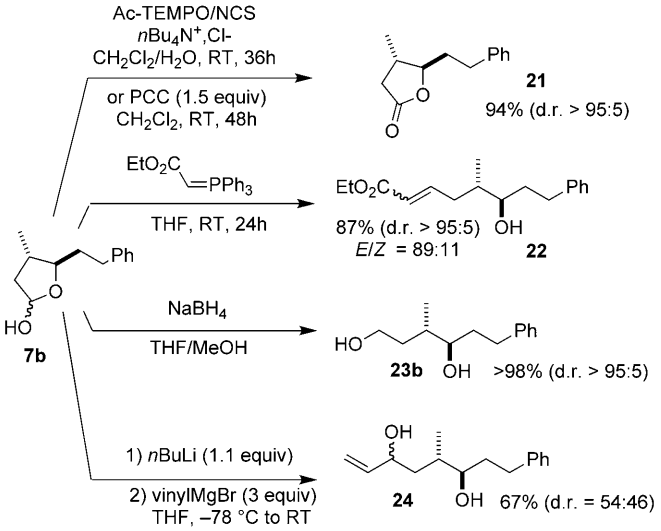
Functionalization of γ-lactols and 4-methylene-γ-lactols: The versatility of the resulting γ-lactols was illustrated by various transformations. For instance, reaction with allyltrimethyl silane,[33,34] thiophenol, or Et_3SiH[33] in the presence of $BF_3{\cdot}Et_2O$ gave the corresponding tetrahydrofurans **18**–**20** in good yields (>80% from **7b**, Scheme 10).



Scheme 10. Illustration of the versatility of γ-lactols by using their reactivity as oxonium ion precursors.

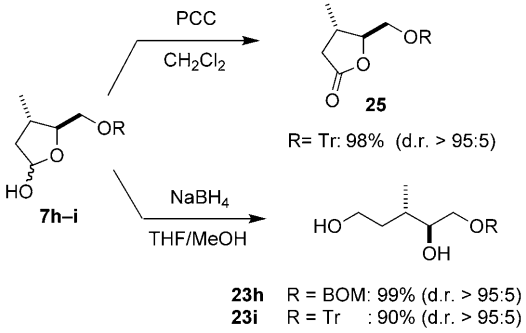
Oxidation of γ-lactol **7b** could be achieved by the use of Ac-2,2,6,6-tetramethylpiperidine *N*-oxide (Ac-TEMPO) in the presence of *N*-chlorosuccinimide (NCS) under phase-transfer conditions, or alternatively in the presence of pyridinium chlorochromate (PCC), leading to lactone **21** in quantitative yield (Scheme 11). Olefination with three equivalents of a stabilized phosphorous ylide was carried out in THF at room temperature and gave **22** in 87% yield as an 89:11 mixture of *E*/*Z* isomers. Ring-opening of lactol **7b** could also be achieved under mild conditions either with sodium borohydride in THF/MeOH or by the use of a vinyl Grignard reagent, following metallation with *n*BuLi, to give 1,4-diols **23b** and **24**, respectively.

More interestingly, PCC oxidation of **7i**, for which the hydroxyl group was protected as a highly acid-sensitive triphenylmethyl ether, gave lactone **25** in high yield as a single diastereoisomer. Reduction of γ-lactols **7h** and **7i**, which both possess an acid-sensitive protecting group for the hydroxyl moiety, into the corresponding mono-protected triols **23h** and **23i** could also be achieved in high yields (99 and



Scheme 11. Illustration of the versatility of γ-lactols by using their reactivity as masked aldehydes.

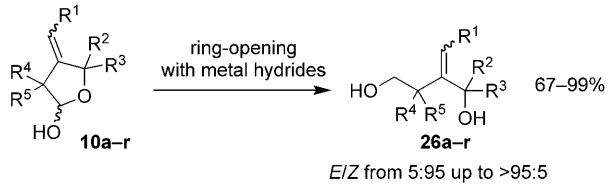
90% yield, respectively) under very mild conditions (Scheme 12). Note that the latter transformations could not be achieved directly from cyclic acetals obtained by the classical Ueno–Stork reaction.



Scheme 12. Oxidation and reduction of γ-lactols possessing acid-sensitive functionalities.

The reactivity of 4-methylene-γ-lactols with various nucleophiles was then investigated. We first turned our attention to the ring-opening of methylene-, alkylidene-, and arylidene-γ-lactols with hydrides. Gratifyingly, lactols **10a**–**r** were efficiently converted into the corresponding 1,4-diols **26a**–**r** under mild reaction conditions, according to Scheme 13. In the case of alkylidene- and arylidene-γ-lactols, the diols were obtained as an *E*/*Z* mixture of diastereoisomers, thus allowing *E*/*Z* ratio (for lactols **10f**–**r**) and the diastereomeric C_2–C_4 ratio (for lactols **10c**) to be determined at this stage. The results are presented in Table 3.

The reduction of 4-methylene-γ-lactols **10a**–**d** (Table 3, entries 1–4) could be easily achieved at room temperature by using sodium borohydride in THF/MeOH, leading to the



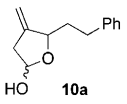
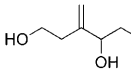
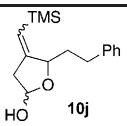
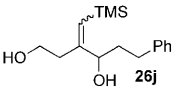
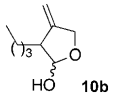
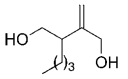
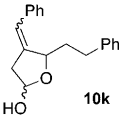
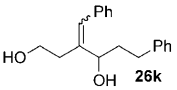
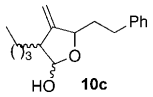
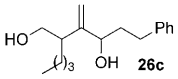
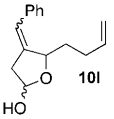
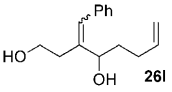
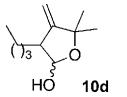
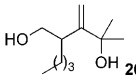
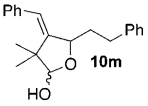
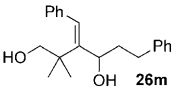
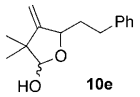
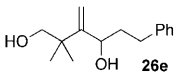
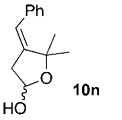
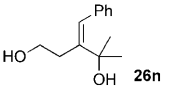
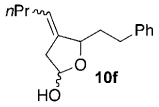
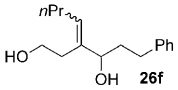
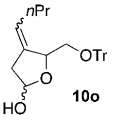
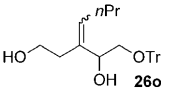
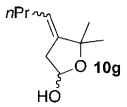
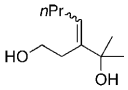
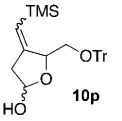
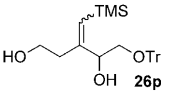
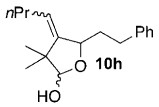
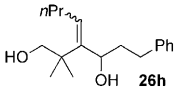
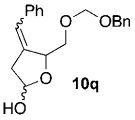
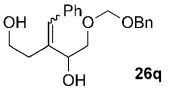
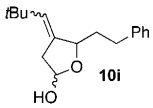
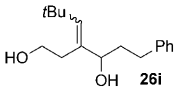
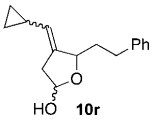
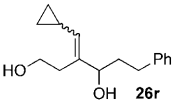
Scheme 13. Reduction of 4-methylene-γ-lactols into 1,4-diols.

desired 1,4-diols **26a–d** in good to high yields (67–99%). On the other hand, compound **10e** containing a *gem*-dimethyl substitution next to the hemiacetal center proved to be unreactive under similar reaction conditions.

In this case, a more powerful reducing agent, such as lithium aluminum hydride was needed to give diol **26e** in high yield (Table 3, entry 5). Similarly, other hindered lactols, such as alkylidene- and arylidene-4-methylene-γ-lactols **10h** and **10m** (Table 3, entries 8 and 13) required the use of $LiAlH_4$ for the reduction into the corresponding diols **26h** and **26m** (99 and 85% yields, respectively), whereas nonhindered alkylidene- and arylidene-4-methylene-γ-lactols **10f**, **10g**, **10i–l**, **10n**, **10o**, **10q**, and **10r** could be reduced in good to high yields with the use of a milder reducing agent (Table 3, entries 6, 7, 9–12, 14, 15, 17, and 18). In the case of the highly acid-sensitive γ-lactols **26p**, the best results were obtained with sodium bis(2-methoxyethoxy)aluminumhydride (Red-Al) in CH_2Cl_2.

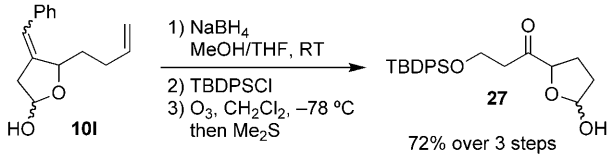
Interestingly, 4-methylene-γ-lactol **10l** could be conveniently converted into lactol **27** in a three-step sequence involving the ring-opening of **10l** with sodium borohydride to give diol **26l**, followed by selective protection of the primary hydroxyl group and oxidative cleavage of the two carbon–carbon double bonds with ozone. The resulting γ-hydroxy al-

Table 3. Reduction of γ-lactols **10a–r** into 1,4-diols with hydrides.

Entry	Substrate[a]	Product	Yield [%][b]	d.r.[c]	Entry	Substrate[a]	Product	Yield [%][b]	d.r.[c]
1	 **10a**	 **26a**	99	–	10	 **10j**	 **26j**	82	31:69
2	 **10b**	 **26b**	92	–	11	 **10k**	 **26k**	91	26:74
3	 **10c**	 **26c**	67	62:38[d]	12	 **10l**	 **26l**	93	28:72
4	 **10d**	 **26d**	99	–	13	 **10m**	 **26m**	85[e]	>95:5
5	 **10e**	 **26e**	99[e]	–	14	 **10n**	 **26n**	94	5:95
6	 **10f**	 **26f**	97	71:29	15	 **10o**	 **26o**	78	37:63
7	 **10g**	 **26g**	91	33:67	16	 **10p**	 **26p**	67[f]	17:83
8	 **10h**	 **26h**	99[e]	62:38	17	 **10q**	 **26q**	87	26:74
9	 **10i**	 **26i**	99	82:18	18	 **10r**	 **26r**	80	53:47

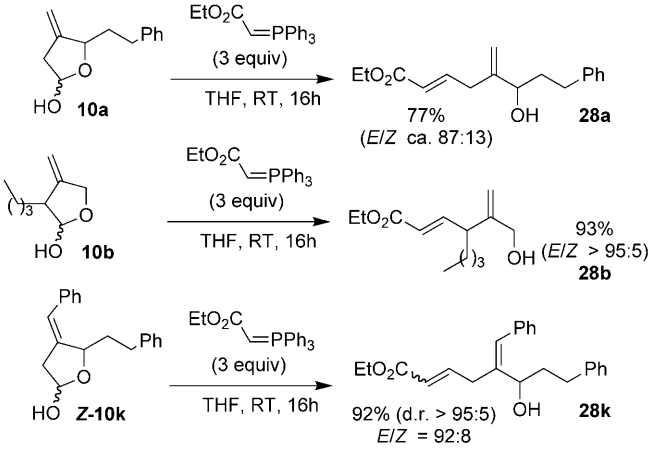
[a] All reactions were carried out with $NaBH_4$ in MeOH/THF at room temperature, unless otherwise stated. [b] Yields of isolated products. [c] Selectivity *E*/*Z* determined by NMR spectroscopy (NOE measurements). [d] d.r. C_2–C_4. [e] $LiAlH_4$ was used. [f] Red-Al was used.

dehyde spontaneously cyclized into lactol **27** (72% yield for the three steps) giving an entry to 2,5-disubstituted tetrahydrofuran derivatives (Scheme 14).



Scheme 14. Three-step sequence for the preparation of lactol **27** from lactol **10l**. TBDPS = *tert*-butyldiphenylsilyl.

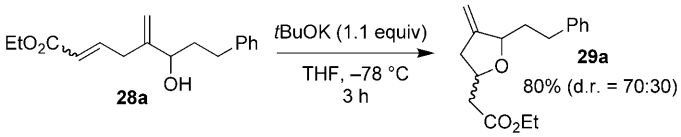
The reactivity of alkylidene- and arylidene-γ-lactols under Wittig–Horner conditions was then investigated. Olefination reactions proved successful, as illustrated by the reaction of **10a–b** and (*Z*)-**10k** with a stabilized phosphorous ylide delivering 1,4-dienes **28a–b** and **28k** in high yields, without migration of the double bond (Scheme 15). Whilst 5-substituted-γ-lactols **10a** and (*Z*)-**10k** led to the desired 1,4-dienes in good to high yields but with only moderate levels of diastereoselectivity in favor of the *E* isomer (*E*/*Z* ca. 90:10), the olefination reaction from **10b** proved to be highly stereoselective, the corresponding diene **28b** being obtained exclusively as the *E* isomer with no traces of the *Z* isomer detected by NMR spectroscopic analysis of the crude reaction mixture.



Scheme 15. Olefination of 4-methylene-γ-lactols by using stabilized phosphorous ylides.

Gratifyingly, attempts at cyclizing diene **28a** under basic conditions (1.1 equiv of *t*BuOK) revealed the desired methylene-tetrahydrofurans **29a** without migration of the exocyclic carbon–carbon double bond (Scheme 16).

Contrary to saturated lactols, such as **7b**, functionalization of 4-methylene-γ-lactols, such as **10a**, in the presence of Lewis acids proved thus far unsuccessful. The high sensitivity to acidic media of this class of lactols might account for this observation. On the other hand, more stable 4-arylidene-γ-lactols could engage in new carbon–carbon bond-forming reactions, as illustrated by the highly diastereoselective allylation of (*Z*)-**10k** by using allyltrimethylsilane in the presence of $BF_3{\cdot}Et_2O$, which led to the corresponding polysubstituted tetrahydrofuran **30** with a complete control of the stereochemistry (Scheme 17).



