DOI: 10.1002/ejoc.201300869

An Approach to the Carbon Backbone of Bielschowskysin, Part 1: Photocyclization Strategy

Martin Himmelbauer,[a] Jean-Baptiste Farcet,[a] Julien Gagnepain,[a] and Johann Mulzer*[a]

Keywords: Natural products / Total synthesis / Asymmetric synthesis / Cycloaddition / Terpenoids

Several macrocyclization reaction attempts of highly advanced precursors toward a total synthesis of marine diterpene bielschowskysin are disclosed. Biomimetic [2+2]-photocyclization reactions were applied to construct the cyclobutane core in these intermediates, which could be accessed along scalable high-yielding reaction sequences from cheap enantiopure starting-materials.

Introduction

In 2003 Rodríguez et al. reported the isolation of bielschowskysin (**1**) along with other congeners from the Caribbean Sea plume *Pseudopterogorgia kallos*,[1] among which **1** and providencin (**2**)[2] are the only ones bearing unusual cyclobutane moieties (Figure 1). Owing to its densely functionalized furanocembranoid structure featuring an unprecedented tricyclo[9.3.0.0^{2,10}]tetradecane ring system and eleven stereogenic centers, bielschowskysin has attracted considerable interest from the scientific community.[3] Furthermore, the compound shows significant biological activity against the malaria-causing protozoan parasite *Plasmodium falciparum* and two human cancer cell lines.

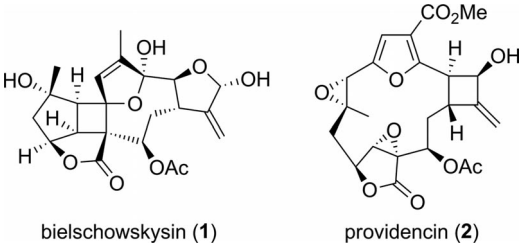
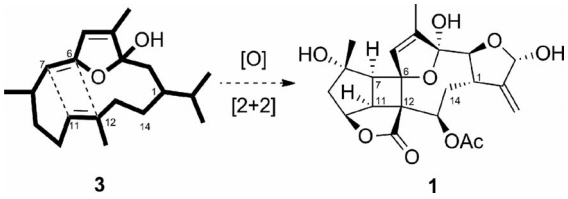


Figure 1. Structures of bielschowskysin and providencin.

The members of the furanocembranoid family display a wide degree of functionalization. Nonetheless, they appear to be biogenetically interconnected.[4] Thus, the cyclobutane moiety of bielschowskysin has been postulated to arise from a transannular [2+2]-cycloaddition reaction of much simpler macrocyclic precursor **3** (Scheme 1). We report two entirely different approaches to the full carbon backbone of bielschowskysin. The present article deals with the biomimetic [2+2]-photocyclization reaction, whereas the following paper presents a non-photochemical route.[5]



Scheme 1. Biosynthetic [2+2]-cycloaddition reaction forming bielschowskysin.

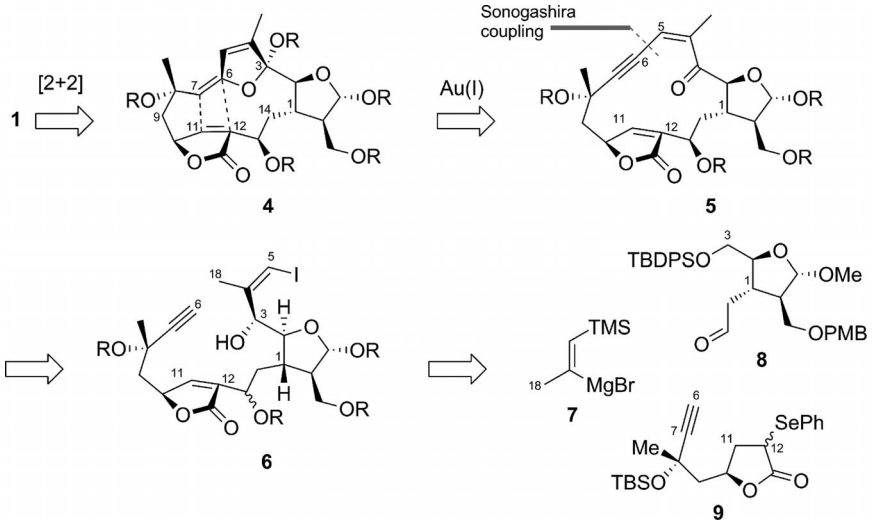
Results and Discussion

Our retrosynthetic considerations were centered on the photochemical ring contraction[6] of 14-membered carbocycle **4** (Scheme 2). A gold-mediated cyclization reaction[7] of macrocyclic enyne **5** was expected to generate the required *exo*-methylene dihydrofuran ring. Palladium-mediated intramolecular Sonogashira reaction[8] of vinyl iodide **6** should close the 14-membered carbon macrocycle. As outlined in Scheme 2, precursor **6** could be assembled from three rather simple building blocks. Thus, aldol reaction of seleno lactone **9** and aldehyde **8** was planned to form the southern part and the enone functionality in **6**, which is essential for the [2+2]-cycloaddition reaction, which could be established by regioselective oxidative elimination of the selenide. After that, vinyl magnesium species **7** could introduce the vinyl moiety for the later macrocyclization reaction.

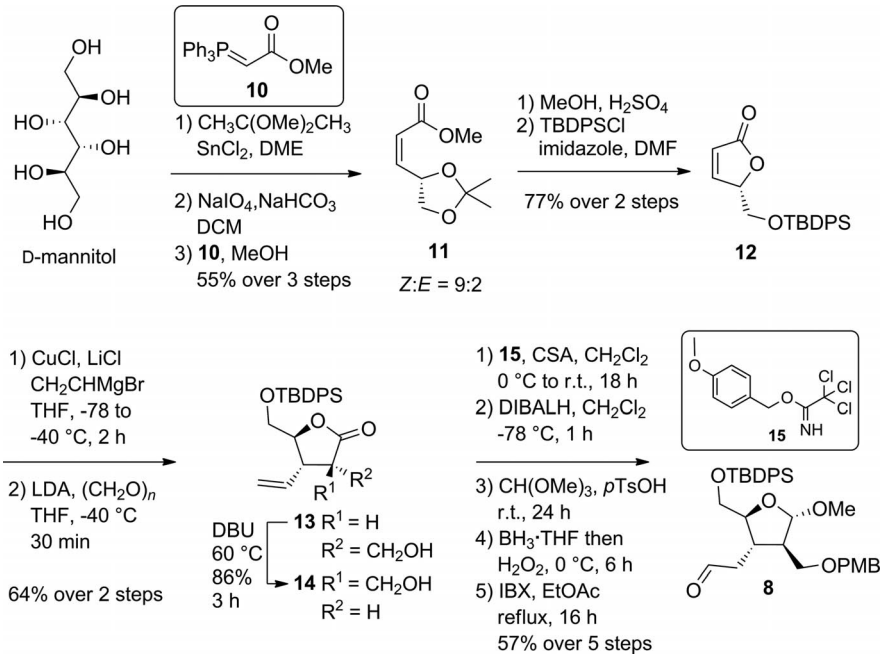
The synthesis of aldehyde **8** commenced with D-mannitol, which was converted into enantiomerically pure butenolide **12** in five steps (Scheme 3).[9] We noticed that the

[a] Department of Organic Chemistry, University of Vienna, Währinger Straße 38, 1090 Vienna, Austria
E-mail: johann.mulzer@univie.ac.at
http://mulzer.univie.ac.at/

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201300869.



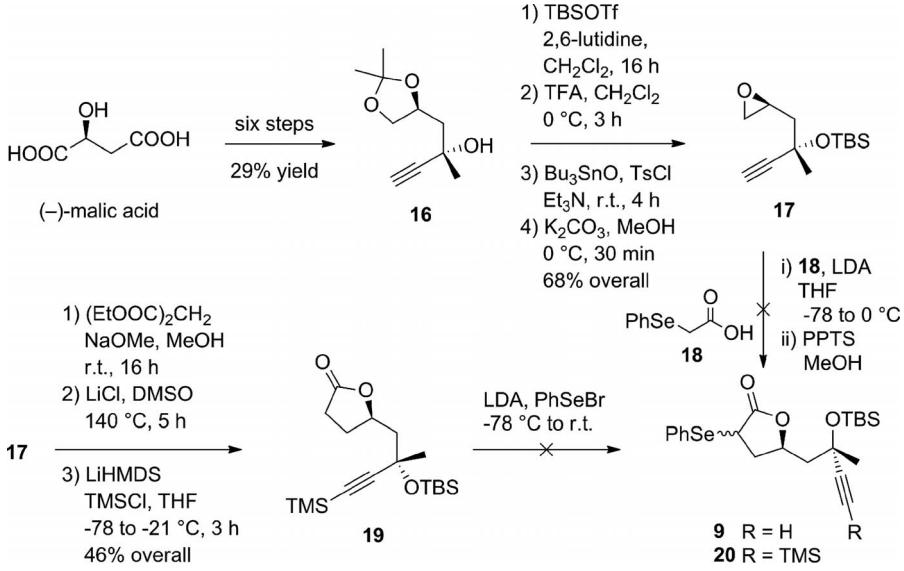
Scheme 2. Initial retrosynthesis based on a transannular [2+2]-cycloaddition reaction.



Scheme 3. Synthesis of the eastern section of the backbone, fragment **8**.

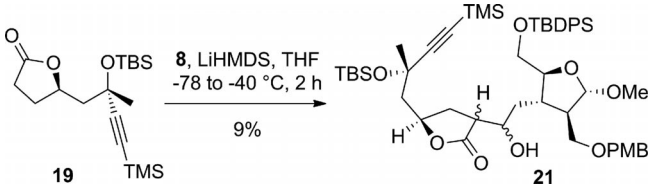
bulky *tert*-butyldiphenylsilyl (TBDPS) protecting group in **12** was essential for the stereochemical outcome of the copper-mediated Michael addition reaction of vinyl magnesium bromide. Unexpectedly, the introduction of the α-hydroxymethylene group met with problems. Neither in situ generation of formaldehyde,[10] nor introduction of gaseous formaldehyde gave satisfying results. However, deprotonation of the γ-butyrolactone followed by addition of a freshly prepared solution of formaldehyde in tetrahydrofuran (THF; see **14** in Experimental Section) resulted in a 4:1 mixture of diastereoisomers **13** and **14**. As expected, 2,3-*cis* lactone **13** could be epimerized to all-*trans* **14** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) at elevated temperatures. Finally, *p*-methoxybenzyl ether (PMB) protection, reduction of the lactone, acetalization of the anomeric center and a hydroboration/oxidation reaction sequence provided desired aldehyde **8**.

For the synthesis of the western section of the backbone, alkyne building block **9** (Scheme 4), known acetonide **16**[3a,3b] was converted into epoxide **17** in 68% yield over four steps. Various attempts to form α-phenylselenyl lactone **9** in a single step by opening the epoxide with the dianion of phenylselenyl acetic acid failed.[11] Thus, epoxide **17** was converted into γ-butyrolactone **19** by opening the epoxide with diethylmalonate followed by Krapcho decarboxylation[12] and protection of the terminal alkyne. Unfortu-



Scheme 4. Synthesis of the western section of the backbone, alkyne **19**.

nately, **19** could not be α-selenylated by any means. Thus, we coupled intermediates **19** and **8** (Scheme 5) and tried to introduce the selenide in the next step. Unfortunately, the yield of the aldol reaction was unacceptably low.



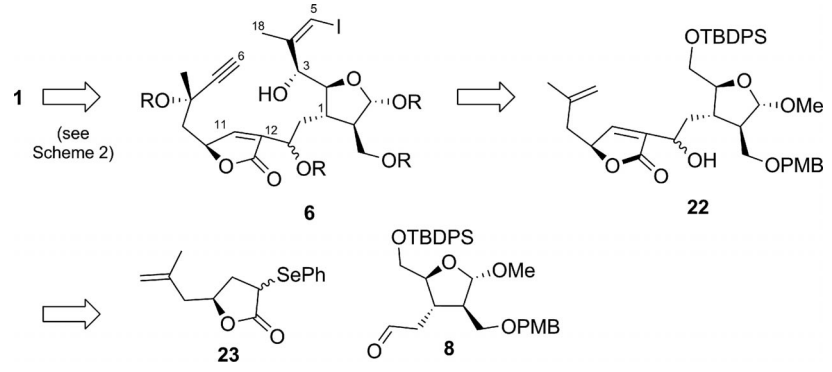
Scheme 5. Building block coupling.

In view of these failures we decided to add fragment **8** to seleno lactone **23** (Scheme 6), which is readily available from (*R*)-glycidol in three steps[11] (Scheme 7). If the coupling indeed gave **22**, elaboration of the isopropenyl moiety (Scheme 6) might still lead to envisaged intermediate **6**.

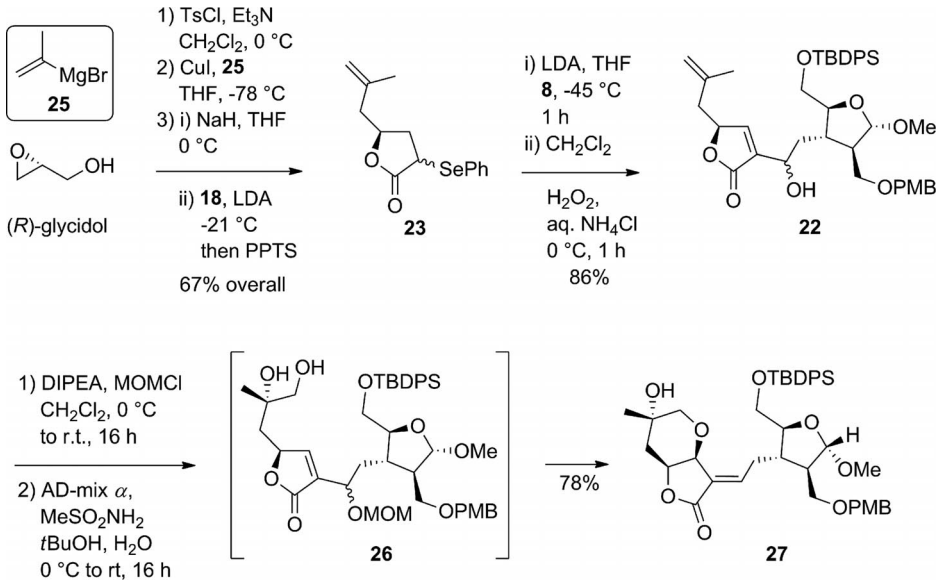
To our delight, the aldol reaction smoothly furnished the desired coupling product as a mixture of all four possible diastereoisomers (Scheme 7). Oxidative elimination of the phenylselenyl group gave butenolide **22** as a mixture of two diastereoisomers, which was used directly in the next reaction. After protection of the free secondary alcohol a SAD reaction was performed. Interestingly but unproductively, the primary product **26** underwent a S_N2' reaction under OMOM elimination to generate compound **27**.

At this juncture we decided to abandon the transannular [2+2]-approach and to modify our strategy as shown in Scheme 8. Thus, aldol addition of **32** and **8** should provide precursor **31**, which in an allene–olefin [2+2]-photocyclization reaction should lead to polycycle **30**. Further transformations should be directed toward **29** as the substrate of a ring-closing metathesis (RCM) reaction to give dihydrofuran **28**.

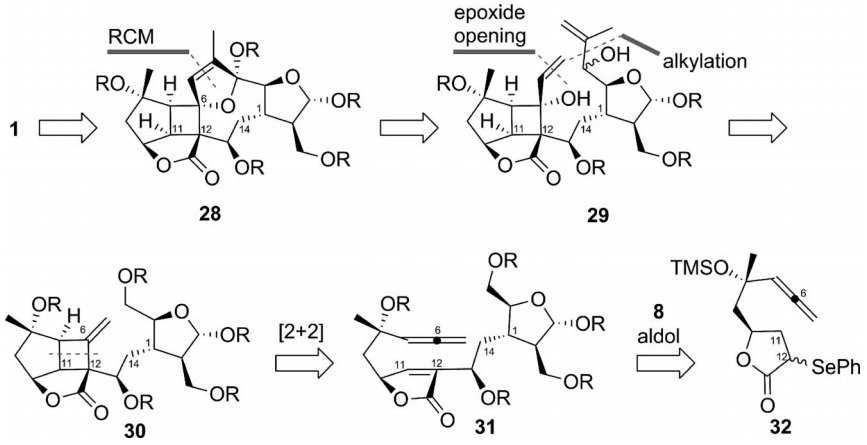
To start with, epoxide **36** was synthesized from **33** in two steps (Scheme 9). Regioselective addition of diethylmalon-



Scheme 6. Altered retrosynthesis.



Scheme 7. Fragment coupling and formation of pyran **27**.

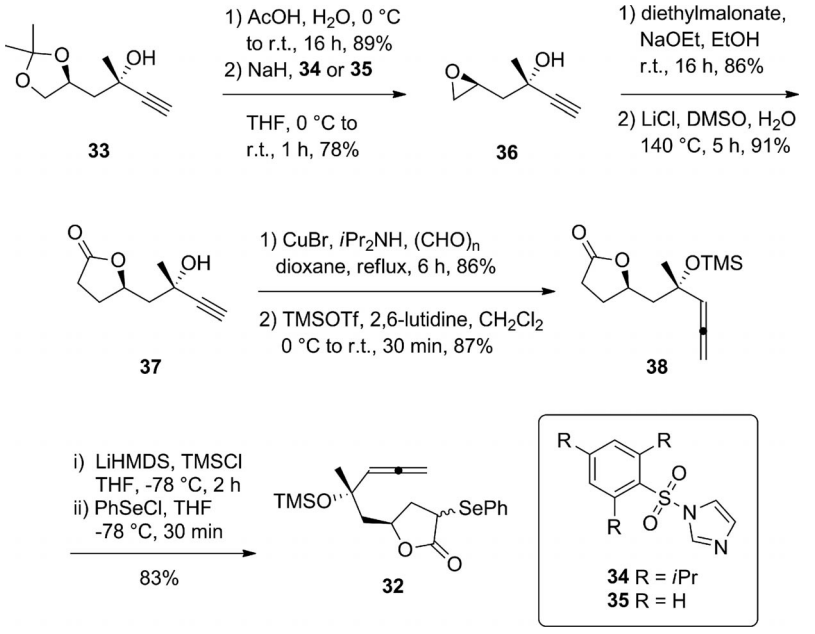


Scheme 8. Retrosynthesis based on an allene–olefin [2+2]-photocyclization reaction.

