Highly Stereoselective Radical Cyclization of Haloacetals Controlled by the Acetal Center

Félix Villar,[a] Tanja Kolly-Kovac,[a, b] Olivier Equey,[a] and Philippe Renaud*[a, b]

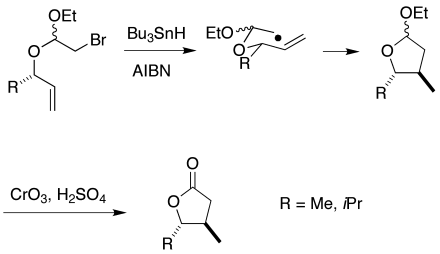
Abstract: A systematic investigation of radical haloacetal cyclizations (Ueno–Stork reaction) where the acetal center is the unique stereogenic element is reported. This highly diastereoselective reaction can be used for the preparation of polysubstituted tetrahydrofurans and γ-lactones. We report herein the full experimental details of reactions where up to three new chiral centers are created. To demonstrate the potential of this approach, short syntheses of (+)-eldanolide and of tricyclic acetals related to biologically active lignans have been achieved.

Keywords: asymmetric synthesis · cyclizations · haloacetals · lactones · radical reactions

Introduction

Eighteen years ago, Ueno and Stork reported independently the very efficient 5-*exo* cyclization of bromoacetals.[1–6] This reaction is one of the most useful radical reaction described to date and has been applied for the synthesis of natural products.[4, 7–14] The use of chiral alcohol allows the synthesis of polysubstituted lactones in enantiomerically pure form with good to excellent diastereoselectivity (Scheme 1).[4, 15] In these processes, the allylic chiral center controls completely the stereochemical outcome of the reaction. Apparently, the second stereogenic center at the acetal does not influence the diastereoselectivity of the reaction. In the original work, chair-like transition states where the ethoxy group is either occupying an axial or an equatorial position were proposed (Scheme 1).[3] These first experiments suggested that the control of the stereochemical outcome of Ueno–Stork cyclizations from the acetal center is very hypothetical. However, several reports indicates that the role of the acetal center was overlooked, and that it has a determinant influence at several occasions[16–19] can provide some degree of stereocontrol.[20–23]

Therefore, a few years ago, we started a systematic investigation of cyclization reactions where the acetal center is the unique stereogenic element.[12, 13, 24] We report here our effort to define the scope and limitations of this approach.



Scheme 1. Stereoselective Ueno–Stork reactions for the synthesis of *trans*-β,γ-disubstituted γ-butyrolactone.

Application to the synthesis of optically pure lactones such as (+)-eldanolide, the pheromone of the male African sugarcane stem borer *Eldana saccharina*, is described. A stereoselective cascade cyclization reaction leading to tricyclic compounds is also described. A computational study of the stereoselectivity of the reaction is described in the following paper.[25]

Results and Discussion

Diastereoselectivity of the cyclization reactions

4-Substituted 2-alkoxytetrahydrofurans: The bromoacetals **1–6** have been prepared by treatment of a mixture of the corresponding enol ethers and allylic alcohols with NBS. The cyclization reactions were conducted at $-78\,^{\circ}C$ using tributyltin hydride and triethylborane/oxygen as initiator [Eq. (1)] results are summarized in Table 1. In all cases, the major

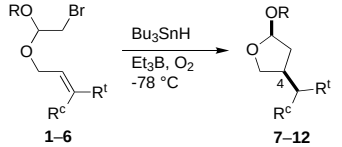


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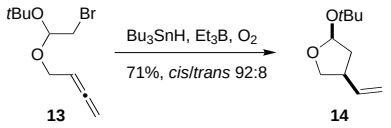
Table 1. Radical cyclization of **1**–**6** according to Equation (1).

Entry	Bromide	OR	R^t	R^c	Product	Yield [%]	*cis*/*trans*
1	**1**	OEt	H	H	**7**	71	>98:2
2	**2**	O*t*Bu	H	H	**8**	68	>98:2
3	**3**	OEt	*n*Pr	H	**9**	75	92:8
4	**4**	O*t*Bu	*n*Pr	H	**10**	71	92:8
5	**5**	OEt	Me	Me	**11**	80	77:23
6	**6**	O*t*Bu	Me	Me	**12**	83	77:23

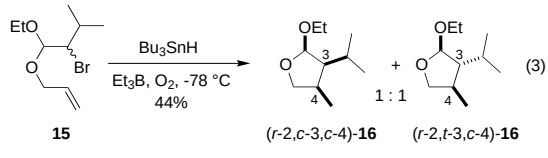
tetrahydrofuran product **7**–**12** possesses a *cis* configuration. The size of the alkoxy group has no influence on the stereochemical outcome as demonstrated by comparing entries 1, 3 and 5 (OR = OEt) with entries 2, 4 and 6 (OR = O*t*Bu), respectively. However, the substitution of the alkene moiety has a marked influence. With terminal alkenes (R^t and R^c = H), the *cis* isomer was produced with an excellent stereoselectivity (entries 1 and 2, *cis*/*trans* >98:2). When the alkene moiety is monosubstituted at the terminal position (R^t = *n*Bu, R^c = H), the stereoselectivity decreased (*cis*/*trans* 92:8). With an alkene disubstituted at the terminal position ($R^t = R^c$ = Me), the *cis*/*trans* ratio dropped to 77:23 (entries 5 and 6).

Finally, a good control of the stereochemistry was obtained with the allene **13**. Cyclization of **13** afforded 2-*tert*-butoxy-4-vinyl tetrahydrofuran **14** as a *cis*/*trans* 92:8 mixture [Eq. (2)].



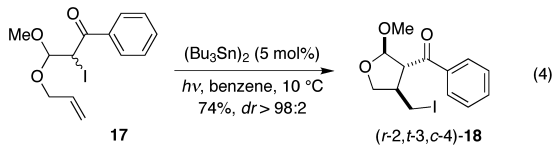
(2)

3,4-Disubstituted 2-alkoxytetrahydrofurans: The isopropyl substituted system **15** was examined first. Under our standard radical cyclization conditions, the tetrahydrofuran **16** was isolated as a 1:1 mixture of isomers [Eq. (3)], the stereochemistry at C(4) is fully controlled by the acetal center but the stereochemistry at C(3) is not controlled.



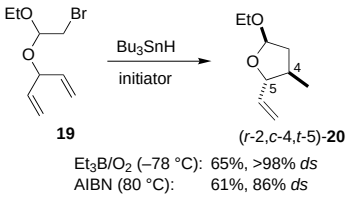
(3)

The α-iodoketone **17** was examined next. Under iodine atome transfer conditions (5 mol% $Bu_3SnSnBu_3$, *hv*, 10 °C),[26] the reaction afforded (*r*-2,*t*-3,*c*-4)-**18** as a single diastereomer [Eq. (4)].[27] The relative configuration of the main isomer was assigned from difference NOE spectra.



(4)

4,5-Disubstituted 2-alkoxytetrahydrofurans: The radical precursors **19** and **21** are easily prepared from 1,4-pentadien-1-ol and 4-hydroxy-4-methyl-2,5-cyclohexadien-1-one by haloacetalization with ethyl vinyl ether and *tert*-butyl vinyl ether, respectively. Reaction of **19** with tributyltin hydride at −78 °C furnishes essentially (*r*-2,*c*-4,*t*-5)-**20** [Eq. (5)]. At 80 °C, the



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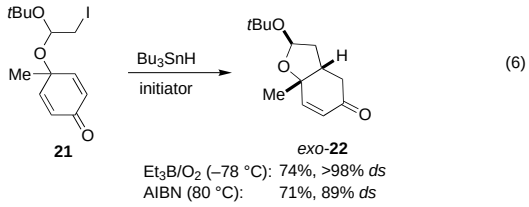
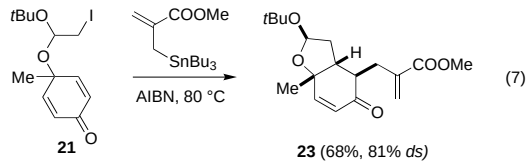
stereoselectivity drops to 86% *ds*. The reaction of **21** leading to the bicyclic compound **22** shows the same tendency [Eq. (6)]: a very high diastereoselectivity in favor of the *exo*



(6)

isomer is achieved at low temperatures whereas lower stereocontrol (89% *ds*) is observed at 80 °C. Interestingly, the cyclization of **21** can be coupled with an allylation of the final radical enolate to give **23** [Eq. (7)]. Three new chiral centers



(7)

are generated in this process with a diastereoselectivity of 81% *ds* at 80 °C. This allylation process does not work efficiently at lower temperature.

3,4,5-Trisubstituted 2-alkoxytetrahydrofurans: The *gem*-dimethyl substituted bromide **24** was prepared from 1-ethoxy-2-methyl-propene. At low temperature, it affords predominantly the (*r*-2,*c*-4,*t*-5)-**25** [Eq. (8)]. The *gem*-dimethyl substitution induces a slight decrease of the diastereoselectivity relative to the unsubstituted system [compare with Eq. (5)]. The

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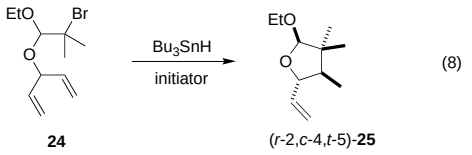

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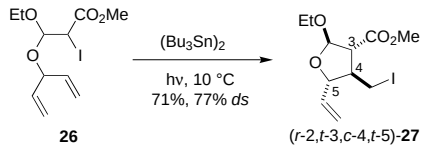
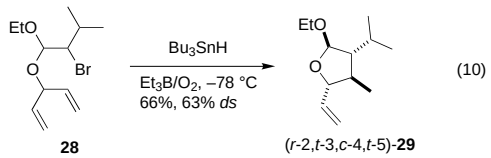
α-iodoester **26** is prepared from the corresponding enolether and gives the polysubstituted tetrahydrofuran **27** under iodine atom transfer conditions at 10 °C [Eq. (9)]. Three new chiral



(9)

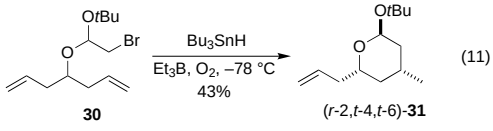
centers are created during this process and the major isomer (*r*-2,*t*-3,*c*-4,*t*-5)-**27** represents 77% of the whole mixture of diastereomers. The isopropyl derivative **28** has also been examined [Eq. (10)]. The control of the stereochemistry at the



(10)

C(3) center is moderate (63% *ds*) and (*r*-2,*t*-3,*c*-4,*t*-5)-**29** is isolated as major isomer. However, two out of the three newly formed centers (C(4) and C(5)) are created with high stereocontrol since the principal minor isomer is epimeric at position C(3).

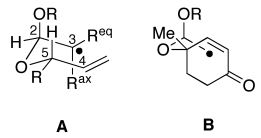
Tetrahydropyran derivatives: The stereochemical outcome of 6-*exo* cyclizations leading to tetrahydropyran derivatives can also be controlled by the acetal center. For instance, the desymmetrization of 1,6-heptadien-4-ol via the acetal **30** is totally diastereoselective at -78 °C [Eq. (11)]. The moderate



(11)

yield of this process is due to the formation of the acyclic reduced product. The relative configuration of the 2,4,6-trisubstitued tetrahydropyran **31** was deduced from ^{1}H NMR coupling constants. Beckwith has recently reported a related example of stereoselective bromoacetal cyclization leading to 2,4-disubstituted tetrahydropyran.[22]

Discussion of the stereochemical outcome: The stereochemical outcome of the above reactions for all acyclic precursors can be rationalized by a chair-like transition state where the alkoxy substituent occupies an axial position (Scheme 2, model **A**). The substituent at C(5) lies in a pseudoequatorial

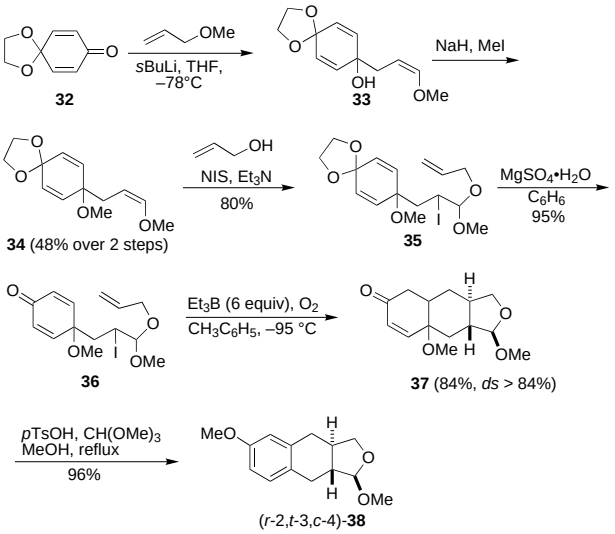


Scheme 2. Model for the Ueno–Stork cyclization controlled by the acetal center.[25]

position as predicted by the Beckwith–Houk model. The substituent at C(3) can occupy either a pseudoaxial (R^{ax}) position which would minimize the steric interactions with the C(2)-alkoxy substituents, or a equatorial (R^{eq}) position as in the Beckwith–Houk model. An exception to this model is the reaction of the cyclic haloacetal **21**. In this case, the major isomer arises from the twist-like transition state **B**. Interestingly, in both models, the *exo*-alkoxy group is in a pseudoaxial position that allows to maximize the anomeric effect. The models presented in Scheme 2 are based on the results of the ab inito calculations that are reported in the following paper.[25]

Cascade cyclization process

Polycyclic lactones are substructure of many natural products. Our interest in the synthesis of analogues of (−)-podophyllotoxin,[28, 29] a tetracyclic lignan with potent antimitotic activity, prompted us to examine a cascade cyclization process for the preparation of tricyclic lactones. To validate such an approach, the iodoacetal **36** was prepared from the monoprotected 1,4-benzoquinone **32** by allylation with lithiated allyl methyl ether followed by methylation of the tertiary alcohol, iodoacetalization with *N*-iodosuccinimide and allyl alcohol and deprotection of the dioxolanyl acetal with hydrated magnesium sulfate (Scheme 3). Treatment of the iodoacetal



Scheme 3. Preparation of the tricyclic acetal **38** related to podophyllotoxin.

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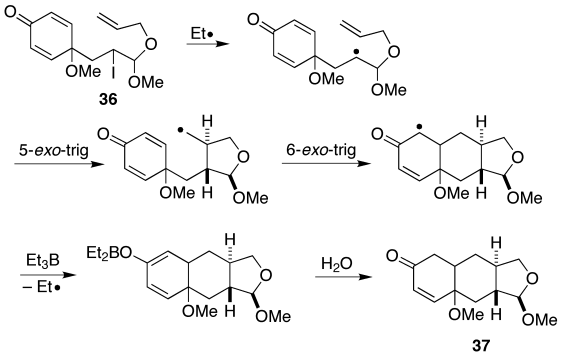
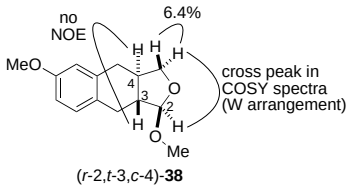
36 with triethylborane in toluene at $-95\,^{\circ}C$ afforded the desired tricyclic compound **37** in good yield. The efficiency of this tin-free cyclization is striking and best explained by the mechanism depicted in Scheme 3. Indeed, this reaction is mediated by a stoichiometric amount of triethylborane which reacts with the tricylic enolate radical to give a boron enolate and an ethyl radical that can abstract an iodine atom from the substrate and propagates the chain reaction (Scheme 4).[30] The diastereoselectivity (84% *ds*) is remarkable considering



Scheme 4. Proposed mechanism for the triethylborane mediated cyclization of **36**.

that the position 3 of 3,4-disubstituted 2-alkoxytetrahydrofuran is usually difficult to control (see below) and that four new stereogenic centers are created in a single reaction. After treatment of the major isomer with *p*-toluenesulfonic acid in methanol and trimethyl orthoformate, the aromatic compound (*r*-2,*t*-3,*c*-4)-**38** was isolated and its *trans* relative

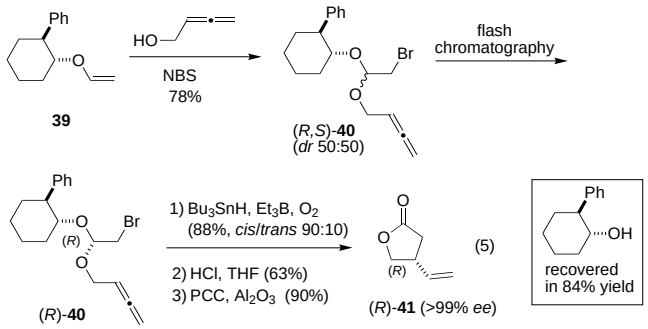


configuration was unambiguously established from NOE difference and COSY spectra.

Preparation of optically pure lactones

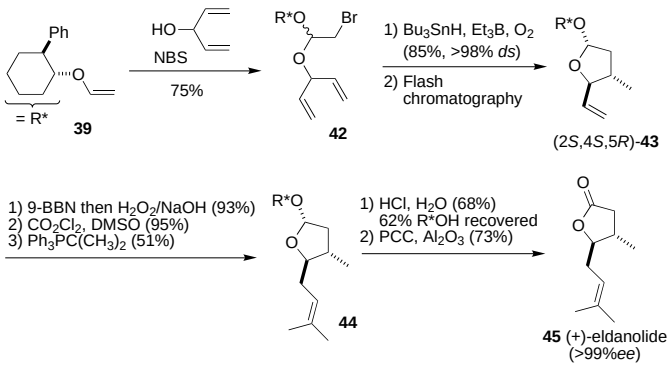
Optically pure chiral enol ethers are easily available from diverse chiral alcohols and are very valuable starting material for asymmetric synthesis.[31] Since our reactions are producing acetals as final products, it was anticipated that the chiral alcohol could be recovered by simple hydrolysis. We have previously shown [Eq. (1), Table 1] that the size of the *exo*-alkoxy group has no influence on the stereochemistry of the radical cyclization, therefore, we were expecting that the acetal center will be the only control element of the cyclization reactions.