Scheme 16. Base-mediated Michael cyclization of diene **28a**.

Scheme 17. Functionalization of (*Z*)-**10k** with allyltrimethylsilane.

Conclusion

We have reported herein that thermally labile α-bromo aluminum acetal species derived from *O*-allyl-α-bromo esters by reduction with DIBAL-H are very useful intermediates, which are stable enough at low temperature to engage in radical cyclization at a low temperature in the presence of nBu_3SnH and Et_3B/O_2. This one-pot process led to γ-lactols in good to excellent yields. The scope of this reaction could be extended to include the related *O*-propargyl-α-bromo esters, giving access to polysubstituted methylene γ-lactols, a class of highly acid-sensitive compounds the preparation of which by using the classical Ueno–Stork approach proved to be rather difficult. This one-pot procedure appears quite general and efficient, especially when disubstituted alkynyl side chains are employed as radical acceptors. This very simple approach tolerates substitution at the different positions of the starting α-bromo ester derivatives with a high flexibility. Relative to the classical cyclization of α-halo acetals, several advantages of the approach reported here can be highlighted. First, the precursors are easily prepared in high yields by simple esterification of allylic or propargylic alcohols with α-bromo acids by using standard procedures. The mild reaction conditions are compatible with acid-sensitive functionalities, such as labile hydroxy protecting groups. Finally, the versatility of saturated and unsaturated γ-lactols produced by this reaction makes them particularly attractive for further transformations. The classical radical cyclization of α-halo acetals pioneered by Ueno and Stork produces cyclic acetals. The latter represent a protected form of the corresponding aldehyde moiety and are unreactive under basic conditions. On the contrary, the γ-lactols obtained by using the Radic[Al] process could engage directly in reduc-

tion reactions with hydrides under mild conditions, as well in carbon–carbon bond-forming reactions, thus complementing nicely the classical approach. The application of this methodology for the total synthesis of macrolides is currently underway in our laboratory.

Experimental Section

General considerations: All reactions were performed under an argon atmosphere. THF and toluene were distilled from sodium/benzophenone and sodium, respectively. DIBAl-H and *n*-tributyltin hydride were purchased from Acros Organics and Et_3B (1 M in hexanes) from Aldrich. Flash column chromatography (FC): SDS-CarloErba Silica gel 60 ACC (40–63 μm). TLC: Merck silica gel 60 F_{254} analytical plates; detection either with UV (254 nm) or dipping in a solution of $KMnO_4$ (3 g), K_2CO_3 (20 g), NaOH 5% (5 mL) in H_2O (300 mL) or in a solution of vanillin (1 g), H_2SO_4 96% (2 mL) in EtOH (200 mL) and subsequent heating. ^1H and ^{13}C NMR spectra were recorded on a BRUKER ARX300 ($^1H=300$, $^{13}C=75$ MHz) and a BRUKER Avance3 ($^1H=400$, $^{13}C=100$ MHz); chemical shifts (δ) are reported in parts per million (ppm) and coupling constants (J) in Hertz (Hz); chemical shifts in ppm relative to tetramethylsilane ($\delta=0$ ppm) or $CHCl_3$ for ^1H ($\delta=7.26$ ppm) and $CDCl_3$ for ^{13}C ($\delta=77.16$ ppm) for spectra recorded in $CDCl_3$; chemical shift in ppm relative to benzene ($\delta=7.16$ ppm) for ^1H ($\delta=7.16$ ppm) and C_6D_6 for ^{13}C ($\delta=128.02$ ppm) for spectra recorded in C_6D_6. LRMS: Thermo-Finnigan DSQII quadripolar spectrometer (coupled with a TraceUltra GC apparatus); chemical ionization (CI) and electronic impact (EI, 70 eV) *m*/*z* (%); instrument Thermo-Finnigan LCQ Advantage; electrospray ionization (ESI). HRMS: instruments Thermo-Finnigan MAT 95 XL spectrometer or BRUCKER microTOF QII; ionizations (CI, ESI, and EI, 70 eV). IR spectra were recorded on a BRUKER Vector 22 spectrometer; frequencies are reported in cm^{-1}. Melting points (m.p.) were determined on a Stuart Scientific apparatus 7SMP3.

General procedure GP1 for the preparation of γ-lactols: DIBAl-H (4.2 mL, 1.2 M in toluene, 5.0 mmol) was added dropwise to a solution of α-bromoester (5.0 mmol) in toluene (40 mL) under argon at −78 °C. After complete disappearance of the starting material (15 min, TLC monitoring), Et_3B (2.5 mL, 1 M in hexanes, 2.5 mmol), nBu_3SnH (1.34 mL, 5.0 mmol), and air (ca. 1 mL) were simultaneously added dropwise at −78 °C. The mixture was kept at −78 °C until complete disappearance of alcohol (TLC monitoring, vanillin revelation). The cold bath was removed and the reaction mixture quenched by a saturated aqueous solution of NaF. The reaction mixture was stirred vigorously overnight, then placed in a separatory funnel and diluted with CH_2Cl_2 without agitating. The organic phase was collected and the procedure repeated twice. The aqueous phase was then extracted several times with CH_2Cl_2. The resulting organic phase was dried over Na_2SO_4, filtered, concentrated in vacuo, and the residue was purified by flash chromatography.

General procedure GP2 for the preparation of γ-lactols: DIBAL-H (8.4 mL, 1.2 M in toluene, 10.0 mmol) was added dropwise to a solution of α-bromoester (5.0 mmol) in toluene (40 mL) under argon at −78 °C. After complete disappearance of the starting material (15 min, TLC monitoring), Et_3B (2.5 mL, 1 M in hexanes, 2.5 mmol) and nBu_3SnH (1.34 mL, 5.0 mmol) were simultaneously added dropwise at −78 °C. The mixture was kept at −78 °C until complete disappearance of alcohol (TLC monitoring, vanillin revelation). The cold bath was removed and the reaction mixture quenched by a saturated aqueous solution of NaF. The reaction mixture was stirred vigorously overnight, then placed in a separatory funnel and diluted with CH_2Cl_2 without agitating. The organic phase was collected and the procedure repeated twice. The aqueous phase was then extracted twice with CH_2Cl_2. The resulting organic phase was dried over Na_2SO_4, filtered, concentrated in vacuo, and the residue was purified by flash chromatography.

4-Methylene-5-phenethyltetrahydro-2-furanol (10a): The title compound was prepared according to the general procedure GP1 from α-bromoester **9a** (0.57 g, 2 mmol). Flash chromatography (petroleum ether/Et_2O 70:30) gave **10a** (0.27 g, 67%) as a colorless oil. ^1H NMR (C_6D_6, 300 MHz; mixture of two isomers at the hemiacetal center): $\delta=7.33$–7.15 (m, 10H; two isomers), 5.55 (brs, 1H; major isomer), 5.47 (brs, 1H; minor isomer), 4.96 (s, 1H; major isomer), 4.92 (s, 1H; minor isomer), 4.84 (s, 1H; major isomer), 4.79 (s, 1H; minor isomer), 4.76 (brs, 1H; major isomer), 4.47 (br d, $J=9.0$ Hz, 1H; minor isomer), 3.67 (brs, 2H; OH, two isomers), 3.09–2.76 (m, 4H; two isomers), 2.61–2.47 (m, 4H; two isomers), 2.23–1.83 ppm (m, 4H; two isomers); ^{13}C NMR (C_6D_6, 75 MHz; mixture of two isomers at the hemiacetal center): $\delta=149.8$ (C, minor isomer), 149.6 (C, major isomer), 142.44 (C, minor isomer), 142.40 (C, major isomer), 128.9 ($2CH_{Ar}$), 128.8 ($2CH_{Ar}$), 128.7 ($4CH_{Ar}$), 126.1 ($2CH_{Ar}$), 105.5 (CH_2, minor isomer), 105.4 (CH_2, major isomer), 97.7 (CH, minor isomer), 97.3 (CH, major isomer), 80.3 (CH, minor isomer), 78.7 (CH, major isomer), 41.0 (CH_2, minor isomer), 40.6 (CH_2, major isomer), 39.4 (CH_2, minor isomer), 37.7 (CH_2, major isomer), 32.6 (CH_2, minor isomer), 31.9 ppm (CH_2, major isomer); IR (neat): $\tilde{\nu}=3403$, 3025, 2933, 2860, 1668, 1605, 1495, 1453, 1177, 1028, 889, 700 cm^{-1}; MS (ESI^+): *m*/*z*: for $C_{13}H_{16}O_2$: 227 $[M+Na]^+$; HRMS (ESI^+): *m*/*z*: calcd for $C_{13}H_{16}O_2$: 227.1043 $[M+Na]^+$; found: 227.1032; TLC: $R_f=0.48$ (petroleum ether/Et_2O 50:50).

3-Butyl-4-methylenetetrahydro-2-furanol (10b): The title compound was prepared according to the general procedure GP1 from α-bromoester **9b** (1.17 g, 5 mmol). Flash chromatography (petroleum ether/Et_2O 70:30) gave **10b** (0.64 g, 82%) as a colorless oil. ^1H NMR (CD_3OD, 300 MHz; mixture of two isomers at the hemiacetal center): $\delta=5.41$ (d, $J=4.8$ Hz, 1H; minor isomer), 5.16 (d, $J=0.9$ Hz, 1H; major isomer), 5.00–4.97 (m, 2H; major isomer), 4.95–4.90 (m, 2H; minor isomer), 4.51–4.33 (m, 4H; two isomers), 2.56–2.37 (m, 2H; two isomers), 1.70–1.18 (m, 12H; two isomers), 1.02–0.87 ppm (m, 6H; two isomers); ^{13}C NMR (CD_3OD, 75 MHz; mixture of two isomers at the hemiacetal center): $\delta=151.7$ (C, major isomer), 151.2 (C, minor isomer), 105.6 (CH_2, major isomer), 104.2 (CH, major isomer), 103.9 (CH_2, minor isomer), 99.6 (CH, minor isomer), 70.5 (CH_2, minor isomer), 70.3 (CH_2, major isomer), 52.4 (CH, major isomer), 49.2 (CH, minor isomer), 33.3 (CH_2, major isomer), 31.2 (CH_2, minor isomer), 30.4 (CH_2, major isomer), 27.5 (CH_2, minor isomer), 24.1 (CH_2, minor isomer), 23.8 (CH_2, major isomer), 14.4 ppm ($2CH_3$, two isomers); IR (neat): $\tilde{\nu}=3404$, 2956, 2930, 2859, 1456, 1436, 1027, 931, 885 cm^{-1}; MS (CI^+): *m*/*z*: for $C_9H_{16}O_2$: 157 $[M+H]^+$; HRMS (CI^+): *m*/*z*: calcd for $C_9H_{16}O_2$: 157.1229 $[M+H]^+$; found: 157.1227; TLC: $R_f=0.64$ (petroleum ether/Et_2O 50:50).

3-Butyl-4-methylene-5-phenethyltetrahydro-2-furanol (10c): The title compound was prepared according to the general procedure GP1 from α-bromoester **9c** (0.68 g, 2 mmol). Flash chromatography (petroleum ether/Et_2O 70:30) gave **10c** (0.40 g, 77%) as a colorless oil. ^1H NMR (C_6D_6, 300 MHz; mixture of four isomers): $\delta=7.25$–7.05 (m, 20H), 5.47–5.15 (m, 4H), 4.88–4.42 (m, 12H), 3.64–2.45 (m, 12H, 4H; OH), 2.15–1.80 (m, 8H), 1.76–1.13 (m, 24H), 0.92–0.81 ppm (m, 12H); ^{13}C NMR (C_6D_6, 75 MHz; mixture of four isomers): $\delta=154.4$ (C), 154.1 (C), 153.7 (C), 153.5 (C), 142.52 (C_{Ar}), 142.47 (C_{Ar}), 142.43 (C_{Ar}), 142.37 (C_{Ar}), 128.9 ($4CH_{Ar}$), 128.8 ($4CH_{Ar}$), 128.7 ($8CH_{Ar}$), 126.1 ($4CH_{Ar}$), 105.5 (CH_2), 105.4 (CH_2), 104.1 (CH_2), 103.8 (CH_2), 102.8 (CH), 102.2 (CH), 98.2 (CH), 97.8 (CH), 80.2 (CH), 80.1 (CH), 79.6 (CH), 79.2 (CH), 52.2 (CH), 52.0 (CH), 49.0 (CH), 48.5 (CH), 39.5 (CH_2), 39.3 (CH_2), 38.6 (CH_2), 38.2 (CH_2), 33.4 (CH_2), 32.8 (CH_2), 32.60 (CH_2), 32.57 (CH_2), 32.2 (CH_2), 31.9 (CH_2), 30.4 (CH_2), 30.2 (CH_2), 30.0 (CH_2), 29.5 (CH_2), 27.1 (CH_2), 26.6 (CH_2), 23.4 (CH_2), 23.0 ($2CH_2$), 23.0 (CH_2), 14.3 (CH_3), 14.3 (CH_3), 14.2 ppm ($2CH_3$); IR (neat): $\tilde{\nu}=3403$, 3026, 2930, 2858, 1496, 1456, 1029, 888, 748, 699 cm^{-1}; MS (ESI^+): *m*/*z*: for $C_{17}H_{24}O_2$: 283 $[M+Na]^+$; HRMS (ESI^+): *m*/*z*: calcd for $C_{17}H_{24}O_2$: 283.1669 $[M+Na]^+$; found: 283.1661; TLC: $R_f=0.79$ (petroleum ether/Et_2O 50:50).