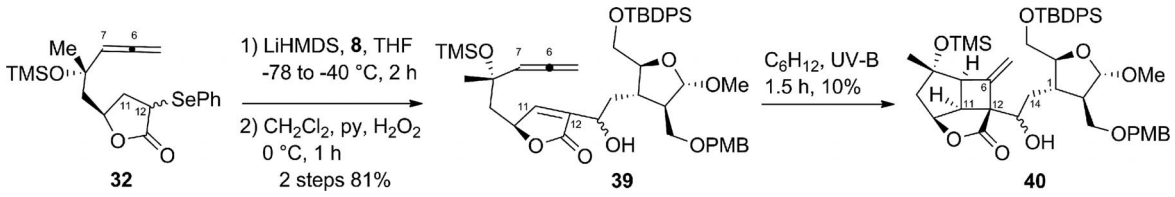
ate, cyclization to the corresponding lactone and Krapcho decarboxylation gave γ-butyrolactone **37** in fair yield. Copper-mediated formation of the allene through the Searles-Crabbé protocol[13] proceeded with high yield and was exceptionally easy to carry out. Protection of the tertiary alcohol and α-selenylation delivered lactone **32** in scalable seven steps with an overall yield of 35%. Interestingly, in situ formation of a trimethylsilyl enol ether and the use of phenylselenyl chloride instead of the more reactive bromide were essential to stop the reaction after mono-selenylation.

Aldol coupling of building block **32** with **8** and regioselective oxidative elimination of the selenide uneventfully gave **39** as a mixture of diastereoisomers (Scheme 10). Without separation, a plethora of irradiation conditions was tested, some of which are outlined in Table 1. In many cases complex product mixtures were formed, and we found that irradiation of **39** with a sunlamp destroyed the starting material in a few minutes. On narrowing the spectrum we either isolated starting material or detected traces of presumptive product in the mass-spectrum of the reaction mixture. Eventually, irradiation of **39** with UV-B light in cyclohexane for 2.5 h allowed the isolation of 10% (Table 1, Entry 13), of desired [3.2.0]-carbocycle **40** as a diastereoisomeric mixture. Purification by column chromatography allowed partial separation of the C13-epimers. Thus, for the first time the crucial all-carbon quaternary center at C-12 of **1** was established.

We reasoned that the formation of complex mixtures in the photoreaction might be a result of the presence of the aryl chromophores in our substrate and decided to remove the PMB and the TBDPS-protecting groups in the [2+2]-cycloaddition reaction precursor. The synthesis of the eastern section of the backbone containing a tetrahydrofuran ring was redesigned accordingly (Scheme 11).



Scheme 9. Synthesis of the western section of the backbone, allene building block **32**.



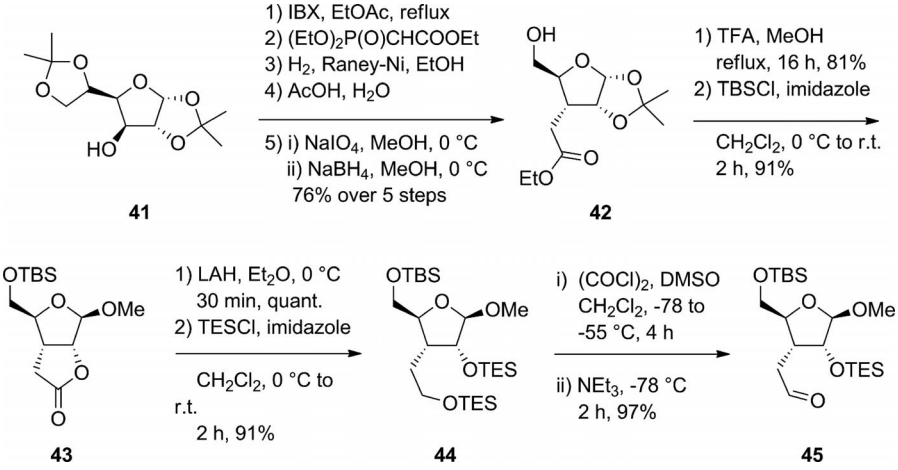
Scheme 10. Fragment coupling and [2+2]-photocyclization reaction.

Table 1. [2+2]-photocyclization reaction conditions of **39** to **40**.

Entry[a]	Solvent	Conditions[b]	Yield
1	EtOH	750 W, > 100 nm, 30 °C, 0.5 h	decomp.
2	acetone	750 W, > 100 nm, 30 °C, 0.5 h	decomp.
3	hexane/CH_2Cl_2	750 W, > 100 nm, 30 °C, 0.5 h	decomp.
4	hexane/CH_2Cl_2	6 W, > 350 nm, r.t., 3 h	SM
5	EtOH	6 W, > 350 nm, r.t., 3 h	SM
6	hexane	6 W, > 350 nm, r.t., 9 h	SM
7	MeOH	6 W, > 350 nm, r.t., 9 h	SM
8	acetone	2×6 W, > 350 nm, r.t., 9 h	SM
9	cy	750 W, > 100 nm, 30 °C, 0.5 h	**40**, traces
10	cy	750 W, > 350 nm, 30 °C, 0.5 h	decomp.
11	cy	2×6 W, > 350 nm, r.t., 7 h	**40**, traces
12	cy	8×6 W, 320–400 nm, r.t., 7 h	SM
13	cy	8×6 W, 280–320 nm, r.t., 1.5 h	**40**, 10%

[a] All solutions were 0.001 M and freshly degassed prior to use. [b] In all entries quartz tubes were used as reaction vessels.

To circumvent the experimentally tedious 1,4-addition α-alkylation procedure of **12** (Scheme 3) we started from diacetone D-glucofuranose (**41**; Scheme 11), from which known α-D-ribofuranose **42**[14] was prepared in five steps along an optimized scalable sequence. Thus, 2-iodoxybenzoic acid (IBX) oxidation of **41** was followed by Horner–Wittig reaction giving an α,β-unsaturated ester. In contrast to the literature procedures, which either required aqueous workup, prolonged reaction-times or high pressure for acquiring acceptable yields, we were able to hydrogenate the double bond with Raney-nickel in ethanol in an ultrasound bath at 1 atm of hydrogen pressure over 2 h. Removal of the acetonide, glycol cleavage and reductive workup yielded primary alcohol **42**. Acid catalyzed acetalization of the anomeric center and protection of the primary alcohol gave lactone **43**. After reduction to the diol, silyl protection and



Scheme 11. Synthesis of the new building block towards to new eastern section of the backbone.

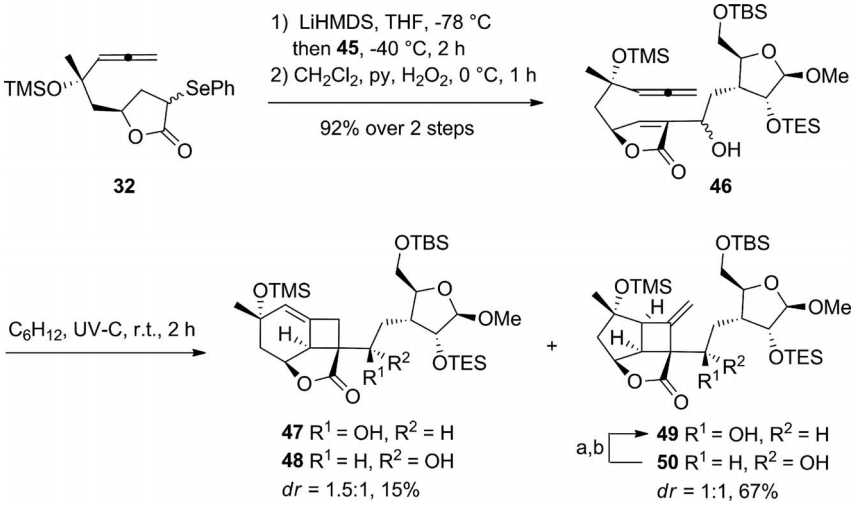
subsequent Swern oxidation reaction afforded desired aldehyde **45**.

Deprotonation of **32**, addition of **45** and oxidative elimination of the phenylselenide furnished [2+2]-photocyclization precursor **46** (Scheme 12) with a *dr* of about 1:1. Capitalizing on our earlier results a solution of **46** in freshly degassed cyclohexane was irradiated with UV-B light for 18 h to give 57% of diastereoisomeric cyclobutanes **49** and **50**. As the UV-spectrum of **46** revealed an absorption maximum at 235 nm, UV-light of 200–280 nm was applied. Gratifyingly the reaction time was reduced to 2 h and the yield of cyclization products **49**/**50** was increased to 67%. Additionally 15% of undesired regioisomers **47**/**48** were formed. After separation of the isomers, "wrong" diastereoisomer **50** was recycled to **49** by an oxidation–reduction sequence, and all ensuing reactions were carried out with enantiomerically pure **49** and **50**.

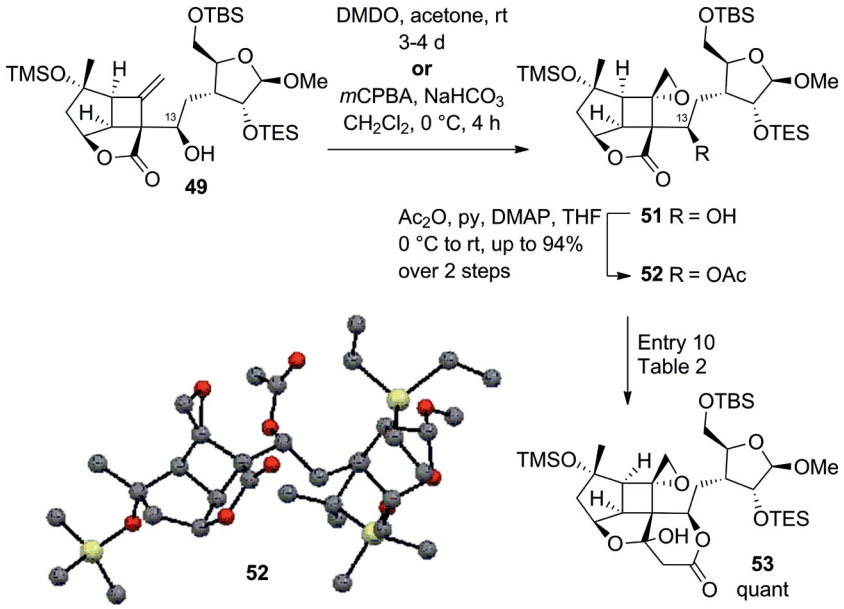
Next we epoxidized the *exo*-methylene group of **49** with dimethyldioxirane (DMDO) and found that a free 13-OH group was necessary to obtain reasonable diastereoselectivity (6:1) (Scheme 13). In presence of a 13-OAc (13-OTMS) the *dr* dropped to 2:1 (1:1). With *m*CPBA the reaction was much faster and gave higher yields with a *dr* of 4:1. To assign the relative configuration, crystalline acetate **52** was prepared and subjected to single crystal diffraction.[15]

For the opening of the epoxide, a number of nucleophiles were tested both with the free alcohol and the acetate, to no avail (Table 2). Interestingly, on **52** the lithium acetylide ethylenediamine complex acted as base and furnished pentacycle **53** in quantitative yield over 15 min at 0 °C, whereas **51** led to complex product mixtures. The *exo*-methylene group of **47** was subjected to a variety of alternative functionalizations (dihydroxylation, ozonolysis, hydroboration, 1,3-dipolar cycloaddition reactions) with disappointing results.

Being aware of the rich potential of transition metal catalyzed C–C connections between olefins and alkynes,[7] we envisage propargylic alcohol **56** as a suitable substrate for



Scheme 12. Fragment coupling and improved [2+2]-photocyclization. (a) TPAP, NMO, 4 Å MS, CH_2Cl_2, 0 °C; (b) (*S*)-2-(–)-methyl-CBS oxazaborolidine, BH_3·THF, THF, –78 to –40 °C, 33% + 66% of **50**.

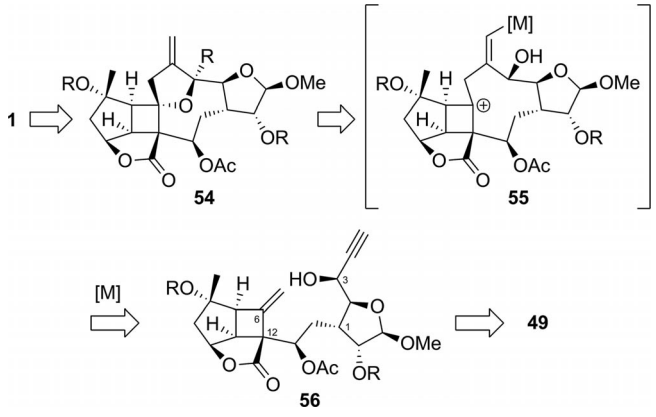


Scheme 13. Synthesis and X-ray structure of **52** and formation of pentacycle **53**.

Table 2. Conditions for the epoxide opening.

Entry	Conditions	Yield
1	**52**, Me_3SI, *n*BuLi, THF, –78 °C, 8 h	SM
2	**52**, Me_3SI, *n*BuLi, THF, –21 °C, 8 h	SM
3	**52**, Me_3SI, *n*BuLi, THF, 0 °C to room temp., 10 h	SM
4	**52**, isopropenylMgBr, CuI, THF; –78 °C to 0 °C, 24 h	SM
5	**52**, Me_3SBF_4, *n*BuLi, THF, –21 °C, 24 h	SM
6	**52**, Me_3SBF_4, *n*BuLi, THF, –21 °C to r.t., 24 h	SM
7	**52**, $CH_2CHMgBr$, *n*BuLi, CuCN, THF; –78 °C to r.t., 12 h	SM
8	**52**, $CH_2CHMgBr$, *n*BuLi, CuCN, $BF_3{\cdot}OEt_2$ THF, –78 °C to r.t., 12 h	SM
9	**52**, PhSH, 0.5 M NaOH, dioxane, reflux, 16 h	decomp.
10	**52**, Lithium acetylide ethylenediamine complex THF, DMSO, 0 °C, 15 min	**53**, quant.

closing both nine-membered carbocycle **55** and the furan moiety in **54** in a single step (Scheme 14). The introduction of the alkyne into **49/50** through aldehydes **59** and **60**[3h] is outlined in Scheme 15.

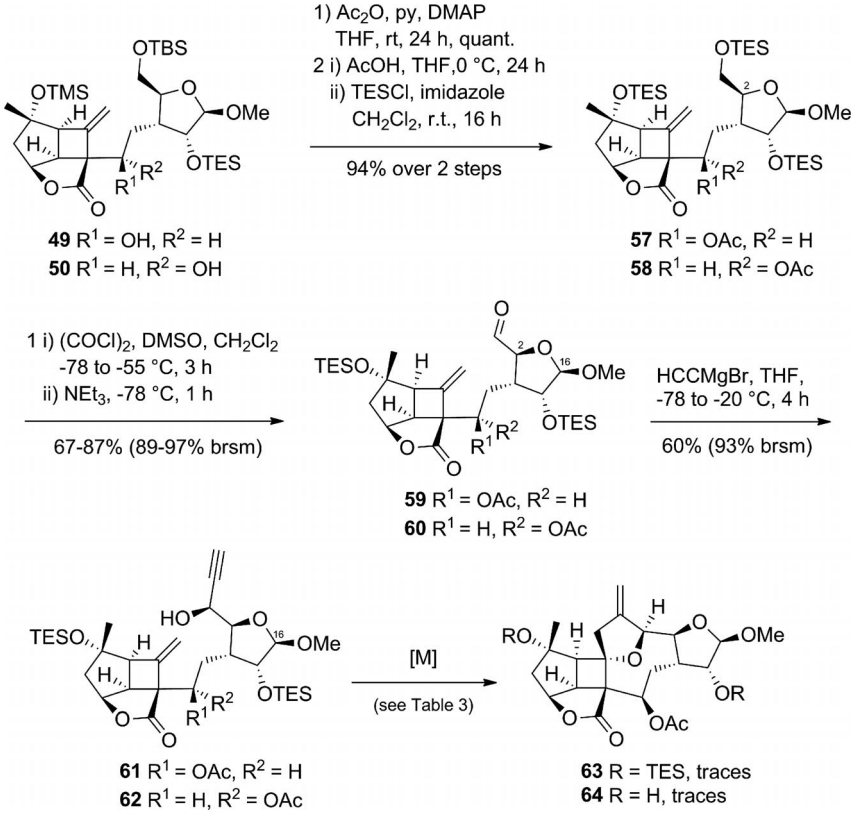


Scheme 14. Retrosynthesis based on transition-metal-mediated cyclization reaction of the carbon core of bielschowskysin.

At the end, propargylic alcohol **61** was formed in good overall yield as a single diastereoisomer, and subjected to macrocyclization (Table 3, Scheme 15). Although mass analysis indicated the formation of the desired product in some cases, we were not able to obtain a suitable NMR spectra.

Trying to close a macrocyclic ether **66** by treating enyne **61** with NBS[16] (Scheme 16) only led to formation of **65** (connectivity and relative configuration of the bromides were determined by 2D-NMR spectroscopic analysis). In another attempt, aldehyde **59** was oxidized to carboxylic acid **67** that was subjected to several halo-lactonization and Wacker cyclization reaction conditions (Scheme 16, Table 4),[17] but the substrate either was unreactive or decomposed without revealing any trace of products **68**–**71**.

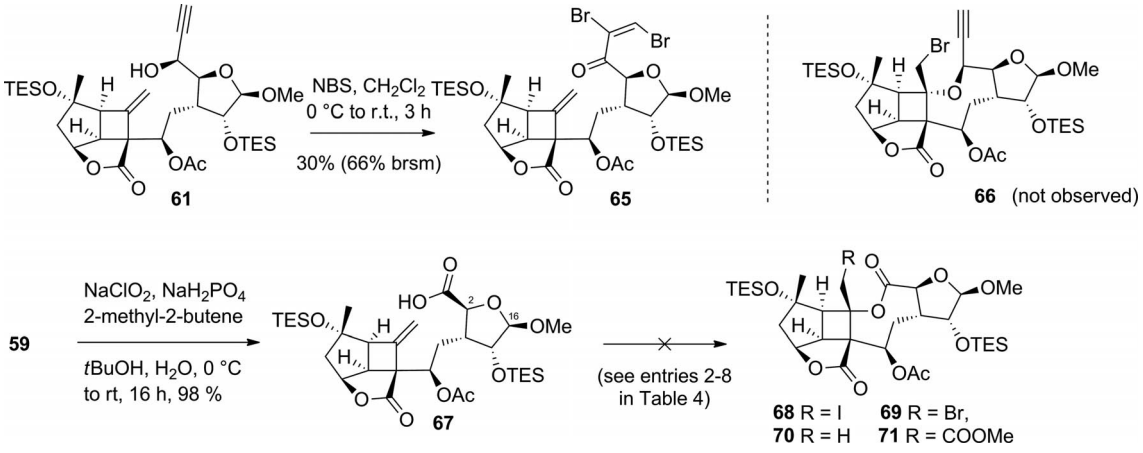
To get more flexibility in the eastern section building block and to obtain a suitable protecting group pattern we decided to modify the synthesis of **46** and prepared derivatives **75**, **76** and **77** along scalable and reliable routes (Scheme 17).