Synthesis of 3-vinyl-γ-butyrolactone: 3-Vinyl-γ-butyrolactone is an important building block widely that has been used in several natural product synthesis.[32–35] The acetal **40** has been prepared from the (1*R*,2*S*)-2-phenylcyclohexyl vinyl ether **39**[36] and 1,2-butadien-4-ol. The bromoacetalization furnished **40** as a 1:1 mixture of two diastereomers which were separated by flash chromatography.[23, 37] Reaction of the diastereomerically pure (*R*)-**40** with tributyltin hydride gave the 2-alkoxy-4-vinyl tetrahydrofuran in 88% yield as a *cis*/*trans* 90:10 mixture. After elimination of the minor diastereomer by flash chromatography, hydrolysis of the pure *cis* isomer followed by oxidation of the lactol gave the enantiomerically pure (>99% *ee*) lactone **41** (Scheme 5). During the hydrolysis step, the chiral auxiliary was recovered in 84% yield.



Scheme 5. Preparation of the enantiomerically enriched (>99% *ee*) lactone (*R*)-**41**.

Synthesis of (+)-eldanolide: The utility of our approach was demonstrated by the preparation of the naturally occuring (+)-eldanolide, the pheromone of the male African sugarcane stem borer *Eldana saccharina* (Scheme 6).[38–48] For this purpose, the bromoacetal **42** was prepared from the chiral



Scheme 6. Synthesis of (+)-eldanolide.

vinyl ether **39** by bromoacetalization with 1,4-pentadien-3-ol. The haloacetalization step is not stereoselective, the required diastereomerically pure **42** could be obtained after flash chromatography; however, since the separation of the diastereomers is easier after the cyclization reaction, the mixture of diastereomers was used for the next step. The bromoacetal **42** (1:1 mixture of two diastereomers) was submitted to cyclization conditions to afford **43** as a 1:1 mixture of two diastereoisomers, the cyclization process is completely diastereoselective (*ds* > 98%) for each diastereomer of **42**. At this stage, the two diastereomers were separated by flash

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chromatography and (2*S*,4*S*,5*R*)-**43** was used for the rest of the synthesis. The γ-chain was modified in a straightforward manner by hydroboration, Swern oxidation and Wittig reaction. Finally, hydrolysis of the acetal **44** furnished the lactol together with recovered (1*R*,2*S*)-2-phenylcyclohexanol (62%). Oxidation of the lactol with PCC gave (+)-eldanolide **45** (optical purity >99% by gas chromatography on a chiral column).

Conclusion

We have demonstrated on several examples that the Ueno–Stork radical cyclization of haloacetal can be highly stereoselective. The key element for the control of the stereochemical outcome is the acetal center. This allows an excellent control of the stereochemistry at C(4) and C(5) of the newly formed tetrahydrofuran. The control of the stereochemistry at C(3) is lower due to antagonist effect of the two neighbouring substituents. The used of easily recovered chiral auxiliary offers an entry for the synthesis of enantiomerically pure compounds. At the moment, the diastereoselectivity of the haloacetalization step is not controlled and separation of the diastereomers by chromatography is necessary. Further efforts toward stereoselective haloacetalization reaction are currently underway in our laboratory and will be reported in due course.

Experimental Section

General remarks: THF was freshly distilled from K under N_2; CH_2Cl_2 and benzene from CaH_2 under N_2; toluene from Na under N_2. Et_3B solution (1M) in hexane or toluene was freshly prepared from commercially available Et_3B (95%, Aldrich). Other reagents were obtained from commercial sources and used as received. Flash column chromatography (FC) and filtration: Baker silica gel (0.063–0.200 mm); AcOEt, Et_2O, CH_2Cl_2 and hexane as eluents. Thin-layer chromatography (TLC): Merck silica gel 60 F_{254} analytical glass plates; detection either with UV or by spraying with a solution of vanillin or a solution of 25 g phosphomolybdic acid, 10 g $Ce(SO_4)_2 \cdot 4H_2O$, 60 mL conc. H_2SO_4 and 940 mL H_2O with subsequent heating. FT-IR: Mattson Unicam 5000 and Perkin Elmer 1600. NMR: Varian Gemini 200 (^{1}H 200 MHz, ^{13}C 50.3 MHz), Bruker AM 360 (^{1}H 360 MHz, ^{13}C 90.5 MHz), Bruker Avance DRX 500 (^{1}H 500.13 MHz, ^{13}C 125.8 MHz), Bruker DRX 400 (^{1}H 400 MHz, ^{13}C 100.6 MHz); chemical shift in ppm relative to tetramethylsilane (=0 ppm) or $CHCl_3$ (=7.26 ppm) for ^{1}H and $CDCl_3$ (=77.0 ppm) for ^{13}C. Intensity of the NOE effect: w (weak), m (medium), s (strong). MS: Vacuum Generators Micromass VG 70/70E, DS 11-250 and VG Autospec; CI (CH_4), EI (70 eV). High resolution mass spectra (HRMS) were recorded on a FTICR mass spectrometer Bruker 4.7 BioApex II and VG Autospec. Elementary analysis: Ilse Beetz, Mikroanalytisches Laboratorium, 96317 Kronach (Germany).

General procedure 1 (GP 1): *N*-Halosuccinimide (10 mmol) was added in portions to a solution of enol ether (10 mmol) and alcohol (11 mmol) in CH_2Cl_2 (10 mL) cooled at $-20\,^\circ$C. The resulting mixture was stirred at the same temperature for 2–3 h until disappearance of the starting material. The mixture was diluted with hexane, filtered and washed successively with KOH (5%), water and NaCl. After drying and evaporation of the solvent, the residue was purified by FC (hexane/Et_2O).

General procedure 2 (GP 2): A solution of the haloacetal (2.1 mmol) and Bu_3SnH (735 mg, 2.5 mmol) in toluene (52 mL) was cooled at $-78\,^\circ$C and a 1M solution of Et_3B in hexane (2.9 mL, 2.9 mmol) was added. Air (2.0 mL) was then bubbled into the reaction mixture with a syringe. The solution was kept at $-78\,^\circ$C for 3 h. A 1M NaOH solution (30 mL) was added and the heterogeneous mixture was stirred for 2 h at rt. The organic layer was washed with H_2O, dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by flash chromatography (pentane/Et_2O) to afford the tetrahydrofuran. The diasteroisomeric ratios were determined by ^{1}H NMR before and after FC. Attempts to measure the diasteroselectivity by GC failed due to partial decomposition of the products. The relative configuration have been assigned by NOE difference experiments.

General procedure 3 (GP 3): A solution of Bu_3SnH (735 mg, 2.52 mmol), AIBN (17 mg, 0.11 mmol) and the haloacetal (2.1 mmol) was heated under reflux in benzene (20 mL). The reaction was monitored by TLC. After cooling, a 1M NaOH solution (30 mL) was added and the heterogeneous mixture was stirred for 2 h at rt. The organic layer was washed with H_2O, dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by FC (hexane/Et_2O).

General procedure 4 (GP 4): A solution of the haloacetal (1 mmol) and $(Bu_3Sn)_2$ (58 mg, 0.1 mmol) in benzene (5 mL) was irradiated with a sun lamp for 2 h at 10 °C. A KF aqueous solution was added and the mixture was stirred for 2 h. The organic layer was washed with water, dried over $MgSO_4$ and evaporated. The crude product was purified by FC (hexane/Et_2O).

3-(2-Bromo-1-ethoxyethoxy)-1-propene (1): According to GP 1 from ethyl vinyl ether (1.13 g, 15.7 mmol), allyl alcohol (1.00 g, 17.2 mmol) and NBS (2.79 g, 15.7 mmol). The bromoacetal **1** (2.73 g, 76%) was obtained as a colorless oil after FC (hexane/Et_2O 40:1). IR (KBr): $\tilde{\nu}$ = 3081, 2978, 2877, 1423, 1346, 1126, 1057 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): δ = 5.97 (m, 1H, C*H*=CH_2), 5.25 (dq, J = 1.8, 17.4 Hz, 1H, CH=C*H*H), 5.20 (dq, J = 1.2, 10.4 Hz, 1H, CH=CH*H*), 4.72 (t, J = 5.5 Hz, 1H, OC*H*CH_2Br), 4.16 (ddt, J = 1.5, 5.5, 12.8 Hz, 1H, OC*H*HCH=CH_2), 4.07 (ddt, J = 1.5, 6.1, 12.2 Hz, 1H, OCH*H*CH=CH_2), 3.75–3.53 (m, 2H, C*H*$_2$CH$_3$), 3.38 (d, J = 5.2 Hz, 2H, OCHC*H*$_2$Br), 1.23 (t, J = 7.0 Hz, 3H, CH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 134.0 (d), 117.4 (t), 100.9 (d), 67.6 (t), 62.4 (t), 31.7 (t), 15.17 (q); CI-MS (CH_4): m/z (%): 209 (3) [M^+], 165 (74), 163 (72), 153 (97), 152 (100), 115 (84), 85 (5), 83 (8); elemental analysis calcd for $C_7H_{13}O_2Br$ (209.08): C 40.21, H 6.27; found: C 40.34, H 6.21.

3-(2-Bromo-1-*tert*-butoxyethoxy)-1-propene (2): According to GP 1 from *tert*-butyl vinyl ether (2.07 g, 20.7 mmol), allyl alcohol (1.20 g, 20.7 mmol) and NBS (3.68 g, 20.7 mmol). The bromoacetal **2** (3.73 g, 91%) was obtained as a colorless oil after FC (hexane/Et_2O 40:1). IR (KBr): $\tilde{\nu}$ = 3082, 2978, 2953, 2874, 1369, 1182, 1109, 925 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): δ = 5.95–5.86 (m, 1H, C*H*=CH_2), 5.30 (dq, J = 1.8, 17.4 Hz, 1H, CH=C*H*H), 5.17 (dq, J = 1.5, 10.4 Hz, 1H, CH=CH*H*), 4.92 (t, J = 5.5 Hz, 1H, OC*H*CH_2Br), 4.08–4.06 (m, 2H, OCHC*H*$_2$Br), 3.39 (dd, J = 5.8, 10.7 Hz, 1H,C*H*HCH=), 3.29 (dd, J = 5.2, 10.4 Hz, 1H, CH*H*CH=), 1.27 (s, 9H, *t*Bu); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 134.4 (d), 116.8 (t), 95.7 (d), 75.1 (s), 64.8 (t), 33.1 (t), 28.6 (q); CI-MS (CH_4): m/z (%): 239 (13) [M^++H], 237 (14), 221 (17), 181 (100), 179 (97), 165 (68), 163 (67), 115 (47), 101 (14), 57 (99); elemental analysis calcd for $C_9H_{17}O_2Br$ (237.14): C 45.59, H 7.23; found: C 45.39, H 7.06.

1-(2-Bromo-1-ethoxyethoxy)-2-hexene (3): According to GP 1 from ethyl vinyl ether (655 mg, 9.1 mmol), 2-hexen-1-ol (1.0 g, 10.0 mmol) and NBS (1.62 g, 9.1 mmol). The bromoacetal **3** (1.78 g, 78%) was obtained as a colorless oil after FC (hexane/Et_2O 40:1). IR (KBr): $\tilde{\nu}$ = 2959, 2872, 1436, 1377, 1187, 1118, 1055, 970 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): δ = 5.72–5.69 (m, 1H, OCH_2CH=CH), 5.60–5.52 (m, 1H, CH=C*H*CH_2), 4.70 (t, J = 5.5 Hz, 1H, OC*H*CH_2Br), 4.11 (ddd, J = 1.2, 6.1, 11.9 Hz, 1H, OC*H*HCH=CH), 4.02 (ddd, J = 0.9, 6.4, 11.6 Hz, 1H, OCH*H*CH=CH), 3.71–3.50 (m, 2H, OC*H*$_2$CH$_3$), 3.38 (d, J = 5.5 Hz, 2H, OCHC*H*$_2$Br), 2.06–2.00 (m, 2H, CH=CHC*H*$_2$CH$_2$), 1.46–1.36 (m, 2H, $CH_2CH_2CH_3$), 1.24 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 0.90 (t, J = 7.6 Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 135.3 (d), 125.6 (d), 100.6 (d), 67.7 (t), 62.3 (t), 34.3 (t), 31.9 (t), 22.2 (t), 15.2 (q), 13.7 (q); CI-MS (CH_4): (2) [M^+], 235 (19), 233 (18), 211 (13), 165 (14), 153 (90), 151 (89), 125 (16), 83 (100); elemental analysis calcd (%) for $C_{10}H_{19}O_2Br$ (251.16): C 47.82, H 7.63; found: C 47.69, H 7.60.

1-(2-Bromo-1-*tert*-butoxyethoxy)-2-hexene (4): According to GP 1 from *tert*-butyl vinyl ether (910 mg, 9.1 mmol), 2-hexen-1-ol (1.0 g, 10.0 mmol) and NBS (1.62 g, 9.1 mmol). The bromoacetal **4** (1.8 g, 71%) was obtained as a colorless oil after FC (hexane/Et_2O 40:1). IR (KBr): $\tilde{\nu}$ = 2974, 2872, 1464, 1367, 1110, 1010, 969 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$):

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$\delta = 5.71-5.66$ (m, 1H, $OCH_2CH{=}CH$), 5.58–5.50 (m, 1H, $CH{=}CHCH_2$), 4.88 (t, $J = 5.5$ Hz, 1H, $OCHCH_2Br$), 4.01 (dd, $J = 0.9$, 6.1 Hz, 2H, $OCHCH_2Br$), 3.39 (dd, $J = 5.5$, 10.4 Hz, 1H, $OCHHCH{=}CH$), 3.28 (dd, $J = 5.5$, 10.4 Hz, 1H, $OCHHCH{=}CH$), 2.05–2.00 (m, 2H, $CH{=}CHCH_2CH_2$), 1.40–1.31 (m, 2H, $CH_2CH_2CH_3$), 1.26 (s, 9H, *t*Bu), 0.89 (t, $J = 7.3$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 134.5$ (d), 125.1 (d), 95.7 (d), 75.0 (s), 67.0 (t), 33.3 (t), 28.6 (q), 22.2 (t), 13.7 (q); CI-MS (CH_4): *m*/*z* (%): 279 (1) [M^+], 183 (9), 181 (13), 179 (13), 164 (12), 157 (15), 139 (13), 99 (9), 83 (100), 57 (56); elemental analysis calcd for $C_{12}H_{23}O_2Br$ (279.22): C 51.62, H 8.30; found: C 51.63, H 8.26.

1-(2-Bromo-1-ethoxyethoxy)-3-methyl-2-butene (5): According to GP 1 from ethyl vinyl ether (1.20 g, 16.6 mmol), 3-methyl-2-buten-1-ol (1.57 g, 18.3 mmol) and NBS (2.95 g, 16.6 mmol). The bromoacetal **5** (2.66 g, 81%) was obtained as a colorless oil after FC (hexane/Et_2O 20:1). IR (KBr): $\tilde{\nu} =$ 2975, 2879, 1444, 1348, 1118, 1056, 684 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.40$ (m, 1H, $CH{=}CMe_2$), 4.70 (t, $J = 5.5$ Hz, 1H, $OCHCH_2Br$), 4.14 (dd, $J = 7.0$, 11.3 Hz, 1H, $OCHHCH{=}CMe_2$), 4.08 (dd, $J = 7.2$, 11.4 Hz, 1H, $OCHHC{=}CMe_2$), 3.74–3.55 (m, 2H, CH_2CH_3), 3.39 (d, $J = 5.5$ Hz, 2H, $OCHCH_2Br$), 1.76 (s, 3H, CH_3), 1.70 (s, 3H, CH_3), 1.25 (t, $J = 7.0$ Hz, 3H, CH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 137.7$ (s), 120.3 (d), 100.8 (d), 63.2 (t), 62.1 (t), 31.8 (t), 25.8 (q), 18.0 (q), 15.2 (q); CI-MS (CH_4): *m*/*z* (%): 236 (10) [$M^+ - H$], 171 (10), 153 (100), 151 (99), 125 (34), 123 (37), 101 (63), 85 (78), 83 (41), 69 (46); elemental analysis calcd for $C_9H_{17}O_2Br$ (237.14): C 45.59, H 7.23; found: C 45.56, H 7.21.