3-Butyl-5,5-dimethyl-4-methylenetetrahydro-2-furanol (10d): The title compound was prepared according to the general procedure GP2 from α-bromoester **9d** (653 mg, 2.5 mmol). Flash chromatography (petroleum ether/Et_2O 80:20) gave **10d** (365 mg, 79%) as a colorless oil. ^1H NMR (C_6D_6, 300 MHz; mixture of two isomers at the hemiacetal center): $\delta=$ 5.36 (dd, $J=3.7$, 3.9 Hz, 1H), 5.23 (brs, 1H), 4.81–4.75 (m, 4H), 3.63 (d, $J=2.8$ Hz, 1H; OH), 3.30 (d, $J=2.2$ Hz, 1H; OH), 2.70 (t, $J=7.0$ Hz,

1H), 2.59–2.55 (m, 1H), 1.71–1.18 (m, 12H), 1.55 (s, 3H), 1.52 (s, 3H), 1.31 (s, 3H), 1.30 (s, 3H), 0.89 (t, $J=7.0$ Hz, 3H), 0.83 ppm (t, $J=6.9$ Hz, 3H); ^{13}C NMR (C_6D_6, 75 MHz; mixture of two isomers at the hemiacetal center): $\delta=159.6$ (C), 158.8 (C), 104.6 (CH_2), 103.1 (CH_2), 102.0 (CH), 97.4 (CH), 83.4 (C), 83.1 (C), 52.5 (CH), 48.4 (CH), 33.4 (CH_2), 31.6 (CH_3), 30.6 (CH_3), 30.4 (CH_3), 30.2 (CH_2), 30.1 (CH_3), 29.8 (CH_2), 26.8 (CH_2), 23.4 (CH_2), 23.0 (CH_2), 14.3 (CH_3), 14.2 ppm (CH_3); IR (neat): $\tilde{\nu}=3403$, 2957, 2871, 1662, 1460, 1190, 1000, 885 cm^{-1}; MS (ESI$^+$): m/z: for $C_{11}H_{20}O_2$: 207 $[M+Na]^+$; HRMS (ESI$^+$): m/z: calcd for $C_{11}H_{20}O_2$: 207.1356 $[M+Na]^+$; found: 207.1361; TLC: $R_f=0.68$ (petroleum ether/Et_2O 50:50).

3,3-Dimethyl-4-methylene-5-phenethyltetrahydro-2-furanol (10e): The title compound was prepared according to the general procedure GP2 from α-bromoester **9e** (618 mg, 2 mmol). Flash chromatography (petroleum ether/Et_2O 80:20) gave **10e** (270 mg, 57%) as a colorless oil. ^{1}H NMR (CD_3OD, 300 MHz; mixture of two isomers at the hemiacetal center): $\delta=7.28$–7.12 (m, 10H; two isomers), 5.01 (s, 1H; major isomer), 4.93 (s, 1H; minor isomer), 4.91 (d, $J=15.7$ Hz, 1H; major isomer), 4.90 (d, $J=15.7$ Hz, 1H; major isomer), 4.86 (d, $J=17.1$ Hz, 1H; minor isomer), 4.85 (d, $J=17.1$ Hz, 1H; minor isomer), 4.63–4.58 (m, 1H; major isomer), 4.47–4.41 (m, 1H; minor isomer), 2.93–2.64 (m, 4H; two isomers), 2.03–1.77 (m, 4H; two isomers), 1.12 (s, 3H; major isomer), 1.10 (s, 3H; major isomer), 1.09 (s, 3H; minor isomer), 1.08 ppm (s, 3H; minor isomer); ^{13}C NMR (CD_3OD, 75 MHz; mixture of two isomers at the hemiacetal center): $\delta=160.9$ (C, major isomer), 160.6 (C, minor isomer), 143.6 (C_{Ar}, minor isomer), 143.4 (C_{Ar}, major isomer), 129.52 (4CH_{Ar}, major isomer), 129.42 (4CH_{Ar}, major isomer), 126.8 (CH_{Ar}, major isomer), 126.7 (CH_{Ar}, minor isomer), 105.3 (CH, major isomer), 105.2 (CH, minor isomer), 103.6 (CH_2, major isomer), 103.4 (CH_2, minor isomer), 80.0 (CH, major isomer), 79.8 (CH, minor isomer), 47.7 (C, major isomer), 47.5 (C, minor isomer), 40.2 (CH_2, minor isomer), 39.5 (CH_2, major isomer), 33.4 (CH_2, minor isomer), 33.2 (CH_2, major isomer), 28.5 (CH_3, major isomer), 27.1 (CH_3, minor isomer), 21.7 (CH_3, major isomer), 21.2 ppm (CH_3, minor isomer); IR (neat): $\tilde{\nu}=3396$, 3026, 2959, 2928, 2868, 2521, 1496, 1454, 1030, 992, 699 cm^{-1}; MS (ESI$^+$): m/z: for $C_{15}H_{20}O_2$: 255 $[M+Na]^+$; HRMS (ESI$^+$): m/z: calcd for $C_{15}H_{20}O_2$: 255.1356 $[M+Na]^+$; found: 255.1350; TLC: $R_f=0.76$ (petroleum ether/Et_2O 50:50).

4-Butylidene-5-phenethyltetrahydro-2-furanol (10f): The title compound was prepared according to the general procedure GP1 from α-bromoester **9f** (1.61 g, 5 mmol). Flash chromatography (petroleum ether/Et_2O 60:40) gave **10f** (0.96 g, 78%, E/Z 71:29) as a colorless oil. ^{1}H NMR (CD_3OD, 300 MHz; mixture of four diastereoisomers): $\delta=7.34$–7.11 (m, 20H), 5.57–5.23 (m, 8H), 4.73–4.32 (m, 4H), 2.90–2.32 (m, 16H), 2.11–1.69 (m, 16H), 1.48–1.32 (m, 8H), 0.95–0.87 ppm (m, 12H); ^{13}C NMR (CD_3OD, 75 MHz; mixture of four diastereoisomers): $\delta=143.7$ (C), 143.6 (C), 143.4 (2C), 141.4 (C_{Ar}), 141.15 (C_{Ar}), 141.10 (C_{Ar}), 140.08 (C_{Ar}), 129.59 (2CH_{Ar}), 129.53 (2CH_{Ar}), 129.49 (2CH_{Ar}), 129.47 (4CH_{Ar}), 129.38 (4CH_{Ar}), 129.35 (2CH_{Ar}), 126.81 (2CH_{Ar}), 126.76 (CH_{Ar}), 126.71 (CH_{Ar}), 123.5 (CH), 122.7 (CH), 121.9 (CH), 121.8 (CH), 99.2 (CH), 98.8 (CH), 98.1 (CH), 97.7 (CH), 81.3 (CH), 79.5 (CH), 79.3 (CH), 78.1 (CH), 42.1 (CH_2), 41.4 (CH_2), 40.6 (CH_2), 39.9 (CH_2), 38.7 (CH_2), 38.4 (2CH_2), 38.3 (CH_2), 33.13 (CH_2), 33.05 (CH_2), 32.96 (CH_2), 32.89 (CH_2), 32.41 (CH_2), 32.35 (CH_2), 32.2 (CH_2), 32.1 (CH_2), 23.9 (2CH_2), 23.7 (2CH_2), 14.22 (2CH_3), 14.17 ppm (2CH_3); IR (neat): $\tilde{\nu}=3403$, 3025, 2956, 1603, 1495, 1454, 1177, 1029, 698 cm^{-1}; MS (ESI$^+$): m/z: for $C_{16}H_{22}O_2$: 269 $[M+Na]^+$; HRMS (ESI$^+$): m/z: calcd for $C_{16}H_{22}O_2$: 269.1512 $[M+Na]^+$; found: 269.1521; TLC: $R_f=0.33$ (major isomer), 0.28 (minor isomer) (petroleum ether/Et_2O 60:40).

4-Butylidene-5,5-dimethyltetrahydro-2-furanol (10g): The title compound was prepared according to the general procedure GP2 from α-bromoester **9g** (0.74 g, 3 mmol). Flash chromatography (petroleum ether/Et_2O 60:40) gave **10g** (0.50 g, 99%, E/Z 63:37) as a pale-yellow oil. ^{1}H NMR (C_6D_6, 300 MHz; 63:37 mixture of E/Z isomers): $\delta=5.59$ (d, $J=4.6$ Hz, 1H; E isomer), 5.49 (d, $J=4.6$ Hz, 1H; Z isomer), 5.15–5.05 (m, 2H; two isomers), 4.54 (brs, 1H; OH, E isomer), 4.46 (brs, 1H; OH, Z isomer), 2.74–2.48 (m, 4H; two isomers), 2.02–1.75 (m, 4H; two isomers), 1.68 (s, 3H; Z isomer), 1.56 (s, 3H; E isomer), 1.37 (s, 3H; Z isomer), 1.35–1.21 (m, 4H; two isomers), 1.29 (s, 3H; E isomer), 0.83 (t, $J=7.3$ Hz, 3H; E isomer), 0.83 ppm (t, $J=7.3$ Hz, 3H; Z isomer); ^{13}C NMR (C_6D_6, 75 MHz; 63:37 mixture of E/Z isomers): $\delta=145.7$ (C, E isomer), 143.9 (C, Z isomer), 121.3 (CH, Z isomer), 119.8 (CH, E isomer), 97.0 (CH, E isomer), 96.5 (CH, Z isomer), 83.1 (C, E isomer), 82.1 (C, Z isomer), 42.7 (CH_2, Z isomer), 37.5 (CH_2, E isomer), 32.0 (CH_2, E isomer), 30.9 (CH_2, E isomer), 30.5 (CH_3, Z isomer), 29.9 (CH_3, Z isomer), 29.8 (CH_3, E isomer), 28.3 (CH_3, Z isomer), 23.5 (CH_2, Z isomer), 22.9 (CH_2, E isomer), 13.9 (CH_3, Z isomer), 13.8 ppm (CH_3, E isomer); IR (neat): $\tilde{\nu}=$ 3406, 2963, 2930, 2871, 1456, 1360, 1142, 1071, 967, 827 cm^{-1}; MS (ESI$^+$): m/z: for $C_{10}H_{18}O_2$: 193 $[M+Na]^+$; HRMS (ESI$^+$): m/z: calcd for $C_{10}H_{18}O_2$: 193.1191 $[M+Na]^+$; found: 193.1199; TLC: $R_f=0.54$ (petroleum ether/Et_2O 50:50).

4-Butylidene-3,3-dimethyl-5-phenethyltetrahydro-2-furanol (10h): The title compound was prepared according to the general procedure GP2 from α-bromoester **9h** (0.70 g, 2 mmol). Flash chromatography (petroleum ether/Et_2O 60:40) gave **10h** (0.28 g, 50%) as a colorless oil. ^{1}H NMR (C_6D_6, 300 MHz; mixture of four isomers): $\delta=7.27$–7.05 (m, 20H), 5.14–4.35 (m, 12H), 3.09–2.75 (m, 10H), 2.74 (d, $J=3.5$ Hz, 1H; OH), 2.65 (d, $J=3.3$ Hz, 1H; OH), 2.24–1.67 (m, 16H), 1.36 (s, 3H), 1.33–1.21 (m, 8H), 1.25 (s, 3H), 1.174 (s, 3H), 1.167 (s, 3H), 1.13 (s, 3H), 1.12 (s, 3H), 1.06 (s, 3H), 1.03 (s, 3H), 0.87–0.76 ppm (m, 12H); ^{13}C NMR (C_6D_6, 75 MHz; mixture of four isomers): $\delta=150.0$ (C), 148.6 (C), 148.2 (C), 147.9 (C), 142.7 (2C_{Ar}), 142.6 (C_{Ar}), 142.4 (C_{Ar}), 129.0 (2CH_{Ar}), 128.95 (2CH_{Ar}), 128.91 (2CH_{Ar}), 128.85 (2CH_{Ar}), 128.7 (8CH_{Ar}), 126.14 (2CH_{Ar}), 126.07 (2CH_{Ar}), 121.5 (CH), 121.2 (CH), 119.9 (CH), 119.7 (CH), 105.7 (CH), 105.5 (CH), 105.2 (CH), 104.4 (CH), 80.1 (CH), 79.8 (CH), 78.42 (CH), 78.37 (CH), 46.6 (C), 46.5 (C), 46.0 (C), 45.9 (C), 39.8 (CH_2), 39.3 (CH_2), 39.0 (CH_2), 38.4 (CH_2), 33.2 (CH_2), 33.1 (CH_2), 32.7 (CH_2), 32.5 (CH_2), 30.9 (2CH_2), 29.8 (CH_2), 29.6 (CH_2), 28.2 (CH_3), 27.7 (CH_3), 26.7 (CH_3), 25.5 (CH_3), 23.6 (2CH_2), 23.2 (2CH_2), 22.0 (CH_3), 21.9 (CH_3), 21.6 (CH_3), 21.2 (CH_3), 14.0 (2CH_3), 13.89 (CH_3), 13.85 ppm (CH_3); IR (neat): $\tilde{\nu}=3403$, 3025, 2958, 2870, 1496, 1464, 1456, 1029, 748, 699 cm^{-1}; MS (ESI$^+$): m/z: for $C_{18}H_{26}O_2$: 297 $[M+Na]^+$; HRMS (ESI$^+$): calcd for $C_{18}H_{26}O_2$: 297.1825 $[M+Na]^+$; found: 297.1824; TLC: $R_f=0.72$ (petroleum ether/Et_2O 50:50).

4-(2,2-Dimethylpropylidene)-5-phenethyltetrahydro-2-furanol (10i): The title compound was prepared according to the general procedure GP1 from α-bromoester **9i** (1.68 g, 5 mmol). Flash chromatography (petroleum ether/Et_2O 50:50) gave **10i** (0.96 g, 74%, E/Z 82:18) as a colorless oil.