Scheme 15. Introduction of the alkyne and transition-metal-mediated cyclization reaction attempts.

Table 3. Conditions for the transition-metal-mediated cyclization reaction.

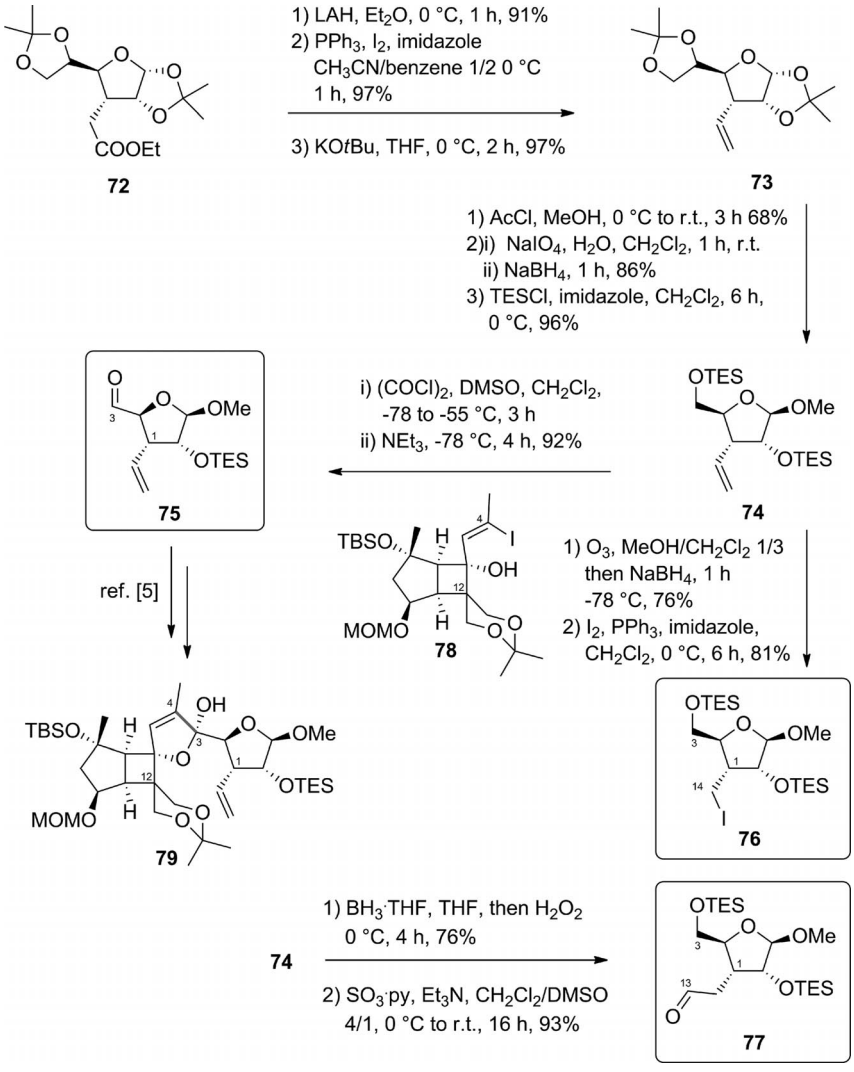
Entry	SM	Conditions	Yield
1	**61**	$[(PPh_3)Au]NTf_2$, CH_2Cl_2, –78 to 0 °C, 24 h	**63**, traces
2	**61**	$PtCl_2$, toluene, 75 °C, 2 d	**64**, traces
3	**61**	$[(PPh_3)Au]Cl$, $AgSbF_6$, CH_2Cl_2, 0 °C, 1 h	**61** - global TES
4	**61**	$[(PPh_3)Au]Cl$, $AgSbF_6$, MeOH, 0 °C, 6 h	**61** - global TES
5	**61**	$[(CH_3CN)_4Cu]PF_6$, toluene, 80 °C, 5 h	**63**, traces
6	**61** - global TES	$[(PPh_3)Au]NTf_2$, CH_2Cl_2, 0 °C to r.t., 1 h	decomp.



Scheme 16. Additional macrocyclization reaction attempts.

Table 4. Conditions for alternative macrocyclization reactions.

Entry	SM	Conditions	Yield
1	**61**	NBS, CH_2Cl_2, 50 °C, 5 h	**65**, 66%
2	**67**	NIS, $CDCl_3$, 40 °C, 2 h	SM
3	**67**	I_2, $NaHCO_3$, CH_2Cl_2, 40 °C, 6 h	SM
4	**67**	NBS. CH_3CN, 82 °C, 3 h	decomp.
5	**67**	$PdCl_2$, CuCl, O_2, DMF, r.t., 16 h	decomp.
6	**67**	$PdCl_2$, CuCl, O_2,$NaHCO_3$ DMF, r.t., 16 h	decomp.
7	**67**	$PdCl_2$, CuCl, CO, CH_3CN, MeOH, 140 °C, 4 h	SM
8	**67**	$Pd(OAc)_2$, CuCl, CO, CH_3CN, MeOH, 140 °C, 6 h	SM

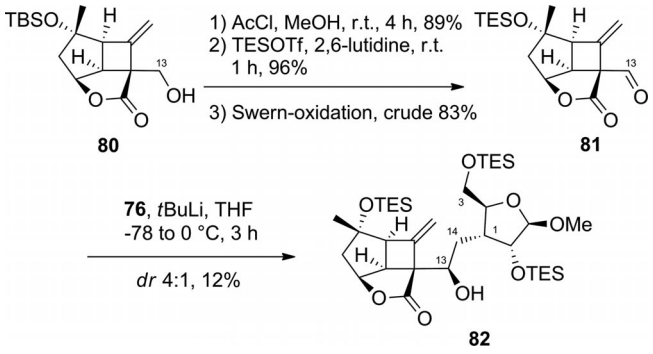


Scheme 17. New flexible route to the eastern section tetrahydrofuran moiety.

Metal halogen exchange of iodide **76** and addition of the lithium derivative to aldehyde **81**, which was derived from our earlier intermediate **80**[3f,3g] in three steps, delivered **82** with a *dr* of 4:1 at C-13 but low yield (Scheme 18).

In parallel, we repeated the aldol coupling by using partners **83** and **77** and now adduct **84** was formed in high yield and a *dr* of 3:1. The [2+2]-photocycloaddition reaction of the diastereoisomeric mixture gave pure **82** in 51% yield after separation (Scheme 19).

With a straightforward synthesis of **82** in hand we attempted to close the macrocycle. On one hand we envisaged an *endo*-selective Heck reaction[18] of **86** to form a suitable nine-membered carbon macrocycle (Scheme 20). Alternatively a RCM reaction[19] of **87** was tried to construct the



Scheme 18. Alternative synthesis of the southern section hemisphere of Bielschowskysin.

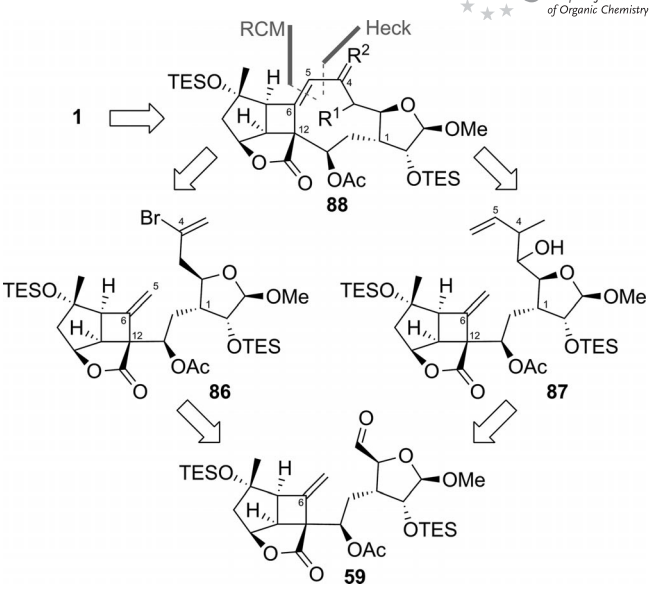
tricyclo[9.3.0.0^{2,10}]tetradecane framework of bielschowskysin.

The results of the Heck reaction have already been described in detail.[3h] Instead of desired diene **91**, acetate **92** was obtained (Scheme 21), presumably along an unprecedented mechanistic pathway as outlined in Scheme 22.

An interesting detail is the formation of vinyl cyanide **93**. Though we have no plausible explanation yet, in all experiments leading to **93**, $Pd(OAc)_2$ has been used as catalyst, and dimethylformamide as solvent and plausible "CN" source.

The formation of macrocycle **92** with the wrong ring size does not necessarily put an end to our synthesis because there are a number of options available to achieve a suitable ring expansion, one of which is tentatively suggested in Scheme 23.

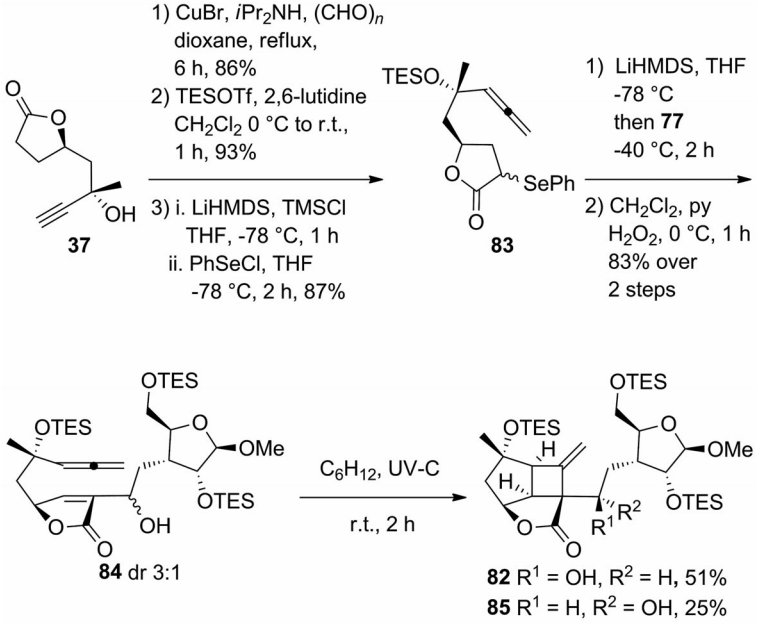
Thus, saponification of the acetate group at C-5 in **92** followed by oxidation to the aldehyde and Baeyer–Villiger oxidation should provide **III**. Dihydroxylation of the *exo*-methylene bond, mesylation of the primary alcohol at C-5′



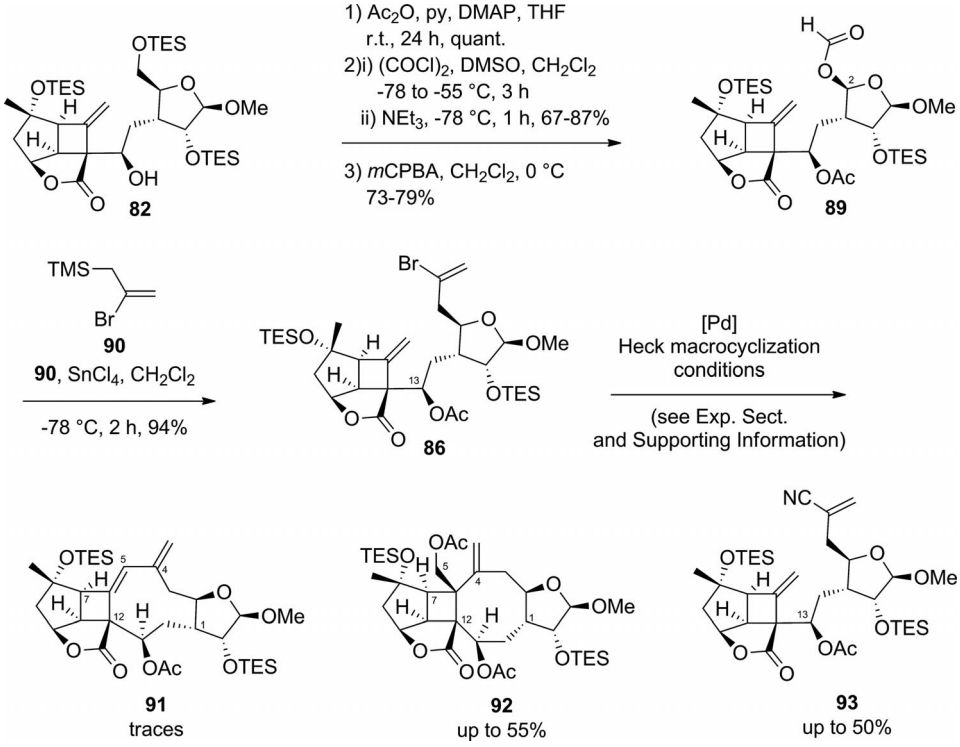
Scheme 20. Heck- and RCM-macrocyclization reaction strategies.

followed by Wagner–Meerwein rearrangement forming the $\Delta^{6,5'}$ bond should deliver the desired nine-membered macrocycle and the ketone at C-4 in **V**. Elimination of the formate and an olefination should give diene **91**, which can be processed to the natural product over a few steps mainly consisting of protecting group operations and oxidations.

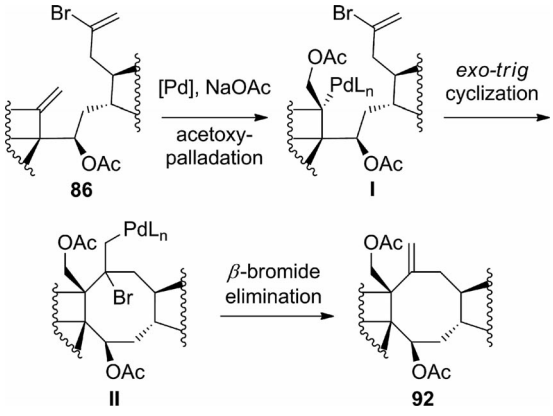
In parallel to the Heck-type cyclization reaction we tried to set the stage for the RCM approach and various attempts to introduce an allyl appendage at aldehyde **59/60** were initiated (Scheme 24). Conventional treatment with allylmagnesium halides, allyl-zinc species, Brown-allylation[20] and Duthaler–Hafner allyl complex[21] all failed. Finally, reaction of **59/60** with allyltrimethylsilane or (*Z*)-crotyltrimethylsilane (**94**) and tin tetrachloride afforded **95** to **98** as insepa-

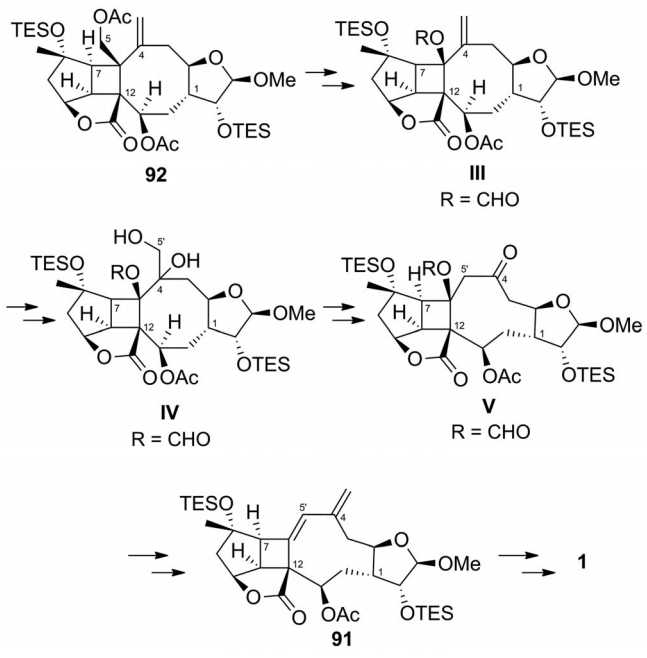


Scheme 19. Improved [2+2]-photocyclization reaction to **82**.



Scheme 21. Results from the palladium-catalyzed macrocyclization reaction attempts.