1-(2-Bromo-1-*tert*-butoxyethoxy)-3-methyl-2-butene (6): According to GP 1 from *tert*-butyl vinyl ether (0.34 g, 3.43 mmol), 3-methyl-2-buten-1-ol (0.33 g, 3.80 mmol) and NBS (2.97 g, 0.61 mmol). The bromoacetal **6** (0.65 g, 72%) was obtained as a colorless oil after FC (hexane/Et_2O 20:1). IR (KBr): $\tilde{\nu} =$ 2975, 1446, 1366, 1179, 1100, 1014, 935 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.37-5.30$ (m, 1H, $CH{=}CMe_2$), 4.89 (t, $J = 5.8$ Hz, 1H, $OCHCH_2Br$), 4.05 (d, $J = 7.0$ Hz, 2H, $OCHCH_2Br$), 3.41 (dd, $J = 5.5$, 10.4 Hz, 1H, $OCHHCH{=}C$), 3.30 (dd, $J = 5.8$, 10.7 Hz, 1H, $OCHHCH{=}C$), 1.75 (s, 3H, CH_3), 1.68 (s, 3H, CH_3), 1.27 (s, 9H, *t*Bu); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 136.8$ (s), 120.8 (d), 95.8 (d), 74.9 (s), 60.6 (t), 33.3 (t), 28.7 (q), 25.7 (q), 18.0 (q); CI-MS (CH_4): *m*/*z* (%): 267 (6) [$M + 3$], 265 (6) [$M^+ + 1$], 199 (10), 197 (10), 181 (100), 179 (98), 155 (74), 143 (86), 137 (28), 125 (68); elemental analysis calcd for $C_{11}H_{21}O_2Br$ (265.19): C 49.82, H 7.98; found: C 49.81, H 7.89.

***cis*-2-Ethoxy-4-methyltetrahydrofuran (7)**: The reaction was performed in CH_2Cl_2 due to the high volatility of the resulting tetrahydrofuran. According to the GP 2 from bromoacetal **1** (438 mg, 2.1 mmol), Bu_3SnH (735 mg, 2.52 mmol) and 1M Et_3B (2.9 mL, 2.9 mmol) in CH_2Cl_2 (52 mL). After flash chromatography (pentane/Et_2O 40:1), *cis*-**7** (71%, 98% *ds*) was obtained as a colorless oil. IR (KBr): $\tilde{\nu} =$ 2974, 2876, 1446, 1373, 1112, 1076, 987 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.13$ (dd, $J = 3.1$, 5.5 Hz, 1H, $OCHCH_2$), 3.93 (t, $J = 6.7$ Hz, 1H, $OCHHCHMe$), 3.75 (dq, $J = 7.0$, 9.5 Hz, 1H, $OCHHCH_3$), 3.49–3.40 (m, 2H, $OCHHCHMe$, $OCHHCH_3$), 2.32–2.20 (m, 2H, CH_2), 1.49–1.42 (m, 1H, $CHMe$), 1.20 (t, $J = 7.0$ Hz, 3H, OCH_2CH_3), 1.08 (d, $J = 6.7$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta =$ 104.7 (d), 73.2 (t), 63.1 (t), 40.8 (t), 33.0 (d), 17.1 (q), 15.3 (q); CI-MS (CH_4): *m*/*z* (%): 131 (12) [M^++H], 113 (13), 85 (100), 73 (41); HRMS (CI/isobutane): calcd for $C_7H_{15}O_2$: 131.10665, found: 131.10661 [M^++H].

***cis*-4-Methyl-2-*tert*-butoxytetrahydrofuran (8)**: According to GP 2 from the bromoacetal **2** (0.5 g, 2.1 mmol), Bu_3SnH (735 mg, 2.52 mmol) and 1M Et_3B (2.9 mL, 2.9 mmol) to afford the acetal *cis*-**8** (226 mg, 68%, 98% *ds*) as a colorless oil after FC (pentane/Et_2O 10:1). IR (KBr): $\tilde{\nu} =$ 2974, 2876, 1460, 1366, 1259, 1194, 1018, 993 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta =$ 5.40 (dd, $J = 4.3$, 1H, 5.2 Hz, $OCHCH_2$), 3.87 (t, $J = 7.9$ Hz, 1H, $OCHHCHCH_3$), 3.46 (t, $J = 8.2$ Hz, 1H, $OCHHCHCH_3$), 2.27–2.18 (m, 2H, $OCHCH_2CHCH_3$), 1.43–139 (m, 1H, $CHCH_3$), 1.25 (s, 9H, *t*Bu), 1.07 (d, $J = 6.4$ Hz, 3H, CH_3); NOE difference spectra (500 MHz): $\delta = 5.41-5.38$ (*t*BuOC*H*) → 2.27–2.18 (2.05%), 1.26–1.21 (1.71%), 3.90–3.83 ($OCHH$) → 3.49–3.43 (6.57%), 2.27–2.18 (1.37%), 1.26–1.21 (0.14%), 3.49–3.43 ($OCHH$) → 3.90–3.83 (6.89%), 2.27–2.18 (0.57%), 1.26–1.21 (0.36%), 1.08–1.05 (1.80%), 2.27–2.18 (*t*BuOCHC*H*H) → 5.41–5.38 (1.21%), 3.90–3.83 (0.56%), 3.49–3.43 (0.11%), 1.43–1.39 (4.25%), 1.26–1.21 (0.25%), 1.08–1.05 (1.0%), 1.43–1.39 (*CH*Me) → 5.41–5.38 (0.46%), 3.49–3.43 (0.36%), 2.27–2.18 (7.06%), 1.08–1.05 (2.29%), 1.08–1.05 (CH-C*H*$_3$) → 3.49–3.43 (0.49%), 2.26–2.18 (0.87%); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 99.6$ (d), 74.0 (s), 73.1 (t), 42.1 (t), 33.2 (d), 28.9 (q), 17.0 (q); MS-CI (CH_4): *m*/*z* (%): 159 (36) [M^++H], 103 (27), 101 (18), 85 (100), 57 (33); HRMS (CI, isobutane): calcd for $C_9H_{19}O_2$: 159.13795; found: 159.13791 [M^++H].

***cis*-4-Butyl-2-ethoxytetrahydrofuran (9)**: According to GP 2 from the bromoacetal **3** (220 mg, 0.84 mmol), Bu_3SnH (294 mg, 1.01 mmol) and 1M Et_3B (1.2 mL, 1.2 mmol) to afford the acetal **9** (115 mg, 75%, *cis*/*trans* 92:8) as a colorless oil after FC (pentane/Et_2O 40:1). *cis*-**9**: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.12$ (dd, $J = 3.4$, 5.5 Hz, 1H, $OCHCH_2$), 3.93 (t, $J = 7.9$ Hz, 1H, $OCHHCH$), 3.78–3.70 (dq, $J = 7.0$, 9.5 Hz, 1H, $OCHHCH_3$), 3.48–3.42 (m, 2H, $OCHHCHnBu$, $OCHHCH_3$), 2.30–2.23 (m, 1H, $CHnBu$), 2.18–2.09 (m, 1H, $OCHCHH$), 1.50–1.40 (m, 3H, $OCHCHH$, CH_2nPr), 1.34–1.17 (m, 4H, $CH_2CH_2CH_2CH_3$), 1.20 (t, $J = 7.0$ Hz, 3H, OCH_2CH_3), 0.89 (t, $J = 7.1$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 104.4$ (d), 71.9 (t), 63.0 (t), 39.2 (t), 38.7 (d), 32.7 (t), 30.9 (t), 22.8 (t), 15.3 (q), 14.0 (q); *trans*-**9**: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 4.05$ (t, $J = 7.9$ Hz, 1H, $OCHH$); *cis*/*trans*-**9**: IR (KBr): $\tilde{\nu} = 2960$, 2926, 2860, 1446, 1404, 1114, 1043, 1004 cm^{-1}; EI-MS: *m*/*z* (%): 173 (9) [M^++H], 128 (13), 127 (96), 109 (45), 99 (22), 85 (52), 83 (51), 75 (61), 70 (66), 57 (100); elemental analysis calcd (%) for $C_{10}H_{20}O_2$ (172.27): C 69.72, H 11.70; found: C 69.86, H 11.83.

***cis*-2-*tert*-Butyl-4-butyltetrahydrofuran (10)**: According to GP 2 from the bromoacetal **4** (243 mg, 0.84 mmol), Bu_3SnH (294 mg, 1.01 mmol) and 1M solution Et_3B (1.2 mL, 1.2 mmol) to afford the acetal **10** (126 mg, 71%, *cis*/*trans* 92:8) as a colorless oil after FC (pentane/Et_2O 40:1). *cis*-**10**: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.38$ (dd, $J = 4.6$, 5.8 Hz, 1H, $OCHCH_2$), 3.87 (t, $J =$ 7.6 Hz, 1H, $OCHHCHnBu$), 3.49 (t, $J = 8.2$ Hz, 1H, $OCHHCHnBu$), 2.26–2.18 (m, 1H, $CHnBu$), 2.13–2.03 (m, 1H, $OCHCHH$), 1.45–1.37 (m, 3H, $OCHCHH$, $CHCH_2nPr$), 1.33–1.18 (m, 4H, CH_2-CH_2CH_3), 1.22 (s, 9H, *t*Bu), 0.88 (t, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta =$ 99.4 (d), 73.9 (s), 71.1 (t), 40.4 (t), 38.9 (d), 32.4 (t), 30.9 (t), 29.0 (q), 22.8 (t), 14.1 (q); *trans*-**10**: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 4.06$ (t, $J = 7.6$ Hz, 1H, $OCHH$), 3.37 (dd, $J = 7.0$ Hz, $J = 8.2$ Hz, 1H, $OCHH$); *cis*/*trans*-**10**: IR (KBr): $\tilde{\nu} = 2972$, 2930, 2860, 1467, 1365, 1199, 1008 cm^{-1}; CI-MS (CH_4): *m*/*z* (%): 201 (76) [M^++H], 145 (18), 128 (9), 127 (100), 109 (7); elemental analysis calcd for $C_{10}H_{24}O_2$ (200.32): C 71.94, H 12.08; found: C 71.96, H 11.90.

***cis*-2-Ethoxy-4-isopropyltetrahydrofuran (11)**: According to GP 2 from the bromoacetal **5** (0.5 g, 2.1 mmol), Bu_3SnH (735 mg, 2.52 mmol) and 1M Et_3B (2.9 mL, 2.9 mmol) to afford the acetal **11** (266 mg, 80%, *cis*/*trans* 77: 23) as a colorless oil after FC (pentane/Et_2O 20:1). *cis*-**11**: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.13$ (dd, $J = 3.7$, 5.8 Hz, 1H, $OCHCH_2$), 3.91 (t, $J = 7.6$ Hz, 1H, $OCHHCHiPr$), 3.79–3.66 (m, 1H, $CHHCH_3$), 3.54–3.39 (m, 2H, $OCHH$-$CHiPr$, $CHHCH_3$), 2.30–2.21 (m, 1H, OCH_2CHiPr), 1.90–1.80 (m, 1H, $CHMe_2$), 1.60–1.42 (m, 2H, $OCHCH_2CH$), 1.20 (t, $J = 7.0$ Hz, 3H, CH_2CH_3), 0.92 (d, $J = 6.7$ Hz, 3H, CH_3), 0.87 (d, $J = 6.7$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 104.6$ (d), 70.6 (t), 63.1 (t), 46.7 (d), 37.9 (d), 31.6 (d), 21.1 (q), 21.6 (q), 15.3 (q); *trans*-**11**: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.09$ (d, $J = 4.9$ Hz, 1H, $OCHCH_2$), 4.05 (t, $J = 8.2$ Hz, 1H, $OCHHCHiPr$), 1.2 (t, $J = 7.0$ Hz, 3H, CH_2CH_3), 0.91 (d, $J = 6.7$ Hz, 3H, CH_3), 0.86 (d, $J = 6.7$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 104.2$ (d), 71.6 (t), 62.5 (t), 44.3 (d), 37.6 (t), 32.3 (d), 21.5 (q), 21.3 (q), 15.3 (q); *cis*/*trans*-**11**: IR (KBr): $\tilde{\nu} = 2962$, 2874, 1467, 1371, 1114, 1068, 1006 cm^{-1}; MS-CI (CH_4): *m*/*z* (%): 159 (13) [M^++H], 157 (19) [$M^+ - H$], 127 (8), 113 (100), 95 (16), 85 (43), 75 (14), 56 (19); HRMS (CI, isobutane): calcd for $C_9H_{19}O_2$: 159.13795; found: 159.13794 [M^++H].

***cis*-4-Isopropyl-2-*tert*-butoxytetrahydrofuran (12)**: According to GP 2 from the bromoacetal **6** (0.3 g, 1.13 mmol), Bu_3SnH (395 mg, 1.36 mmol) and 1M Et_3B (1.6 mL, 1.6 mmol) to afford the acetal **12** (174 mg, 83%, *cis*/*trans* 77:23) as a colorless oil after FC (pentane/Et_2O 20:1). *cis*-**12**: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.40$ (dd, $J = 5.4$, 5.5 Hz, 1H, $OCHCH_2$), 3.87 (t, $J =$ 7.9 Hz, 1H, $OCHHCHiPr$), 3.56 (dd, $J = 8.2$, 10.1 Hz, 1H, $OCHHCHiPr$), 2.24–2.18 (m, 1H, $CHiPr$), 1.91–1.74 (m, 1H, $CHMe_2$), 1.58–1.41 (m, 2H, $OCHCH_2$), 1.24 (s, 9H, *t*Bu), 0.92 (d, $J = 6.7$ Hz, 3H, CH_3), 0.86 (d, $J =$ 6.4 Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 99.6$ (d), 74.0 (s), 70.5 (t), 46.6 (d), 39.1 (t), 31.6 (d), 28.9 (q), 21.8 (q), 21.6 (q); *trans*-**12**: ^{1}H NMR (360 MHz): $\delta = 4.08$ (t, $J = 7.9$ Hz, 1H, $OCHHCHiPr$), 3.44 (t, $J = 7.9$ Hz, 1H, $OCHHCHiPr$), 1.23 (s, 9H, *t*Bu), 0.91 (d, $J = 6.7$ Hz, 3H, CH_3), 0.87 (d, $J = 6.4$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 99.2$ (d), 73.9 (s), 71.1 (t), 44.4 (d), 38.7 (t), 32.3 (d), 21.3 (q), 21.2 (q); *cis*/*trans*-**12**: IR (KBr): $\tilde{\nu} = 2972$, 2874, 1469, 1365, 1197, 1006 cm^{-1}; MS-CI (CH_4): *m*/*z* (%): 187 (16) [M^++H], 141 (7), 131 (45), 129 (21), 113 (100), 95 (17), 85 (12), 69 (7), 57 (40); HRMS (CI, isobutane): calcd for $C_{11}H_{23}O_2$: 187.16925; found: 187.16905 [M^++H].

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4-(2-Bromo-1-*tert*-butoxyethoxy)-1,2-butadiene (13): According to GP 1 from *tert*-butyl vinyl ether (750 mg, 7.5 mmol), 2,3-butadien-1-ol (525 mg, 3.80 mmol) and NBS (1.33 g, 7.5 mmol). The bromoacetal **13** (1.20 g, 64%) was obtained as a colorless oil after FC (hexane/Et_2O 40:1). IR (KBr): $\tilde{\nu}$ = 2978, 2939, 1957, 1471, 1369, 1105, 846 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$): δ = 5.25 (quint, J = 6.7 Hz, 1H, OCH_2CH=C=CH_2), 4.93 (t, J = 5.5 Hz, 1H, $OCHCH_2Br$), 4.80 (dt, J = 2.4, 6.7 Hz, 2H, CH=C=CHH), 4.10 (dt, J = 2.4, 6.7 Hz, 2H, OCH_2CH=C), 3.39 (dd, J = 5.8, 10.7 Hz, 1H, OCHCHHBr), 3.29 (dd, J = 5.5, 10.7 Hz, 1H, OCHCHHBr), 1.27 (s, 9H, *t*Bu); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 209.1 (s), 95.7 (d), 88.0 (d), 76.0 (t), 75.1 (s), 62.0 (t), 33.3 (t), 28.7 (q); MS-CI (CH_4): *m*/*z* (%): 251 (12) [M^++2], 249 (13) [M^+], 181 (34), 176 (36), 127 (71), 113 (23), 109 (19), 57 (100); elemental analysis calcd for $C_{10}H_{17}O_2Br$ (249.15): C 48.21, H 6.88; found: C 47.83, H 6.99.

***cis*-2-*tert*-Butyl-4-vinyltetrahydrofuran (14)**: According to GP 2 from the bromoacetal **13** (523 mg, 2.1 mmol), Bu_3SnH (735 mg, 2.52 mmol) and 1M solution Et_3B (2.94 mL, 2.94 mmol) to afford the acetal **14** (252 mg, 71%, *cis*/*trans* 92:8) as a colorless oil after FC (pentane/Et_2O 40:1). *cis*-**14**: ^1H NMR (360 MHz, $CDCl_3$): δ = 5.82 (ddd, J = 8.6, 10.4, 17.1 Hz, 1H, CHCH=CH_2), 5.43 (dd, J = 4.0, 5.5 Hz, 1H, OC$H$$CH_2$), 5.09–5.54 (m, 2H, CHCH=CH_2), 3.88 (t, J = 7.9 Hz, 1H, OCHHCH), 3.62 (t, J = 8.5 Hz, 1H, OCHHCH), 2.85–2.73 (m, 1H, CHCH=CH_2), 2.26 (ddd, J = 5.8, 8.9, 13.4 Hz, 1H, OCHCHH), 1.64 (ddd, J = 4.0, 8.5, 12.8 Hz, 1H, OCHCHH), 1.26 (s, 9H, *t*Bu); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 139.0 (d), 115.1 (t), 99.4 (d), 74.0 (s), 70.8 (t), 43.3 (d), 40.5 (t), 28.9 (q); *trans*-**14**: ^1H NMR (360 MHz, $CDCl_3$): δ = 4.10 (t, J = 7.9 Hz, 1H, OCHH), 3.49 (t, J = 7.3 Hz, 1H, OCHH); *cis*/*trans*-**14**: IR (KBr): $\tilde{\nu}$ = 3080, 2964, 2872, 1643, 1365, 1194, 1010, 914 cm^{-1}; CI-MS (CH_4): *m*/*z* (%): 171 (5) [M^++H], 115 (29), 97 (100), 85 (3), 69 (6), 57 (60); HRMS (CI, isobutane): calcd for $C_{10}H_{19}O_2$: 171.13795; found: 171.13807 [M^++H].