Major isomer: ^{1}H NMR (C_6D_6, 300 MHz; E isomer, mixture of two isomers at the hemiacetal center): $\delta=7.25$–7.04 (m, 10H), 5.47 (d, $J=$ 5.0 Hz, 1H; major isomer), 5.40 (brs, 1H; minor isomer), 5.17 (dd, $J=$ 2.2, 4.7 Hz, 1H; major isomer), 5.11 (dd, $J=2.4$, 4.5 Hz, 1H; minor isomer), 4.69 (brd, $J=7.9$ Hz, 1H; major isomer), 4.40 (brd, $J=9.5$ Hz, 1H; minor isomer), 3.03–2.39 (m, 10H; two isomers), 2.18–1.74 (m, 4H; two isomers), 0.99 (s, 9H; major isomer), 0.97 ppm (s, 9H; minor isomer); ^{13}C NMR (C_6D_6, 75 MHz; E isomer, mixture of two isomers at the hemiacetal center): $\delta=142.7$ (2C, E isomer), 137.5 (C_{Ar}, E isomer), 136.9 (C_{Ar}, E isomer), 131.21 (CH, E isomer), 131.18 (CH, E isomer), 129.0 (2CH_{Ar}), 128.9 (2CH_{Ar}), 128.7 (4CH_{Ar}), 126.1 (2CH_{Ar}, E isomer), 99.0 (CH, E isomer), 97.9 (CH, E isomer), 82.2 (CH, E isomer), 80.0 (CH, E isomer), 40.5 (CH_2, E isomer), 38.4 (CH_2, E isomer), 37.7 (CH_2, E isomer), 37.6 (CH_2, E isomer), 33.0 (CH_2, E isomer), 32.9 (C, E isomer), 32.8 (C, E isomer), 32.0 (CH_2, E isomer), 30.5 ppm (6CH_3, E isomer); IR (neat): $\tilde{\nu}=3406$, 3025, 2953, 2864, 1495, 1455, 1212, 1028, 878, 746, 699 cm^{-1}; MS (ESI$^+$): m/z: for $C_{17}H_{24}O_2$: 283 $[M+Na]^+$; HRMS (ESI$^+$): m/z: calcd for $C_{17}H_{24}O_2$: 283.1669 $[M+Na]^+$; found: 283.1671; TLC: $R_f=0.51$ (major isomer) (petroleum ether/Et_2O 50:50).

Relevant signals for the minor isomer: ^{1}H NMR (C_6D_6, 300 MHz; Z isomer, mixture of two isomers at the hemiacetal center): $\delta=5.24$ (brs, 1H), 5.07–5.02 (m, 2H), 4.87 (brd, $J=10.6$ Hz, 1H), 0.94 (s, 9H), 0.90 ppm (s, 9H); ^{13}C NMR (C_6D_6, 75 MHz; mixture of four isomers): $\delta=142.5$ (C, Z isomer), 142.3 (C, Z isomer), 137.5 (C_{Ar}, Z isomer), 135.9 (C_{Ar}, Z isomer), 133.3 (CH, Z isomer), 131.7 (CH, Z isomer), 126.2 (2CH_{Ar}, Z isomer), 97.4 (CH, Z isomer), 96.1 (CH, Z isomer), 77.4 (CH, Z isomer), 76.0 (CH, Z isomer), 43.4 (CH_2, Z isomer), 42.5 (CH_2, Z

isomer), 39.8 (CH_2, *Z* isomer), 39.1 (CH_2, *Z* isomer), 33.9 (C, *Z* isomer), 33.8 (C, *Z* isomer), 32.9 (CH_2, *Z* isomer), 32.3 (CH_2, *Z* isomer), 30.7 ppm ($6CH_3$, *Z* isomer); IR (neat): $\tilde{\nu}$ = 3406, 3025, 2953, 2864, 1495, 1455, 1212, 1028, 878, 746, 699 cm^{-1}; MS (ESI^+): *m*/*z*: for $C_{17}H_{24}O_2$: 283 $[M+Na]^+$; HRMS (ESI^+): *m*/*z*: calcd for $C_{17}H_{24}O_2$: 283.1669 $[M+Na]^+$; found: 283.1671; TLC: R_f = 0.42 (minor isomer) (petroleum ether/Et_2O 50:50).

5-Phenethyl-4-(1-trimethylsilylmethylidene)tetrahydro-2-furanol (10j): The title compound was prepared according to the general procedure GP1 from α-bromoester **9j** (3.53 g, 10 mmol). Flash chromatography (petroleum ether/Et_2O 80:20) gave **10j** (2.6 g, 94%, *E*/*Z* 31:69) as a colorless oil. ^1H NMR (C_6D_6, 300 MHz; mixture of four isomers): δ = 7.29–7.04 (m, 20H), 5.63–5.27 (m, 8H), 4.90–4.86 (m, 1H), 4.72–4.69 (m, 1H), 4.64–4.60 (m, 1H), 4.41–4.36 (m, 1H), 4.28 (d, *J* = 3.3 Hz, 1H; OH), 4.16–4.10 (m, 3H; OH), 3.07–2.43 (m, 16H), 2.40–1.75 (m, 8H), 0.10 (s, 9H), 0.08 (s, 9H), 0.03 (s, 9H), 0.02 ppm (s, 9H); ^{13}C NMR (C_6D_6, 75 MHz; mixture of four isomers): δ = 159.1 (C), 158.5 (C), 158.3 (C), 158.0 (C), 142.5 ($2C_{Ar}$), 142.3 (C_{Ar}), 142.2 (C_{Ar}), 129.1 ($4CH_{Ar}$), 128.96 ($2CH_{Ar}$), 128.93 ($2CH_{Ar}$), 128.83 ($2CH_{Ar}$), 128.77 ($2CH_{Ar}$), 128.71 ($4CH_{Ar}$), 126.22 (CH_{Ar}), 126.17 (CH_{Ar}), 126.12 ($2CH_{Ar}$), 120.9 (CH), 120.0 (CH), 118.5 (CH), 118.3 (CH), 98.4 (CH), 98.1 (CH), 97.6 (CH), 97.0 (CH), 82.5 (CH), 80.7 (CH), 80.0 (CH), 78.3 (CH), 44.7 (CH_2), 44.0 (CH_2), 40.6 (CH_2), 40.5 (CH_2), 40.3 (CH_2), 39.6 (CH_2), 39.4 (CH_2), 37.8 (CH_2), 32.83 (CH_2), 32.78 (CH_2), 32.2 (CH_2), 32.0 (CH_2), 0.03 ($6CH_3$), −0.08 ($3CH_3$), −0.43 ppm ($3CH_3$); IR (neat): $\tilde{\nu}$ = 3403, 3025, 2951, 1637, 1496, 1453, 1248, 1029, 858, 699 cm^{-1}; MS (ESI^+): *m*/*z*: for $C_{16}H_{24}O_2Si$: 299 $[M+Na]^+$; HRMS (ESI^+): *m*/*z*: calcd for $C_{16}H_{24}O_2Si$: 299.1443 $[M+Na]^+$; found: 299.1443; TLC: R_f = 0.57 (major isomer), 0.68 (minor isomer) (petroleum ether/Et_2O 50:50).

5-Phenethyl-4-(1-phenylmethylidene)tetrahydro-2-furanol (10k): The title compound was prepared according to the general procedure GP1 from α-bromoester **9k** (3.75 g, 10.5 mmol). Flash chromatography (petroleum ether/Et_2O 80:20) gave **10k** (2.6 g, 88%, *E*/*Z* 26:74) as a white powder. ^1H NMR (C_6D_6, 300 MHz; mixture of four isomers): δ = 7.25–7.17 (m, 40H), 6.24–6.09 (m, 4H), 5.62–5.52 (m, 4H), 5.31 (br d, *J* = 8.5 Hz, 1H), 5.01 (br d, *J* = 9.4 Hz, 1H), 4.88 (br d, *J* = 6.2 Hz, 1H), 4.53 (br d, *J* = 9.2 Hz, 1H), 4.04 (d, *J* = 2.0 Hz, 2H; OH), 3.97 (d, *J* = 3.8 Hz, 1H; OH), 3.85 (d, *J* = 2.5 Hz, 1H; OH), 2.95–2.51 (m, 16H), 2.07–1.63 ppm (m, 8H); ^{13}C NMR (C_6D_6, 75 MHz; mixture of four isomers): δ = 143.3 (2C), 142.4 (2C), 142.3 (2C), 141.8 (2C), 137.9 (2C), 137.2 (2C), 129.3 ($4CH_{Ar}$), 129.1 ($4CH_{Ar}$), 129.0 ($4CH_{Ar}$), 128.9 ($4CH_{Ar}$), 128.7 ($4CH_{Ar}$), 128.62 ($4CH_{Ar}$), 128.60 ($4CH_{Ar}$), 128.55 ($4CH_{Ar}$), 126.9 ($2CH_{Ar}$), 126.7 ($2CH_{Ar}$), 126.2 ($2CH_{Ar}$), 126.1 ($2CH_{Ar}$), 122.6 (CH), 121.7 (CH), 121.41 (CH), 121.36 (CH), 98.9 (CH), 97.9 (CH), 97.3 (CH), 96.5 (CH), 82.2 (CH), 80.2 (CH), 78.4 (CH), 77.0 (CH), 42.7 ($2CH_2$), 39.8 (CH_2), 39.3 (CH_2), 39.2 (CH_2), 38.0 (CH_2), 36.3 (CH_2), 34.9 (CH_2), 32.6 (CH_2), 32.5 (CH_2), 31.99 (CH_2), 31.95 ppm (CH_2); IR (neat): $\tilde{\nu}$ = 3417, 3022, 2940, 1602, 1496, 1242, 1069, 667 cm^{-1}; MS (ESI^+): *m*/*z*: for $C_{19}H_{20}O_2$: 303 $[M+Na]^+$; HRMS (ESI^+): *m*/*z*: calcd for $C_{19}H_{20}O_2$: 303.1361 $[M+Na]^+$; found: 303.1360; TLC: R_f = 0.54 (minor isomer), 0.39 (major isomer) (petroleum ether/Et_2O 50:50); m.p. 70–72 °C.

5-(3-Butenyl)-4-(1-phenylmethylidene)tetrahydro-2-furanol (10l): The title compound was prepared according to the general procedure GP1 from α-bromoester **9l** (1.22 g, 4 mmol). Flash chromatography (petroleum ether/Et_2O 70:30) gave **10l** (0.84 g, 91%, *E*/*Z* 22:78) as a colorless oil. ^1H NMR (C_6D_6, 300 MHz; mixture of four isomers): δ = 7.20–6.96 (m, 20H), 6.25–6.13 (m, 4H), 5.96–5.65 (m, 4H), 5.47–4.50 (m, 16H), 3.11 (dd, *J* = 1.3, 3.4 Hz, 1H; OH), 3.04 (d, *J* = 3.3 Hz, 1H; OH), 3.00 (d, *J* = 3.8 Hz, 1H; OH), 2.92 (dd, *J* = 1.1, 3.2 Hz, 1H; OH), 2.78–2.17 (m, 16H), 2.01–1.43 ppm (m, 8H); ^{13}C NMR (C_6D_6, 75 MHz; mixture of four isomers): δ = 143.7 (C), 142.8 (C), 142.7 (C), 142.5 (C), 138.70 (CH), 138.67 (CH), 138.31 (CH), 138.26 (CH), 138.0 (C_{Ar}), 137.8 (C_{Ar}), 137.5 (C_{Ar}), 137.4 (C_{Ar}), 128.61 ($4CH_{Ar}$), 128.58 ($8CH_{Ar}$), 128.54 ($4CH_{Ar}$), 126.8 ($4CH_{Ar}$), 122.6 (CH), 121.8 (CH), 121.4 (2CH), 115.3 (CH_2), 115.2 (CH_2), 115.0 (CH_2), 114.9 (CH_2), 98.8 (CH), 97.8 (CH), 97.3 (CH), 96.5 (CH), 82.4 (CH), 80.3 (CH), 78.9 (CH), 77.3 (CH), 42.71 (CH_2), 42.67 (CH_2), 39.4 (CH_2), 39.3 (CH_2), 37.3 (CH_2), 35.3 (CH_2), 34.3 (CH_2), 32.6 (CH_2), 30.7 (CH_2), 30.6 (CH_2), 30.0 (CH_2), 29.9 ppm (CH_2); IR (neat): $\tilde{\nu}$ = 3396, 3024, 2974, 2940, 2850, 1750, 1494, 1447, 1118, 1073, 749, 696 cm^{-1}; MS (ESI^+): *m*/*z*: for $C_{15}H_{18}O_2$: 253 $[M+Na]^+$; HRMS (ESI^+): *m*/*z*: calcd for $C_{15}H_{18}O_2$: 253.1199 $[M+Na]^+$; found: 253.1197; TLC: R_f = 0.45 (*Z* isomer), 0.51 (*E* isomer) (petroleum ether/Et_2O 50:50).

3,3-Dimethyl-5-phenethyl-4-[(*E*)-1-phenylmethylidene]tetrahydro-2-furanol (10m): The title compound was prepared according to the general procedure GP2 from α-bromoester **9m** (1.92 g, 5 mmol). Flash chromatography (petroleum ether/Et_2O 70:30) gave **10m** (0.89 g, 58%, *E*/*Z* > 95:5) as a colorless oil. ^1H NMR (C_6D_6, 300 MHz; mixture of two isomers at the hemiacetal center): δ = 7.27–6.93 (m, 20H; two isomers), 6.28 (d, *J* = 1.9 Hz, 1H; major isomer), 6.24 (d, *J* = 2.0 Hz, 1H; minor isomer), 4.80–4.75 (m, 2H; two isomers), 4.69 (d, *J* = 4.9 Hz, 1H; major isomer), 4.48 (ddd, *J* = 2.3, 3.1, 9.6 Hz, 1H; minor isomer), 3.10–2.52 (m, 4H), 2.20–1.93 (m, 6H), 1.18 (s, 3H; major isomer), 1.05 (s, 3H; minor isomer), 1.01 (s, 3H; minor isomer), 1.00 ppm (s, 3H; major isomer); ^{13}C NMR (C_6D_6, 75 MHz; mixture of two isomers at the hemiacetal center): δ = 151.19 (C), 151.15 (C), 142.6 (C_{Ar}), 142.4 (C_{Ar}), 137.9 (C_{Ar}), 137.8 (C_{Ar}), 129.3 ($4CH_{Ar}$), 129.0 ($4CH_{Ar}$), 128.9 ($4CH_{Ar}$), 128.7 ($4CH_{Ar}$), 126.8 ($2CH_{Ar}$), 126.2 ($2CH_{Ar}$), 122.2 (CH), 122.0 (CH), 106.0 (CH), 105.6 (CH), 81.0 (CH), 80.1 (CH), 47.2 (C), 46.8 (C), 39.8 ($2CH_2$), 32.8 ($2CH_2$), 28.2 (CH_3), 26.0 (CH_3), 21.2 (CH_3), 20.9 ppm (CH_3); IR (neat): $\tilde{\nu}$ = 3395, 3024, 2931, 1601, 1495, 1454, 1029, 699 cm^{-1}; MS (ESI^+): *m*/*z*: for $C_{21}H_{24}O_2$: 331 $[M+Na]^+$; HRMS (ESI^+): *m*/*z*: calcd for $C_{21}H_{24}O_2$: 331.1674 $[M+Na]^+$; found: 331.1674; TLC: R_f = 0.53 (petroleum ether/Et_2O 60:40).