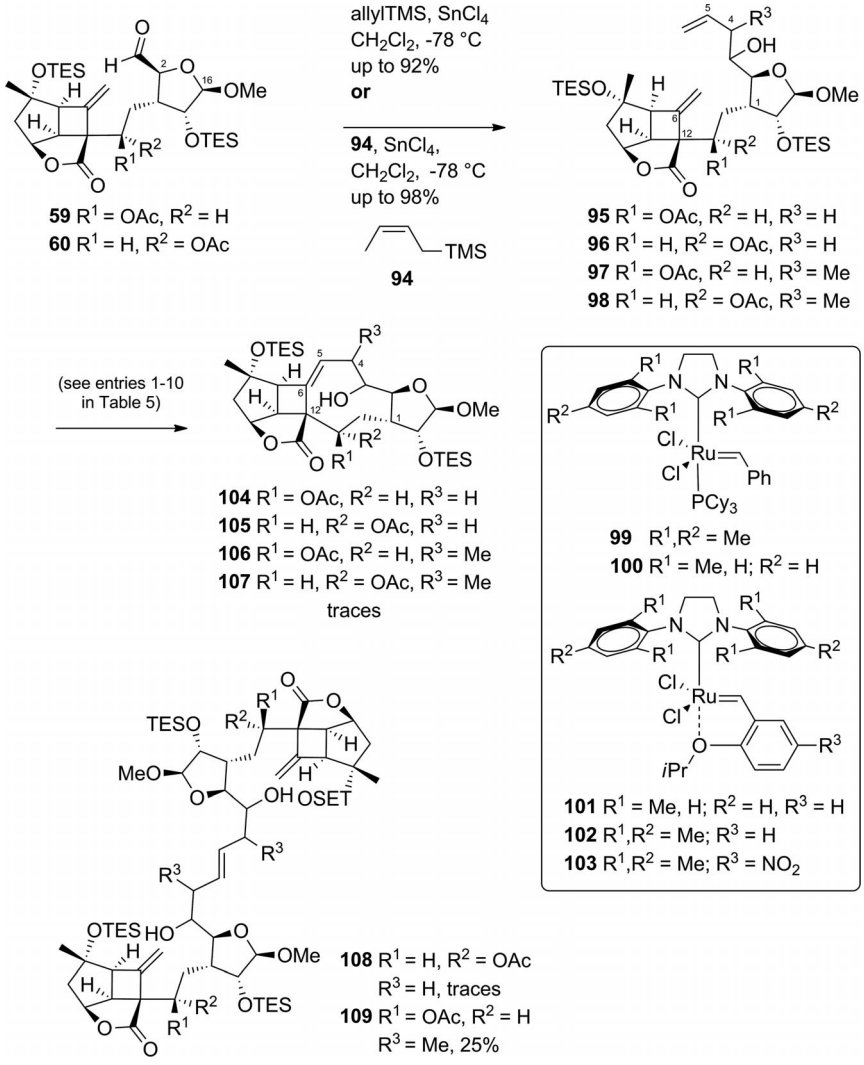
Scheme 22. Mechanistic explanation for the carbo-oxygenation.

Scheme 23. Tentative conversion of **92** to desired macrocycle **91**.

rable mixtures of diastereoisomers along with some unreacted aldehyde. These mixtures were used in the RCM experiments (Scheme 24, Table 5).

A broad spectrum of catalysts and solvents were employed (Table 5). Specifically, conventional Grubbs 2nd generation catalyst **99**,[22] Grubbs–Hoveyda II catalyst **102**, **100**, Stevens catalyst **101**,[23] fast initiating Nitro-Grela catalyst **103**,[24] and the doping-effect of poly-fluorinated solvents on the RCM reaction were tested.[25] In most cases complex product mixtures were obtained and indeed, in some cases traces of desired macrocycles **104** to **107** were identified in the mass spectrum. Predominantly however, homodimers **108** and **109** were obtained.

From the dimerization products we reasoned that replacing the terminal vinyl group by an isobutene appendage would facilitate the RCM reaction with the *exo*-methylene group in the *neo*-pentyl position.[26] Therefore, cross metathesis of **97** to **110** with isobutene was initiated (Table 5,



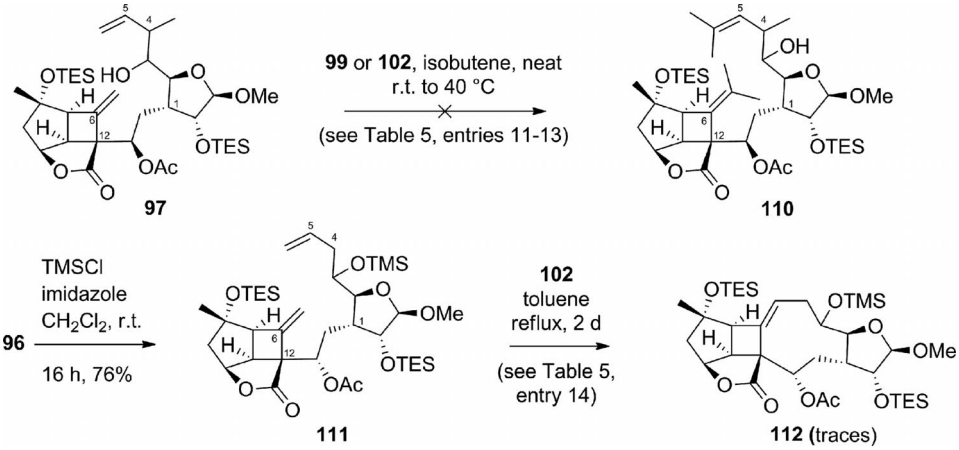
Scheme 24. Ring closing metathesis reaction attempts.

Table 5. Metathesis reaction conditions.

Entry	SM	Conditions	Yield
1[a]	**96**	**99** (0.4 equiv.), benzene (0.001 M), reflux, 24 h	**105**, traces
2[a]	**96**	**102** (0.4 equiv.), benzene (0.001 M), reflux, 24 h	**108**, traces
3[a]	**96**	**102** (0.4 equiv.), toluene (0.001 M), reflux, 24 h	**105**, traces.
4[a]	**95**	**102** (0.3 equiv.), toluene (0.001 M), reflux, 30 h	**104**, traces
5[a]	**97**	**102** (0.3 equiv.), toluene (0.0005 M), reflux, 18 h	**109**, 15%
6[a]	**97**	**101** (0.2 equiv.), toluene (0.0005 M), reflux, 36 h	SM
7[a]	**97**	**103** (0.2 equiv.), toluene (0.0005 M), reflux, 36 h	SM
8[b]	**97**	**103** (0.2 equiv.), toluene (0.0005 M), reflux, 16 h	SM
9[a]	**97**	**103** (0.2 equiv.), toluene (0.0005 M), reflux, 20 h	**109**, 25%
10[a]	**97**	**99** (0.2 equiv.), hexafluorobenzene (0.001 M), reflux, 38 h	**109**, 24%
11[b]	**97**	**99** (0.1 equiv.), isobutene (0.01 M), reflux, 16 h	SM
12[b]	**97**	**99** (0.1 equiv.), isobutene (0.01 M), 45 °C, 24 h	SM
13[b]	**97**	**102** (0.3 equiv.), isobutene (0.01 M), 45 °C, 24 h	SM
14[a]	**111**	**102** (0.4 equiv.), toluene (0.001 M), reflux, 48 h	**112**, traces

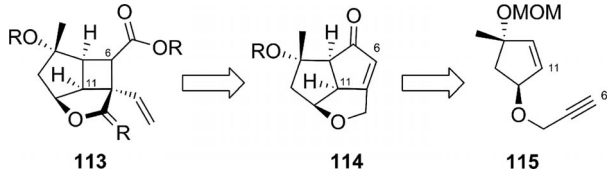
[a] Catalyst constantly added as 0.005 M solution through a syringe pump over 8 h. [b] Catalyst added in one portion as a solid.

Entries 11–12; Scheme 25), but no reaction occurred under these conditions. Finally, the free 3-OH in **96** was protected as silyl ether **111**. Disappointingly, this did not improve the outcome of the RCM reaction (Table 5, Entry 14; Scheme 25), leading only to traces of desired macrocycle **112**.



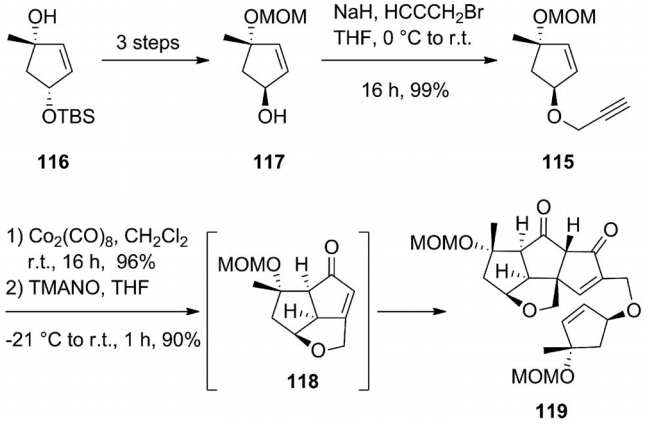
Scheme 25. Additional metathesis reaction experiments.

Having sizeable quantities of iodide **76** in hand, we thought of accessing the western section [3.2.0]-carbocyclic structure of bielschowskysin through a totally different strategy (Scheme 26). This approach was centered on a Pauson–Khand reaction[27] of **115** to form cyclopentenone **114**, which after 1,4-addition reaction and contraction of the five-membered ring by either Favorskii[28] or Wolff rearrangement[29] should lead to cyclobutane **113**.



Scheme 26. Pauson–Khand strategy to construct the cyclobutane moiety.

Thus, prostaglandin precursor **116**[30] was readily converted into **115** (Scheme 27). After formation of the stable hexacarbonyldicobalt complex a trimethylamine *N*-oxide (TMANO) induced Pauson–Khand reaction (PKR) was performed. Interestingly, the intramolecular PKR to **118** was followed by an intermolecular PKR with a second molecule of **115** to furnish highly functionalized poly-cycle **119**



Scheme 27. Pauson–Khand reaction cascade.

in excellent yield. This remarkable cascade generated three cycles and four stereogenic centers, including an all carbon quaternary center, in a single step. After conducting the reaction at lower temperatures and at higher dilution intermediate **118** could be identified in an inseparable mixture with an uncharacterized side product. As pentacycle **119** features a *cis,trans,cis*-triquinane terpene-type core, this serendipitous result may be useful in other synthetic ventures.

Conclusions

In conclusion, in this part of our bielschowskysin project we were able to synthesize several advanced macrocyclization precursors. Stereoselective high-yielding syntheses of building blocks representing the eastern section hemisphere of the target compound have led to optically active tetrahydrofuran building blocks **8**, **45**, and **75**–**77**, which may be also useful in other syntheses. Our initial synthetic plan was modified and optimized, so that the biomimetic [2+2]-photocyclization reaction could be carried out on a large scale and provided the [3.2.0]-carbocyclic core of bielschowskysin in a stereoselective manner. Except for an epoxidation, the *exo*-methylene group proved exceptionally unreactive to numerous transformations. Various RCM reactions, instead of closing the desired nine-membered macrocycle, exclusively led to dimers **108** and **109**. However, macrocyclization under Jeffery–Heck conditions was successful, and, through an unprecedented carbo-oxygenation, led to highly functionalized macrocycle **92**, which had the wrong ring size, but eight correctly substituted stereocenters in place. At present, synthetic efforts to enlarge the eight-membered ring to the desired nine-membered one are well underway in our laboratory.

Experimental Section

General Remarks: All moisture and oxygen sensitive reactions were carried out in flame-dried glassware under a slight argon overpressure. All solvents (except dichloromethane and methanol) were purchased as the highest available grade from Sigma–Aldrich, Acros Organics or Fischer Chemicals. Anhydrous dichloromethane was purified by filtration through alumina under argon immediately be-

fore use. Methanol was heated at reflux for several hours over sodium before being distilled. NEt_3, iPr_2NEt and 2,6-lutidine were distilled from CaH_2 before use. All other reagents were used as received from Sigma–Aldrich, Acros Organics, Fischer Chemicals, TCI or ABCR unless otherwise stated. Preparative column chromatography was performed with silica gel 60 from Merck (0.040–0.063 μm, 240–400 mesh). All NMR spectra were measured with a Bruker AV400, DRX400 or DRX600 instrument. Chemical shifts are referenced to the solvent residual peaks ($CDCl_3$ ^1H, δ = 7.26 ppm, ^{13}C, δ = 77.16 ppm). Infrared spectra were recorded as thin films of pure products with an ATR-unit attached to a Bruker Vertex 70 instrument. High-resolution mass spectra were measured with a Bruker MaXis (ESI-TOF) instrument with a resolution of 10,000. A P341 Perkin–Elmer polarimeter equipped with in a 10 cm cell and a Na-lamp (589 nm) was used for optical rotation measurements.

(3*R*,4*S*,5*S*)-5-{[(*tert*-Butyldiphenylsilyl)oxy]methyl}-3-(hydroxymethyl)-4-vinyldihydrofuran-2(3*H*)-one (14): In a round-bottomed flask copper chloride (35 mg, 0.35 mmol) and lithium chloride (37 mg, 0.87 mmol) were gently dried with a heat gun in vacuo. The flask was carefully purged with argon and equipped with a rubber septum. The solids were digested in THF (20 mL) at room temperature and cooled to –78 °C. Vinyl magnesium bromide (5.7 mL, 5.70 mmol) was added to the vigorously stirred mixture by syringe over 10 min. After 30 min, to the resulting beige milky suspension, a solution of butenolide **12** (1.54 g, 4.37 mmol) was added dropwise in THF (20 mL) through a cannula over 30 min at –78 °C. After 1 h the resulting yellow solution was warmed to –40 °C and stirred for an additional hour. The resulting dark red reaction mixture was quenched with satd. aq. NH_4Cl (40 mL) and warmed to room temperature. The aqueous phase was separated and extracted with diethyl ether (3× 20 mL). The combined organic phases were washed with water (40 mL), satd. aq. NaCl (40 mL) dried with $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (SiO_2, hexane/EtOAc, 6:1) afforded the desired 1,4 adduct as a pale yellow gum (1.38 g, 3.62 mmol) in 83%. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.78–7.65 (m, 4 H), 7.47–7.38 (m, 6 H), 5.76 (ddd, *J* = 17.6, 9.6, 8.0 Hz, 1 H), 5.13 (d, *J* = 17.6 Hz, 1 H), 5.11 (d, *J* = 9.6 Hz, 1 H), 4.25 (ddd, *J* = 6.8, 3.5, 2.7 Hz, 1 H), 3.93 (dd, *J* = 11.6, 2.7 Hz, 1 H), 3.73 (dd, *J* = 11.6, 3.5 Hz, 1 H), 3.20 (dddd, *J* = 8.9, 8.4, 8.0, 6.8 Hz, 1 H), 2.82 (dd, *J* = 17.6, 8.9 Hz, 1 H), 2.44 (dd, *J* = 17.6, 8.4 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 175.9, 136.4, 136.0, 135.5, 132.9, 132.5, 129.9, 127.8, 117.3, 104.5, 84.6, 63.3, 40.7, 35.0, 26.7, 19.2 ppm.

Preparation of the Formaldehyde Solution: Paraformaldehyde (3.8 g, 126 mmol) was placed in a two-necked round-bottomed flask equipped with a rubber septum and an argon inlet on one side, and a glass bridge filled with fresh calcium chloride on the other. The glass bridge was connected to a second two-necked round-bottomed flask that acted as a water trap, which was cooled to 0 °C. The second neck was equipped with a rubber septum and a thick Teflon cannula that reached into dry THF (28 mL) at –40 °C that was stored in a third two-necked round-bottomed flask equipped with a bubbler on the remaining neck. The flask containing formaldehyde was heated in an oil bath to 150 °C under a constant stream of argon (one bubble per second through THF). Heating was continued for 15 min after all the formaldehyde was gone (overall 2 h). The resulting clear solution was kept at –40 °C and used immediately without purification in the alkylation reaction.

A solution of diisopropylamine (1.75 mL, 12.3 mmol) in THF (16 mL) was dropwise treated with *n*BuLi (1.6 M in hexane, 7.4 mL, 11.7 mmol) at –21 °C. After 5 min the resulting solution was warmed to 0 °C for 30 min. At –40 °C a solution of the 1,4 adduct (3.9 g, 10.2 mmol) in THF (12 mL) was added dropwise over 15 min and the resulting solution was left for 1 h. The freshly prepared cold solution of formaldehyde was added through a Teflon cannula over 2 min and the resulting turbid reaction mixture was allowed to stir for an additional 30 min. The reaction was quenched with satd. aq. NH_4Cl (30 mL). The aqueous phase was separated and extracted with diethyl ether (2× 40 mL). The combined organic phases were washed with satd. aq. NaCl (40 mL), dried with $MgSO_4$, filtered, and concentrated in vacuo resulting in a 2:1 mixture of diastereoisomers. Purification by flash column chromatography (SiO_2, hexane/EtOAc, 6:1) yielded **14** (2.21 g, 5.40 mmol) and **13** (1.11 g, 2.69 mmol) as single diastereoisomers in combined 79% yield. Analytic data for **13**: ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.67–7.65 (m, 4 H), 7.47–7.38 (m, 6 H), 5.88 (dt, *J* = 17.0, 9.9 Hz, 1 H), 5.22–5.20 (m, 1 H), 5.19–5.15 (m, 1 H), 4.36 (dt, *J* = 5.3, 3.1 Hz, 1 H), 3.94–3.84 (m, 2 H), 3.92 (dd, *J* = 11.7, 3.0 Hz, 1 H), 3.72 (dd, *J* = 11.7, 3.3 Hz, 1 H), 3.29 (td, *J* = 14.5, 5.2 Hz, 1 H), 3.04 (dt, *J* = 10.2, 5.1 Hz, 1 H), 2.18 (dd, *J* = 7.0, 4.8 Hz, 1 H), 1.55 (1 H), 1.06 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 176.8, 135.8 (2 C), 135.7 (2 C), 134.7, 133.1 (2 C), 132.9, 130.0, 128.0 (4 C), 119.9, 83.2, 62.4, 59.8, 48.8, 43.2, 26.9 (3 C), 19.4 ppm. HRMS (ESI): calcd. for $C_{24}H_{30}O_4SiNa$ $[M + Na]^+$ 433.1811; found 433.1815.

Epimerization of 13: Alcohol **13** (611 mg, 1.15 mmol) was dissolved in toluene (5 mL) and DBU (170 μL, 1.13 mmol). The resulting solution was heated to 60 °C for 3 h. The organic phase was washed with 1 N HCl (2× 5 mL) and water (5 mL), dried with $MgSO_4$, filtered, concentrated under reduced pressure and subjected to column chromatography (SiO_2, hexane/EtOAc, 6:1). Desired alcohol **14** (529 mg, 1.0 mmol) was isolated as a colorless oil in 86% yield. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.68–7.65 (m, 4 H), 7.46–7.37 (m, 6 H), 5.68 (ddd, *J* = 16.9, 10.3, 8.3 Hz, 1 H), 5.21–5.16 (m, 2 H), 4.22 (ddd, *J* = 9.5, 4.0, 2.6 Hz, 1 H), 4.00–3.95 (m, 1 H), 3.96 (dd, *J* = 11.7, 2.7 Hz, 1 H), 3.78–3.72 (m, 1 H), 3.74 (dd, *J* = 11.9, 3.8 Hz, 1 H), 3.18 (dt, *J* = 11.4, 9.1 Hz, 1 H), 2.67 (ddd, *J* = 11.6, 5.8, 4.0 Hz, 1 H), 2.35 (dd, *J* = 7.5, 5.6 Hz, 1 H), 1.06 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 178.3, 135.8 (2 C), 135.7 (2 C), 133.9, 133.0 (2 C), 132.6, 130.1, 128.0 (4 C), 119.4, 84.2, 63.8, 60.3, 46.3, 43.9, 26.9 (3 C), 19.4 ppm. HRMS (ESI): calcd. for $C_{24}H_{30}O_4SiNa$ $[M + Na]^+$ 433.1811; found 433.1816. IR: $\tilde{\nu}$ = 3481, 2932, 1859, 1770, 1472, 1428, 1113, 1047, 929, 703 cm^{-1}. $[\alpha]_D^{23}$ = +12.7, ($CHCl_3$, *c* = 1.2). R_f (hexane/EtOAc, 3:1) = 0.28.