2-Bromo-1-ethoxy-3-methyl-1-(2-propenoxy)-butane (15): According to GP 1 from ethyl 3-methyl 1-butenyl ether (2.6 g, 23.0 mmol), allyl alcohol (1.3 g, 23.0 mmol) and NBS (4.1 g, 23.0 mmol). The bromoacetal **15** (1.4 g, 24%) was obtained as a colorless oil after FC (hexane/Et_2O). IR (KBr): $\tilde{\nu}$ = 3082, 2970, 2933, 2877, 1464, 1386, 1112, 1055, 925 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$): δ = 6.00–5.90 (m, 1H, OCH_2CH=), 5.33 (dq, J = 1.5, 17.1 Hz, 1H, CHH=CH), 5.19 (dq, J = 1.5, 10.5 Hz, 1H, CHH=CH), 4.64 (d, J = 7.9 Hz, 1H, OCHCHBr), 4.15 (ddt, J = 1.5, 5.5, 8.9 Hz, 2H, OCH_2CH=CH_2), 4.02 (dd, J = 3.1, 7.6 Hz, 1H, OCHCHBr), 3.73–3.53 (m, 2H, OCH_2CH_3), 2.15–2.07 (m, 1H, CH(CH_3)$_2$), 1.22 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 1.07 (d, J = 7.0 Hz, 3H, CH_3), 0.95 (d, J = 7.0 Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 134.2 (d), 117.1 (t), 102.5 (d), 67.8 (t), 63.9 (d), 62.6 (t), 29.4 (d), 21.9 (q), 17.3 (q), 15.2 (q); CI-MS (CH_4): *m*/*z* (%): 206 (7) [M^+ − 45], 204 (7), 195 (26), 193 (26), 171 (10), 115 (100), 113 (21), 85 (32), 73 (24), 57 (13); elemental analysis calcd for $C_{10}H_{19}O_2Br$ (251.16): C 47.82, H 7.63; found: C 47.78, H 7.65.

(*r*-2,*c*-3,*c*-4)- and (*r*-2,*t*-3,*c*-4)-2-Ethoxy-4-methyl-3-isopropyltetrahydrofuran (16): According to GP 2 from the bromoacetal **15** (527 mg, 2.1 mmol), Bu_3SnH (735 mg, 2.52 mmol) and 1M solution Et_3B (2.94 mL, 2.94 mmol) to afford the acetal **16** (160 mg, 44%, 1:1 mixture of two diasteromers) after FC (pentane/Et_2O 40:1). These diastereomers were separated by FC and characterized. Their relative stereochemistry was assigned by NOE experiments.

(*r*-2,*c*-3,*c*-4)-**16**: ^1H NMR (360 MHz, $CDCl_3$): δ = 4.88 (d, J = 4.9 Hz, 1H, OCHCH*i*Pr), 4.03 (t, J = 7.0 Hz, 1H, OCHHCHMe), 3.74 (dq, J = 7.0, 9.8 Hz, 1H, OC$H$$HCH_3$), 3.67 (dd, J = 2.1, 8.2 Hz, 1H, O-CH*i*Pr), 3.37 (dq, J = 7.0, 9.8 Hz, 1H, OCH$H$$CH_3$), 2.25 (dq, J = 2.1, 7.3 Hz, 1H, C$H$$CH_3$), 1.91–1.82 (m, 1H, C$H$($CH_3$)$_2$), 1.61 (ddd, J = 4.9, 7.3, 12.2 Hz, 1H, CH*i*Pr), 1.20 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 1.10 (d, J = 7.0 Hz, 3H, CH-CH_3), 0.95 (d, J = 6.1 Hz, 3H, CH_3), 0.93 (d, J = 6.4 Hz, 3H, CH_3). NOE difference spectra (500 MHz): 4.90–4.87 (EtOCH) → 4.05–4.00 (w), 3.78–3.65 (m), 3.41–3.33 (s), 1.64–1.58 (s), 0.99–0.90 (m), 4.05–4.00 (OCHH) → 3.69–3.65 (s), 2.30–2.21 (m), 1.64–1.58 (w), 3.69–3.65 (OCHH) → 4.90–4.00 (m), 4.05–4.00 (s), 1.20–1.15 (m), 2.30–2.21 (CH_3CH) → 4.05–4.00 (s), 3.69–3.65 (w), 1.64–1.58 (s), 1.11–1.09 (s), 0.92–0.90 (m), 1.64–1.58 (CH*i*Pr) → 4.90–4.87 (s), 4.05–4.00 (w), 2.30–2.21 (m), 0.98–0.90 (s); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 104.2 (d), 75.6 (t), 62.9 (t), 55.0 (d), 33.0 (d), 24.0 (d), 21.8 (q), 21.5 (q), 16.0 (q), 15.4 (q).

(*r*-2,*t*-3,*c*-4)-**16**: ^1H NMR (360 MHz, $CDCl_3$): δ = 4.82 (d, J = 2.8 Hz, 1H, OCHCH*i*Pr), 3.94 (t, J = 7.9 Hz, 1H, OCHHCHMe), 3.72 (dq, J = 7.0, 9.8 Hz, 1H, OC$H$$HCH_3$), 3.50–3.40 (m, 2H, OCH$H$CHMe, OCH$H$$CH_3$), 2.02–1.93 (m, 1H, C$H$Me), 1.75–1.65 (m, 1H, C$H$($CH_3$)$_2$), 1.48 (dt, J = 2.8, 7.3 Hz, 1H, CH*i*Pr), 1.20 (t, J = 7.0 Hz, 3H, OCH_2CH_3), 1.05 (d, J = 6.7 Hz, 3H, $CHCH_3$), 0.95 (d, J = 2.8 Hz, 3H, CH_3), 0.94 (d, J = 2.8 Hz, 3H, CH_3). NOE difference spectra (500 MHz): 4.83–4.80 (EtOCH) → 3.96–3.90 (w), 3.77–3.68 (m), 3.50–3.40 (s), 2.13–1.93 (w), 1.74–1.65 (m), 1.50–1.44 (m), 1.23–1.17 (m), 0.97–0.91 (s), 3.96–3.90 (OCHH) → 3.50–3.40 (s), 2.13–1.93 (m), 2.13–1.93 ($CHCH_3$) → 4.83–4.80 (m), 3.96–3.90 (s), 3.50–3.40 (m), 1.74–1.65 (m), 1.50–1.44 (m), 1.07–1.03 (s), 0.97–0.91 (s), 1.74–1.65 (C$H$$Me_2$) → 4.83–4.80 (m), 2.13–1.93 (w), 1.50–1.44 (w), 0.97–0.91 (s), 1.50–1.44 (CH-*i*Pr) → 4.83–4.80 (m), 2.13–1.93 (m), 1.74–1.65 (m), 1.07–1.03 (m), 0.97–0.91 (s), 1.07–1.03 (CH-CH_3) → 3.50–3.40 (s), 2.13–1.93 (s), 1.50–1.44 (s); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 108.2 (d), 73.7 (t), 63.0 (t), 60.1 (d), 36.8 (d), 29.8 (d), 20.7 (q), 17.2 (q), 15.4 (q).

Mixture of diasteroisomers: IR (KBr): $\tilde{\nu}$ = 2962, 2933, 2874, 1469, 1375, 1114, 1076, 1028, 981 cm^{-1}; CI-MS (CH_4): *m*/*z* (%): 173 (15) [M^++H], 171 (19), 155 (13), 127 (100), 115 (10), 97 (12), 83 (11); HRMS (ESI): calcd for $C_{10}H_{20}O_2Na$: 195.13554; found: 195.13565.

2-Iodo-3-(2-propenoxy)-3-methoxy-1-phenyl-1-propanone (17): *N*-Iodosuccinimide (1.4 g, 6.2 mmol) was added in portions at 0 °C protected from the light to a solution of the 3-methoxy-1-phenylpropenone (1.0 g, 6.2 mmol) and allyl alcohol (1.70 g, 29.4 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred at rt for 2 d. Hexane was added and the precipitated was filtered off. The filtrate was washed with H_2O and NaCl, dried and evaporated. FC (hexane/Et_2O 10:1) afforded **17** (1.26 g, 59%) as a yellow oil and starting material (0.32 g, 32%). IR (KBr): $\tilde{\nu}$ = 3067, 2989, 2931, 1680, 1597, 1448, 1294, 1047 cm^{-1}. Major diasteroisomer: ^1H NMR (360 MHz, $CDCl_3$): δ = 7.96 (d, J = 7.3 Hz, 2H, arom. H), 7.59 (t, J = 7.3 Hz, 1H, arom. H), 7.47 (t, J = 7.6 Hz, 2H, arom. H), 5.79 (ddt, J = 5.8, 10.4, 17.1 Hz, 1H, OCH_2CH=CH_2), 5.43 (d, J = 8.6 Hz, 1H, MeOCHCHI), 5.16 (d, J = 8.2 Hz, 1H, MeOCHCHI), 5.22–5.10 (m, 2H, OCH_2CH=CH_2), 4.21–4.10 (m, 2H, OCH_2CH=CH_2), 3.49 (s, 3H, CH_3O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 193.4 (s), 134.4 (s), 133.8 (d), 133.7 (d), 128.8 (d), 128.6 (d), 117.6 (t), 103.4 (d), 70.3 (t), 54.0 (d), 24.3 (q); CI-MS (CH_4): *m*/*z* (%): 347 (7) [M^++H], 329 (13), 315 (99), 289 (61), 267 (13), 219 (60), 189 (51), 163 (68), 160 (20), 101 (100); elemental analysis calcd for $C_{13}H_{15}IO_3$ (346.17): C 45.11; H 4.37; found: C 45.15, H 4.37.

(*r*-2,*t*-3,*c*-4)-[4-(Iodomethyl)-2-methoxytetrahydro-3-furanyl](phenyl)methanone (18): A solution of iodoacetal **17** (2.5 g, 7.25 mmol) and $(Bu_3Sn)_2$ (5%, 0.21 g, 0.36 mmol) in benzene (36 mL) was irradiated with a sun lamp at 10 °C for 3 h. Then a saturated aqueous solution of KF (20 mL) was added and the resulting mixture was stirred for 2 h. The organic phase was washed with H_2O, dried over $MgSO_4$ and evaporated under reduced pressure. Purification by FC (hexane/Et_2O 8:1) gave **18** (1.85 g, 74%, one diastereomer) as a yellow oil. IR (KBr): $\tilde{\nu}$ = 3061, 2933, 2833, 1687, 1597, 1448, 1379, 1228, 1064 cm^{-1}; ^1H NMR (500 MHz, [D_8]toluene): δ = 8.00 (dd, J = 1.3, 8.4 Hz, 2 arom. H), 7.14–6.97 (m, 3 arom. H), 4.91 (d, J = 2.1 Hz, 1H, MeOCHCH), 3.98 (dd, J = 7.7, 8.4 Hz, 1H, OCHHCHCH_2I), 3.62 (dd, J = 2.0, 6.0 Hz, 1H, MeOCHCHCOPh), 3.54 (t, J = 8.4 Hz, 1H, OCHHCHCH_2I), 3.16–3.12 (m, 1H, OCHHCHCH_2I), 3.06 (s, 3H, CH_3O), 2.79 (dd, J = 6.6, 9.8 Hz, 1H, CHCHHI), 2.70 (dd, J = 7.9, 9.7 Hz, 1H, CHCHHI). NOE difference spectra (500 MHz): 4.91–4.89 (MeOCH) → 8.02–7.98 (1.45%), 3.63–3.60 (1.09%), 4.01–3.96 (OCHH) → 8.02–7.98 (0.05%), 4.91–4.89 (0.18%), 3.56–3.50 (10.74%), 3.16–3.11 (2.46%), 3.63–3.60 (MeOCHCHCOPh) → 8.02–7.98 (8.11%), 4.91–4.89 (1.50%), 4.01–3.96 (0.29%), 2.82–2.78 (1.61%), 2.72–2.68 (1.73%), 3.56–3.50 (OCHH) → 4.01–3.96 (11.53%), 2.82–2.78 (1.01%), 2.72–2.68 (1.35%), 3.16–3.11 (CH-CH_2I) → 8.02–7.98 (0.40%), 7.14–6.97 (0.92%), 4.91–4.89 (0.56%), 4.01–3.96 (2.26%), 3.63–3.60 (0.73%), 3.56–3.50 (0.09%), 2.82–2.78 (1.11%), 2.72–2.68 (1.12%); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 196.3 (s), 134.0 (s), 133.7 (d), 128.8 (d), 107.4 (d), 73.0 (t), 61.1 (d), 55.3 (d), 42.8 (q), 6.4 (t); CI-MS (CH_4): *m*/*z*: 347 (10) [M^++H], 315 (100), 287 (40), 219 (28), 159 (32), 105 (100); elemental analysis calcd for $C_{13}H_{15}IO_3$ (346.17): C 45.11, H 4.37; found: C 45.15, H 4.47.

3-(2-Bromo-1-ethoxy)-1,4-pentadiene (19): According to GP 1 from ethyl vinyl ether (0.72 g, 10 mmol), 1,4-pentadien-3-ol (840 mg, 10 mmol) and NBS (1.78 g, 10 mmol). FC (hexane/Et_2O 40:1) gave **19** (2.02 g, 86%) as a colorless oil. IR (KBr): $\tilde{\nu}$ = 3029, 2978, 2883, 1420, 1115, 1028, 928 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$): δ = 5.92–5.71 (m, 2H, 2CH=CH_2), 5.32–5.15 (m, 4H, 2CH_2=CH), 4.77 (t, J = 5.2 Hz, 1H, OC$H$$CH_2Br$), 4.54 (tt, J = 1.2, 6.1 Hz, 1H, CH(CH=CH_2)$_2$), 3.65 (dq, J = 7.0, 9.2 Hz, 1H, CH_3CHH), 3.58 (dq, J = 7.0, 9.5 Hz, 1H, CH_3CHH), 3.39 (dd, J = 2.7, 5.2 Hz, 2H, CH_2Br),

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1.23 (t, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 137.4$ (d), 136.9 (d), 117.5 (t), 116.3 (t), 99.5 (d), 78.8 (d), 62.0 (t), 32.1 (t), 15.2 (q); MS (EI): m/z (%): 153 (65) [$M^+ - 81$], 151 (65) [$M^+ - 83$], 125 (36), 123 (37), 67 (100), 65 (20); elemental analysis calcd for $C_9H_{15}O_2Br$ (235.12): C 45.98, H 6.43; found: C 46.00, H 6.38.

5-Ethoxy-3-methyl-2-vinyltetrahydrofuran (20): According to the GP 2 from **19** (0.49 g, 2.1 mmol), Bu_3SnH (735 mg, 2.5 mmol) and a 1M solution of Et_3B in hexane (2.9 mL, 2.9 mmol). FC (hexane/Et_2O 10:1) gave **20** (0.21 g, 65%, 98% *ds*). IR (KBr): $\tilde{\nu} = 3082$, 2974, 2876, 1448, 1375, 1107, 985, 923 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.77$ (ddd, $J = 7.3$, 10.4, 17.4 Hz, 1H, C*H*=CH_2), 5.32–5.16 (m, 2H, CH_2=CH), 5.15 (dd, $J = 4.0$, 5.8 Hz, 1H, OC*H*CH_2), 3.93 (t, $J = 8.2$ Hz, 1H, C*H*CH=CH_2), 3.79 (dq, $J = 7.0$, 9.5 Hz, 1H, CH_3C*H*H), 3.45 (dq, $J = 7.0$, 9.5 Hz, 1H, CH_3CH*H*), 2.40 (ddd, $J = 5.8$, 8.9, 13.4 Hz, 1H, OCHC*H*H), 1.91–1.77 (m, 1H, C*H*Me), 1.57 (ddd, $J = 3.7$, 9.2, 13.1 Hz, 1H, OCHCH*H*), 1.20 (t, $J = 7.0$ Hz, 3H, CH_3), 1.03 (d, $J = 6.4$ Hz, 3H, CH_3). NOE difference spectra (500 MHz): 5.83–5.72 (OCHC*H*=CH_2) → 5.20–5.16 (s), 3.97–3.90 (m), 1.89–1.79 (m), 5.16–5.12 (EtOC*H*) → 5.83–5.72 (m), 3.50–3.41 (m), 2.45–2.36 (m), 3.97–3.90 (OC*H*CH=CH_2) → 5.83–5.72 (m), 5.31–5.25 (s), 1.89–1.79 (m), 1.56–1.48 (m), 1.05–1.01 (s), 2.45–2.36 (EtOCHC*H*H) → 5.16–5.12 (m), 1.89–1.79 (m), 1.56–1.48 (s), 1.89–1.79 (C*H*-Me) → 5.83–5.72 (m), 5.16–5.12 (w), 3.97–3.90 (w), 2.45–2.36 (m), 1.56–1.48 (w), 1.05–1.01 (s), 1.56–1.48 (EtOCHCH*H*) → 5.16–5.12 (w), 3.97–3.90 (w), 2.45–2.36 (s), 1.89–1.79 (w), 1.05–1.01 (m), 1.05–1.01 (CH-C*H*$_3$) → 3.97–3.90 (s), 1.89–1.79 (s), 1.56–1.48 (s); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 137.1$ (d), 117.2 (t), 103.7 (d), 85.4 (d), 63.4 (t), 41.2 (t), 39.2 (d), 15.8 (q), 15.3 (q); MS (EI): m/z (%): 157 (5) [M^++H], 111 (69), 100 (100), 93.10 (71), 85 (74), 82 (27), 72 (38), 67 (76), 57 (74); HRMS (CI, isobutane): calcd for $C_9H_{15}O_2$: 155.10665; found: 155.10660 [$M^+ - H$].