5,5-Dimethyl-4-[(*Z*)-1-phenylmethylidene]tetrahydro-2-furanol (10n): The title compound was prepared according to the general procedure GP2 from α-bromoester **9n** (1 g, 3.55 mmol). Flash chromatography (petroleum ether/Et_2O 60:40) gave **10n** (0.69 g, 94%, *E*/*Z* 5:95) as a white powder. ^1H NMR (C_6D_6, 300 MHz): δ = 7.21–7.04 (m, 5H), 6.43 (br s, 1H), 5.51–5.49 (m, 1H), 4.19 (br s, 1H; OH), 2.82 (ddd, *J* = 2.4, 4.3, 15.3 Hz, 1H), 2.69 (dt, *J* = 1.3, 15.3 Hz, 1H), 1.54 (s, 3H), 1.37 ppm (m, 3H); ^{13}C NMR (C_6D_6, 75 MHz): δ = 147.2 (C), 138.1 (C_{Ar}), 129.2 ($2CH_{Ar}$), 128.2 ($2CH_{Ar}$), 126.9 (CH_{Ar}), 122.1 (CH), 96.0 (CH), 82.5 (C), 43.6 (CH_2), 30.0 (CH_3), 29.5 ppm (CH_3); IR (KBr): $\tilde{\nu}$ = 3385, 3077, 2992, 2929, 1439, 1361, 1069, 1022, 966, 706 cm^{-1}; MS (ESI^+): *m*/*z*: for $C_{13}H_{16}O_2$: 227 $[M+Na]^+$; HRMS (ESI^+): *m*/*z*: calcd for $C_{13}H_{16}O_2$: 227.1034 $[M+Na]^+$; found: 227.1043; TLC: R_f = 0.42 (petroleum ether/Et_2O 50:50); m.p. 69–71 °C.

4-Butylidene-5-trityloxymethyltetrahydro-2-furanol (10o): The title compound was prepared according to the general procedure GP1 from α-bromoester **9o** (1.47 g, 3 mmol). Flash chromatography (petroleum ether/Et_2O 50:50) gave **10o** (0.89 g, 72%, *E*/*Z* 37:63) as a colorless oil. ^1H NMR (C_6D_6, 300 MHz; mixture of four isomers): δ = 7.65–7.61 (m, 24H), 7.17–6.99 (m, 36H), 5.66–5.60 (m, 4H), 5.28–5.08 (m, 4H), 5.03–4.62 (m, 4H), 4.36 (d, *J* = 6.7 Hz, 1H; OH), 4.07 (d, *J* = 6.8 Hz, 1H; OH), 3.67–3.21 (m, 10H), 2.73–2.40 (m, 8H), 1.86–1.53 (m, 8H), 1.29–0.97 (m, 8H), 0.80–0.66 ppm (m, 12H); ^{13}C NMR (C_6D_6, 75 MHz; mixture of four isomers): δ = 144.8 ($3C_{Ar}$), 144.7 ($3C_{Ar}$), 144.3 ($6C_{Ar}$), 137.9 (C), 137.7 (C), 137.5 (C), 137.0 (C), 129.34 ($12CH_{Ar}$), 129.28 ($12CH_{Ar}$), 128.14 ($12CH_{Ar}$), 128.07 ($12CH_{Ar}$), 127.3 ($6CH_{Ar}$), 127.2 ($6CH_{Ar}$), 123.6 (CH), 123.0 (CH), 122.2 (CH), 121.8 (CH), 98.9 (CH), 98.7 (CH), 98.2 (CH), 97.8 (CH), 87.7 (2C), 87.0 (2C), 80.9 (CH), 79.5 (CH), 79.3 (CH), 78.2 (CH), 68.0 (CH_2), 67.6 (CH_2), 67.4 (CH_2), 66.6 (CH_2), 41.5 ($2CH_2$), 38.4 (CH_2), 37.5 (CH_2), 32.2 (CH_2), 32.1 (CH_2), 31.5 (CH_2), 31.4 (CH_2), 23.0 ($2CH_2$), 22.8 (CH_2), 22.7 (CH_2), 13.92 ($2CH_3$), 13.89 ppm ($2CH_3$); IR (neat): $\tilde{\nu}$ = 3406, 3022, 2956, 2870, 1596, 1490, 1448, 1222, 1074, 957, 705 cm^{-1}; MS (ESI^+): *m*/*z*: for $C_{28}H_{30}O_3$: 437 $[M+Na]^+$; HRMS (ESI^+): *m*/*z*: calcd for $C_{28}H_{30}O_3$: 437.2087 $[M+Na]^+$; found: 437.2087; TLC: R_f = 0.43 (major isomer), 0.50 ppm (minor isomer) (petroleum ether/Et_2O 40:60).

4-(1-Trimethylsilylmethylidene)-5-trityloxymethyltetrahydro-2-furanol (10p): The title compound was prepared according to the general procedure GP1 from α-bromoester **9p** (4.35 g, 8.35 mmol). Flash chromatography (petroleum ether/Et_2O 80:20) gave **10p** (2.75 g, 74%, *E*/*Z* 17:83) as a white powder. ^1H NMR (CD_3OD, 300 MHz; mixture of four isomers): δ = 7.53–7.41 (m, 24H), 7.29–7.17 (m, 36H), 5.69–5.36 (m, 8H), 4.86–4.42 (m, 4H), 3.59–2.37 (m, 16H), 0.11 (s, 9H), 0.10 (s, 9H), −0.17 (s, 9H), −0.22 ppm (s, 9H); ^{13}C NMR (CD_3OD, 75 MH

z; mixture of four isomers): δ=156.8 (C), 156.7 (C), 156.3 (C), 155.9 (C), 145.42 ($6C_{Ar}$), 145.35 ($6C_{Ar}$), 130.1 ($6CH_{Ar}$), 130.0 ($18CH_{Ar}$), 128.8 ($18CH_{Ar}$), 128.7 ($6CH_{Ar}$), 128.1 ($9CH_{Ar}$), 128.0 ($3CH_{Ar}$), 122.9 (CH_2), 122.8 (CH_2), 121.2 (CH_2), 120.4 (CH_2), 99.5 (CH), 99.0 (CH), 98.8 (CH), 98.0 (CH), 87.7 (4C), 83.4 (CH), 82.5 (CH), 81.7 (CH), 80.2 (CH), 70.3 (CH_2), 69.3 (CH_2), 68.9 (CH_2), 67.6 (CH_2), 46.0 (CH_2), 45.0 (CH_2), 41.5 (CH_2), 41.4 (CH_2), −0.07 ($3CH_3$), −0.18 ($3CH_3$), −0.35 ($3CH_3$), −0.41 ppm ($3CH_3$); IR (neat): $\tilde{\nu}$=3413, 3058, 3032, 2950, 1652, 1490, 1448, 1248, 1075, 836, 705 cm^{-1}; MS (ESI^+): *m/z*: for $C_{28}H_{32}O_2Si$: 467 $[M+Na]^+$; HRMS (ESI^+): *m/z*: calcd for $C_{19}H_{20}O_2Si$: 467.2013 $[M+Na]^+$; found: 467.1994; TLC: R_f=0.58 (petroleum ether/Et_2O 50:50); m.p. 57–59 °C.

5-Benzyloxymethoxymethyl-4-(1-phenylmethylidene)tetrahydro-2-furanol (10q): The title compound was prepared according to the general procedure GP1 from α-bromoester **9q** (0.92 g, 2.27 mmol). Flash chromatography (petroleum ether/Et_2O 70:30) gave **10q** (0.51 g, 69%, *E*/*Z* 24:74) as a white gum. ^{1}H NMR (C_6D_6, 300 MHz; mixture of four isomers): δ= 7.32–6.95 (m, 40H), 6.31–6.14 (m, 4H), 5.65–4.71 (m, 8H), 4.71–3.49 (m, 28H), 2.82–2.49 ppm (m, 8H); ^{13}C NMR (C_6D_6, 75 MHz; mixture of four isomers): δ=140.0 (2C), 139.8 (2C), 138.5 (C_{Ar}), 138.2 (C_{Ar}), 137.7 (C_{Ar}), 137.6 (C_{Ar}), 137.2 ($4C_{Ar}$), 128.7 ($8CH_{Ar}$), 128.5 ($16CH_{Ar}$), 128.2 ($8CH_{Ar}$), 127.7 ($2CH_{Ar}$), 127.6 ($2CH_{Ar}$), 127.0 ($2CH_{Ar}$), 126.9 ($2CH_{Ar}$), 123.7 (CH), 123.2 (CH), 122.2 (2CH), 99.2 (CH), 98.5 (CH), 97.5 (CH), 96.9 (CH), 94.8 (CH_2), 94.6 ($2CH_2$), 94.5 (CH_2), 82.1 (CH), 80.5 (CH), 79.2 (CH), 78.1 (CH), 71.0 (CH_2), 69.4 (CH_2), 69.3 ($2CH_2$), 69.1 ($3CH_2$), 68.6 (CH_2), 43.8 (CH_2), 42.9 (CH_2), 40.4 (CH_2), 39.4 ppm (CH_2); IR (KBr): $\tilde{\nu}$=3446, 3033, 2955, 2880, 1652, 1495, 1448, 1026, 749, 697 cm^{-1}; MS (ESI^+): *m/z*: for $C_{20}H_{22}O_4$: 349 $[M+Na]^+$; HRMS (ESI^+): *m/z* calcd for $C_{20}H_{22}O_4$: 349.1410 $[M+Na]^+$; found: 349.1409; TLC: R_f=0.27 (*Z* isomer), 0.32 (*E* isomer) (petroleum ether/Et_2O 40:60).

4-(1-Cyclopropylmethylidene)-5-phenethyltetrahydro-2-furanol (10r): The title compound was prepared according to the general procedure GP1 from α-bromoester **9r** (1.61 g, 5 mmol). Flash chromatography (petroleum ether/Et_2O 50:50) gave **10r** (0.95 g, 78%, *E*/*Z* 52:48) as a colorless oil. ^{1}H NMR (C_6D_6, 300 MHz; mixture of four isomers): δ=7.28–7.04 (m, 20H), 5.60–5.49 (m, 4H), 5.02–4.38 (m, 8H), 3.71 (br d, *J*= 3.0 Hz, 1H; OH), 3.53 (br d, *J*=2.9 Hz, 1H; OH), 3.49 (br s, 1H; OH), 3.47 (br s, 1H; OH), 3.07–2.35 (m, 16H), 2.33–1.73 (m, 8H), 1.18–0.89 (m, 4H), 0.57–0.37 (m, 8H), 0.24–0.09 ppm (m, 8H); ^{13}C NMR (C_6D_6, 75 MHz; mixture of four isomers): δ=142.70 (C), 142.66 (2C), 142.63 (C), 138.6 (C_{Ar}), 138.5 (C_{Ar}), 138.4 (C_{Ar}), 137.6 (C_{Ar}), 129.0 ($4CH_{Ar}$), 128.8 ($4CH_{Ar}$), 128.7 ($8CH_{Ar}$), 126.3 (CH), 126.1 ($4CH_{Ar}$), 125.5 (CH), 124.8 (CH), 124.7 (CH), 98.6 (CH), 98.4 (CH), 97.7 (CH), 97.4 (CH), 80.8 (CH), 79.2 (CH), 78.9 (CH), 77.8 (CH), 41.1 (CH_2), 40.7 (CH_2), 39.9 (CH_2), 38.9 (CH_2), 38.0 (CH_2), 37.83 (CH_2), 37.78 (CH_2), 37.4 (CH_2), 32.7 (CH_2), 32.63 (CH_2), 32.1 (CH_2), 31.9 (CH_2), 12.1 (CH), 12.0 (CH), 11.23 (CH), 11.19 (CH), 7.5 (CH_2), 7.4 (CH_2), 7.0 (CH_2), 6.9 ($2CH_2$), 6.8 (CH_2), 6.71 (CH_2), 6.66 ppm (CH_2); IR (neat): $\tilde{\nu}$=3396, 3025, 3001, 2929, 1652, 1495, 1454, 1354, 1028, 957, 699 cm^{-1}; MS (ESI^+): *m/z*: for $C_{16}H_{20}O_2$: 267 $[M+Na]^+$; HRMS (ESI^+): *m/z*: calcd for $C_{16}H_{20}O_2$: 267.1356 $[M+Na]^+$; found: 267.1348; TLC: R_f=0.52 (*E* isomer), 0.46 (*Z* isomer) (petroleum ether/Et_2O 50:50).