2-((2*S*,3*S*,4*R*,5*S*)-2-{[(*tert*-Butyldiphenylsilyl)oxy]methyl}-5-methoxy-4-{[(4-methoxybenzyl)oxy]methyl}tetrahydrofuran-3-yl)acetaldehyde (8): To a solution of alcohol **14** (5.0 g, 12.2 mmol) and freshly prepared 4-methoxybenzyl-2,2,2-trichloroacetimidate (7.0 g, 24.9 mmol) in CH_2Cl_2 (80 mL) was added camphor sulfonic acid (CSA; 140 mg, 0.6 mmol) at 0 °C. The resulting pale yellow solution was warmed to room temperature overnight. After 18 h, water (50 mL) was added and stirring was continued for an additional hour. The organic phase was separated, dried with $MgSO_4$, filtered and concentrated under reduced pressure. Flash column chromatography (SiO_2, hexane/EtOAc, 12:1) yielded the desired PMB protected alcohol (5.94 g, 11.2 mmol, 92%) as pale yellow oil. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.68–7.66 (m, 4 H), 7.45–7.36 (m, 4 H), 7.21 (d, *J* = 8.5 Hz, 2 H), 6.84 (d, *J* = 8.7 Hz, 2 H), 5.66 (ddd, *J* = 17.0, 10.3, 8.4 Hz, 1 H), 5.14–5.08 (m, 2 H), 4.51 (d, *J* = 11.8 Hz, 1 H), 4.43 (d, *J* = 11.9 Hz, 1 H), 4.18 (ddd, *J* = 9.5, 4.2, 2.7 Hz, 1 H), 3.93 (dd, *J* = 11.8, 2.7 Hz, 1 H), 3.81–3.78 (m, 1 H), 3.79 (s, 3 H), 3.75 (dd, *J* = 11.8, 4.3 Hz, 1 H), 3.61 (dd, *J* = 9.7, 3.5 Hz, 1 H), 3.37–3.30 (m, 1 H), 2.62 (dt, *J* = 11.2, 3.7 Hz,

1 H), 1.04 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 175.8, 159.3, 135.8 (2 C), 135.7 (2 C), 135.4, 133.3, 133.0, 130.2, 129.93, 129.92, 129.3 (2 C), 127.9 (4 C), 119.1, 113.9 (2 C), 82.7, 73.1, 65.6, 62.8, 55.4, 47.7, 43.3, 26.8 (3 C), 19.4 ppm. HRMS (ESI): calcd. for $C_{32}H_{38}O_5SiNa$ [M + Na]$^+$ 553.2386; found 553.2388. IR: $\tilde{\nu}$ = 3000, 2858, 1777, 1513, 1247, 1113, 1008, 823, 702, 504 cm^{-1}. $[\alpha]_D^{20}$ = +0.63, ($CHCl_3$, c = 0.64). R_f (hexane/EtOAc, 3:1) = 0.37.

To a solution of the PMB ether (4.34 g, 8.2 mmol) in CH_2Cl_2 (100 mL) was added diisobutylaluminium hydride (DIBALH; 25 wt.-% in toluene, 9.3 mL, 16.3 mmol) through a syringe at –78 °C over 10 min. The resulting reaction mixture was allowed to stir at this temperature for 1 h before the reaction was carefully quenched with satd. aq. Na/K tartrate (100 mL). The resulting biphasic mixture was vigorously stirred for 2 h. The aqueous phase was separated and extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with water (100 mL) and satd. aq. NaCl (100 mL), dried with $MgSO_4$ and filtered. Evaporation of all volatiles provided the desired lactol at a *dr* of 2:1 as a pale yellow oil, which was used without further purification in the next reaction.

The residue was dissolved in trimethyl orthoformate (40 mL) and pyridinium *p*-toluenesulfonate (PPTS; 18 mg, 0.1 mmol) was added. The reaction was stirred at room temperature for 24 h after which satd. aq. $NaHCO_3$ (20 mL) was added. The aqueous phase was separated and extracted with diethyl ether (3 × 20 mL). The combined organic phases were washed with water (40 mL) and satd. aq. NaCl (40 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, hexane/EtOAc, 6:1) yielded the desired acetal (3.6 g, 6.6 mmol, 80%). Major diastereoisomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.70–7.67 (m, 4 H), 7.43–7.34 (m, 6 H), 7.23 (d, J = 8.7 Hz, 2 H), 6.86 (d, J = 8.7 Hz, 2 H), 5.71 (ddd, J = 16.9, 10.1, 8.8 Hz, 1 H), 4.95 (dd, J = 10.1, 1.6 Hz, 1 H), 4.94–4.90 (m, 1 H), 4.91 (d, J = 2.4 Hz, 1 H), 4.46 (d, J = 11.8 Hz, 1 H), 4.41 (d, J = 11.8 Hz, 1 H), 3.90 (ddd, J = 8.7, 7.9, 3.0 Hz, 1 H), 3.82 (dd, J = 9.4, 2.9 Hz, 1 H), 3.80 (s, 3 H), 3.70 (dd, J = 11.2, 4.7 Hz, 1 H), 3.43 (dd, J = 9.5, 5.2 Hz, 1 H), 3.38 (s, 3 H), 3.38–3.35 (m, 1 H), 2.40 (dd, J = 16.6, 8.6 Hz, 1 H), 2.26–2.20 (m, 1 H), 1.05 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.3, 138.1, 135.9 (2 C), 135.8 (2 C), 133.8 (2 C), 130.6, 129.7 (2 C), 129.3 (2 C), 127.75 (2 C), 127.73 (2), 116.7, 113.9 (2 C), 107.6, 82.8, 72.7, 69.4, 64.2, 55.4, 55.2, 52.8, 47.4, 27.0 (3 C), 19.5 ppm. HRMS (ESI): calcd. for $C_{33}H_{42}O_5SiNa$ [M + Na]$^+$ 569.2699; found 569.2697. IR: $\tilde{\nu}$ = 2999, 2931, 2858, 1613, 1513, 1248, 1112, 1007, 823, 703 cm^{-1}. $[\alpha]_D^{23}$ = +15.7, ($CHCl_3$, c = 0.42). R_f (hexane/EtOAc, 3:1) = 0.48.

To a solution of the acetal (1.3 g, 2.38 mmol) in THF (24 mL) was added BH_3·THF (1.0 M in THF, 7.2 mL, 7.2 mmol) at 0 °C over 10 min. After 5 h of stirring at 0 °C, 1 M NaOH (6 mL) and hydrogen peroxide (30 wt.-%, 3 mL) were added sequentially and the resulting biphasic mixture was stirred for an additional hour at that temperature. Sat. aq. $Na_2S_2O_3$ (15 mL) was added and the aqueous phase was separated and extracted with diethyl ether (3 × 20 mL). The combined organic phases were washed with water (20 mL) and satd. aq. NaCl (20 mL), dried with $MgSO_4$ and concentrated under reduced pressure. After column chromatography (SiO_2, hexane/EtOAc, 6:1) the desired alcohol (1.0 g, 1.7 mmol, 75%) was obtained as pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.71–7.67 (m, 4 H), 7.45–7.35 (m, 6 H), 7.20 (d, J = 8.7 Hz, 2 H), 6.85 (d, J = 8.7 Hz, 2 H), 4.72 (s br., 1 H), 4.43 (d, J = 11.5 Hz, 1 H), 4.40 (d, J = 11.5 Hz, 1 H), 3.82 (ddd, J = 8.2, 4.8, 3.8 Hz, 1 H), 3.79 (s, 3 H), 3.77 (dd, J = 11.2, 3.6 Hz, 1 H), 3.72 (dd, J = 11.2, 4.9 Hz, 1 H), 3.65–3.56 (m, 2 H), 3.52 (dd, J = 8.7, 6.8 Hz, 1 H), 3.31 (s, 3 H), 3.24 (t, J = 9.0 Hz, 1 H), 2.34–2.29 (m, 1 H), 1.96–1.90 (m, 1 H), 1.69–1.59 (m, 1 H), 1.58–1.51 (m, 1 H), 1.07 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.5, 135.9 (2 C), 135.8 (2 C), 133.6, 133.5, 129.84 (2 C), 129.83 (2 C), 129.7, 127.83 (2 C), 127.81 (2 C), 114.0 (2 C), 107.3, 84.3, 73.2, 71.7, 65.2, 61.2, 55.4, 54.6, 51.4, 40.0, 36.1, 27.0 (3 C), 19.4 ppm. HRMS (ESI): calcd. for $C_{33}H_{44}O_6SiNa$ [M + Na]$^+$ 587.2805; found 587.2814. IR: $\tilde{\nu}$ = 3470, 2932, 2859, 1613, 1472, 1249, 1112, 1080, 823, 703 cm^{-1}. $[\alpha]_D^{21}$ = +20.1, ($CHCl_3$, c = 0.30). R_f (hexane/EtOAc, 3:1) = 0.21.

A suspension of the alcohol (244 mg, 0.43 mmol) and IBX (242 mg, 0.86 mmol) in EtOAc (4.3 mL) was heated to reflux for 16 h. The fine suspension was cooled to room temperature and hexane (5 mL) was added. The mixture was filtered through a pad of Celite, which was rinsed with hexane (5 mL). The remaining colorless filtrate was concentrated under reduced pressure. The residue was subjected to column chromatography (SiO_2, hexane/EtOAc, 8:1), which gave desired aldehyde **8** (239 mg, 0.42 mmol, 98%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.65 (t, J = 1.3 Hz, 1 H), 7.69–7.65 (m, 4 H), 7.45–7.35 (m, 6 H), 7.21 (d, J = 8.7 Hz, 2 H), 6.85 (d, J = 8.7 Hz, 2 H), 4.86 (d, J = 1.0 Hz, 1 H), 4.41 (d, J = 11.6 Hz, 1 H), 4.36 (d, J = 11.6 Hz, 1 H), 3.80 (s, 3 H), 3.79–3.77 (m, 1 H), 3.77–3.75 (m, 2 H), 3.44–3.34 (m, 2 H), 3.31 (s, 3 H), 2.65 (ddd, J = 17.6, 8.4, 1.6 Hz, 1 H), 2.54 (ddd, J = 17.6, 5.4, 1.2 Hz, 1 H), 2.23–2.16 (m, 1 H), 2.15–2.10 (m, 1 H), 1.06 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 201.3, 159.1, 135.7 (2 C), 135.6 (2 C), 133.3, 133.3, 130.3, 129.73, 129.71, 129.2 (2 C), 127.69 (2 C), 127.78 (2 C), 113.8 (2 C), 107.2, 82.9, 72.7, 70.4, 64.9, 55.2, 54.6, 52.4, 48.1, 36.4, 26.9 (3 C), 19.3 ppm. HRMS (ESI): calcd. for $C_{33}H_{42}O_6SiNa$ [M + Na]$^+$ 585.2648; found 585.2665. IR: $\tilde{\nu}$ = 2932.5, 1759.8, 1613.7, 1514.5, 1428.5, 1249.3, 1180.5, 1112.2, 823.9, 704.0 cm^{-1}. $[\alpha]_D^{22}$ = +0.5, ($CHCl_3$, c = 1.1). R_f (hexane/EtOAc, 3:1) = 0.44.

***tert*-Butyldimethyl({(*S*)-2-methyl-1-[(*S*)-oxiran-2-yl]but-3-yn-2-yl}oxy)silane (17):** Tertiary alcohol **16** (5.96 g, 32.3 mmol) and 2,6-lutidine (7.6 mL, 65.3 mmol) were dissolved in CH_2Cl_2 (130 mL) and cooled to 0 °C. Trifluoromethanesulfonic acid *tert*-butyldimethylsilyl ester (TBSOTf ; 8.2 mL, 35.7 mmol) was added dropwise through a syringe over 10 min. The resulting pale yellow solution was stirred at that temperature for 16 h followed by addition of satd. aq. NH_4Cl (50 mL). The organic phase was separated, dried with $MgSO_4$ and concentrated under reduced pressure providing the crude TBS ether (9.0 g, 30 mmol, 93%), which was exceptionally clean and used in the next step without further purification. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.37–4.31 (m, 1 H), 4.14 (dd, J = 8.1, 5.8 Hz, 1 H), 3.63 (t, J = 8.0 Hz, 1 H), 2.45 (s, 1 H), 2.12 (dd, J = 13.8, 4.3 Hz, 1 H), 1.90 (dd, J = 13.8, 7.6 Hz, 1 H), 1.50 (s, 3 H), 1.38 (s, 3 H), 1.35 (s, 3 H), 0.87 (s, 9 H), 0.18 (s, 3 H), 0.17 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 107.9, 88.1, 72.8, 72.7, 70.4, 67.3, 48.8, 31.4, 27.0, 26.0, 25.9 (3 C), 18.2, –2.7, –3.06 ppm. HRMS (EI): calcd. for $C_{15}H_{27}NaO_3SiNa$ [M – CH_3]$^+$ 283.1729; found 183.1722.

The alkyne (50 mg, 0.17 mmol) was dissolved in CH_2Cl_2 (2 mL) and cooled to 0 °C. Trifluoroacetic acid (TFA; 85 μL, 1.1 mmol) was added. After 3 h satd. aq. $KHCO_3$ (10 mL) and CH_2Cl_2 (10 mL) were added. The aqueous phase was separated and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried with $MgSO_4$, filtered and concentrated under reduced pressure giving the desired vicinal diol (39 mg, 15 mmol, 90%) as colorless oil, which was clean enough to carry on to the next reaction without further purification. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.31–4.25 (m, 1 H), 3.81 (s, 1 H), 3.66–3.61 (m, 1 H), 3.51–3.46 (m, 1 H), 2.53 (s, 1 H), 2.19–2.16 (m, 1 H), 1.92 (dd, J = 14.2,

9.7 Hz, 1 H), 1.69 (dd, J = 14.3, 1.6 Hz, 1 H), 1.56 (s, 3 H), 0.89 (s, 9 H), 0.26 (s, 3 H), 0.25 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 86.6, 73.7, 70.9, 70.3, 66.9, 47.3, 32.0, 25.7 (3 C), 18.0, –2.6, –3.1 ppm. HRMS (ESI): calcd. for $C_{13}H_{26}O_3SiNa$ [M + Na]$^+$ 281.1549; found 281.1555. IR: $\tilde{\nu}$ = 3311, 2929, 2858, 1670, 1463, 1254, 1120, 983, 838, 778 cm^{-1}. $[\alpha]_D^{20}$ = –1.6, ($CHCl_3$, c = 0.25). R_f (hexane/EtOAc, 1:1) = 0.50.

To a solution of the vicinal diol (1.2 g, 4.6 mmol) and tributyltin oxide (25 mg, 0.02 mmol) in CH_2Cl_2 (50 mL) was added tosyl chloride (970 μL, 5.1 mmol) followed by triethylamine (711 μL, 5.1 mmol) at 0 °C. The resulting mixture was warmed to room temperature after 15 min and stirred for a further 4 h. Water (30 mL) was added, the aqueous phase was separated and extracted with CH_2Cl_2 (30 mL). The combined organic phases were dried with $MgSO_4$, filtered and the volatiles were removed under reduced pressure. The remaining residue was subjected to column chromatography (SiO_2, hexane/EtOAc, 8:1) yielding the desired terminal tosylate (1.68 g, 4.1 mmol) as a colorless oil in 87%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.80 (d, J = 8.3 Hz, 2 H), 7.33 (d, J = 8.5 Hz, 2 H), 4.39–4.34 (m, 1 H), 3.98 (s, 1 H), 3.97 (s, 1 H), 3.65 (s, 1 H), 2.51 (s, 1 H), 2.43 (s, 3 H), 1.83 (dd, J = 14.3, 9.0 Hz, 1 H), 1.77 (dd, J = 14.3, 2.5 Hz, 1 H), 1.52 (s, 3 H), 0.84 (s, 9 H, s), 0.22 (s,3 H), 0.21 (s,3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 144.9, 133.0, 129.9 (3 C), 128.2 (3 C), 86.1, 74.0, 73.2, 70.6, 67.7, 47.1, 31.9, 25.7 (3 C), 21.7, 18.0, 17.6, –2.62, –3.16 ppm. HRMS (ESI): calcd. for $C_{20}H_{32}O_5SSiNa$ [M + Na]$^+$ 435.1637; found 435.1644. IR: $\tilde{\nu}$ = 3286 2984, 2921, 2887, 1463, 1409, 1298, 1164, 1126, 999 cm^{-1}. $[\alpha]_D^{20}$ = –21.4, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 4:1) = 0.48.

At 0 °C, K_2CO_3 (1.4 g, 10.3 mmol) was added to a solution of the tosylate (1.64 g, 3.97 mmol) in methanol (40 mL). After 30 min, Et_2O/Hex (1:1, 30 mL) was added and the resulting solids were removed by filtration. The organic phase was washed with water (20 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Crude epoxide **17** (877 mg, 3.65 mmol, 92%) was used in the next step without further purification. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.21–3.16 (m, 1 H), 2.79 (t, J = 4.5 Hz, 1 H), 2.54 (dd, J = 5.0, 2.7 Hz, 1 H), 2.47 (s, 1 H), 1.97 (dd, J = 13.8, 5.7 Hz, 1 H), 1.80 (dd, J = 13.8, 5.6 Hz, 1 H), 1.54 (s, 3 H), 0.88 (s, 9 H), 0.20 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 87.9, 72.7, 67.9, 49.1, 48.0, 46.9, 31.1, 25.8 (3 C), 18.2, –2.7, –3.1 ppm. HRMS (EI): calcd. for $C_{12}H_{21}O_2Si$ [M – CH_3]$^+$ 225.1311; found 225.1306. IR: $\tilde{\nu}$ = 2992, 2956, 2987, 1473, 1427, 1304, 1165, 1135, 1047, 996 cm^{-1}. $[\alpha]_D^{20}$ = –9.7, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 4:1) = 0.81.