4-[1-(*tert*-Butoxy)-2-iodomethoxy]-4-methyl-2,5-cyclohexadien-1-one (21): According to the GP 1 from *tert*-butyl vinyl ether (1.00 g, 10 mmol), 4-hydroxy-4-methyl-2,5-cyclohexadien-1-one[49] (1.24 g, 10 mmol) and NIS (2.25 g, 10 mmol) in CH_2Cl_2 (10 mL). The resulting mixture was stirred at rt overnight protected from the light. After usual workup, FC (hexane/Et_2O 5:1) gave **21** (2.80 g, 80%) as a colorless oil. IR (KBr): $\tilde{\nu} = 3043$, 2978, 2931, 1668, 1631, 1338, 1091 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 7.04$ (dd, $J = 3.1$, 5.1 Hz, 1H, C*H*=CH), 7.01 (dd, $J = 3.1$, 5.1 Hz, 1H, C*H*=CH), 6.31 (dd, $J = 3.1$, 10.1 Hz, 1H, C*H*=CH), 6.22 (dd, $J = 3.1$, 10.1 Hz, 1H, C*H*=CH), 4.69 (dd, $J = 4.0$, 5.8 Hz, 1H, OC*H*CH_2I), 3.15 (dd, $J = 4.0$, 5.8 Hz, 2H, CH_2I), 1.48 (s, 3H, CH_3), 1.19 (s, 9H, *t*Bu); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 185.0$ (s), 152.5 (d), 151.2 (d), 129.6 (d), 128.0 (d), 95.0 (d), 75.4 (s), 72.5 (s), 29.1 (q), 27.5 (q), 10.0 (q); MS (EI): m/z (%): 351 (2) [M^++H], 153 (25), 125 (63), 124 (16), 109 (20), 108 (14), 107 (100), 77 (28), 57 (66), 53 (12); elemental analysis calcd for $C_{13}H_{19}O_3I$ (350.20): C 44.59, H 5.47; found: C 44.41, H 5.45.

2-(*tert*-Butoxy)-7a-methyl-2,3,3a,4,5,7a-hexahydrobenzo[*b*]furan-5-one (22): According to the GP 2 from the iodoacetal **21** (0.74 g, 2.1 mmol), Bu_3SnH (735 mg, 2.52 mmol) and a 1M solution of Et_3B in hexane (2.9 mL, 2.9 mmol). FC (hexane/Et_2O 5:1) afforded **22** (0.35 g, 74%, 98% ds). According to the GP 3 from the iodoacetal **21** (0.18 g, 0.5 mmol), Bu_3SnH (174 mg, 0.60 mmol) and AIBN (4 mg, 0.025 mmol) gave **22** (0.08 g, 71%, 89% *ds*). IR (KBr): $\tilde{\nu} = 3032$, 2976, 2872, 1689, 1369, 1099 cm^{-1}. *exo*-**22** (major diastereomer): ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 6.50$ (dd, $J = 1.8$, 10.8 Hz, 1H, C*H*=CHMe), 5.84 (d, $J = 10.4$ Hz, 1H, C*H*=CO), 5.29 (d, $J = 5.2$ Hz, 1H, OC*H*CH_2), 2.88–2.78 (m, 1H, C*H*CH_2CO), 2.64 (dd, $J = 5.5$, 17.0 Hz, 1H, CHC*H*HC=O), 2.54 (dd, $J = 2.1$, 16.8 Hz, 1H, CHCH*H*C=O), 1.96 (dd, $J = 7.0$, 12.5 Hz, 1H, C*H*HCH-O), 1.86 (dt, $J = 5.2$, 12.5 Hz, 1H, CH*H*CH-O), 1.52 (s, 3H, CH_3), 1.23 (s, 9H, *t*Bu-O). NOE difference spectra (500 MHz): 5.31–5.27 (*t*BuOC*H*) → 1.91–1.81 (s), 1.25–1.22 (s), 2.87–2.78 (*t*BuOCHCH$_2$C*H*) → 2.68–2.51 (s), 1.99–1.92 (m), 1.91–1.81 (w), 1.53–1.51 (m), 1.99–1.92 (*t*BuOCHC*H*H) → 5.31–5.27 (w), 2.87–2.78 (m), 1.91–1.81 (s), 1.25–1.22 (m), 1.91–1.81 (*t*BuOCHCH*H*) → 5.31–5.27 (s), 1.99–1.92 (s), 1.53–1.51 (C*H*$_3$) → 2.87–2.78 (s), 2.67–2.59 (m); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 197.6$ (s), 151.8 (d), 126.0 (d), 97.1 (d), 79.3 (s), 74.1 (s), 41.6 (d), 39.7 (t), 39.4 (t), 29.1 (q), 25.6 (q). *endo*-**22** (minor diastereomer): ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 6.70$ (dd, $J = 1.8$, 10.1 Hz, 1H, C*H*=CH), 1.73 (s, 3H, CH_3), 1.21 (s, 9H, *t*BuO); MS (CI, CH_4): m/z (%): 225 (12) [M^++H], 197 (32), 169 (86), 152 (13), 150 (100), 122 (8), 57 (13); elemental analysis calcd for $C_{13}H_{20}O_3$ (224.30): C 69.51, H 8.97; found: C 69.61, H 8.99.

Methyl-2-{[2-(*tert*-butoxy)-7a-methyl-5-oxo-2,3,3a,4,5,7a-hexahydro-1-benzofuran-4-yl]methyl}acrylate (23): A solution of 2-(methoxycarbonyl)-propenyltributylstannane (1.55 g, 4 mmol), AIBN (4 mg, 0.025 mmol) and the iodoacetal **21** (0.18 g, 0.5 mmol) in benzene (6 mL) was heated under reflux. The reaction was monitored by TLC until disappearance of the starting material. An aqueous KF solution was added and the mixture was stirred at rt for 2 h. The organic layer was washed with H_2O, dried over $MgSO_4$ and evaporated. FC (hexane/Et_2O 2:1) gave **23** (0.11 g, 68%, 81% *ds*) as a mixture of diastereomers. IR (KBr): $\tilde{\nu} = 3030$, 2976, 1722, 1680, 1440, 1347, 1199, 1143 cm^{-1}. Major diastereomer: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 6.50$ (dd, $J = 1.5$, 10.1 Hz, 1H, C*H*=CHCMe), 6.26 (d, $J = 1.2$ Hz, 1H, C*H*H=CCO_2Me), 5.80 (d, $J = 10.1$ Hz, 1H, C*H*=CO), 5.56 (d, $J = 1.2$ Hz, 1H, CH*H*=CCO_2Me), 5.27 (d, $J = 5.2$ Hz, 1H, OCHCH$_2$), 3.76 (s, 3H, CH_3O), 2.75–2.72 (m, 2H, C*H*C=O, C*H*CHCO), 2.64–2.62 (m, 2H, CH_2C=CH_2), 2.03 (ddd, $J = 0.9$, 7.0, 12.8 Hz, 1H, C*H*HCHCHCO), 1.85 (dt, $J = 5.2$, 12.5 Hz, 1H, CH*H*CHCHCO), 1.59 (s, 3H, CH_3), 1.23 (s, 9H, *t*BuO). NOE difference spectra (500 MHz): 5.29–5.24 (*t*BuOC*H*) → 2.06–1.99 (0.70%), 1.90–1.81 (5.67%), 1.25–1.21 (6.37%), 2.78–2.70 (*t*BuOCHCH$_2$C*H*) → 2.65–2.60 (0.31%), 2.06–1.99 (2.43%), 1.90–1.81 (0.48%), 1.61–1.58 (1.41%), 2.65–2.60 (CH_2C=CH_2) → 2.78–2.70 (2.73%), 1.61–1.58 (2.04%), 2.06–1.99 (*t*BuOCHC*H*H) → 5.29–5.24 (1.95%), 2.78–2.70 (7.79%), 1.90–1.81 (23.54%), 1.90–1.81 (*t*BuOCHCH*H*) → 5.29–5.24 (9.28%), 2.78–2.70 (2.92%), 2.06–1.99 (18.91%), 1.61–1.58 (CH_3) → 2.78–2.70 (2.72%), 2.65–2.60 (2.01%), 1.25–1.21 (0.13%); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 199.8$ (s), 166.9 (s), 149.8 (d), 137.5 (t), 127.4 (s), 124.9 (d), 96.9 (d), 78.3 (s), 74.1 (s), 51.8 (q), 47.9 (d), 46.0 (d), 41.1 (t), 35.1 (t), 29.1 (q), 28.8 (q). Minor diastereoisomer: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 6.66$ (dd, $J = 1.22$, 10.07 Hz, 1H, C*H*=CH), 5.59 (d, $J = 1.22$ Hz, 1H, *t*BuOC*H*), 3.79 (s, 3H, CH_3), 1.19 (s, 9H, *t*BuO); MS (CI, CH_4): m/z (%): 323 (8) [M^++H], 267 (21), 235 (30), 217 (63), 169 (24), 151 (100), 136 (15), 57 (78); elemental analysis calcd for $C_{18}H_{26}O_5$ (322.46): C 67.06, H 8.13; found: C 67.10, H 8.09.

3-(2-Bromo-1-ethoxy-2-methylpropoxy)-1,4-pentadiene (24): According to GP 1 from 1-ethoxy-2-methyl-1-propene[50] (1.00 g, 10 mmol), 1,4-pentadien-3-ol (840 mg, 10 mmol) and NBS (1.78 g, 10 mmol). FC (hexane/Et_2O 20:1) afforded **24** (1.12 g, 43%) as a colorless oil. IR (KBr): $\tilde{\nu} = 3084$, 2978, 2876, 1464, 1383, 1112, 1055, 927 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.92–5.73$ (m, 2H, 2C*H*=CH_2), 5.32–5.15 (m, 4H, 2CH_2=CH), 4.56 (tt, $J = 0.9$, 5.8 Hz, 1H, C*H*(CH=CH_2)$_2$), 4.54 (s, 1H, OC*H*CBrMe$_2$), 3.82 (dq, $J = 7.0$, 9.1 Hz, 1H, CH_3C*H*H), 3.68 (dq, $J = 7.0$, 9.2 Hz, 1H, CH_3CH*H*), 1.74 (s, 3H, CH_3), 1.73 (s, 3H, CH_3), 1.23 (t, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 137.7$ (d), 137.1 (d), 117.7 (t), 116.2 (t), 105.2 (d), 80.4 (d), 67.1 (t), 29.1 (q), 28.4 (q), 15.4 (q); MS (EI): m/z (%): 181 (63) [$M^+ - 81$], 179 (65) [$M^+ - 83$], 153 (9), 151 (9), 75 (20), 67 (100); elemental analysis calcd for $C_{11}H_{19}O_2Br$ (263.18): C 50.20, H 7.28; found: C 50.83, H 7.46.

2-Ethoxy-3,3,4-trimethyl-5-vinyltetrahydrofuran (25): According to the GP 2 from the bromoacetal **24** (0.55 g, 2.1 mmol), Bu_3SnH (735 mg, 2.5 mmol) and a 1M solution of Et_3B in hexane (2.9 mL, 2.9 mmol). FC (hexane/Et_2O 10:1) gave **25** (0.29 g, 75%, 86% *ds*) as a mixture of diastereomers. According to the GP 3 from **24** (0.55 g, 2.1 mmol), Bu_3SnH (735 mg, 2.52 mmol) and AIBN (17 mg, 0.11 mmol), compound **25** (0.34 g, 88%, 74% *ds*) was obtained after FC. IR (KBr): $\tilde{\nu} = 3082$, 2974, 2877, 1645, 1469, 1388, 1109, 1020, 922 cm^{-1}. (*r*-2,*c*-4, *t*-5)-**25** (major): ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.80$ (ddd, $J = 7.3$, 10.1, 17.1, 1H, C*H*=CH_2), 5.23 (ddd, $J = 0.9$, 1.5, 17.1 Hz, 1H, CH*H*=CH), 5.13 (ddd, $J = 0.9$, 1.5, 10.1 Hz, 1H, C*H*H=CH), 4.69 (s, 1H, OC*H*CMe$_2$), 4.00 (dd, $J = 7.3$, 8.2 Hz, 1H, C*H*CH=CH_2), 3.82 (dq, $J = 7.0$, 9.5 Hz, 1H, CH_3C*H*H), 3.48 (dq, $J = 7.0$, 9.8 Hz, 1H, CH_3CH*H*), 1.57 (dq, $J = 7.0$, 8.2 Hz, 1H, C*H*Me), 1.20 (t, $J = 7.0$ Hz, 3H, C*H*$_3$CH$_2$), 1.00 (s, 3H, CH_3), 0.87 (s, 3H, CH_3), 0.86 (d, $J = 6.7$ Hz, 3H, CHC*H*$_3$); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 138.8$ (d), 116.0 (t), 111.1 (d), 84.8 (d), 64.5 (t), 48.5 (d), 43.9 (s), 25.9 (q), 16.0 (q), 15.3 (q), 11.2 (q). Minor diastereoisomer: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 4.51$ (s, 1H, OC*H*CMe$_2$), 3.95 (t, $J = 8.5$ Hz, 1H, C*H*CH=CH_2); elemental analysis calcd for $C_{11}H_{20}O_2$ (183.99): C 71.70, H 10.94; found: C 71.42, H 10.93.

Methyl 3-ethoxy-2-iodo-3-[(1-vinyl-2-propenyl)-oxy]propanoate (26): NIS (2.92 g, 13 mmol) at 0 °C was added in portions to a solution of methyl (*E*)-3-ethoxy-2-propenoate[51] (1.69 g, 13 mmol) and 1,4-pentadien-3-ol (0.93 g, 11 mmol) in CH_2Cl_2 (10 mL). The resulting mixture, protected from the light, was stirred at rt for 3 d. The precipitate was diluted in hexane and

filtered off. The filtrate was washed with sat. $Na_2S_2O_3$, brine and dried. Evaporation in vacuo afforded a yellow oil that was purified by FC (hexane/Et_2O 10:1) to give the iodoacetal **26** (2.24 g, 60%). IR (KBr): $\tilde{\nu}$ = 3082, 2978, 2895, 1741, 1435, 1303, 1253, 1109, 1030, 929 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$): δ = 5.85–5.60 (m, 2H, 2 C*H*=CH_2), 5.30–5.15 (m, 4H, 2 CH_2=CH), 5.03 (d, J = 8.6 Hz, 1H, C*H*ICO_2Me), 4.55 (dt, J = 1.2, 7.3 Hz, 1H, C*H*(CH=CH_2)$_2$), 4.46 (d, J = 8.5 Hz, 1H, OC*H*$HICO_2Me$), 3.82–3.61 (m, 2H, OCH_2CH_3), 3.73 (s, 3H, CH_3O), 1.24 (t, J = 7.3 Hz, 3H, CH_3CH_2O); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 169.9 (s), 137.2 (d), 136.4 (d), 117.7 (t), 116.4 (t), 100.2 (d), 79.7 (d), 61.6 (t), 52.8 (d), 21.4 (q), 14.9 (q); MS (EI): m/z (%): 257 (56) [M^+ − 83], 229 (17), 197 (17), 169 (19), 127 (12), 103 (19), 89 (34), 67 (100), 55 (16); elemental analysis calcd for $C_{11}H_{17}O_4I$ (340.16): C 38.84, H 5.04; found: C 39.10, H 5.18.

Methyl 2-ethoxy-4-iodomethyl-5-vinyltetrahydro-3-furancarboxylate (27): According to the GP 4 from the iodoacetal **26** (0.34 g, 1 mmol) and $(Bu_3Sn)_2$ (58 mg, 0.1 mmol). FC (hexane/Et_2O 5:1) afforded **27** (0.24 g, 71%, 77% ds). IR (KBr): $\tilde{\nu}$ = 3082, 2978, 1739, 1437, 1199 cm^{-1}. (*r*-2,*t*-3,*c*-4,*t*-5)-**27** (major): ^1H NMR (360 MHz, $CDCl_3$): δ = 5.85 (ddd, J = 7.6, 10.2, 17.2 Hz, 1H, C*H*=CH_2), 5.39 (dt, J = 1.1, 17.1 Hz, 1H, C*H*H=CH), 5.33 (d, J = 2.5 Hz, 1H, OC*H*$CHCO_2Me$), 5.28 (ddd, J = 0.8, 1.4, 10.2 Hz, 1H, CH*H*=CH), 4.25 (t, J = 8.0 Hz, 1H, C*H*CH=CH_2), 3.77 (dq, J = 7.0, 9.7 Hz, 1H, CH_3CHH), 3.75 (s, 3H, CH_3), 3.49 (dq, J = 7.0, 9.4 Hz, 1H, CH_3CH*H*), 3.39 (dd, J = 4.9, 10.3 Hz, 1H, CHC*H*HI), 3.28 (dd, J = 6.3, 10.3 Hz, 1H, CHCH*H*I), 3.00 (dd, J = 2.5, 7.4 Hz, 1H, C*H*CO_2Me), 2.29 (m, 1H, CH), 1.22 (t, J = 7.2 Hz, 3H, CH_3CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 171.7 (s), 135.7 (d), 118.9 (t), 104.5 (d), 84.2 (d), 63.5 (d), 57.7 (d), 52.5 (q), 48.7 (d), 15.1 (q), 6.0 (q). Minor diastereomer: ^1H NMR (360 MHz, $CDCl_3$): δ = 4.38 (t, J = 7.9 Hz, 1H, C*H*CH=CH_2); MS (EI): m/z (%): 341 (4) [M^++H], 295 (100), 254 (7), 127 (4), 58 (6); elemental analysis calcd for $C_{11}H_{17}IO_4$ (340.16): C 38.84, H 5.04; found: C 38.74, H 5.09.