(2*S,3*R**)-3-Methyl-2-phenetyltetrahydrofuran (18)**: BF_3·Et_2O (390 μL, 3 mmol) was added dropwise to a solution of lactol **7b** (310 mg, 1.5 mmol) and triethylsilane (720 μL, 4.5 mmol) in CH_2Cl_2 (20 mL) under argon at −78 °C. After completion of the reaction (TLC monitoring), the mixture was allowed to reach −30 °C and a saturated solution of $NaHCO_3$ was added. The aqueous phase was extracted with CH_2Cl_2 (×2) and the resulting organic phase was dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash chromatography (petroleum ether/Et_2O 95:5) gave **18** (0.24 g, 82%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ= 7.23–7.07 (m; 5H; Ar), 3.83–3.71 (m, 2H), 3.25 (dt, *J*=3.5, 8.1 Hz, 1H), 2.77 (ddd, *J*=5.2, 10.7, 13.7 Hz, 1H), 2.58 (ddd, *J*=6.2, 10.5, 13.7, 1H), 2.07–1.96 (m, 1H), 1.85–1.59 (m, 3H), 1.52–1.40 (m, 1H), 0.94 ppm (d, *J*=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=142.6 (CqAr), 128.5 (2CAr), 128.4 (2CAr), 125.8 (CAr), 85.4, 66.9, 39.2, 36.4, 34.9, 33.0, 17.4 ppm; IR (neat): $\tilde{\nu}$=3025, 2927, 2870, 1603, 1453, 1107, 1039, 746, 699 cm^{-1}; MS (CI^+): *m/z*: $C_{13}H_{18}O$: 208 $[M+NH_4]^+$, 191 $[M+H]^+$; HRMS (EI^+): *m/z*: calcd for $C_{13}H_{18}O$: 190.1353 $[M]^+$; found: 190.1357; TLC: R_f=0.37 (petroleum ether/Et_2O 95:5).

(2*S,3*R**,5*S**)-5-Allyl-3-methyl-2-phenetyltetrahydrofuran (19)**: BF_3·Et_2O (390 μL, 3 mmol) was added dropwise to a solution of lactol **7b** (310 mg, 1.5 mmol) and allyltrimethylsilane (730 μL, 4.5 mmol) in CH_2Cl_2 (22 mL) under argon at −78 °C. After completion of the reaction (TLC monitoring), the mixture was allowed to reach −30 °C and a saturated solution of $NaHCO_3$ was added. The aqueous phase was extracted with CH_2Cl_2 (×2) and the resulting organic phase was dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash chromatography (petroleum ether/Et_2O 98:2) gave **19** (0.30 g, 86%, d.r.=85:15) as a colorless oil.

Major isomer: ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.30–7.13 (m, 5HAr), 5.83 (tdd, *J*=7.0, 10.2, 17.1 Hz, 1H), 5.13–5.03 (m, 2H), 4.05–3.95 (m, 1H), 3.37 (dt, *J*=4.1, 7.4 Hz, 1H), 2.82 (ddd, *J*=5.5, 10.6, 13.7 Hz, 1H), 2.66 (ddd, *J*=6.2, 10.4, 13.7 Hz, 1H), 2.43–2.32 (m, 1H), 2.28–2.14 (m, 1H), 1.95–1.73 (m, 4H), 1.63–1.54 (m, 1H), 0.99 ppm (d, *J*=6.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=142.6 (CqAr), 135.3 (C), 128.5 (2CAr), 128.4 (2CAr), 125.8 (CAr), 116.8, 85.8, 77.2, 41.0, 39.3, 38.2, 36.6, 32.7, 17.8 ppm; IR (neat): $\tilde{\nu}$=3063, 2955, 2870, 1641, 1454, 1108, 1031, 913, 699 cm^{-1}; MS (CI^+): *m/z*: for $C_{16}H_{22}O$: 248 $[M+NH_4]^+$, 231 $[M+H]^+$; HRMS (EI^+): *m/z*: calcd for $C_{16}H_{22}O$: 230.1671 $[M]^+$: found: 230.1670; TLC: R_f=0.57 (petroleum ether/Et_2O 95:5).

(2*S,3*R**,5*R**)- + (2*S**,3*R**,5*R**)-3-Methyl-2-phenetyl-5-phenylsulfanyltetrahydrofuran (20)**: BF_3·Et_2O (390 μL, 3 mmol) was added dropwise to a solution of lactol **7b** (310 mg, 1.5 mmol) and thiophenol (460 μL, 4.5 mmol) in CH_2Cl_2 (20 mL) under argon at −78 °C. After completion of the reaction (TLC monitoring), the mixture was allowed to reach −30 °C and a saturated solution of $NaHCO_3$ was added. The aqueous phase was extracted with CH_2Cl_2 (×2) and the resulting organic phase was dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash chromatography (petroleum ether/Et_2O 98:2) gave **20** (0.36 g, 81%, d.r.=65:35) as a colorless oil.

Major isomer: ^{1}H NMR (C_6D_6, 300 MHz): δ=7.69 (d, *J*=7.2 Hz, 2H; Ar), 7.18–6.95 (m, 8H; Ar), 5.55 (dd, *J*=6.3, 6.6 Hz, 1H), 3.65 (dt, *J*= 3.0, 8.3 Hz, 1H), 2.85 (ddd, *J*=5.2, 9.8, 14.0 Hz, 1H), 2.66 (ddd, *J*=7.1, 9.6, 14.0 Hz, 1H), 2.30–2.18 (m, 1H), 1.81–1.60 (m, 2H), 1.51–1.34 (m, 2H), 0.68 ppm (d, *J*=6.1 Hz, 3H); ^{13}C NMR (C_6D_6, 75 MHz): δ=142.3 (CqAr), 137.5 (CqAr), 131.0 (2CAr), 129.0 (2CAr), 128.8 (2CAr), 128.6 (2CAr), 126.7 (CAr), 126.1 (CAr), 86.1, 83.2, 41.9, 38.8, 35.2, 33.0, 15.9 ppm; IR (neat): $\tilde{\nu}$=3024, 2928, 2869, 1583, 1453, 1090, 1026, 741, 699 cm^{-1}; MS (CI^+): *m/z*: for $C_{19}H_{22}OS$: 316 $[M+NH_4]^+$; HRMS (EI^+): *m/z*: calcd for $C_{19}H_{22}OS$: 298.1391 $[M]^+$; found: 298.1391; TLC: R_f=0.58 (major isomer) (petroleum ether/Et_2O 95:5).

Minor isomer: ^{1}H NMR (C_6D_6, 300 MHz): δ=relevant signals 7.67 (d, *J*=7.3 Hz, 2H; Ar), 5.51 (dd, *J*=3.0, 6.3, 7.2 Hz, 1H), 3.41 (dt, *J*=3.6, 8.7 Hz, 1H), 0.65 ppm (d, *J*=6.4 Hz, 3H); ^{13}C NMR (C_6D_6, 75 MHz): δ= 142.5 (CqAr), 136.9 (CqAr), 131.4 (2CAr), 129.0 (2CAr), 128.8 (2CAr), 128.6 (2CAr), 126.8 (CAr), 126.0 (CAr), 87.1, 86.4, 41.9, 38.4, 37.5, 33.1, 16.9 ppm; IR (neat): $\tilde{\nu}$=3024, 2928, 2869, 1583, 1453, 1090, 1026, 741, 699 cm^{-1}; MS (CI^+): *m/z*: for $C_{19}H_{22}OS$: 316 $[M+NH_4]^+$; HRMS (EI^+): *m/z*: calcd for $C_{19}H_{22}OS$: 298.1391 $[M]^+$; found: 298.1391; TLC: R_f=0.50 (minor isomer) (petroleum ether/Et_2O 95:5).

(4*R,5*R**)-4-Methyl-5-phenetyltetrahydro-2-furanone (21)**: To a solution of lactol **7b** (0.573 g, 2.8 mmol) in CH_2Cl_2 (28 mL) were successively added a solution of $NaHCO_3$/K_2CO_3 (0.5 mol L^{-1}/H_2O, 28 mL), tBu_4NCl (0.078 g, 0.28 mmol), *N*-chlorosuccinimide (0.742 g, 5.6 mmol), and Ac-TEMPO (0.209 g, 1.0 mmol) at room temperature. The reaction mixture was stirred vigorously at room temperature until completion (NMR spectroscopic monitoring, ca. 36 h). The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (×3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash column chromatography on silica gel (petroleum ether/Et_2O 60:40) gave **21** (0.535 g, 94%, d.r.> 95:5) as a colorless oil. ^{1}H NMR (C_6D_6, 300 MHz): δ=7.18–7.00 (m, 5H; Ar), 3.37 (dt, *J*=7.6, 4.9 Hz, 1H), 2.71–2.62 (m, 1H), 2.48 (dt, *J*=13.9, 8.5 Hz, 1H), 2.06 (dd, *J*=16.8, 7.9 Hz, 1H), 1.53–1.28 (m, 4H), 0.33 ppm (d, *J*=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=176.6, 141.0, 128.6 (2C), 128.5 (2C), 126.2, 86.4, 37.2, 36.3, 35.9, 32.1, 17.3 ppm; IR (neat): $\tilde{\nu}$=3061, 3026, 2932, 1774, 1602, 1495, 1454, 1383,

1360, 1330, 1305, 1257, 1203, 1144, 1027, 937, 751, 701 cm^{-1}; MS (CI^+): m/z: for $C_{13}H_{16}O_2$: 222.1 $[M+NH_4]^+$, 205.1 $[M+H]^+$; HRMS (CI^+): m/z: calcd for $C_{13}H_{16}O_2$: 205.1223 $[M+H]^+$; found: 205.1219; TLC: $R_f=0.31$ (petroleum ether/Et_2O 60:30).

(*E*)-(5*R,6*S**)-6-Hydroxy-5-methyl-8-phenyl-2-octenoic ethyl ester ((*E*)-22)**: (Carbethoxymethylene)triphenylphosphorane (1.04 g, 3 mmol) was added to a solution of lactol **7b** (206 mg, 1 mmol) in CH_2Cl_2 (20 mL) at room temperature. The solution was stirred at room temperature until completion (NMR spectroscopic monitoring, 16 h). The solvent was removed under reduced pressure. Flash column chromatography on silica gel (petroleum ether/Et_2O 60:40) gave **22** (0.24 g, 87%, d.r. (E/Z)= 89:11) as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): $\delta=7.32$–7.17 (m, 5H; Ar), 6.93 (ddd, $J=6.9$, 8.1, 15.3 Hz, 1H), 5.82 (dt, $J=1.3$, 15.3 Hz, 1H), 4.18 (q, $J=7.1$ Hz, 2H), 3.51–3.44 (m, 1H), 2.93–2.80 (m, 1H), 2.71–2.61 (m, 1H), 2.47–2.38 (m, 1H), 2.13–2.02 (m, 1H), 1.88–1.65 (m, 3H), 1.50 (brs, 1H; OH), 1.29 (t, $J=7.1$ Hz, 3H), 0.92 ppm (d, $J=6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=166.7$, 148.1, 142.1 (CqAr), 128.6 (2CAr), 128.5 (2CAr), 126.0 (CAr), 122.8, 74.9, 60.3, 38.7, 35.8, 35.2, 32.4, 15.8, 14.4 ppm; IR (neat): $\tilde{\nu}=3464$, 3026, 2930, 1718, 1701, 1496, 1454, 1269, 1043, 700 cm^{-1}; MS (CI^+): m/z: for $C_{17}H_{24}O_3$: 294 $[M+NH_4]^+$, 277 $[M+H]^+$; HRMS (ESI^+): m/z: calcd for $C_{17}H_{24}O_3$: 299.1623 $[M+Na]^+$; found: 299.1621; TLC: $R_f=0.26$ (petroleum ether/Et_2O 60:40).

(*Z*)-(5*R, 6*S**)-6-Hydroxy-5-methyl-8-phenyl-2-octenoic ethyl ester ((*Z*)-22)**: ^1H NMR ($CDCl_3$, 300 MHz): $\delta=7.33$–7.15 (m, 5H; Ar), 6.28 (ddd, $J=7.3$, 9.1, 11.5 Hz, 1H), 5.82 (dt, $J=1.3$, 11.5 Hz, 1H), 4.18 (q, $J=$ 7.1 Hz, 2H), 3.44–3.38 (m, 1H), 2.93–2.77 (m, 2H), 2.70–2.58 (m, 2H), 1.92–1.64 (m, 3H), 1.60 (brs, 1H; OH), 1.29 (t, $J=7.1$ Hz, 3H), 0.94 ppm (d, $J=7.0$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=167.1$, 148.7, 142.6 (CqAr), 128.6 (2CAr), 128.5 (2CAr), 125.8 (CAr), 121.0, 74.6, 60.3, 39.6, 35.9, 32.4, 32.0, 16.1, 14.4 ppm.

(3*R,4*S**)-3-Methyl-6-phenylhexane-1,4-diol (23b)**: According to the general procedure GP3 from lactol **7b** (0.50 g, 2.4 mmol). Flash chromatography (petroleum ether/Et_2O 20:80) gave **23b** (0.47 g, 90%, d.r.> 95:5) as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): $\delta=7.27$–7.12 (m, 5H), 3.74 (ddd, $J=4.9$, 6.5, 10.9 Hz, 1H), 3.62 (ddd, $J=5.1$, 6.9, 10.9 Hz, 1H), 3.44 (ddd, $J=3.6$, 5.7, 9.0 Hz, 1H), 3.06 (s, 2H; OH), 2.85 (ddd, $J=$ 5.6, 9.8, 13.8 Hz, 1H), 2.65 (ddd, $J=6.7$, 9.7, 13.8 Hz, 1H), 1.88–1.55 (m, 5H), 0.93 ppm (d, $J=6.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=142.4$, 128.6 (2C), 128.5 (2C), 125.9, 75.2, 60.4, 36.8, 36.4, 35.4, 32.4, 16.6 ppm; IR (neat): $\tilde{\nu}=3330$, 3025, 2932, 2876, 1603, 1454, 1055, 748, 699 cm^{-1}; MS (CI^+): m/z: for $C_{13}H_{20}O_2$: 226 $[M+NH_4]^+$, 209 $[M+H]^+$; HRMS (CI^+): m/z: calcd for $C_{13}H_{20}O_2$: 209.1542 $[M+H]^+$; found: 209.1542; TLC: $R_f=$ 0.46 (petroleum ether/Et_2O 10:90).