(*R*)-5-{(*S*)-2-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-4-(trimethylsilyl)but-3-yn-1-yl}dihydrofuran-2(3*H*)-one (19): Sodium (0.93 g, 40.5 mmol) was added to ethanol (42 mL) at room temp. After the evolution of gas ceased, diethylmalonate (3.8 mL, 25.2 mmol) was added dropwise. The resulting solution was stirred for 1 h at room temperature. A solution of epoxide **17** (1.22 g, 5.1 mmol) in EtOH (12 mL) was added over 10 min and the resulting mixture was stirred for 16 h. Diethyl ether (100 mL), satd. aq. NH_4Cl (50 mL) and water (100 mL) were added. The aqueous phase was separated and extracted with diethyl ether (3× 50 mL). The combined organic phases were washed with water (50 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure providing the desired malonate as a mixture of diastereoisomers that was used in the next reaction without further purification.

A solution of the malonate (2.0 g, 5.6 mmol) and LiCl (480 mg, 11.3 mmol) in dimethyl sulfoxide (DMSO; 12 mL) and water (0.1 mL) was heated to 140 °C and stirred at this temperature for 5 h. The resulting brown mixture was cooled to room temperature and quenched with satd. aq. NH_4Cl (10 mL) and H_2O (10 mL). The aqueous phase was extracted with diethyl ether (3× 20 mL) and the combined organic phases were dried with $MgSO_4$, filtered and evaporated to give a viscous brown oil. Purification by flash column chromatography (SiO_2, hexane/EtOAc, 3:1) afforded the desired lactone (1.43 g, 5.1 mmol, 91%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.79 (ddd, J = 12.1, 8.8, 6.0 Hz, 1 H), 2.53 (dd, J = 9.9, 1.1 Hz, 1 H), 2.51 (d, J = 9.5 Hz, 1 H), 2.48 (s, 1 H), 2.45–2.39 (m, 1 H), 2.20 (dd, J = 14.3, 6.0 Hz, 1 H), 2.09–1.99 (m, 1 H), 1.98 (dd, J = 14.2, 5.6 Hz, 1 H), 1.5 (s, 3 H), 0.88 (s, 9 H), 0.194 (s, 3 H), 0.191 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 177.2, 87.9, 77.7, 73.0, 67.1, 50.4, 31.3, 29.5, 29.0, 25.8 (3 C), 18.2, –2.7, –3.0 ppm. HRMS (ESI): calcd. for $C_{15}H_{26}O_3SiNa$ [M + Na]$^+$ 305.1549; found 305.1546. IR: $\tilde{\nu}$ = 2929, 2856, 1780, 1463, 1253, 1166, 1113, 1002, 838, 778 cm^{-1}. $[\alpha]_D^{20}$ = –27.8, ($CHCl_3$, c = 0.54). R_f (hexane/EtOAc, 3:1) = 0.31.

To a solution of alkyne (50 mg, 0.18 mmol) in THF (2 mL), lithium bis(trimethylsilyl)amide (LiHMDS; 390 μL, 0.39 mmol) was added dropwise at –78 °C. Trimethylsilyl chloride (TMSCl; 52 μL, 0.41 mmol) was added dropwise through a syringe. The resulting mixture was gradually warmed to –21 °C over 3 h. The reaction was quenched with satd. aq. NH_4Cl (5 mL) and diethyl ether (5 mL) was added to the biphasic mixture. The aqueous phase was separated and extracted with diethyl ether (3× 5 mL). The combined organic phases were washed with satd. aq. NaCl (10 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (SiO_2, hexane/EtOAc, 3:1) of the remaining residue gave **19** (31 mg, 0.08 mmol, 49%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.78 (dq, J = 8.4, 6.0 Hz, 1 H), 2.52 (d, J = 9.8 Hz, 1 H), 2.51 (d, J = 9.4 Hz, 1 H), 2.41 (sext, 1 H), 2.19 (dd, J = 14.1, 5.5 Hz, 1 H), 2.04 (dq, J = 12.5, 9.1 Hz, 1 H), 1.94 (dd, J = 14.1, 6.3 Hz, 1 H), 1.50 (s, 3 H), 0.87 (s, 9 H), 0.19 (s, 3 H), 0.18 (s, 3 H), 0.16 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 177.3, 109.7, 89.2, 77.9, 77.2, 67.3, 50.2, 31.5, 29.4, 29.0, 25.9 (3 C), 18.2, 0.2 (3 C), –2.7, –3.0 ppm. HRMS (ESI): calcd. for $C_{18}H_{34}O_3Si_2Na$ [M + Na]$^+$ 377.1944; found 377.1949. IR: $\tilde{\nu}$ = 2956, 2857, 1780, 1462, 1360, 1251, 1165, 1110, 1000, 838 cm^{-1}. $[\alpha]_D^{23}$ = –16.4, ($CHCl_3$, c = 0.7). R_f (hexane/EtOAc, 3:1) = 0.45.

Secondary Alcohol 21: To a solution of **19** (30 mg, 0.08 mmol) in THF (1 mL) was added LiHMDS (93 μL, 0.09 mmol) at –78 °C. The resulting pale yellow solution was cooled to –40 °C for 30 min, then to –78 °C and a solution of **8** (52 mg, 0.09 mmol) in THF (1 mL) was added. The reaction was warmed to –40 °C over 1 h and stirred for 2 h. The reaction was quenched with satd. aq. NH_4Cl (5 mL) and diethyl ether (5 mL) was added to the biphasic mixture. The aqueous phase was separated and extracted with diethyl ether (3× 5 mL). The combined organic phases were washed with satd. aq. NaCl (10 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the residue by column chromatography (SiO_2, hexane/EtOAc, 10:1) provided **21** as inseparable mixture of all four possible diastereoisomers (7 mg, 0.01 mmol). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.71–7.66 (m, 4 H), 7.44–7.35 (m, 6 H), 7.22–7.17 (m, 2 H), 6.88–6.84 (m, 2 H), 4.86–4.81 (m, 1 H), 4.69–4.63 (m, 1 H), 4.47–4.36 (m, 1 H), 4.23–4.10 (m, 1 H), 3.84–3.68 (m, 5 H), 3.54–3.39 (m, 2 H), 3.34–3.28 (m, 3 H), 3.23–3.17 (m, 1 H), 2.63–2.39 (m, 2 H), 2.33–2.15 (m, 3 H), 2.11–2.02 (m, 2 H), 1.99–1.84 (m, 2 H), 1.49 (s, 3 H), 1.07 (s, 9 H), 0.86 (s, 9 H), 0.18 (s, 6 H), 0.16 (s, 6 H), 0.13 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.6, 159.5, 150.3, 135.9 (2 C), 135.7 (2 C), 133.3, 133.3, 130.3, 129.9, 129.8, 129.2 (2 C), 127.9 (2 C), 127.8 (2 C), 114.2 (2 C), 107.3, 107.4, 84.6, 84.2, 78.2, 73.4,

72.8, 71.7, 66.9, 64.8, 55.4, 54.6, 52.4, 47.1, 41.0. 40.1, 38.7, 29.8, 27.9 (3 C), 26.9 (3 C), 19.3, 19.5. 2.4 (3 C), –2.7, –3.0 ppm. HRMS (ESI): calcd. for $C_{51}H_{76}O_9Si_3Na$ $[M + Na]^+$ 939.4695; found 939.4685. IR: $\tilde{\nu}$ = 3479, 2988, 2878, 1721, 1501, 1453, 1393, 1267, 1101, 992 cm^{-1}. $[\alpha]_D^{20}$ = –11.3, ($CHCl_3$, c = 0.3). R_f (hexane/EtOAc, 3:1) = 0.38.

Butyrolactone 22: To a solution of diisopropylamine (150 μL, 1.06 mmol) in THF (2.8 mL) was added dropwise *n*BuLi (1.6 M in hexane, 633 μL, 1.0 mmol) at –21 °C. 10 min after the addition the resulting solution was put to 0 °C for 30 min and thereafter cooled to –78 °C. A solution of seleno lactone **22** (274 mg, 0.93 mmol) in THF (3.6 mL) was added dropwise over 10 min. The mixture was warmed to –60 °C before aldehyde **8** (475 mg, 0.84 mmol) in THF (3.6 mL) was added over 10 min. The mixture was further warmed to –45 °C over 1 h. Sat. aq. NH_4Cl (15 mL) was added, the layers were separated and the aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic phases were washed with water (20 mL) and satd. aq. NaCl (20 mL), dried with $MgSO_4$ and concentrated under reduced pressure. The obtained yellow oil was used without purification in the next step.

The mixture of diastereoisomers was dissolved in CH_2Cl_2 (7.8 mL), cooled to 0 °C and satd. aq. NH_4Cl (0.8 mL) and H_2O_2 (30 wt.-%, 1.6 mL, 14 mmol) were added. After 1 h satd. aq. $Na_2S_2O_3$ (10 mL) was added and stirring was continued for an additional 30 min. The separated aqueous layer was extracted with diethyl ether (3 × 15 mL). The combined organic phases were washed with water (15 mL), satd. aq. NaCl (15 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude residue by column chromatography (SiO_2, hexane/EtOAc, 3:1) gave **22** (512 mg, 0.73 mmol, 86%) as a mixture of diastereoisomers. Diastereoisomer A: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.71–7.66 (m, 4 H), 7.44–7.35 (m, 6 H), 7.22 (d, J = 8.8 Hz, 2 H), 7.04 (t, J = 1.5 Hz, 1 H), 6.86 (d, J = 8.6 Hz, 2 H), 4.96 (ddt, J = 7.7, 6.3, 1.4 Hz, 1 H), 4.91 (br. s, 1 H), 4.81 (br. s, 1 H), 4.69 (s, 1 H), 4.55–4.51 (m, 1 H), 4.44 (br. s, 2 H), 3.90 (d, J = 5.7 Hz, 1 H), 3.88–3.84 (m, 1 H), 3.80 (s, 3 H), 3.77 (dd, J = 11.1, 3.5 Hz, 1 H), 3.71 (dd, J = 11.2, 4.6 Hz, 1 H), 3.58 (dd, J = 8.6, 6.3 Hz, 1 H), 3.30 (s, 3 H), 3.28 (dd, J = 9.0, 1.1 Hz, 1 H), 3.22 (dd, J = 12.5, 6.3 Hz, 1 H), 2.42–2.34 (m, 2 H), 2.29 (dd, J = 14.4, 6.1 Hz, 1 H), 2.15–2.08 (m, 1 H), 1.90 (ddd, J = 13.8, 10.7, 3.1 Hz, 1 H), 1.78 (br. s, 3 H), 1.66 (ddd, J = 13.7, 9.7, 4.0 Hz, 1 H), 1.06 (br. s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.1, 159.6, 148.6, 140.0, 137.1, 135.9 (4 C), 135.8 (2 C), 133.54, 133.49, 129.8 (4 C), 129.5, 127.9 (2 C), 127.8 (2 C), 114.3, 114.1 (2 C), 107.1, 84.2, 80.1, 73.4, 71.7, 65.6, 64.7, 55.4, 54.5, 51.5, 41.5, 38.82, 38.77, 27.0 (3 C), 23.1, 19.4 ppm. HRMS (ESI): calcd. for $C_{41}H_{52}O_8SiNa$ $[M + Na]^+$ 723.3329; found 723.3325. IR: $\tilde{\nu}$ = 3386, 2967, 2930, 2889, 1773, 1752, 1467, 1365, 1277, 1034 cm^{-1}. $[\alpha]_D^{20}$ = –16.6, ($CHCl_3$, c = 0.8). R_f (hexane/EtOAc, 3:1) = 0.29. Diastereoisomer B: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = δ = 7.71–7.67 (m, 4 H), 7.44–7.35 (m, 6 H), 7.22–7.17 (m, 3 H), 6.87–6.84 (m, 2 H), 5.03–4.99 (m, 1 H), 4.91 (br. s, 1 H), 4.81 (br. s, 1 H), 4.70 (s, 1 H), 4.46 (d, J = 11.9 Hz, 1 H), 4.42–4.39 (m, 1 H), 4.40 (d, J = 11.6 Hz, 1 H), 3.85–3.81 (m, 2 H), 3.79 (s, 3 H), 3.79–3.75 (m, 2 H), 3.57 (dd, J = 8.5, 6.3 Hz, 1 H), 3.31 (s, 3 H), 3.27 (t, J = 9.1 Hz, 1 H), 2.49–2.44 (m, 1 H), 2.39 (dd, J = 14.5, 7.1 Hz, 1 H), 2.28 (dd, J = 14.5, 6.5 Hz, 1 H), 2.06–2.00 (m, 1 H), 1.95–1.88 (m, 1 H), 1.79 (br. s, 3 H), 1.65–1.60 (m, 1 H) 1.07 (br. s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.6, 159.1, 148.6, 139.9, 137.0, 135.9 (2 C), 135.8 (2 C), 133.6, 133.5, 129.9, 129.8, 129.7 (2 C), 129.4, 127.91 (2 C), 127.85 (2 C), 114.4, 114.1 (2 C), 107.3, 84.5, 80.1, 73.3, 71.6, 67.1, 64.8, 55.4, 54.6, 52.4, 41.6, 40.9, 39.9, 27.1 (3 C), 23.1, 19.5 ppm. HRMS (ESI): calcd. for $C_{41}H_{52}O_8SiNa$ $[M + Na]^+$ 723.3329; found 723.3334. IR: $\tilde{\nu}$ = 3407, 2975, 2936, 2904, 1779, 1746, 1467, 1392, 1292, 1015 cm^{-1}. $[\alpha]_D^{20}$ = –11.2, ($CHCl_3$, c = 0.65). R_f (hexane/EtOAc, 3:1) = 0.28.

Pyran 27: To a solution of **22** (1.27 g, 1.8 mmol) as a mixture of diastereoisomers in diisopropylethylamine (3.0 mL) was added dropwise chloromethyl methyl ether (MOMCl; 410 μL, 5.4 mmol). The resulting solution was stirred at room temperature for 16 h. Sat. aq. NH_4Cl (10 mL) and diethyl ether (20 mL) were added. The aqueous phase was separated and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with satd. aq. NaCl (20 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude oil gave the desired MOM-protected secondary alcohol (1.05 g, 1.4 mmol, 78%) as a pale yellow oil. Diastereoisomer A: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.72–7.66 (s, 4 H), 7.42–7.35 (s, 6 H), 7.23 (d, J = 8.6 Hz, 2 H), 7.13 (s, 1 H), 6.86 (d, J = 8.6 Hz, 2 H), 4.97 (t, J = 6.8 Hz, 1 H), 4.91 (br. s, 1 H), 4.89 (s, 1 H), 4.79 (br. s, 1 H), 4.51 (s, 2 H), 4.42–4.40 (m, 3 H), 3.79 (s, 3 H), 3.76 (s, 1 H), 3.70 (dd, J = 11.9, 5.5 Hz, 1 H), 3.36–3.34 (m, 2 H), 3.32 (s, 3 H), 3.24 (s, 3 H), 2.40 (dd, J = 14.4, 7.3 Hz, 1 H), 2.34–2.26 (m, 2 H), 1.99–1.93 (m, 1 H), 1.86 (t, J = 6.4 Hz, 2 H), 1.78 (s, 3 H), 1.73 (d, J = 15.3 Hz, 1 H), 1.05 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.6, 159.3, 149.7, 139.9, 135.9 (2 C), 135.8 (2 C), 135.6, 133.69, 133.66, 130.5, 129.8 (2 C), 129.5 (2 C), 127.80 (2 C), 127.78 (2 C), 114.5, 113.9 (2 C), 107.7, 96.0, 83.8, 79.9, 72.7, 71.1, 70.8, 64.8, 56.1, 55.4, 54.6, 52.2, 41.6, 38.7, 38.2, 27.0 (3 C), 23.1, 19.43 ppm. HRMS (ESI): calcd. for $C_{43}H_{56}O_9SiNa$ $[M + Na]^+$ 767.3591; found 767.3582. IR: $\tilde{\nu}$ = 2954, 2928, 2888, 1756, 1749, 1421, 1383, 1227, 1117, 987 cm^{-1}. $[\alpha]_D^{20}$ = –26.1, ($CHCl_3$, c = 0.5). R_f (hexane/EtOAc, 3:1) = 0.48. Diastereoisomer B: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.72–7.67 (m, 4 H), 7.44–7.36 (m, 6 H), 7.22 (d, J = 8.6 Hz, 2 H), 7.02 (s, 1 H), 6.85 (d, J = 8.6 Hz, 2 H), 4.95–4.91 (m, 1 H), 4.88 (s, 1 H), 4.87 (br. s, 1 H), 4.76 (br. s, 1 H), 4.47 (d, J = 6.8 Hz, 1 H), 4.45 (d, J = 6.7 Hz, 1 H), 4.40 (d, J = 11.8 Hz, 1 H), 4.37 (d, J = 11.6 Hz, 1 H), 4.31 (t, J = 6.5 Hz, 1 H), 3.91–3.87 (m, 1 H), 3.82 (dd, J = 11.3, 3.0 Hz, 1 H), 3.79 (s, 3 H), 3.69 (dd, J = 11.2, 5.2 Hz, 1 H), 3.34 (s, 3 H), 3.34–3.30 (m, 2 H), 3.23 (s, 3 H), 2.33–2.20 (m, 3 H), 1.99–1.94 (m, 2 H), 1.74 (s, 3 H), 1.31–1.27 (m, 1 H), 1.06 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 400 MHz): δ = 171.4, 159.3, 150.4, 139.8, 135.9 (2 C), 135.8 (2 C), 134.8, 133.8, 133.6, 130.5, 129.8, 129.7, 129.4 (2 C), 127.81 (2 C), 127.78 (2 C), 114.4, 113.9 (2 C), 107.4, 95.6, 84.3, 79.8, 72.8, 71.0, 70.8, 65.3, 55.9, 55.4, 54.6, 52.6, 41.4, 38.6, 38.5, 27.01 (3 C), 23.1, 19.4 ppm. HRMS (ESI): calcd. for $C_{43}H_{56}O_9SiNa$ $[M + Na]^+$ 767.3591; found 767.3596. IR: $\tilde{\nu}$ = 2954, 2928, 2888, 1756, 1749, 1421, 1383, 1227, 1117, 987 cm^{-1}. $[\alpha]_D^{20}$ = –23.4, ($CHCl_3$, c = 0.6). R_f (hexane/EtOAc, 3:1) = 0.41.