3-(2-Bromo-1-ethoxy-3-methylbutoxy)-1,4-pentadiene (28): According to GP 1 from (*Z*/*E*)-1-ethoxy-3-methyl-1-butene[50] (1.14 g, 10 mmol), 1,4-pentadien-3-ol (840 mg, 10 mmol) and NBS (1.78 g, 10 mmol). FC (hexane/Et_2O 20:1) gave **28** (0.47 g, 17%) as a colorless oil. Mixture of diastereomers. IR (KBr): $\tilde{\nu}$ = 3084, 2968, 2877, 1464, 1386, 1109, 1035, 925 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$): δ = 5.95–5.65 (m, 2H, 2 C*H*=CH_2), 5.32–5.15 (m, 4H, 2 CH_2=CH), 4.70 (d, J = 7.0 Hz, 1H, OC*H*CHBr), 4.56 (t, J = 6.1 Hz, 1H, C*H*(CH=CH_2)$_2$), 4.03 (dd, J = 3.1, 7.3 Hz, 1H, OCHC*H*Br), 3.68–3.56 (m, 2H, CH_3CH_2O), 2.18–2.05 (m, 1H, C*H*$(CH_3)_2$), 1.20 (t, J = 7.0 Hz, 3H, CH_3CH_2O), 1.01 (d, J = 6.7 Hz, 3H, CH_3), 0.96 (d, J = 6.7 Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 137.6 (d), 137.5 (d), 117.6 (t), 116.3 (t), 100.8 (d), 79.4 (d), 64.5 (d), 61.4 (t), 29.4 (d), 22.0 (q), 17.7 (q), 15.2 (q); MS (EI): m/z (%): 195 (98) [M^+ − 81], 193 (100) [M^+ − 83], 167 (8), 165 (8), 137 (26), 113 (84), 85 (57), 75 (31), 55 (62); HRMS (ESI): calcd for $C_{12}H_{21}O_2BrNa$: 299.06171; found: 299.06128.

2-Ethoxy-3-*iso*propyl-4-methyl-5-vinyltetrahydrofuran (29): According to the GP 2 from the bromoacetal **28** (0.58 g, 2.1 mmol), Bu_3SnH (735 mg, 2.5 mmol) and a 1M solution of Et_3B in hexane (2.9 mL, 2.9 mmol). FC (hexane/Et_2O 40:1) gave **29** (0.27 g, 66%, 63:37 mixture of diastereomers). The two diastereomers were separated by further FC. (*r*-2,*t*-3,*c*-4,*t*-5)-**29** (major): ^1H NMR (500 MHz, $CDCl_3$): δ = 5.79 (ddd, J = 7.5, 10.3, 17.2 Hz, 1H, CH=CH_2), 5.27 (ddd, J = 1.0, 1.7, 17.2 Hz, 1H, C*H*H=CH), 5.17 (ddd, J = 0.8, 1.7, 10.3 Hz, 1H, CH*H*=CH), 4.83 (d, J = 2.7 Hz, 1H, OC*H*CH*i*Pr), 3.99 (t, J = 8.3 Hz, 1H, C*H*CH=CH_2), 3.77 (dq, J = 7.1, 9.7 Hz, 1H, CH_3CHH), 3.45 (dq, J = 7.0, 9.7 Hz, 1H, CH_3CH*H*), 1.73–1.68 (m, 1H, C*H*-Me_2), 1.59–1.55 (m, 1H, C*H*Me), 1.51–1.46 (m, 1H, C*H*i*Pr*), 1.20 (t, J = 7.1 Hz, 3H, CH_3CH_2), 1.1 (d, J = 6.4 Hz, 3H, CHC*H*$_3$), 0.95 (d, J = 2.7 Hz, 3H, CH_3), 0.93 (d, J = 2.7 Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 137.2 (d), 117.2 (t), 107.1 (d), 85.9 (d), 63.1 (t), 60.3 (d), 42.9 (d), 29.8 (d), 20.7 (q), 20.5 (q), 16.0 (q), 15.3 (q). **29** (minor): ^1H NMR (360 MHz, $CDCl_3$): δ = 5.86 (ddd, J = 6.7, 10.4, 17.1 Hz, 1H, C*H*=CH_2), 5.20 (dt, J = 1.5, 17.1 Hz, 1H, C*H*H=CH), 5.04 (dt, J = 1.2, 10.4 Hz, 1H, CH*H*=CH), 4.97 (d, J = 4.6 Hz, 1H, OC*H*CH*i*Pr), 4.21 (dquint, J = 1.2, 6.4 Hz, 1H, C*H*CH=CH_2), 3.76 (dq, J = 7.3, 9.8 Hz, 1H, CH_3C*H*H), 3.40 (dq, J = 7.2, 9.7 Hz, 1H, CH_3CH*H*), 2.04–1.94 (m, 1H, C*H*Me), 1.91–1.80 (m, 1H, C*H*Me_2), 1.72–1.65 (m, 1H, C*H*i*Pr*), 1.20–1.14 (m, 6H, CH_3CH_2, CH_3), 0.94 (d, J = 6.4 Hz, 3H, CH_3), 0.90 (d, J = 6.7 Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 139.5 (d), 114.0 (t), 104.9 (d), 87.6 (d), 62.9 (t), 53.4 (d), 39.1 (d), 23.9 (d), 21.8 (q), 21.5 (q), 16.0 (q), 15.4 (q). Mixture of isomers of **29**. IR (KBr): $\tilde{\nu}$ = 3082, 2960, 2876, 1465, 1377, 1093, 989, 922 cm^{-1}; HRMS (CI, isobutane): calcd for $C_{12}H_{23}O_2$: 199.16925; found: 199.17066 [M^++H].

4-(2-Bromo-1-*tert*-butoxyethoxy)-1,6-heptadiene (30): According to the GP 1 from 1,6-heptadien-3-ol (1.0 g, 8.9 mmol), *tert*-butyl vinyl ether (0.89 g, 8.9 mmol) and NBS (1.58 g, 8.9 mmol). FC (hexane/Et_2O 40:1) afforded the bromoacetal **30** (1.74 g, 67%) as a colorless oil. IR (KBr): $\tilde{\nu}$ = 3076, 2978, 2935, 1641, 1367, 1033, 914 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$): δ = 5.91–5.78 (m, 2H, C*H*=CH_2), 5.12–5.02 (m, 4H, CH_2=CH), 4.87 (dd, J = 4.6, 6.1 Hz, 1H, OCHCH_2Br), 3.66 (m,1H, OC*H*$(CH_2CH$=$CH_2)_2$), 3.36 (dd, J = 6.1, 10.7 Hz, 1H, OCHC*H*HBr), 3.27 (dd, J = 4.3, 10.4 Hz, 1H, OCHCH*H*Br), 2.31 (t, J = 6.4 Hz, 4H, 2 CH_2CH=CH_2), 1.27 (s, 9H, *t*Bu); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 134.7 (d), 134.3 (d), 117.6 (t), 117.1 (t), 95.9 (d), 74.8 (s), 38.8 (t), 38.2 (t), 34.5 (t), 28.9 (q); MS (EI): m/z (%): 293 (4) [M^++2], 291 (3) [M^+], 219 (26), 217 (26), 201 (9), 199 (9), 169 (40), 127 (56), 95 (100), 81 (39), 57 (65); elemental analysis calcd for $C_{13}H_{23}O_2Br$ (291.23): C 53.62, H 7.96; found: C 53.48, H 8.13.

6-(3-Propenyl)-4-methyltetrahydro-2*H*-pyran-2-yl *tert*-butyl ether (31): According to the GP 2 from the bromoacetal **30** (0.61 g, 2.1 mmol), Bu_3SnH (735 mg, 2.5 mmol) and a 1M solution of Et_3B in hexane (2.9 mL, 2.9 mmol). FC gave the acetal **31** (0.19 g, 43%) as a single diastereomer. IR (KBr): $\tilde{\nu}$ = 3078, 2976, 2930, 2872, 1458, 1375, 1112, 1001 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 5.82 (ddt, J = 7.0, 10.3, 17.0 Hz, 1H, C*H*=CH_2), 5.15 (dm, J = 3.3 Hz, 1H, *t*BuOC*H*CH_2), 5.05 (ddt, J = 1.4, 2.1, 17.1 Hz, 1H, C*H*H=CH), 5.00 (ddt, J = 1.1, 2.1, 10.1 Hz, 1H, CH*H*=CH), 3.91 (dddd, J = 2.2, 5.6, 7.1, 11.6 Hz, 1H, OC*H*CH_2CH=CH_2), 2.20 (dtt, J = 1.3, 6.9, 14.1 Hz, 1H, C*H*HCH=CH_2), 2.12 (dddt, J = 1.0, 6.1, 7.3, 14.1 Hz, 1H, CH*H*CH=CH_2), 1.98 (tqt, J = 6.5 Hz, 1H, C*H*Me), 1.60 (ddt, J = 1.5, 3.8, 12.9 Hz, 1H, OCH(CH_2CH=CH_2)C*H*H), 1.54 (ddt, J = 1.5, 3.0, 12.9 Hz, 1H, *t*BuOCHC*H*H), 1.22 (s, 9H, *t*Bu), 1.21 (ddd, J = 3.7, 12.3, 12.9 Hz, 1H, *t*BuOCHCH*H*), 0.86 (d, J = 6.5 Hz, 3H, CH_3), 0.85 (ddd, J = 11.7, 11.7, 12.9 Hz, 1H, OCH(CH_2CH=CH_2)CH*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 135.5 (d), 116.2 (t), 91.8 (d), 73.7 (s), 67.8 (d), 40.9 (t), 40.0 (t), 39.8 (t), 28.8 (q), 24.2 (d), 22.3 (q); MS (EI): m/z (%): 213 (16) [M^++H], 171 (11), 157 (43), 139 (78), 115 (38), 95 (27), 69 (22), 57 (100); HRMS (ESI): calcd for $C_{13}H_{24}O_2Na$: 235.16685; found: 235.16711.

8-Methoxy-8-[(2*Z*)-3-methoxyprop-2-enyl]-1,4-dioxaspiro[4.5]deca-6,9-diene (34): Allyl methyl ether (656 mg, 9.1 mmol) dissolved in THF (5 mL) was added to a 0.5M solution of *s*BuLi (9.8 mmol) in dry THF at −78 °C. After 30 min a solution of ketone **32**[52] (690 mg, 4.5 mmol) in THF (5 mL) was added. The reaction medium was kept at −78 °C for 1 h. After dilution with Et_2O, H_2O was added and the solution was allowed to warm up to rt. The aqueous phase was extracted with Et_2O and the organic layer was dried and evaporated to give crude alcohol **33** (880 mg). To a suspension of NaH (912 mg, ca. 50% in paraffin, 19 mmol) in dry THF (15 mL) was added at 0 °C the crude alcohol **33** (880 mg) dissolved in THF (5 mL) and the mixture was allowed to warm up to rt. After 20 min, MeI (1.2 mL, 19 mmol) was added at 0 °C and the mixture was stirred at rt overnight. H_2O was added and the mixture was extracted with Et_2O. The organic layer was dried over $MgSO_4$ and evaporated, FC (hexane/ethylacetate 10:1) gave the vinyl ether **34** (521 mg, 2.2 mmol, 48% from **32**) as a colorless oil. IR ($CHCl_3$): $\tilde{\nu}$ = 3020, 2936, 2889, 2827, 1666, 1464, 1407, 1206, 1109 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$): δ = 5.92 (d, J = 10.5 Hz, 2H, 2 C*H*=CHC(OMe)), 5.90–5.93 (m, 1H, C*H*OMe), 5.77 (d, J = 10.4 Hz, 2H, 2 CH=C*H*C(OMe)), 4.23 (dt, J = 6.4, 7.3 Hz, 1H, CH_2C*H*=CH), 4.02 (s, 4H, OCH_2CH_2O), 3.51 (s, 3H, OCH_3), 3.09 (s, 3H, OCH_3), 2.36 (d, J = 7.3 Hz, 2H, CH_2CH=CH); ^{13}C NMR (90.5 MHz, $CDCl_3$): δ = 147.8 (d), 134.7 (d), 129.9 (d), 99.9 (d), 99.2 (s), 73.7 (s), 65.2 (t), 65.0, 59.3 (q), 51.8 (q), 34.4 (t); EI-MS: m/z (%): 238 (3) [M^+], 167 (100), 136 (18), 115 (21), 95 (26), 72 (82); HRMS (ESI-MS): calcd for $C_{13}H_{18}O_4Na$: 261.10973; found: 261.10943 [M^++Na].

8-[3-(Allyloxy)-2-iodo-3-methoxypropyl]-8-methoxy-1,4-dioxaspiro[4.5]-deca-6,9-diene (35): According to GP 1 from enol ether **34** (5.76 g, 24 mmol), allyl alcohol (11 mL), NEt_3 (2.3 mL, 12 mmol) and NIS (16.3 g, 72 mmol, addition at −50 °C) in CH_2Cl_2 (70 mL). FC (CH_2Cl_2/Et_2O 60:1) gave the iodoacetal **35** (8.2 g, 19.4 mmol, 81%) as a colorless oil. IR ($CHCl_3$): $\tilde{\nu}$ = 3007, 2936, 2889, 2829, 1464, 1406, 1336, 1206, 1116, 967 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$): δ = 6.20–5.80 (m, 5H, 2 C*H*=C*H*C(OMe), CH_2=C*H*), 5.28 (dm, J = 17.2 Hz, 1H, C*H*H=CH), 5.16 (dm, J = 10.4 Hz, 1H, CH*H*=CH), 3.93–4.17 (m, 8H, CHCH_2O, OCH_2CH_2O, IC*H*C*H*OMe), 3.34 (s, 3H, OCH_3), 3.07 (s, 3H, OCH_3), 2. 51 (dd, J = 15.3, 4.3 Hz, 1H, C*H*HCI), 2.26 (dd, J = 15.4, 6.6 Hz, 1H, CH*H*CI);

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^{13}C NMR (90.5 MHz, $CDCl_3$): $\delta = 134.4$ (d), 134.0 (d), 130.9 (d), 130.8 (d), 117.2 (t), 104.7 (d), 98.9 (s), 73.6 (s), 68.9 (t), 65.4 (t), 65.1 (t), 55.3 (q), 51.6 (q), 44.8 (t), 25.82 (d); EI-MS: *m*/*z* (%): 422 (1.1) [M^+], 167 (100), 233 (1.6), 149 (22), 128 (12), 107 (11), 101 (70), 71 (15), 41 (63); HRMS (EI-MS): calcd for $C_{16}H_{23}O_5I$: 422.05903; found 422.05902 [M^+].

4-[3-(Allyloxy)-2-iodo-3-methoxypropyl]-4-methoxycyclohexa-2,5-dien-1-one (36): A solution of **35** (5.27 g, 12.5 mmol) in benzene (2 L) saturated with H_2O (0.5 mL) was stirred for 1 h with anhydrous $MgSO_4$ (210 g) until the TLC shows no starting material. The mixture was filtered and the filtrate was concentrated to give **36** (4.50 g, 11.9 mmol, 95%) as a yellow oil that was used without further purification for the next step. IR ($CHCl_3$): $\tilde{\nu} = 3009$, 2933, 1670, 1635, 1507, 1460, 1394, 1071, 929, 861 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 6.90$ (dd, $J = 10.5$, 3.2 Hz, 1H, CH=C*H*C=O), 6.76 (dd, $J = 10.0$, 3.2 Hz, 1H, CH=C*H*C=O), 6.34–6.39 (m, 2H, 2C*H*=CHC=O), 5.87 (ddt, $J = 17.3$, 10.4, 5.9 Hz, 1H, CH_2=C*H*), 5.28 (dd, $J = 17.3$, 1.4 Hz, 1H, C*H*H=CH), 5.18 (d, $J = 10.5$, 1H, CH*H*=CH), 4.23 (d, $J = 4.1$, 1H, C*H*OMe), 4.12 (dd, $J = 12.7$, 5.5 Hz, 1H, C*H*HCl), 4.02 (dd, $J = 12.7$, 5.9 Hz, 1H, CH*H*Cl), 3.95 (ddd, $J = 8.2$, 4.5, 3.2, 1H, CHI), 3.38 (s, 3H, OCH_3), 3.16 (s, 3H, OCH_3), 2.71 (dd, $J = 15.4$, 2.7 Hz, 1H, C*H*HCl), 2.27 (dd, $J = 15.9$, 8.2 Hz, 1H, CH*H*Cl); ^{13}C NMR (90.5 MHz, $CDCl_3$): $\delta = 185.2$ (s),150.6 (d), 149.6 (d), 133.7 (d), 131.7 (d), 131.6 (d), 117.6 (t), 105.4 (d), 74.7 (s), 69.1 (t), 55.6 (d), 52.8 (q), 44.4 (t), 23.9 (q); EI-MS: *m*/*z* (%): 378 (0.2) [M^+], 41 (100), 289 (1.4), 255 (1.4), 210 (12), 162 (25),152 (19), 123 (64), 101 (81), 71 (29); HRMS (EI-MS): calcd for $C_{14}H_{19}O_4I$: 378.03281; found 378.03275 [M^+].