(3*R,4*R**)-5-Benzyloxymethoxy-3-methyl-1,4-pentanediol (23h)**: According to the general procedure GP3 from lactol **7h** (0.15 g, 0.6 mmol). Flash chromatography (Et_2O) gave **23h** (0.15 g, 99%, d.r.>95:5) as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): $\delta=7.40$–7.25 (m, 5H), 4.79–4.77 (m, 2H), 4.61 (s, 2H), 3.76–3.68 (m, 2H), 3.63–3.50 (m, 3H), 3.51 (brs, 2H; OH), 1.85–1.67 (m, 2H), 1.61–1.49, (m, 1H), 0.92 ppm (d, $J=6.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=137.6$ (Cq), 128.5 (2C), 127.9 (2C), 127.8, 95.1, 74.4, 71.2, 69.7, 60.3, 36.1, 33.8, 16.5 ppm; IR (neat): $\tilde{\nu}=3386$, 2931, 2880, 1652, 1454, 1381, 1114, 1047, 739, 698 cm^{-1}; MS (ESI^+): m/z: for $C_{14}H_{22}O_4$: 277 $[M+Na]^+$; HRMS (ESI^+): m/z: calcd for $C_{14}H_{22}O_4$: 277.1416 $[M+Na]^+$; found: 277.1415; TLC: $R_f=0.25$ (Et_2O).

(3*R,4*R**)-3-Methyl-5-trityloxy-1,4-pentanediol (23i)**: According to the general procedure GP3 from lactol **7i** (0.37 g, 1 mmol). Flash chromatography (petroleum ether/Et_2O 10:90) gave **23i** (0.34 g, 90%, d.r.>95:5) as a white gum. ^1H NMR (C_6D_6, 300 MHz): $\delta=7.68$ (d, $J=7.6$ Hz, 6H), 7.30–7.10 (m, 9H), 3.76–3.54 (m, 5H), 3.46 (dd, $J=3.0$, 9.0 Hz, 1H), 3.35 (dd, $J=6.9$, 9.0 Hz, 1H), 2.00–1.86 (m, 1H), 1.80–1.69 (m, 1H), 1.58–1.45 (m, 1H), 0.81 ppm (d, $J=6.8$ Hz, 3H); ^{13}C NMR (C_6D_6, 75 MHz): $\delta=$ 144.6 (3Cq), 129.2 (6C), 128.3 (6C), 127.3 (3C), 87.1 (Cq), 75.3, 66.7, 60.4, 36.3, 34.2, 16.7 ppm; IR (neat): $\tilde{\nu}=3374$, 2969, 2878, 1490, 1448, 1050, 763, 706 cm^{-1}; MS (ESI^+): m/z: for $C_{25}H_{28}O_3$: 399 $[M+Na]^+$, 774 $[2M+Na]^+$; HRMS (ESI^+): m/z: calcd for $C_{25}H_{28}O_3$: 399.1936 $[M+Na]^+$; found: 399.1938; TLC: $R_f=0.62$ (Et_2O).

(3*R,5*R**,6*S**)- + (3*S**,5*R**,6*S**)-5-Methyl-8-phenyl-oct-1-ene-3,6-diol (24)**: *n*BuLi (0.4 mL, 2.5 M/hexanes, 1 mmol) was added dropwise to a solution of lactol **7b** (206 mg, 1 mmol) in THF (15 mL) at −78 °C. The solution was stirred for 30 min and vinylmagnesium bromide (3 mL, 1 M/THF, 3 mmol) was added dropwise. The solution was allowed to warm to room temperature. After 3 h at room temperature, the mixture was quenched with NH_4Cl saturated solution and extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash chromatography (petroleum ether/Et_2O 50:50) gave **24** (0.16 g, 67%, d.r.=56:44) as a colorless oil. ^1H NMR (C_6D_6, 300 MHz; mixture of two isomers): $\delta=7.21$–7.03 (m, 10H; Ar, two isomers), 5.89–5.73 (m, 2H; two isomers), 5.23 (dt, $J=1.5$, 17.2 Hz, 1H; major isomer), 5.22 (dt, $J=1.5$, 17.1 Hz, 1H; minor isomer), 5.00 (dt, $J=1.5$, 10.3 Hz, 1H; minor isomer), (dt, $J=1.5$, 10.4 Hz, 1H; major isomer), 4.19–4.06 (m, 2H; two isomers), 3.97 (brs, 2H; OH minor isomer), 3.71 (brs, 2H; OH, major isomer), 3.39–3.27 (m, 2H; two isomers), 2.95–2.82 (m, 2H; two isomers), 2.73–2.59 (m, 2H; two isomers), 1.85–1.06 (m, 10H; two isomers), 0.87 (d, $J=6.7$ Hz, 3H; minor isomer), 0.81 ppm (d, $J=6.8$ Hz, 3H; major isomer); ^{13}C NMR (C_6D_6, 75 MHz; mixture of two isomers): $\delta=143.0$ (CqAr, major isomer), 142.9 (CqAr, minor isomer), 142.6 (Cb, major isomer), 142.0 (Cb, minor isomer), 128.9 (4CAr, two isomers), 128.7 (4CAr, two isomers), 126.0 (2CAr, two isomers), 114.1 (minor isomer), 113.5 (major isomer), 75.8 (major isomer), 74.8 (minor isomer), 71.5 (major isomer), 70.0 (minor isomer), 41.9 (major isomer), 39.7 (minor isomer), 36.9 (2C, minor isomer and major isomer), 36.5 (major isomer), 35.9 (minor isomer), 32.8 (minor isomer), 32.5 (major isomer), 17.1 (minor isomer), 17.0 ppm (major isomer); IR (neat): $\tilde{\nu}=3352$, 3025, 2930, 2873, 1495, 1453, 1038, 921, 699 cm^{-1}; MS (CI^+): m/z: for $C_{15}H_{22}O_2$: 252 $[M+NH_4]^+$, 235 $[M+H]^+$, 217 $[M-H_2O+H]^+$; HRMS (ESI^+): m/z: calcd for $C_{15}H_{22}O_2$ $[M+Na]^+$: 257.1517; found: 257.1515; TLC: $R_f=0.32$ (petroleum ether/Et_2O 50:50).

(4*R,5*R**)-4-Methyl-5-trityloxymethyltetrahydro-2-furanone (25)**: Molecular sieves (4 Å) and PCC (325 mg, 1.5 mmol) were added to a solution of lactol **7h** (375 mg, 1 mmol) in CH_2Cl_2. The mixture was stirred at room temperature until completion of the reaction (TLC monitoring, $KMnO_4$) and then filtered through Celite. The solvent was removed under reduced pressure. Flash column chromatography on silica gel (petroleum ether/Et_2O 60:40) gave **25** (0.37 g, 98%) as a white powder. ^1H NMR (C_6D_6, 300 MHz): $\delta=7.53$ (d, $J=7.7$ Hz, 6H), 7.16–6.99 (m, 9H), 3.59 (ddd, $J=3.3$, 4.8, 6.6 Hz, 1H), 3.20 (dd, $J=3.3$, 10.5 Hz, 1H), 2.98 (dd, $J=4.8$, 10.5 Hz, 1H), 2.24 (dd, $J=8.3$, 16.9 Hz, 1H), 1.77–1.63 (m, 1H), 1.54 (dd, $J=8.2$, 16.9 Hz, 1H), 0.35 ppm (d, $J=6.7$ Hz, 3H); ^{13}C NMR (C_6D_6, 75 MHz): $\delta=175.1$, 144.2 (3Cq), 129.0 (6C), 128.3 (6C), 127.4 (3C), 87.4, 84.9, 64.8, 36.6, 32.0, 17.7 ppm; IR (KBr): $\tilde{\nu}=3448$, 3050, 2937, 2868, 1766, 1487, 1446, 1217, 1106, 775 cm^{-1}; MS (ESI^+): m/z: calcd for $C_{25}H_{24}O_3$: 395 $[M+Na]^+$; HRMS (ESI^+): m/z: calcd for $C_{25}H_{24}O_3$: 395.1623 $[M+Na]^+$; found: 395.1623; m.p. 140–141 °C; TLC: $R_f=0.33$ (petroleum ether/Et_2O 60:40).

2-(2-*tert*-Butyldiphenylsilyloxyethyl)-1-phenyl-hepta-1,6-dien-3-ol: Et_3N (210 μL, 1.5 mmol), *tert*-butyldiphenylsilyl chloride (0.418 g, 1.5 mmol), and DMAP (0.012 g, 0.1 mmol) were successively added to a solution of diol **26l** (0.235 g, 1.0 mmol) in CH_2Cl_2 (8 mL) at room temperature. The reaction mixture was stirred at room temperature for 9 h, then quenched with a saturated aqueous solution of $NaHCO_3$ (10 mL). The aqueous phase was extracted with Et_2O (×3). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash chromatography (petroleum ether/toluene/Et_2O 50:40:10) gave the title compound as a mixture of two diastereoisomers (0.446 mg, 93%, E/Z 23:77) as a colorless oil.

Major isomer: ^1H NMR ($CDCl_3$, 400 MHz): $\delta=7.72$–7.68 (m, 4H), 7.46–7.22 (m, 11H), 6.44 (s, 1H), 5.77 (ddt, $J=6.6$, 10.2, 16.9 Hz, 1H), 4.95 (dq, $J=1.7$, 17.0 Hz, 1H), 4.91–4.88 (m, 1H), 4.67 (dt, $J=5.4$, 8.1 Hz, 1H), 3.92 (dt, $J=5.1$, 10.0, 1H), 3.80 (dt, $J=4.6$, 9.1 Hz, 1H), 3.32 (d, $J=$ 5.3 Hz, 1H), 2.64 (ddd, $J=5.3$, 9.2, 14.2 Hz, 1H), 2.32 (ddt, $J=1.1$, 4.6, 14.2 Hz, 1H), 2.16–1.97 (m, 2H), 1.83–1.75 (m, 1H), 1.64–1.55 (m, 1H), 1.08 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta=142.1$, 138.5, 137.3, 135.8, 133.11, 133.08, 130.03, 129.99, 129, 97, 129.0, 128.3, 127.96, 127.94, 126.8, 69.0, 65.9, 35.5, 34.6, 30.2, 27.0, 19.2 ppm; IR (film): $\tilde{\nu}=3430$, 3072, 3052, 2931, 2857, 1491, 1471, 1444, 1428, 1217, 1112, 1073, 1046, 918, 861, 757, 700 cm^{-1}; MS (CI^+): m/z: for $C_{31}H_{38}O_2Si$: 453 $[M-H_2O+H]^+$, 470

$[M+H]^+$; HRMS (ESI^+): m/z: calcd for $C_{31}H_{38}O_2Si$: 493.2533 $[M+Na]^+$; found: 493.2523; TLC: $R_f=0.41$ (petroleum ether/Et_2O 80:20).

Minor isomer: ^1H NMR ($CDCl_3$, 400 MHz): $\delta=7.65$–7.59 (m, 4H), 7.44–7–23 (m, 8H), 7.19–7.14 (m, 3H), 6.60 (s, 1H), 5.86 (ddt, $J=6.6$, 10.2, 16.9 Hz, 1H), 5.05 (dq, $J=1.7$, 17.1 Hz, 1H), 5.00–4.96 (m, 1H), 4.22–4.18 (m, 1H), 3.80–3.71 (m, 1H), 3.13 (d, $J=4.4$ Hz, 1H), 2.62–2.58 (m, 2H), 2.25–2.07 (m, 2H), 1.83–1.65 (m, 2H), 1.04 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta=142.1$, 138.6, 137.5, 135.8, 133.15, 133.09, 129.96, 129.91, 128.82, 128.6, 128.4, 127.91, 127.88, 126.8, 76.6, 63.7, 35.49, 30.36, 30.26, 26.9, 19.2 ppm; TLC: $R_f=0.38$ (petroleum ether/Et_2O 80:20).

3-(*tert*-Butyldiphenylsilyloxy)-1-(5-hydroxytetrahydrofuran-2-yl)-propan-1-one (27): O_3 was introduced to a solution of 2-(2-*tert*-butyldiphenylsilyloxyethyl)-1-phenyl-hepta-1,6-dien-3-ol (0.300 g, 0.63 mmol) in CH_2Cl_2/MeOH (9:1, 40 mL) until persistence of a deep-blue coloration at −78 °C. The excess of ozone was removed under a flow of argon and Me_2S (0.5 mL, 6.8 mmol) was added at −78 °C. The reaction mixture was stirred overnight while the temperature was allowed to slowly reach room temperature. The solvent and the excess of Me_2S were removed under reduced pressure. Flash chromatography (petroleum ether/Et_2O 50:50) gave **27** (0.21 g, 84%) as a colorless oil.

Major isomer: ^1H NMR (C_6D_6, 300 MHz): $\delta=7.93$–7.83 (m, 4H; Ar), 7.37–7.25 (m, 8H; Ar), 5.40–5.34 (m, 1H), 4.30 (t, $J=7.9$ Hz, 1H), 4.13–4.07 (m, 2H), 2.90 (brs, 1H; OH), 2.79 (dt, $J=6.1$, 16.9 Hz, 1H), 2.72–2.64 (m, 1H), 2.16–2.0 (m, 1H), 1.76–1.66 (m, 1H), 1.52–1.39 (m, 2H), 1.26 ppm (s, 9H); ^{13}C NMR (C_6D_6, 75 MHz): $\delta=209.9$, 136.0, 133.9, 130.0, 128.1, 99.81, 84.4, 59.6, 41.2, 33.6, 27.0, 26.3, 19.34 ppm; IR (film): $\tilde{\nu}=3434$, 3072, 3052, 2958, 2931, 2888, 2857, 1719, 1487, 1472, 1462, 1428, 1390, 1361, 1112, 823, 786, 701 cm^{-1}; MS (CI^+): m/z: for $C_{23}H_{30}O_4Si$: 416 $[M+NH_4]^+$; HRMS (ESI^+): m/z: calcd for $C_{23}H_{30}O_4Si$: 421.1813 $[M+Na]^+$; found: 421.1813; TLC: $R_f=0.21$ (petroleum ether/Et_2O 50:50).