The MOM-protected mixture of diastereoisomers (100 mg, 0.13 mmol) was dissolved in *t*BuOH/H_2O (1:1, 1.4 mL), methylsulfonamide (12 mg, 0.28 mmol) and AD-mix-α (190 mg, 0.27 mmol) were added. The resulting mixture was stirred for 16 h, diethyl ether (10 mL) and satd. aq. $NaHS_2O_3$ (5 mL) were added. The aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic extracts were washed with satd. aq. NaCl (10 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the oil by column chromatography (SiO_2, hexane/EtOAc, 3:1) gave pyran **27** (80 mg, 0.11 mmol) in 83% yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.69–7.66 (m, 4 H), 7.44–7.36 (m, 6 H), 7.20 (d, J = 8.0 Hz, 2 H), 6.87–6.85 (m, 3 H), 5.15 (d, J = 5.5 Hz, 1 H), 5.04 (t, J = 6.1 Hz, 1 H), 4.84 (br. s, 1 H), 4.38 (br. s, 2 H), 3.90–3.86 (m, 1 H), 3.80 (br. s, 3 H), 3.76 (dd, J = 11.2, 3.9 Hz, 1 H), 3.72 (dd, J = 11.3, 3.7 Hz, 1 H), 3.47 (d, J = 11.3 Hz, 1 H), 3.36–3.22 (m, 3 H), 3.33 (s, 3 H), 2.63–2.48 (m, 2

H), 2.42 (dd, J = 14.4, 6.6 Hz, 1 H), 2.10–2.03 (m, 2 H), 1.98–1.91 (m, 1 H), 1.88 (br. s, 1 H), 1.12 (s, 3 H), 1.06 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 169.6, 159.4, 145.1, 135.82 (2 C), 135.77 (2 C), 133.51, 133.46, 130.4, 130.2, 129.90, 129.87, 129.4 (2 C), 127.9 (2 C), 127.8 (2 C), 114.0 (2 C), 107.4, 85.9, 83.4, 83.2, 77.4, 72.9, 70.5, 68.2, 64.9, 55.4, 54.8, 51.9, 41.3, 39.3, 34.0, 27.0 (3 C), 24.4, 19.4 ppm. HRMS (ESI): calcd. for $C_{41}H_{52}O_9SiNa$ $[M + Na]^+$ 739.3278; found 739.3287. IR: $\tilde{\nu}$ = 3461, 2943, 2917, 2875, 1763, 1741, 1453, 1399, 1202, 1016 cm^{-1}. $[\alpha]_D^{22}$ = –41.1, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 1:1) = 0.63.

(*S*)-2-Methyl-1-[(*S*)-oxiran-2-yl]but-3-yn-2-ol (36): Alkyne **33** (2.40 g, 13.0 mmol) was dissolved in a mixture of acetic acid (27 mL) and H_2O (1.4 mL) at room temperature. The clear colorless solution was stirred for 24 h and concentrated under reduced pressure. The remaining pale yellow residue was evaporated with toluene (3 × 10 mL) until the smell of AcOH was gone. Purification by flash column chromatography (SiO_2, hexane/EtOAc, 2:1) afforded the corresponding triol as a colorless gum (1.67 g, 89%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.42–4.38 (m, 1 H), 4.05 (br. s, 1 H), 3.68 (dd, J = 11.1, 2.9 Hz, 1 H), 3.51 (dd, J = 10.7, 6.9 Hz, 1 H), 3.33 (br. s, 1 H), 2.51 (s, 1 H), 2.11 (br. s, 1 H), 1.85 (dd, J = 14.4, 10.6 Hz, 1 H), 1.70 (dd, J = 14.4, 2.1 Hz, 1 H) 1.55 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 87.0, 72.3, 71.3, 68.3, 66.8, 43.9, 31.2 ppm. HRMS (ESI): calcd. for $C_7H_{12}O_3$ $[M]^+$ 144.0786; found 144.0791. IR: $\tilde{\nu}$ = 3298, 2983, 2359, 1418, 1133, 1109, 1058, 1036, 1016, 908 cm^{-1}. $[\alpha]_D^{20}$ = –7.9, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 1:2) = 0.19.

A solution of aforementioned triol (3.8 g, 26.4 mmol) in THF (40 mL) was added to a suspension of NaH (5.2 g, 132 mmol) in THF (100 mL) at 0 °C. The resulting heterogeneous mixture was stirred at 0 °C for 30 min, warmed to room temperature and left for 30 min before being cooled to 0 °C again. Solid trisylimidazole **34** (11.5 g, 34.3 mmol) was added in three portions under a constant stream of argon. The resulting reaction mixture was vigorously stirred at 0 °C for 1 h before it was quenched with H_2O (50 mL) and brine (20 mL). The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL), the combined organic phases were dried with $MgSO_4$, filtered and evaporated to give a brown oil. Purification by flash column chromatography (SiO_2, hexane/EtOAc, 1:1) afforded epoxide **36** as a colorless oil (2.36 g, 78%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.34–3.29 (m, 1 H), 3.07 (s, 1 H), 2.81 (dd, J = 4.8, 4.2 Hz, 1 H), 2.53 (dd, J = 4.9, 2.8 Hz, 1 H), 2.50 (s, 1 H), 2.02 (dd, J = 4.2, 14.2 Hz, 1 H), 1.71 (dd, J = 14.2, 7.6 Hz, 1 H), 1.52 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 87.0, 72.1, 67.2, 49.5, 46.7, 45.5, 30.2 ppm. HRMS (EI): calcd. for $C_6H_7O_2$ $[M – CH_3]^+$ 111.0446; found 111.0441. IR: $\tilde{\nu}$ = 3408, 3283, 2985, 2926, 1450, 1410, 1304, 1165, 1135, 1047 cm^{-1}. $[\alpha]_D^{20}$ = –20.5, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 1:2) = 0.58.

(*R*)-5-[(*S*)-2-Hydroxy-2-methylbut-3-ynyl]dihydrofuran-2(3*H*)-one (37): Sodium (1.08 g, 46.8 mmol) was added as small pieces under a constant stream of argon to EtOH (100 mL). After all solids were dissolved, diethylmalonate (14.2 mL, 94 mmol) was added dropwise. A solution of epoxide **36** (2.36 g, 18.7 mmol) in EtOH (100 mL) was added after stirring at room temperature for 15 min. The reaction mixture was left at this temperature for 16 h and quenched with satd. aq. NH_4Cl (50 mL) and H_2O (50 mL). The aqueous phase was extracted with CH_2Cl_2 (4 × 10 mL) and the combined organic phases were dried with $MgSO_4$, filtered and evaporated to give a pale yellow oil. Purification by flash column chromatography (SiO_2, hexane/EtOAc, 4:1) afforded a (1:1.45) diastereoisomeric mixture of the desired malonate as a colorless oil (3.86 g, 86%). Major diastereoisomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.98–4.91 (m, 1 H), 4.28 (dd, J = 7.12, 1.3 Hz, 1 H), 4.24 (dd, J = 7.1, 1.2 Hz, 1 H), 3.61 (dd, J = 11.2, 9.1 Hz, 1 H), 2.68 (dd, J = 9.1, 6.1 Hz, 1 H), 2.65 (dd, J = 9.1, 6.1 Hz, 1 H), 2.52 (s, 1 H), 2.43 (dd, J = 11.2, 9.8 Hz, 1 H), 2.18 (dd, J = 14.8, 8.7 Hz, 1 H), 2.07–2.03 (m, 1 H), 1.56 (s, 3 H), 1.31 (t, J = 1.4 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.2, 167.7, 86.5, 76.9, 72.8, 66.6, 62.4, 48.0, 46.8, 32.9, 30.5, 14.2 ppm. Minor diastereoisomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.19–5.12 (m, 1 H), 4.27 (d, J = 7.1 Hz, 1 H), 4.23 (d, J = 7.1 Hz, 1 H), 3.57 (dd, J = 9.6, 4.1 Hz, 1 H), 2.80 (dd, J = 6.7, 4.1 Hz, 1 H), 2.77 (dd, J = 6.7, 4.1 Hz, 1 H), 2.54 (s, 1 H), 2.39 (dd, J = 11.2, 9.8 Hz, 1 H), 2.20 (m, 1 H), 2.05–2.02 (m, 1 H), 1.55 (s, 3 H), 1.31 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.2, 167.7, 86.4, 77.9, 72.9, 66.6, 62.5, 48.1, 46.5, 32.9, 30.5, 14.2 ppm. HRMS (EI): calcd. for $C_{11}H_{13}O_5$ $[M – CH_3]^+$ 225.0763; found 225.0765. IR: $\tilde{\nu}$ = 3473, 2984, 1767, 1450, 1371, 1260, 1156, 1095, 1035, 1008 cm^{-1}. $[\alpha]_D^{20}$ = –33.5, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 1:1) = 0.51.

Aforementioned malonate (3.8 g, 15.83 mmol) was heated to 140 °C in the presence of LiCl (1.33 g, 31.66 mmol) in a mixture of DMSO (32 mL) and water (1 mL) and stirred for 5 h. The resulting brown mixture was cooled to room temperature and quenched with satd. aq. NH_4Cl (10 mL) and H_2O (30 mL). The aqueous phase was extracted with CH_2Cl_2 (7 × 10 mL) and the combined organic phases were dried with $MgSO_4$, filtered and evaporated to give a viscous brown oil. Purification by flash column chromatography (SiO_2, hexane/EtOAc, 3:1) afforded alcohol **37** as a colorless oil (2.5 g, 94%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.03–4.97 (m, 1 H), 2.72 (br. s, 1 H), 2.54 (dd, J = 9.9, 1.7 Hz, 1 H), 2.53 (d, J = 9.6 Hz, 1 H) 2.52 (s, 1 H), 2.47–2.39 (m, 1 H), 2.09–1.89 (m, 3 H), 1.55 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 176.3, 86.6, 78.5, 72.7, 66.9, 48.2, 30.5, 28.9, 28.3 ppm. HRMS (ESI): calcd. for $C_8H_9O_3$ $[M – CH_3]^+$ 153.0552; found 153.0557. IR: $\tilde{\nu}$ = 3430, 3280, 2985, 2934, 1760, 1357, 1173, 1124, 1035, 1008 cm^{-1}. $[\alpha]_D^{20}$ = –67.2, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 1:2) = 0.41.

(*R*)-5-[(*S*)-2-Methyl-2-(trimethylsilyloxy)penta-3,4-dienyl]dihydrofuran-2(3*H*)-one (38): A heterogeneous mixture of alcohol **37** (2.5 g, 14.9 mmol), paraformaldehyde (1.29 g, 44.6 mmol), iPr$_2$NH (3.2 mL, 22.32 mmol) and CuBr (1.07 g, 7.45 mmol) in 1,4-dioxane (30 mL) was stirred at 125 °C for 6 h. The resulting greenish reaction mixture was cooled to room temperature, filtered through a pad of Celite followed by the addition of satd. aq. NH_4Cl (10 mL) and H_2O (30 mL). The aqueous phase was extracted with CH_2Cl_2 (5 × 10 mL) and the combined organic phases were washed with satd. aq. NaCl (10 mL), dried with $MgSO_4$, filtered and evaporated to give a brown oil. Purification by flash column chromatography (SiO_2, hexane/EtOAc, 2:1) afforded the desired allene as a colorless oil (1.9 g, 86%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.31 (t, J = 6.6 Hz, 1 H), 4.90 (d, J = 6.6 Hz, 2 H), 4.83–4.76 (m, 1 H), 2.51 (d, J = 9.7 Hz, 1 H), 2.49 (d, J = 9.7 Hz, 1 H), 2.40–2.32 (m, 1 H), 2.24 (br. s, 1 H), 2.02 (dd, J = 14.7, 8.5 Hz, 1 H), 1.94–1.82 (m, 2 H), 1.38 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 205.5, 176.9, 99.4, 79.1, 78.1, 70.4, 47.7, 29.4, 28.9, 28.7 ppm. HRMS (EI): calcd. for $C_{10}H_{12}O_2$ $[M]^+$ 164.0839; found 164.0837. IR: $\tilde{\nu}$ = 3423, 2978, 2934, 1956, 1760, 1727, 1457, 1419, 1357, 1289, 1223, 1179, 1114, 1075, 1012, 986, 917, 850 cm^{-1}. $[\alpha]_D^{20}$ = –49.3, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 1:1) = 0.18.

2,6-Lutidine (8.0 mL, 69.1 mmol) and TMSOTf (6.3 mL, 34.6 mmol) were sequentially added to a solution of the tertiary allenic alcohol (4.2 g, 23.0 mmol) in THF (50 mL) at 0 °C. After removal of the cooling bath and additional 30 min, the reaction was quenched with satd. aq. NH_4Cl (50 mL). The aqueous phase was extracted with hexanes (10 mL) and the combined organic

phases were washed with satd. aq. NaCl (20 mL), dried with $MgSO_4$, filtered and evaporated to give a crude colorless oil. Purification by flash column chromatography (SiO_2, hexane/EtOAc, 4:1) afforded lactone **38** as a colorless oil (5.1 g, 87%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.25 (t, J = 6.6 Hz, 1 H), 4.82 (d, J = 6.6 Hz, 2 H), 4.76–4.70 (m, 1 H), 2.50 (dd, J = 8.4, 2.5 Hz, 1 H), 2.48 (d, J = 9.7 Hz, 1 H), 2.36 (sext, J = 6.5 Hz, 1 H), 1.99–1.84 (m, 3 H), 1.39 (s, 3 H), 0.10 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 206.3, 177.4, 99.8, 78.1, 77.9, 72.8, 49.4, 29.8, 29.0, 27.7, 2.4 (3 C) ppm. HRMS (ESI): calcd. for $C_{13}H_{22}O_3SiNa$ [M + Na]$^+$ 277.1233; found 277.1236. IR: $\tilde{\nu}$ = 2955, 1956, 1773, 1249, 1154, 1110, 1078, 1001, 982, 916, 836 cm^{-1}. $[\alpha]_D^{20}$ = –42.3, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 1:1) = 0.64.

2-Phenylselenyl-γ-butyrolactone 32: LiHMDS (1.0 M in toluene, 6.5 mL, 64.9 mmol) and TMSCl (0.83 mL, 64.9 mmol) were sequentially added to a solution of lactone **39** (1.50 g, 5.9 mmol) in THF (30 mL) at –78 °C. After 2 h at –78 °C a solution of PhSeCl (1.24 g, 64.9 mmol) in THF (30 mL) was added over 10 min. After 30 min at –78 °C, the reaction was quenched with satd. aq. NH_4Cl (40 mL). The aqueous phase was extracted with diethyl ether (3 × 20 mL) and the combined organic phases were washed with satd. aq. NaCl (40 mL), dried with $MgSO_4$, filtered and evaporated to give a colorless oil. Purification by flash column chromatography (SiO_2, hexane/EtOAc, 20:1) afforded a 1:1.5 diastereoisomeric mixture of lactone **32** as a colorless oil (2.0 g, 83%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.71–7.63 (m, 3 H), 7.41–7.29 (m, 4.6 H), 5.20 (t, J = 6.6 Hz, 1 H), 5.19 (t, J = 6.6 Hz, 0.5 H), 4.81 (d, J = 6.6 Hz, 3 H), 4.70–4.62 (m, 0.5 H), 4.57–4.48 (m, 1 H), 4.02 (dd, J = 10.1, 9.1 Hz, 0.5 H), 3.91 (dd, J = 6.4, 4.0 Hz, 1 H), 2.79–2.69 (m, 0.5 H), 2.41–2.35 (m, 2 H), 2.01 (dt, J = 13.3, 10.0 Hz, 0.5 H), 1.92 (dd, J = 14.3, 6.3 Hz, 1 H), 1.86–1.76 (m, 1.5 H), 1.70 (dd, J = 14.4, 5.1 Hz, 1 H), 1.35 (s, 1.5 H), 1.32 (s, 3 H), 0.09 (s, 9 H), 0.08 (s, 4.5 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 206.1, 175.8, 136.0, 135.9, 135.6, 128.7, 127.1, 126.8, 99.6, 99.6, 77.8, 76.6, 76.4, 72.6, 49.2, 48.9, 38.3, 37.0, 27.5, 2.2 (3 C) ppm. HRMS (ESI): calcd. for $C_{19}H_{26}O_3SeSiNa$ [M + Na]$^+$ 433.0709; found 433.0715. IR: $\tilde{\nu}$ = 2956, 1956, 1769, 1483, 1251, 1112, 1022, 840, 740 cm^{-1}. $[\alpha]_D^{20}$ = –53.5, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 8:1) = 0.27 (major), 0.32 (minor).

Butenolide 39: A freshly prepared solution of lithium diisopropylamide (LDA; 810 μL, 0.5 M THF, 0.40 mmol; see **22**) was added dropwise to a solution of **32** (153 mg, 0.37 mmol) in THF (1.5 mL) at –78 °C. The resulting pale yellow solution was stirred for 30 min before **8** (190 mg, 0.34 mmol) in THF (2 mL) was added over 10 min. The reaction mixture was gradually warmed to –40 °C over 2 h. Sat. aq. NH_4Cl (10 mL) and diethyl ether (10 mL) were added. The aqueous phase was separated and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with water (15 mL) and satd. aq. NaCl (15 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. NMR spectroscopic analysis of the crude mixture of four diastereoisomers indicated full consumption of **32**. The crude mixture was used in the next step without further purification.