1,8a-Dimethoxy-1,3a,4,4a,5,8a,9,9a-octahydronaphtho[2,3-*c*]furan-6(3*H*)-one (37): A solution of **36** (909 mg, 2.4 mmol) in toluene (60 mL) was cooled to $-90\,^\circ$C and a 1M solution of Et_3B in toluene (12 mL, 12 mmol) was added, followed by addition of air (6 mL) over 6 h with a syringe pump. The solution was filtered over silica gel and the solvent was evaporated under reduced pressure. The crude product was purified by FC (hexane/EtOAc 7:3) to afford **37** (518 mg, 2.06 mmol, 86%, *dr* 84:8:5:2:1, 84% *ds*) as a mixture of 5 diastereomers. The diastereomeric ratios were determined by ^{1}H NMR spectroscopy of the crude product before FC. The major diastereomer was isolated by FC together with one of the minor diastereomers. IR ($CHCl_3$): $\tilde{\nu} = 3009$, 2934, 1678, 1446, 1386, 1206, 1078, 1035, 1010, 972 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 6.79$ (d, $J = 10.4$ Hz, 1H, H_2C=C*H*COMe, minor diast.), 6.67 (dd, $J = 10.0$, 1.8 Hz, 1H, H_2C=C*H*COMe, major diast.), 6.11 (d, $J = 10.5$ Hz, 1H, CH=C*H*C=O, major diast.), 6.06 (d, $J = 10.5$ Hz, 1H, CH=C*H*C=O, minor diast.), 5.06 (d, $J = 4.1$ Hz, 1H, OC*H*OMe, major diast.), 5.01 (d, $J = 3.2$ Hz, 1H, OC*H*OMe, minor diast.), 4.01 (dd, $J = 8.6$, 6.4 Hz, 1H, C*H*HO, minor diast.), 3.80–3.87 (m, 2H, CH_2O, major diast.), 3.69 (dd, $J = 8.2$, 4.5 Hz, 1H, minor diast.), 3.45 (s, 3H, OMe, major diast.), 3.38 (s, 3H, OMe, minor diast.), 3.33 (s, 3H, OMe, major diast.), 3.25 (s, 3H, OMe, major diast.), 3.07 (dd, $J = 16.8$, 5.0 Hz, 1H, C*H*HC=O, major diast.), 2.70 (dd, $J = 16.8$, 4.6 Hz, 1H, CH*H*C=O, minor diast.), 2.56–1.35 (m, 8H, C(O)CH*H*, C*H*C*H*$_2$C*H*, MeOCC*H*$_2$C*H*); ^{13}C NMR (100 MHz, $CDCl_3$): **37** (major): $\delta =$ 199.5 (s), 148.9 (d), 132.6 (d), 108.3 (d), 73.4 (s), 68.7 (t), 57.2 (q), 50.6 (q), 40.3 (t), 39.2 (d), 36.3 (d), 36.2 (d), 28.5 (t). **37** (minor): $\delta = 153.4$ (d), 131.8 (d), 109.8 (d), 71.4 (t), 55.9 (q), 50.8 (q), 43.2 (d), 40.4 (t), 35.0 (d), 33.6 (d), 31.0 (t), 27.2 (t); EI-MS: *m*/*z* (%): 252 (0.7) [M^+], 124 (100), 220 (23), 189 (31), 150 (26), 109 (41), 91 (35), 77 (25), 69 (32), 41 (46); HRMS (EI-MS): calcd for $C_{14}H_{20}O_4$: 252.13616; found: 252.13641 [M^+].

1,6-Dimethoxy-1,3,3a,4,9,9a-hexahydronaphtho[2,3-*c*]furan (38): The enone **37** (538 mg, 2.13 mmol, mixture of diastereomers, 84% *ds*) was dissolved in MeOH (140 mL) in the presence of trimethylorthoformate (14.2 mL) and *p*TsOH (30 mg). The reaction mixture was heated at reflux for 1 h and was allowed to cool down to rt. Sat. $NaHCO_3$ (40 mL) was added and the mixture was extracted with Et_2O. The organic phase was washed with brine (50 mL), dried over MgSO4, and concentrated in vacuo to afford **38** (480 mg, 2.0 mmol, 96%, 87% *ds*). Diastereomers were separated by FC (hexane/EtOAc 20:1).

(*r*-2,*t*-3,*c*-4)-**38** (major): IR ($CHCl_3$): $\tilde{\nu} = 3010$, 2950, 2837, 1612, 1500, 1449, 1368, 1208 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.04$ (d, $J = 7.8$ Hz, 1H, arom. H), 6.73–6.69 (m, 2H, arom. H), 4.71 (s, 1H, C*H*OMe), 4.17 (dd, $J =$ 8.6, 7.1 Hz, 1H, C*H*HO), 3.78 (s, 3H, CH_3OAr), 3.65 (dd, $J = 8.6$, 2.8 Hz, 1H, CH*H*O), 3.33 (s, 3H, CHOC*H*$_3$), 2.87–2.81 (m, 1H, C*H*HCHCOMe), 2.76 (dd, $J = 14.2$, 6.1 Hz, 1H, C*H*HCHCH$_2$O), 2.66–2.59 (m, 1H, CH_2C*H*CH$_2$O), 2.51–2.44 (m, 3H, CH*H*CHCOMe, CH*H*CHCH$_2$O, CH_2C*H*CH$_2$OMe). NOE difference spectra (500 MHz): 4.18–4.11 (C*H*HO) → 3.66–3.64 (20.5%), 2.66–2.59 (6.4%), 3.66–3.64 (CH*H*O) → 4.18–4.11 (22.8%), 2.78–2.74 (1.2%), 2.51–2.48 (2.5%), 2.66–2.59 (CH_2C*H*CH$_2$O) → 4.18–4.11 (5.2%), 3.66–3.64 (0.6%); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 158.2$ (s), 139.3 (s), 129.8 (s), 127.9 (d), 113.3 (d), 111.2 (d), 110.8 (d), 72.3 (d), 55.3 (q), 54.6 (q), 45.9 (d), 37.3 (d), 33.4 (t), 30.3 (t); EI-MS: *m*/*z* (%): 234 (31) [M^+], 172 (100), 202 (82), 159 (71), 144 (28), 128 (53), 115 (56), 91 (27), 77 (21); HRMS (EI-MS): calcd for $C_{14}H_{18}O_3$: 234.12560; found: 234.12584 [M^+].

(1*R*)- and (1*S*)-2-Bromo-1-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]ethyl 2,3-butadienyl ether (40): According to GP 1 from (1*R*,2*S*)-2-phenylcyclohexyl vinyl ether (**39**)[53] (1.11 g, 5.5 mmol), 2,3-butadien-1-ol (0.42 g, 6.05 mmol) and NBS (0.98 g, 5.5 mmol) in CH_2Cl_2 (10 mL). FC (hexane/Et_2O 20:1) gave a 1:1 mixture of the two diasteroisomers of **40** (1.5 g, 78%). The two diasteroisomers were separated by FC (hexane/Et_2O 60:1). (*S*)-**40**: $R_f =$ 0.64 (hexane/Et_2O 5:1); $[\alpha]_D^{21} = -14.8^\circ$ ($c = 1$, CH_2Cl_2); ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 7.31–7.16$ (m, 5 arom. H), 4.91 (quint, $J = 6.4$ Hz, 1H, C*H*=C=CH$_2$), 4.73 (dt, $J = 2.4$, 6.7 Hz, 2H, C*H*$_2$=C=CH), 4.66 (dd, $J =$ 4.6, 6.6 Hz, 1H, OC*H*CH$_2$Br), 3.61 (dt, $J = 4.3$, 10.1 Hz, 1H, OC*H*CHPh), 3.42 (tq, $J = 3.4$, 7.1 Hz, 1H, OC*H*HCH=C), 3.21 (dd, $J = 6.4$, 10.7 Hz, 1H, OCHC*H*HBr), 3.12 (dd, $J = 4.6$, 10.4 Hz, 1H, OCHCH*H*Br), 3.03 (tq, $J =$ 2.4, 6.7 Hz, 1H, OCH*H*CH=C), 2.56 (dt, $J = 3.7$, 10.4 Hz, 1H, OCHC*H*Ph), 2.20–2.13 (m, 1H), 1.92–1.87 (m, 2H), 1.77–1.74 (m, 1H), 1.61–1.50 (m, 1H), 1.42–1.29 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 209.0$ (s), 144.3 (s), 128.2 (d), 1281 (d), 126.3 (d), 99.9 (d), 87.9 (d), 79.5 (d), 75.7 (t), 61.9 (t), 50.8 (d), 33.7 (t), 33.0 (t), 32.4 (t), 25.8 (t), 24.9 (t). (*R*)-**40**: $R_f = 0.60$ (hexane/Et_2O 5:1); $[\alpha]_D^{21} = +1.0^\circ$ ($c = 1.2$, CH_2Cl_2); ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 7.33–7.20$ (m, 5 arom. H), 5.22 (quint, $J = 6.4$ Hz, 1H, C*H*=C=CH), 4.80 (dt, $J = 2.4$, 6.4 Hz, 2H, C*H*$_2$=C=CH), 4.25 (dd, $J = 3.4$, 7.3 Hz, 1H, OC*H*CH$_2$Br), 4.10–3.97 (m, 2H, OC*H*$_2$CH=C), 3.50 (dt, $J =$ 5.8, 10.1 Hz, 1H, OC*H*CHPh), 2.78 (dd, $J = 7.0$, 10.7 Hz, 1H, OCHC*H*HBr), 2.54 (dt, $J = 3.9$, 12.5 Hz, 1H, OCHC*H*Ph), 2.53 (dd, $J =$ 3.4, 10.9 Hz, 1H, OCHCH*H*Br), 2.20–2.16 (m, 1H), 1.92–1.85 (m, 2H), 1.78–1.74 (m, 1H), 1.63–1.29 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta =$ 209.2 (s), 144.0 (s), 128.3 (d), 128.0 (d), 126.7 (d), 101.4 (d), 87.7 (d), 82.2 (d), 75.9 (t), 63.7 (t), 51.5 (d), 34.1 (t), 33.4 (t), 31.5 (t), 25.8 (t), 25.3 (t). Mixture of diastereomers: IR (KBr): $\tilde{\nu} = 3063$, 3028, 2931, 2856, 1957, 1448, 1111, 1037 cm^{-1}; CI-MS (CH_4): *m*/*z* (%): 283 (35), 281 (36), 211 (11), 159 (100), 91 (8).

(1*R*,2*S*)-2-Phenylcyclohexyl-(2*R*,4*R*)-4-vinyltetrahydro-2-furanyl ether: According to GP 2 from (*R*)-**40** (175 mg, 0.5 mmol), Bu_3SnH (174 mg, 0.6 mmol) and 1M solution of Et_3B in hexane (0.8 mL, 0.76 mmol). FC (hexane/Et_2O 20:1) gave (1*R*,2*S*)-2-phenylcyclohexyl-(2*R*,4*R*)-4-vinyltetrahydro-2-furanyl ether (0.12 g, 88%, 90% *ds*). $[\alpha]_D^{21} = +14.2^\circ$ ($c = 1$, CH_2Cl_2); IR (KBr): $\tilde{\nu} = 3028$, 2930, 2858, 1448, 1095, 1049, 1008 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 7.30–7.15$ (m, 5 arom. H), 5.71 (ddd, $J =$ 8.5, 10.1, 18.6 Hz, 1H, C*H*=CH$_2$), 4.94 (ddd, $J = 0.9$, 1.8, 17.1 Hz, 1H, CH=C*H*H), 4.91 (ddd, $J = 0.9$, 1.8, 10.1 Hz, 1H, CH=CH*H*), 4.43 (dd, $J =$ 3.1 5.5 Hz, 1H, OC*H*CH$_2$), 3.81 (t, $J = 8.2$ Hz, 1H, OC*H*HCHCH=CH$_2$), 3.55–3.50 (m, 1H, OC*H*CHPh), 3.52 (t, $J = 8.5$ Hz, 1H, OCH*H*CHCH=CH$_2$), 2.66–2.55 (m, 1H, C*H*CH=CH$_2$), 2.48 (ddd, $J = 3.7$, 10.1, 13.7 Hz, 1H, OCHC*H*Ph), 2.16–2.11 (m, 1H), 1.89–1.71 (m, 4H), 1.61–1.56 (m, 1H), 1.44–1.27 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta =$ 144.5 (s), 138.9 (d), 128.0 (d), 126.1 (d), 115.1 (t), 105.5 (d), 81.6 (d), 70.7 (t), 51.5 (d), 43.0 (d), 39.0 (t), 35.0 (t), 32.9 (t), 25.9 (t), 25.3 (t); CI-MS (CH_4): *m*/*z* (%): 273 (18) [M^++H], 159 (12), 115 (6), 113 (5), 97 (100), 91 (9); elemental analysis calcd (%) for $C_{18}H_{24}O_2$ (272.39): C 79.37, H 8.88; found: C 79.33, H 8.91.

(4*R*)-4-Vinyltetrahydro-2-furanol: A solution of (1*R*,2*S*)-2-phenylcyclohexyl-(2*R*,4*R*)-4-vinyltetrahydro-2-furanyl ether (120 mg, 1.05 mmol) in THF (3 mL) and 10% HCl (2 mL) was kept at rt for 30 min. After extraction with Et_2O, the organic phases were washed with sat. $NaHCO_3$ and H_2O, dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by FC (pentane/Et_2O 4:1) to give (1*R*,2*S*)-phenylcyclohexanol (62 mg, 84%), the (4*R*)-4-vinyltetrahydro-2-furanol (29 mg, 63%) and starting material (10 mg). Mixture of diasteroisomers: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.85$ (ddd, $J = 7.9$, 10.1, 18.3 Hz, 1H, C*H*=CH$_2$, 1 diast.), 5.71 (ddd, $J = 8.2$, 10.4, 18.3 Hz, 1H, CH=CH$_2$, 1 diast.), 5.58–5.54 (m, 1H, HOC*H*CH$_2$), 5.14 (dt, $J = 0.9$, 5.5 Hz, 1H, CH=C*H*H, 1 diast.), 5.08 (dt, $J = 0.9$, 5.5 Hz, 1H, CH=CH*H*, 1 diast.), 5.05–5.01 (m, 2H, CH=C*H*$_2$, 1 diast.), 4.19 (t, $J = 8.2$ Hz, 1H, OC*H*HCHCH=CH$_2$, 1 diast), 3.98 (t, $J = 7.9$ Hz, 1H, OC*H*HCHCH=CH$_2$, 1 diast.), 3.76 (t, $J = 8.2$ Hz,

1H, OCH*H*CHCH=CH_2, 1 diast.), 3.57 (t, J = 8.2 Hz, 1H, OCH*H*CHCH=CH_2, 1 diast.), 3.22–3.10 (m, 1H, C*H*CH=CH_2, 1 diast.), 2.92–2.81 (m, 1H, C*H*CH=CH_2, 1 diast.), 2.63 (broad, 1H, OH, 1 diast.), 2.55 (br s, 1H, OH, 1 diast.), 2.35 (ddd, J = 5.2, 8.9, 13.7 Hz, 1H, OCHC*H*H, 1 diast.), 2.09 (dd, J = 7.5, 12.1 Hz, 1H, OCHCH*H*, 1 diast.), 1.84–1.68 (m, 2H).

(4*R*)-Vinyl-γ-butyrolactone (41):[33, 34] A solution of the (4*R*)-4-vinyltetrahydro-2-furanol (15 mg, 0.13 mmol) in CH_2Cl_2 (2 mL) was added to a mixture of PCC (100 mg, 0.5 mmol) and Al_2O_3 neutral (Woelm N, activity Y, 0.19 g). The orange mixture was stirred overnight, diluted with Et_2O (3 mL) and filtered though Florisil to afford the lactone **41** (13 mg, 90%) as a colorless oil. The optical purity (>99% *ee*) was determined by GC (γ-cyclodextrin 65% diacetoxy, 110 °C. t_R = 39.98 min for (*R*)-**41**. t_R = 40.97 min for (*S*)-**41**). $[\alpha]_D^{21} = -6.4°$ (c = 1 in EtOH) (ref. [34]) $[\alpha]_D^{21} = -5.6°$ (c = 1.6 in EtOH); ^{1}H NMR (360 MHz, $CDCl_3$): δ = 5.78 (ddd, J = 7.3, 10.1, 17.1 Hz, 1H, C*H*=CH_2), 5.20 (dt, J = 1.2, 14.0 Hz, 1H, CH=C*H*H), 5.16 (dt, J = 1.2, 6.8 Hz, 1H, CH=CHH), 4.45 (dd, J = 7.6, 9.2 Hz, 1H, OC*H*HCHCH=CH_2), 4.03 (dd, J = 7.9, 9.2 Hz, 1H, OCH*H*CHCH=CH_2), 3.30–3.18 (m, 1H, C*H*CH=CH_2), 2.68 (dd, J = 8.2, 17.4 Hz, 1H, CO*CH*H), 2.39 (dd, J = 8.2, 17.4 Hz, 1H, COCH*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 176.4 (s), 135.7 (d), 117.5 (t), 72.2 (t), 39.8 (d), 34.1 (t).