Minor isomer: ^1H NMR (C_6D_6, 300 MHz): $\delta=7.93$–7.25 (m, 10H; Ar), 5.40–5.34 (m, 1H), 4.54 (dd, $J=5.2$, 8.9 Hz, 1H), 4.13–4.07 (m, 2H), 2.70–2.64 (m, 2H), 2.26 (brs, 1H; OH), 2.16–2.00 (m, 1H), 1.93–1.83 (m, 1H), 1.76–1.53 (m, 2H), 1.25 ppm (s, 9H); ^{13}C NMR (C_6D_6, 75 MHz): $\delta=$ 208.3, 136.0, 133.9, 130.0, 128.1, 99.75, 83.0, 59.4, 41.3, 32.5, 27.0, 26.5, 19.36 ppm; IR (film): $\tilde{\nu}=3434$, 3072, 3052, 2958, 2931, 2888, 2857, 1719, 1487, 1472, 1462, 1428, 1390, 1361, 1112, 823, 786, 701 cm^{-1}; MS (CI^+): m/z: for $C_{23}H_{30}O_4Si$: 416 $[M+NH_4]^+$; HRMS (ESI^+): m/z: calcd for $C_{23}H_{30}O_4Si$: 421.1813 $[M+Na]^+$; found: 421.1813; TLC: $R_f=0.21$ (petroleum ether/Et_2O 50:50).

(2*E*)-5-(1-Hydroxy-3-phenylpropyl)-2,5-hexadienoic ethyl ester (28a): (Carbethoxymethylene)triphenylphosphorane (1.04 g, 3 mmol) was added to a solution of lactol **10a** (204 mg, 1 mmol) in CH_2Cl_2 (20 mL) at room temperature. The solution was stirred at room temperature for 16 h. Silica was added and the solvent was removed under reduced pressure. Flash column chromatography on silica gel (petroleum ether/Et_2O 60:40) gave **28a** (210 mg, 77%, d.r. (*E*/*Z*) ca. 87:13) as a colorless oil. ^1H NMR (C_6D_6, 300 MHz): $\delta=7.26$–7.04 (m, 5H; Ar+1H), 5.87 (dt, $J=1.4$, 15.6 Hz, 1H), 4.95 (s, 1H), 4.71 (s, 1H), 4.04 (q, $J=7.1$ Hz, 2H), 3.84–3.76 (m, 1H), 2.74–2.49 (m, 4H), 1.73–1.55 (m, 2H+1H; OH), 0.99 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (C_6D_6, 75 MHz): $\delta=166.2$, 149.0, 146.7, 142.3, 128.8, 128.7, 126.1, 123.2, 112.0, 74.0, 60.2, 37.3, 34.2, 32.2, 14.3 ppm; IR (film): $\tilde{\nu}=3500$, 3084, 3061, 3025, 2981, 2935, 2863, 1717, 1652, 1583, 1495, 1453, 1368, 1310, 1271, 1206, 1160, 1041, 987, 911, 865, 806, 749, 699 cm^{-1}; MS (CI^+): m/z: for $C_{17}H_{22}O_3$: 292 $[M+NH_4]^+$, 275 $[M+H]^+$; HRMS (ESI^+): m/z: calcd for $C_{17}H_{22}O_3$: 297.1461 $[M+Na]^+$; found: 297.1457; TLC: $R_f=0.33$ (petroleum ether/Et_2O 50:50).

(2*E*)-4-Butyl-5-(1-hydroxymethyl)-2,5-hexadienoic ethyl ester (28b): (Carbethoxymethylene)triphenylphosphorane (1.04 g, 3 mmol) was added to a solution of lactol **10b** (156 mg, 1 mmol) in CH_2Cl_2 (20 mL) at room temperature. The solution was stirred at room temperature for 16 h. Silica was added and the solvent was removed under reduced pressure. Flash column chromatography on silica gel (petroleum ether/Et_2O 60:40) gave **28b** (210 mg, 93%, d.r. (*E*/*Z*) > 95:5) as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): $\delta=6.84$ (dd, $J=15.6$, 8.5 Hz, 1H), 5.82 (dd, $J=15.6$, 1.0 Hz, 1H), 5.19 (d, $J=0.9$ Hz, 1H), 5.00 (brs, 1H), 4.18 (q, $J=7.1$ Hz, 2H), 4.07 (brs, 2H), 2.87 (q, $J=6.0$ Hz, 2H), 1.63–1.19 (m, 6H), 1.29 (t, $J=7.1$ Hz, 3H), 0.88 ppm (t, $J=6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=166.7$, 151.3, 149.2, 120.9, 110.5, 64.3, 60.3, 45.4, 32.3, 29.4, 22.5, 14.1, 13.8 ppm; IR (film): $\tilde{\nu}=3500$, 2957, 2931, 2871, 2860, 1720, 1640, 1466, 1392, 1334, 1304, 1267, 1213, 1175, 1134, 1096, 1043, 988, 904, 868, 811, 788, 731 cm^{-1}; MS (CI^+): m/z: for $C_{13}H_{22}O_3$: 244 $[M+NH_4]^+$, 227 $[M+H]^+$; HRMS (ESI^+): m/z: calcd for $C_{13}H_{22}O_3$: 249.1461 $[M+Na]^+$; found: 249.1464; TLC: $R_f=0.45$ (petroleum ether/Et_2O 40:60).

Ethyl 2-(4-methylene-5-phenethyl-tetrahydrofuran-2-yl)acetate (29a): *t*BuOK (0.123 g, 1.1 mmol) was added to a solution of diene **28a** (274 mg, 1 mmol) in THF (6 mL) at −78 °C. The solution was stirred at −78 °C for 3 h. The reaction mixture was quenched with a saturated aqueous solution of NH_4Cl (10 mL) and the aqueous phase was extracted with Et_2O (×3). The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash column chromatography on silica gel (petroleum ether/Et_2O 80:20) gave **29a** (219 mg, 80%, d.r. = 70:30) as a colorless oil.

Major isomer: ^1H NMR ($CDCl_3$, 300 MHz): $\delta=7.22$–7.08 (m, 5H), 4.93–4.90 (m, 1H), 4.79–4.77 (m, 1H), 4.28–4.16 (m, 1H), 4.21 (dq, $J=6.5$, 9.1 Hz, 1H), 4.10 (q, $J=7.1$ Hz, 2H), 2.78–2.58 (m, 3H), 2.64 (dd, $J=6.7$, 15.1 Hz, 1H), 2.46 (dd, $J=6.6$, 15.3 Hz, 1H), 2.34–2.19 (m, 1H), 1.90 (dddd, $J=3.8$, 6.5, 10.4, 17.5 Hz, 1H), 1.82–1.68 (m, 1H), 1.20 ppm (t, $J=$ 7.1 Hz, 3H); ^1H NMR ($CDCl_3$, 75 MHz): $\delta=171.16$, 151.0, 142.4, 128.6 (2C), 128.4 (2C), 125.83, 105.6, 80.3, 74.3, 160.6, 40.7, 39.3, 37.2, 31.5, 14.3 ppm; IR (film): $\tilde{\nu}=3083$, 3061, 3025, 2981, 2862, 1734, 1496, 1454, 1433, 1399, 1368, 1312, 1259, 1242, 1193, 1146, 1093, 1042, 885, 749, 700 cm^{-1}; MS (CI^+): for $C_{17}H_{22}O_3$: 292 $[M+NH_4]^+$, 275 $[M+H]^+$; HRMS (ESI^+): m/z: calcd for $C_{13}H_{22}O_3$: 297.1461 $[M+Na]^+$; found: 297.1459; TLC: $R_f=0.57$ (petroleum ether/Et_2O 80:20).

Minor isomer: ^1H NMR ($CDCl_3$, 300 MHz): $\delta=7.22$–7.08 (m, 5H), 4.96–4.94 (m, 1H), 4.82–4.80 (m, 1H), 4.44 (quint., $J=6.6$ Hz, 1H), 4.39–4.31 (m, 1H), 4.10 (q, $J=7.1$ Hz, 2H), 2.78–2.58 (m, 3H), 2.57 (dd, $J=7.0$, 15.2 Hz, 1H), 2.38 (dd, $J=6.8$, 15.2 Hz, 1H), 2.34–2.19 (m, 1H), 1.82–1.68 (m, 2H), 1.20 ppm (t, $J=7.1$ Hz, 3H); ^1H NMR ($CDCl_3$, 75 MHz): $\delta=171.20$, 150.66, 142.2 (minor isomer), 128.6 (2C), 128.4 (2C), 125.85, 104.9, 79.3, 73.8, 160.6, 40.4, 38.6, 37.3, 31.8, 14.3 ppm; IR (film): $\tilde{\nu}=$ 3083, 3061, 3025, 2981, 2862, 1734, 1496, 1454, 1433, 1399, 1368, 1312, 1259, 1242, 1193, 1146, 1093, 1042, 885, 749, 700 cm^{-1}; MS (CI^+): m/z: for $C_{17}H_{22}O_3$: 292 $[M+NH_4]^+$, 275 $[M+H]^+$; HRMS (ESI^+): m/z: calcd for $C_{13}H_{22}O_3$: 297.1461 $[M+Na]^+$; found: 297.1459; TLC: $R_f=0.57$ (petroleum ether/Et_2O 80:20).

(2*E*,5*Z*)-5-(1-Hydroxy-3-phenylpropyl)-6-phenyl-2,5-hexadienoic ethyl ester (28k): (Carbethoxymethylene)triphenylphosphorane (1.04 g, 3 mmol) was added to a solution of lactol (*Z*)-**10k** (280 mg, 1 mmol) in CH_2Cl_2 (20 mL) at room temperature. The solution was stirred at room temperature for 16 h. Silica was added and the solvent was removed under reduced pressure. Flash column chromatography on silica gel (petroleum ether/Et_2O 60:40) gave **29** (322 mg, 92%, d.r. (*E*/*Z*) = 92:8) as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): $\delta=7.30$–7.00 (m, 10H; Ar+1H), 6.35 (s, 1H), 4.95 (dt, $J=1.4$, 15.5 Hz, 1H), 4.77 (dd, $J=4.3$, 9.1 Hz, 1H), 4.21 (q, $J=7.1$ Hz, 2H), 3.25 (ddt, $J=1.4$, 7.0, 16.4 Hz, 1H), 3.08 (ddt, $J=1.2$, 7.4, 16.4 Hz, 1H), 2.81–2.59 (m, 2H), 2.11–1.79 (m, 2H), 1.94 (brs, 1H; OH), 1.30 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=166.7$, 147.7, 141.6, 141.3, 136.6, 129.3, 128.7 ($2C_{Ar}$), 128.6, ($2C_{Ar}$), 128.5 ($2C_{Ar}$), 128.3 ($2C_{Ar}$), 126.9 (C_{Ar}), 126.0 (C_{Ar}), 122.9, 68.7, 60.4, 36.9, 33.4, 32.1, 14.4 ppm; IR (neat): $\tilde{\nu}=3445$, 3024, 2979, 2938, 1717, 1494, 1453, 1267, 1039, 699 cm^{-1}; MS (CI^+): m/z: for $C_{23}H_{26}O_3$: 368 $[M+NH_4]^+$, 350 $[M-H_2O+NH_4]^+$, 333 $[M-H_2O+H]^+$; HRMS (ESI^+): m/z: calcd for $C_{23}H_{26}O_3$: 373.1780 $[M+Na]^+$; found: 373.1770; TLC: $R_f=$ 0.24 (petroleum ether/Et_2O 70:30).

5-Allyl-2-phenethyl-3-[(*Z*)-1-phenylmethyliden]tetrahydrofuran (30): $BF_3{\cdot}Et_2O$ (255 μL, 2 mmol) was added dropwise to a solution of lactol (*Z*)-**10k** (280 mg, 1 mmol) and allyltrimethylsilane (480 μL, 3 mmol) in CH_2Cl_2 (15 mL) under argon at −78 °C. After completion of the reaction (TLC monitoring), the mixture was allowed to reach −30 °C and a saturated solution of $NaHCO_3$ was added. The aqueous phase was extracted with CH_2Cl_2 (×2) and the resulting organic phase was dried over Na_2SO_4, filtered, and concentrated in vacuo. Flash chromatography (petroleum

ether/Et_2O 97:3) gave **30** (210 mg, 68%, d.r. (*cis*/*trans*) > 5:95) as a colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 7.24–7.00$ (m, 10H; Ar), 6.25 (q, $J = 1.9$ Hz, 1H), 5.90 (tdd, $J = 7.0$, 10.5, 17.2 Hz, 1H), 5.15–5.06 (m, 3H), 4.04 (quint., $J = 6.6$ Hz, 1H), 2.86–2.81 (m, 2H), 2.61 (tdd, $J = 1.9$, 6.6, 15.8 Hz, 1H), 2.49–2.40 (m, 1H), 2.32–2.17 (m, 2H), 1.96–1.70 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 145.6$, 141.9 (Cq_{Ar}), 137.4 (Cq_{Ar}), 135.2, 129.2 ($2C_{Ar}$), 128.6 ($2C_{Ar}$), 128.5 ($4C_{Ar}$), 126.6 (C_{Ar}), 126.1 (C_{Ar}), 121.4, 117.0, 77.2, 75.0, 40.4, 40.0, 33.7, 32.5 ppm; IR (neat): $\tilde{\nu} = 3024$, 2923, 2858, 1641, 1601, 1495, 1453, 1043, 913, 697 cm^{-1}; MS (CI^+): *m*/*z*: for $C_{22}H_{24}O$: 322 $[M+NH_4]^+$, 305 $[M+H]^+$; TLC: $R_f = 0.70$ (petroleum ether/Et_2O 95:5).

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