(1*R*)- and (1*S*)-2-Bromo-1-[(1*R*,2*S*)-(2-phenylcyclohexyl)oxy]ethyl 1-vinyl-2-propenyl ether (42): According to GP 1 from **39** (0.72 g, 3.6 mmol), 1,4-pentadien-3-ol (0.45 mL, 3.9 mmol) and NBS (0.73 g, 3.6 mmol) in CH_2Cl_2 (6 mL). FC (hexane/Et_2O 10:1) gave a 1:1 mixture of the two diastereoisomers of **42** (0.98 g, 75%). In preliminary experiments, the diastereoisomers were separated by FC (hexane/Et_2O 80:1) to afford (*R*)-**42** and (*S*)-**42**. However, on larger scale, it was convenient to continue the synthesis with the mixture of diastereoisomers and to separate by FC after the radical cyclization step (*see* below). (1*S*)-**42**: R_f = 0.70 (hexane/Et_2O 5:1); ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.31–7.20 (m, 5 arom. H), 5.86–5.66 (m, 2H, C*H*=CH_2), 5.25–5.15 (m, 4H, CH_2=CH), 4.38 (t, J = 6.1 Hz, 1H, OC*H*(C=CH_2)$_2$), 4.25 (dd, J = 3.5, 6.7 Hz, 1H, OC*H*CH_2Br), 3.46 (dt, J = 4.5, 10.0 Hz, 1H, OC*H*CHPh), 2.75 (dd, J = 6.7, 10.7 Hz, 1H, OCHC*H*HBr), 2.58–2.53 (m, 1H, OCHC*H*Ph), 2.50 (dd, J = 3.5, 10.7 Hz, 1H, OCHCH*H*-Br), 2.19–2.11 (m, 1H), 1.91–1.82 (m, 2H), 1.77–1.71 (m, 1H), 1.61–1.27 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 144.5 (s), 138.1 (d), 137.8 (d), 128.8 (d), 128.6 (d), 127.0 (d), 117.7 (t), 116.6 (t), 101.0 (d), 82.1 (d), 79.1 (d), 51.8 (d), 34.6 (t), 33.8 (t), 32.8 (t), 26.2 (t), 25.7 (t); (1*R*)-**42**: R_f = 0.72 (hexane/Et_2O 5:1); ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.32–7.19 (m, 5 arom. H), 5.60–5.44 (m, 2H, 2C*H*=CH_2), 5.12–4.91 (m, 4H, 2CH=CH_2), 4.57 (dd, J = 3.7, 7.0 Hz, 1H, OC*H*CH_2Br), 3.57–3.53 (m, 1H, OC*H*CHPh), 3.53–3.50 (m, 1H, OC*H*(CH=CH_2), 3.21 (dd, J = 7.0, 10.4 Hz, 1H, OCHC*H*HBr), 3.07 (dd, J = 3.7, 10.7 Hz, 1H, OCHCH*H*Br), 2.61–2.54 (m, 1H, OCHC*H*Ph), 2.13–1.32 (m, 8H, CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 144.8 (s), 138.1 (d), 137.6 (d), 128.7 (d), 128.6 (d), 126.9 (d), 117.6 (t), 116.3 (t), 99.1 (d), 80.2 (d), 77.7 (d), 51.2 (d), 34.3 (t), 33.9 (t), 26.2 (t), 25.4 (t). Mixture of diastereoisomers: IR (KBr): $\tilde{\nu}$ = 3028, 2931, 2858, 1448, 1114, 1028 cm^{-1}; MS (CI-CH_4): m/z (%): 365 (1) [M^+], 283 (6), 225 (14), 175 (16), 159 (100), 91 (11), 67 (51); elemental analysis calcd (%) for for $C_{19}H_{25}O_2Br$ (365.31): C 62.47, H 6.90; found: C 62.43, H 6.83.

(2*S*,4*S*,5*R*)- and (2*R*,4*R*,5*S*)-4-Methyl-5-vinyltetrahydro-2-furanyl (1*R*,2*S*)-2-phenylcyclohexyl ether [(2*S*,4*S*,5*R*)-43 and (2*R*,4*R*,5*S*)-43]: According to GP 2 from **42** (1:1 mixture of diast., 0.98 g, 2.7 mmol), Bu_3SnH (0.94 g, 3.24 mmol) and 1M solution of Et_3B in hexane (3.8 mL, 3.8 mmol). FC (hexane/Et_2O 30:1) gave **43** (0.66 g, 85%). The two diastereomers were separated by FC (hexane/Et_2O 30:1). (2*S*,4*S*,5*R*)-**43**: $[\alpha]_D^{20} = +22.3°$ (c = 1.5, CH_2Cl_2); ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.30–7.15 (m, 5 arom. H), 5.67 (ddd, J = 7.4, 10.1, 17.1 Hz, 1H, C*H*=CH_2), 5.22 (ddd, J = 0.9, 1.5, 17.1 Hz, 1H, CH=C*H*H), 5.13 (ddd, J = 0.9, 1.8, 10.4 Hz, 1H, CH=CH*H*), 4.42 (dd, J = 3.5, 5.5 Hz, 1H, OC*H*CH_2), 3.85 (t, J = 8.2 Hz, 1H, OC*H*CH=CH_2), 3.55 (dt, J = 4.6, 10.4 Hz, 1H, OC*H*CHPh), 2.52–2.45 (m, 1H, OCHC*H*Ph), 2.20–2.13 (m, 1H, C*H*CH_3), 1.90–1.16 (m, 10H), 0.92 (d, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 144.5 (s), 137.5 (d), 128.0 (d), 127.9 (d), 126.1 (d), 116.8 (t), 104.9 (d), 85.2 (d), 81.7 (d), 51.6 (d), 40.9 (t), 39.0 (d), 35.1 (t), 33.0 (t), 25.9 (t), 25.3 (t), 15.8 (q); (2*R*,4*R*,5*S*)-**43**: $[\alpha]_D^{20} = -98.4°$ (c = 0.5, CH_2Cl_2); ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.30–7.23 (m, 5 arom. H), 5.56 (ddd, J = 7.6, 10.4, 18.0 Hz, 1H, C*H*=CH_2), 5.21 (dd, J = 1.8, 5.5 Hz, 1H, OC*H*CH_2), 5.05–4.93 (m, 2H, CH=CH_2), 3.80 (td, J = 4.0, 10.4 Hz, 1H, OC*H*CHPh), 2.60 (t, J = 7.2 Hz, 1H, OC*H*CH=), 2.54–2.46 (m, 1H, OCHC*H*Ph), 2.25–2.16 (m, 1H, C*H*CH_3), 1.91–1.22 (m, 10H, CH_2), 0.66 (d, J = 7.0 Hz, 3H, CH_3); mixture of diastereoisomers: IR (KBr): $\tilde{\nu}$ = 3030, 2930, 2856, 1448, 1084, 987 cm^{-1}; MS (CI, CH_4): m/z (%): 287 (17) [M^++H], 187 (5), 159 (67), 111 (100), 93 (30), 91 (11); elemental analysis calcd for $C_{19}H_{26}O_2$ (286.42): C 79.68, H 9.15; found: C 79.78, H 9.10.

(2*R*,4*S*,5*R*)-4-Methyl-5-(2-hydroxy-ethyl)tetrahydro-2-furanyl-(1*R*,2*S*)-2-phenylcyclohexyl ether: A solution of (2*S*,4*S*,5*R*)-**43** (540 mg, 2.0 mmol) in THF (1 mL) was added to a solution of 9-BBN 0.5M in THF (4.1 mL, 2.1 mmol) under N_2. The solution was heated at reflux for 3 h, cooled at 0 °C and a 3M NaOH solution (2.3 mL) was added dropwise followed by 30% H_2O_2 (2.3 mL). The reaction mixture was stirred at rt for 1 h and extracted with Et_2O. The organic phases were washed with NaCl, dried over $MgSO_4$ and the solvent was removed under reduced pressure. Purification by FC (hexane/Et_2O 2:1) afforded the desired alcohol (0.57 g, 93%). $[\alpha]_D^{20} = +50.0°$ (c = 1, CH_2Cl_2); IR (KBr): $\tilde{\nu}$ = 3421, 2931, 2858, 1602, 1448, 1340, 1064, 993 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.29–7.16 (m, 5 arom. H), 4.43 (dd, J = 3.4, 5.8 Hz, 1H, OC*H*CH_2), 3.77–3.72 (m, 2H, CH_2OH), 3.64 (dt, J = 3.1, 9.2 Hz, 1H, OC*H*CH_2CH_2OH), 3.48 (dt, J = 4.3, 10.1 Hz, 1H, OC*H*CHPh), 2.71 (t, J = 5.8 Hz, 1H, OH), 2.52–2.44 (m, 1H, OCHC*H*Ph), 2.13–2.10 (m, 1H, C*H*CH_3), 1.88–1.11 (m, 12H), 0.92 (d, J = 6.7 Hz, 3H, CHCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 144.9 (s), 128.5 (d), 128.5 (d), 126.5 (d), 105.3 (d), 84.0 (d), 82.5 (d), 62.2 (t), 51.9 (d), 41.0 (t), 38.9 (d), 35.6 (t), 35.5 (t), 33.4 (t), 26.4 (t), 25.8 (t), 16.7 (q); CI-MS: m/z: 305 (5) [M^++H], 257 (11), 159 (5), 129 (100), 111 (5), 85 (22); elemental analysis calcd for $C_{19}H_{28}O_3$ (344.43): C 74.96, H 9.27; found: C 74.83, H 9.17.

2-((2*R*,3*S*,5*R*)-3-Methyl-5-{[(1*R*,2*S*)-2-phenylcyclohexyl]oxy}tetrahydro-2-furanyl)acetaldehyde: A solution of DMSO (0.29 mL, 4.0 mmol) in CH_2Cl_2 (2 mL) was added to a solution of oxalyl chloride (0.18 mL, 2.1 mmol) in CH_2Cl_2 (13 mL) cooled at −78 °C. After 5 min, a solution of the (2*R*,4*S*,5*R*)-4-methyl-5-(2-hydroxy-ethyl)tetrahydro-2-furanyl-(1*R*,2*S*)-2-phenylcyclohexyl ether (0.54 g, 1.8 mmol) in CH_2Cl_2 (1 mL) was added slowly. The white mixture was stirred at −78 °C for 30 min and Et_3N (1.22 mL, 8.8 mmol) was added. The mixture was stirred at rt for 2 h and sat. NaCl (10 mL) was added. The mixture was extracted with CH_2Cl_2 and the organic phase was washed with sat. NaCl, dried over $MgSO_4$ and evaporated under reduced pressure. Purification by FC (hexane/Et_2O 1:1) afforded the desired aldehyde (0.50 g, 95%). $[\alpha]_D^{20} = +23.3°$ (c = 0.3, CH_2Cl_2); IR (KBr): $\tilde{\nu}$ = 2930, 2856, 1728, 1448, 1085, 989 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$): δ = 9.76 (dd, J = 2.1, 3.1 Hz, 1H, C*H*O), 7.29–7.18 (m, 5 arom. H), 4.42 (dd, J = 3.4, 5.8 Hz, 1H, OC*H*CH_2), 3.95 (dt, J = 3.7, 8.6 Hz, 1H, OC*H*CH_2CHO), 3.50 (dt, J = 4.3, 10.1 Hz, 1H, OC*H*CHPh), 2.56 (ddd, J = 2.1, 4.0, 16.2 Hz, 1H, C*H*HCHO), 2.50–2.47 (m, 1H, OCHC*H*Ph), 2.41 (ddd, J = 2.7, 8.2, 15.9 Hz, 1H, CH*H*CHO), 2.15–2.13 (m, 1H, C*H*CH_3), 1.90–1.17 (m, 10H), 0.97 (d, J = 6.4 Hz, 3H, CHCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 201.6 (d), 144.9 (s), 128.5 (d), 128.4 (d), 126.5 (d), 105.3 (d), 82.4 (d), 78.8 (d), 51.9 (d), 47.7 (t), 41.1 (t), 39.0 (d), 35.5 (t), 33.4 (t), 26.4 (t), 25.8 (t), 16.8 (q); MS-CI: m/z: 303 (2) [M^++H], 285 (22), 259 (5), 159 (27), 127 (100), 101 (4), 81 (11); HRMS (ESI-MS): calcd for $C_{19}H_{26}O_3Na$: 325.17741; found: 325.17710 [M^++Na].

(2*R*,4*S*,5*R*)-4-Methyl-5-(3-methyl-2-butenyl)tetrahydro-2-furanyl-(1*R*,2*S*)-2-phenylcyclohexyl ether (44): *n*BuLi (2.21M in hexane, 0.3 mL, 0.66 mmol) was added dropwise to a suspension of isopropyltriphenylphosphonium iodide (0.37 g, 0.86 mmol) in THF (4 mL). The red mixture was stirred at −30 °C for 20 min, cooled at −78 °C and a solution of the 2-((2*R*,3*S*,5*R*)-3-methyl-5-{[(1*R*,2*S*)-2-phenylcyclohexyl]oxy}tetrahydro-2-furanyl)acetaldehyde (0.19 g, 0.66 mmol) in THF (2 mL) was added. The mixture was stirred at the same temperature for 1 h, poured into water, extracted with Et_2O and the organic phases were washed with brine. After drying and evaporation of the solvent the crude product was purified by FC (hexane/Et_2O 40:1) to give **44** (0.11 g, 51%) as a colorless oil. $[\alpha]_D^{20} = +38.5°$ (c = 1, CH_2Cl_2); IR (KBr): $\tilde{\nu}$ = 3030, 2930, 2856, 1448, 1377, 1066, 991 cm^{-1}; ^{1}H NMR (360 MHz): δ = 7.22–7.15 (m, 5 arom. H), 5.16–5.12 (m, 1H, C*H*=CMe_2), 4.40 (dd, J = 3.1, 5.8 Hz, 1H, OC*H*CH_2), 3.56–3.50 (m, 2H, OC*H*CHPh, OC*H*CH_2CH=CMe_2), 2.51–2.44 (m, 1H, OCHC*H*Ph), 2.24–2.08 (m, 3H, CH_2CH=CMe_2, C*H*CH_3), 1.68 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.88–1.12 (m, 10H), 0.92 (d, J = 6.7 Hz, 3H, CHCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 145.1 (s), 133.5 (s), 128.5 (d), 128.4 (d), 126.4 (d), 120.8 (d), 105.0 (d), 84.0 (d), 81.8 (d), 52.0 (d), 41.5 (t), 38.0 (d), 35.5 (t), 33.5 (t), 32.6 (t), 26.4 (t), 26.2 (q), 25.8 (t), 18.4 (q), 17.7 (q);

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MS (CI, CH_4): *m*/*z* (%): 329 (1) [M^++H], 259 (8), 159 (65), 153 (34), 117 (10), 109 (29), 91 (100), 69 (46); HRMS (CI, isobutane): calcd for $C_{22}H_{33}O_2$: 329.24750; found: 329.24887 [M^++H].

(4*S*,5*R*)-4-Methyl-5-(3-methyl-2-butenyl)dihydro-2(3*H*)-furanone [(+)-eldanolide] (45): A solution of **44** (0.12 g, 0.36 mmol) in THF (1.3 mL) and 10% HCl (1 mL) was kept at rt for 30 min. After extraction with Et_2O, the organic phases were washed with sat. $NaHCO_3$ and H_2O, dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by FC (pentane/Et_2O 6:1) to afford (1*R*,2*S*)-phenylcyclohexanol (40 mg, 62%) and the lactol (42 mg, 68%) as a mixture of diastereoisomers. Mixture of diasteroisomers. ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.52$ (dt, $J =$ 3.8, 5.7 Hz, 1H, OC*H*O, 1 diast.), 5.42 (t, $J = 3.6$ Hz, 1H, OC*H*O, 1 diast.), 5.27–5.18 (m, 2H, C*H*=CMe$_2$), 3.78–3.72 and 3.58–3.52 (m, 1H, OC*H*CH$_2$CH=CMe$_2$), 2.70–2.67 and 2.52–2.50 (m, 1H, OH), 2.42–2.03 (m, 8H), 1.92–1.78 (m,1H), 1.73 and 1.72 (2s, 3H, CH_3), 1.53–1.46 (m, 1H), 1.09 and 1.08 (2d, $J = 7.5$ Hz, 3H, CHC*H*$_3$).

A solution of the lactol (0.42 g, 0.25 mmol) in CH_2Cl_2 (4 mL) was added to a mixture of PCC (0.19 g, 0.9 mmol) and Al_2O_3 neutral (Woelm N, activity Y, 0.35 g). The orange mixture was stirred overnight then diluted with Et_2O (6 mL) and filtered through Florisil to afford the (+)-eldanolide **45** (32 mg, 76%) as a colorless oil. The optical purity (>99% *ee*) was determined by GC (γ-cyclodextrin 65% diacetoxy, 140 °C, $t_R = 20.68$ min for (4*S*,5*R*)-**45** and $t_R = 21.23$ min for (4*R*,5*S*)-**45**). $[\alpha]_D^{20} = +43.4°$ ($c = 1$, EtOH) [lit.:[39] $[\alpha]_D^{20} = +51.5°$, $c = 1.15$, MeOH]. All spectral data were in accordance with literature data.[39] ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 5.17$ (brt, 1H, C*H*=CMe$_2$), 4.06 (q, $J = 7.0$ Hz, 1H, OC*H*CH$_2$CH=CMe$_2$), 2.67 (dd, $J = 7.6$, 16.5 Hz, 1H, C*H*HCHCH$_3$), 2.46–2.22 (m, 3H, C*H*CH$_3$, CHC*H*$_2$CH=CMe$_2$), 2.17 (dd, $J = 9.2$, 16.8 Hz, 1H, CH*H*CHCH$_3$), 1.73 (s, 3H, CH_3), 1.64 (s, 3H, CH_3), 1.14 (d, $J = 6.7$ Hz, 3H, CHC*H*$_3$); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 176.4$ (s), 135.4 (s), 118.0 (d), 87.0 (d), 37.1 (t), 35.1 (d), 32.2 (t), 25.8 (q), 17.9 (q), 17.7 (q); MS (CI, CH_4): *m*/*z* (%): 169 (100) [M^++H], 151 (25), 123 (12), 109 (89), 99 (26), 84 (7), 69 (35).

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