The crude oil was dissolved in a mixture of CH_2Cl_2 (3.5 mL) and pyridine (350 μL) and cooled to 0 °C. Hydrogen peroxide (230 μL, 2.0 mmol) was added and the resulting biphasic mixture was stirred at that temperature for 1 h. Sat. aq. $Na_2S_2O_3$ (10 mL) and diethyl ether (20 mL) were added and the resulting biphasic mixture was stirred for another hour. The aqueous phase was extracted with diethyl ether (2 × 10 mL). The combined organic layers were washed with satd. aq. $CuSO_4$ (2 × 15 mL) and water (15 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography (SiO_2, hexane/EtOAc, 6:1) afforded desired butyrolactone **39** (224 mg, 0.28 mmol) as an inseparable mixture of diastereoisomers. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.74–7.67 (m, 4 H), 7.44–7.37 (m, 6 H), 7.25–7.20 (m, 3 H), 7.07–7.02 (m, 0.4 H), 6.89–6.85 (m, 2 H), 5.27 (t, J = 6.6 Hz, 1 H), 5.21–5.15 (m, 1 H), 4.86–4.84 (m, 1 H), 4.72 (d, J = 8.0 Hz, 1 H), 4.57–4.51 (m, 0.5 H), 4.48–4.40 (m, 2.5 H), 4.06 (d, J = 4.2 Hz, 0.5 H), 3.90–3.84 (m, 1.5 H), 3.80–3.68 (m, 4 H), 3.62–3.56 (m, 1 H), 3.31–3.27 (m, 4 H), 3.24–3.21 (m, 0.5 H), 2.49–2.40 (m, 1 H), 2.19–2.14 (m, 0.5 H), 2.07–2.01 (m, 0.5 H), 1.95–1.88 (m, 2 H), 1.82–1.61 (m, 2 H), 1.47 (s, 3 H), 1.09 (s, 4 H), 1.08 (s, 5 H), 0.15 (s, 5 H), 0.14 (s, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 206.3, 172.5, 172.4, 159.6, 159.5, 150.4, 150.2, 136.0, 135.9, 135.8, 135.8, 135.7, 133.6, 133.5, 133.42, 133.38, 133.3, 129.82, 129.80, 129.78, 129.6, 127.9, 127.83, 127.80, 127.77, 114.1, 114.0, 107.3, 107.1, 99, 84.5, 84.2, 78.8, 78.7, 78.2, 78.1, 73.3, 73.2, 72.82, 72.77, 71.7, 71.5, 66.9, 65.7, 64.7, 64.5, 55.3, 54.5, 54.4, 52.4, 51.5, 47.1, 47.0, 40.7, 40.0, 38.8, 38.6, 27.78, 27.76, 27.02, 26.98, 19.41, 19.39, 2.39 ppm. HRMS (ESI): calcd. for $C_{46}H_{62}O_9Si_2Na$ [M + Na]$^+$ 837.3830; found 837.3823. IR: $\tilde{\nu}$ = 3433, 2971, 2921, 2879, 1776, 1429, 1227, 1164, 1023, 973 cm^{-1}. $[\alpha]_D^{20}$ = –13.7, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 2:1) = 0.51.

Cage-Shaped Cyclobutane 40: A 1:1 diastereoisomeric mixture of **39** (25 mg, 0.03 mmol) was dissolved in freshly degassed cyclohexane (13 mL) and placed 1 cm in front of UV-B lamps. The resulting colorless solution was irradiated for 1.5 h. The volatiles were removed under reduced pressure and the resulting yellow oil was subjected to column chromatography (SiO_2, hexane/EtOAc, 8:1) leading to the isolation of a diastereoisomeric mixture of **40** (3 mg, 0.003 mmol, 10%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.71–7.66 (m, 4 H), 7.44–7.35 (m, 6 H), 7.21 (d, J = 8.8 Hz, 2 H), 6.85 (d, J = 8.6 Hz, 2 H), 5.31 (dd, J = 2.6, 1.2 Hz, 1 H), 5.17–5.11 (m, 2 H), 4.75 (br. s, 1 H), 4.45 (d, J = 11.7 Hz, 1 H), 4.40 (d, J = 11.8 Hz, 1 H), 4.01–3.99 (m, 1 H), 3.90–3.83 (m, 1 H), 3.80 (s, 3 H), 3.76–3.74 (m, 2 H), 3.49 (d, J = 2.9 Hz, 1 H), 3.46–3.41 (m, 1 H), 3.30 (s, 3 H), 3.30–3.25 (m, 2 H), 3.09–3.06 (m, 1 H), 2.45 (qd, J = 12.4, 1.8 Hz, 1 H), 2.26–2.20 (m, 1 H), 2.06–1.99 (m, 1 H), 1.92 (dd, J = 14.7, 5.3 Hz, 1 H), 1.65 (td, J = 19.0, 4.2 Hz, 1 H), 1.42–1.38 (m, 4 H), 1.06 (s, 9 H), 0.12 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 177.2, 159.5, 144.8, 135.91 (2 C), 135.86 (2 C), 133.7, 133.5, 130.0, 129.80, 129.78, 129.5 (2 C), 127.82 (2 C), 127.79 (2 C), 114.5, 114.0 (2 C), 107.4, 84.9, 83.9, 83.7, 73.0, 71.5, 69.7, 65.5, 57.90, 57.88, 55.4, 54.6, 51.7, 49.5, 44.4, 39.6, 35.2, 27.0 (3 C), 23.5, 19.4, 2.44 (3 C) ppm. HRMS (ESI): calcd. for $C_{46}H_{62}O_9Si_2Na$ [M + Na]$^+$ 837.3830; found 837.3809. IR: $\tilde{\nu}$ = 3433, 2971, 2921, 2879, 1776, 1429, 1227, 1164, 1023, 973cm^{-1}. $[\alpha]_D^{20}$ = –33.9, ($CHCl_3$, c = 0.08). R_f (hexane/EtOAc, 2:1) = 0.60.

Ethyl 2-[(3a*R*,5S,6R,6aR)-5-(Hydroxymethyl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl]acetate (42): A mixture of diacetone-D-glucofuranose (34.4 g, 127.3 mmol) and IBX (82 g, 292.8 mmol) in EtOAc (1 L) was heated to reflux for 26 h. After the thick suspension reached room temperature, hexane (500 mL) was added and the resulting suspension was filtered through a pad of Celite. The volatiles were removed under reduced pressure and the crude ketone (35.4 g) was used in the olefination reaction without further purification. R_f (hexane/EtOAc, 1:1) = 0.25.

To a solution of PPh_3 (55 g, 209.6 mmol) in EtOAc (360 mL) was added a solution of methyl bromoacetate (32.3 g, 211 mmol) in EtOAc (90 mL) through a dropping funnel over 45 min at 0 °C. The resulting thick white suspension was warmed to room temperature and stirred for 20 h. The solids were collected by filtration, dissolved in CH_2Cl_2 (400 mL) in a separatory funnel and vigor-

ously shaken with 1 M NaOH (300 mL) for 30 min. The aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The organic phases were washed with satd. aq. NaCl (200 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure yielding the Wittig ylide (70 g, 209.3 mmol) as a white solid after extensive drying under high vacuum for 2 h.

A solution of the ylide (50.4 g, 150.7 mmol) in $CHCl_3$ (500 mL) was added through cannula to a solution of the ketone (35.4 g, 137.1 mmol) in $CHCl_3$ (500 mL) at 0 °C over 30 min. After the addition, the reaction mixture was warmed to room temperature and stirred for 16 h resulting in a dark red solution. The volatiles were evaporated and the dark gum was filtered through a short pad of silica (hexane/EtOAc, 2:1). After evaporation the orange gum (40 g, 127.3 mmol, 93%) was used in the next step without further purification. R_f (hexane/EtOAc, 1:1) = 0.70.

To a solution of the α,β-unsaturated ester (20 g, 63.6 mmol) in EtOH (250 mL) was added Raney nickel 2400 (10 g). The round-bottomed flask was sealed with a rubber septum. A rubber balloon charged with H_2 was connected to a needle that reached into the solution. A gas outlet was installed and the flow of the gas was regulated with a hose clamp to about 4 bubbles per second. The round-bottomed flask was placed in an ultra sound bath and treated for 2 h in a fume hood. The balloon was replaced by a balloon filled with argon and the reaction mixture was purged in the ultra sound bath for 30 min. The nickel catalyst was filtered off through a pad of Celite, which was washed with EtOH (2 × 100 mL). Removal of the solvent under reduced pressure gave the desired product as a clean single diastereoisomer (20.0 g, 63.2 mmol, 99%) as a colorless gum, which was used in the next reaction without further purification. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.77 (d, J = 3.8 Hz, 1 H), 4.81 (t, J = 4.2 Hz, 1 H), 4.19–4.13 (m, 2 H), 4.12–4.09 (m, 1 H), 4.00–3.97 (m, 1 H), 3.96–3.92 (m, 1 H), 3.69 (dd, J = 9.9, 7.5 Hz, 1 H), 2.81 (dd, J = 17.4, 4.2 Hz, 1 H), 2.65 (dd, J = 17.4, 10.4 Hz, 1 H), 2.36–2.29 (m, 1 H), 1.50 (s, 3 H), 1.41 (s, 3 H), 1.33 (s, 3 H), 1.31 (s, 3 H), 1.26 (t, J = 7.15 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.5, 112.0, 109.8, 105.2, 81.7 81.1, 78.0, 68.0, 60.7, 44.7, 30.2, 26.9, 26.8, 26.5, 25.4, 14.4 ppm. HRMS (ESI): calcd. for $C_{16}H_{26}O_7Na$ [M + Na]$^+$ 353.1576; found 353.1586. IR: $\tilde{\nu}$ = 2986, 2938, 1734, 1381, 1333, 1241, 1213, 1065, 1016, 847 cm^{-1}. $[\alpha]_D^{22}$ = +69.0, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 1:1) = 0.70.

The crude diacetonide (20.0 g, 63.2 mmol) was dissolved in AcOH/H_2O (2:1, 60 mL). After all of the crude gum was dissolved the solution was stirred at room temperature for 18 h. The volatiles were removed under reduced pressure and the resulting slightly yellow residue was co-evaporated with toluene (5 × 50 mL) until the smell of acetic acid was gone. The desired vicinal diol (17.7 g, 63.2 mmol, 100%) was used in the next reaction without further purification. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.78 (d, J = 3.7 Hz, 1 H), 4.78 (dd, J = 4.6, 4.1 Hz, 1 H), 4.20–4.12 (m, 2 H), 3.84 (dd, J = 10.0, 5.7 Hz, 1 H), 3.80–3.76 (m, 1 H), 3.73–3.68 (m, 2 H), 2.78 (br. s, 1 H), 2.72 (d, J = 6.9 Hz, 2 H), 2.42–2.35 (m, 1 H), 2.25 (br. s, 1 H), 1.49 (s, 3 H), 1.31 (s, 3 H), 1.27 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.1, 112.1, 104.9, 81.9, 81.6, 73.6, 64.1, 61.0, 43.3, 30.6, 26.9, 26.6, 14.4 ppm. HRMS (ESI): calcd. for $C_{13}H_{22}O_7Na$ [M + Na]$^+$ 313.1263; found 313.1256. IR: $\tilde{\nu}$ = 3438, 2924, 2854, 1732, 1460, 1377, 1218, 1168, 1016, 772 cm^{-1}. $[\alpha]_D^{20}$ = +10.0, ($CHCl_3$, c = 0.35). R_f (hexane/EtOAc, 1:1) = 0.18.

The gum (17.7 g, 63.2 mmol, 100%) was dissolved in MeOH (160 mL) and H_2O (20 mL). The solution was cooled to 0 °C and $NaIO_4$ (13.6 g, 63.6 mmol) was added under vigorous stirring. After 1 h at that temperature, glucose (0.5 g, 2.77 mmol) was added to the thick suspension. After 15 min the solids were removed by filtration through a pad of Celite. The residue was washed with MeOH (50 mL). The combined liquids were cooled to 0 °C followed by the careful addition of $NaBH_4$ (3.50 g, 92.5 mmol) in three portions. After 1 h, acetic acid was added carefully until a pH 6 for the solution was reached. The volatiles were removed and the residue was subjected to column chromatography (SiO_2, hexane/EtOAc, 1:1) yielding desired α-D-ribofuranose **42** (13.5 g, 51.8 mmol, 82%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.82 (d, J = 3.6 Hz, 1 H), 4.78 (dd, J = 4.3, 3.8 Hz, 1 H), 4.22–4.11 (m, 2 H), 3.90–3.85 (m, 2 H), 3.59–3.54 (m, 1 H), 2.70 (dd, J = 16.5, 8.1 Hz, 1 H), 2.48–2.41 (m, 1 H), 2.38 (dd, J = 16.5, 5.4 Hz, 1 H), 2.04 (br. s, OH), 1.50 (s, 3 H), 1.32 (s, 3 H), 1.27 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.4, 111.9, 104.9, 81.8, 81.5, 61.6, 61.0, 39.8, 30.0, 26.8, 26.5, 14.3 ppm. HRMS (ESI): calcd. for $C_{12}H_{20}O_6Na$ [M + Na]$^+$ 283.1158; found 283.1153. IR: $\tilde{\nu}$ = 3474, 2985, 2937, 1731, 1374, 1214, 1167, 1112, 1013, 874 cm^{-1}. $[\alpha]_D^{20}$ = +62.9, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 1:1) = 0.33.

(3a*R*,4*S*,6*R*,6a*R*)-4-{[(*tert*-Butyldimethylsilyl)oxy]methyl}-6-methoxytetrahydrofuro[3,4-*b*]furan-2(3*H*)-one (43): A mixture of trifluoroacetic acid (60 mL) and α-D-ribofuranose **42** (9.8 g, 37.7 mmol) in MeOH (370 mL) was heated to reflux for 16 h. The resulting pale yellow solution was concentrated in vacuo and the remaining oil was co-evaporated with toluene (3 × 50 mL). Purification by flash column chromatography (SiO_2, hexane/EtOAc, 1:1 → 1:2) afforded the desired lactone as a pale yellow oil (5.7 g, 81%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.08 (s, 1 H), 4.89 (d, J = 6.8 Hz, 1 H), 4.23 (dd, J = 3.8 Hz, 1 H), 3.73 (dd, J = 12.2, 2.9 Hz, 1 H), 3.57 (dd, J = 12.2, 4.2 Hz, 1 H), 3.46 (s, 3 H), 3.25–3.19 (m, 1 H), 2.86 (dd, J = 18.4, 9.9 Hz, 1 H), 2.52 (dd, J = 18.4, 3.9 Hz, 1 H), 1.25 (br. s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 175.5, 107.8, 89.6, 87.7, 64.7, 55.9, 38.1, 34.1 ppm. HRMS (ESI): calcd. for $C_8H_{12}O_5Na$ [M + Na]$^+$ 211.0582; found 211.0582. IR: $\tilde{\nu}$ = 3412, 2923, 1776, 1454, 1377, 1161, 1106, 1049, 959, 813 cm^{-1}. $[\alpha]_D^{25}$ = –40.3, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 1:4) = 0.29.

To a solution of the primary alcohol (4.1 g, 21.8 mmol) and imidazole (3.6 g, 52.3 mmol) in CH_2Cl_2 (200 mL) was added *tert*-butyldimethylsilyl chloride (3.9 g, 26.1 mmol) as a solid in three portions under an argon stream at room temperature. After stirring for 2 h, the resulting pale yellow reaction mixture was quenched by the addition of water (100 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were washed with water (100 mL) and aq. satd. NaCl (100 mL), dried with $MgSO_4$ and filtered. After evaporation of all volatiles flash column chromatography (SiO_2, hexane/EtOAc, 3:1) of the residue gave lactone **43** (6.0 g, 91%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.06 (s, 1 H), 4.81 (d, J = 6.4 Hz, 1 H), 4.00 (ddd, J = 8.3, 5.1, 4.7 Hz, 1 H), 3.74 (dd, J = 9.8, 5.3 Hz, 1 H), 3.52 (dd, J = 9.8, 8.3 Hz, 1 H), 3.34 (s, 3 H), 3.05–3.00 (m, 1 H), 2.82 (dd, J = 18.1, 9.3 Hz, 1 H), 2.48 (dd, J = 18.1, 2.0 Hz, 1 H), 0.88 (s, 9 H), 0.59 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 175.8, 107.4, 88.1, 87.3, 65.8, 55.0, 40.3, 34.5, 25.9 (3 C), 18.3, –5.2, –5.3 ppm. HRMS (ESI): calcd. for $C_{14}H_{26}O_5SiNa$ [M + Na]$^+$ 325.1447; found 325.1448. IR: $\tilde{\nu}$ = 2953.6, 2930.1, 2857.2, 1787.9, 1471.8, 1254.4, 1154.0, 1106.7, 1004.4, 837.7 cm^{-1}. $[\alpha]_D^{20}$ = –88.3, ($CHCl_3$, c = 0.6). R_f (hexane/EtOAc, 1:2) = 0.73.

***tert*-Butyl[((2*S*,3*R*,4*R*,5*R*)-5-methoxy-4-[(triethylsilyl)oxy]-3-{2-[(triethylsilyl)oxy]ethyl}tetrahydrofuran-2-yl)methoxy]dimethylsilane (44):** A solution of lactone **43** (11.7 g, 38.8 mmol) in diethyl ether (200 mL) was added to a suspension of freshly powdered lithium aluminium hydride pellets (2.5 g, 66.1 mmol) in anhydrous diethyl ether (100 mL) at 0 °C over 30 min under vigorous stirring in a 1 L

round-bottomed flask. After 1 h, satd. aq. NH_4Cl (200 mL) was carefully added at 0 °C followed by the addition of satd. aq. Na/K tartrate (200 mL). The resulting turbid biphasic system was stirred for 2 h and warmed to room temperature. The aqueous phase was separated and extracted with diethyl ether (5× 100 mL). The combined organic phases were washed with satd. aq. NaCl (200 mL) and dried with $MgSO_4$. After evaporation of all volatiles under reduced pressure the desired diol was isolated as colorless sticky oil (11.9 g, quant.) that was used without further purification in the next reaction. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.83 (s, 1 H), 4.18 (d, J = 4.6 Hz, 1 H), 3.95 (dt, J = 8.6, 5.5 Hz, 1 H), 3.86–3.81 (m, 1 H), 3.74 (dd, J = 10.3, 5.2 Hz, 1 H), 3.73–3.67 (m, 1 H), 3.62 (dd, J = 10.3, 5.8 Hz, 1 H), 3.33 (s, 3 H), 3.00 (br. s, 1 H), 2.29 (br. s, 1 H), 2.23–2.17 (m, 1 H), 1.92–1.74 (m, 2 H), 0.90 (s, 9 H), 0.07 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 109.0, 84.3, 77.2, 66.8, 62.0, 54.6, 43.9, 28.9, 26.1 (3 C), 18.5, –5.24, –5.26 ppm. HRMS (ESI): calcd. for $C_{14}H_{30}O_5SiNa$ $[M + Na]^+$ 329.1760; found 329.1749. IR: $\tilde{\nu}$ = 3394, 2929, 2857, 1471, 1254, 1103, 1061, 1036, 951, 837 cm^{-1}. $[\alpha]_D^{20}$ = –28.2, ($CHCl_3$, c = 1.1). R_f (hexane/EtOAc, 1:1) = 0.19.

To a solution of the crude diol (10.9 g, 35.6 mmol) in CH_2Cl_2 (150 mL) and imidazole (9.7 g, 142.5 mmol) was added triethylsilyl chloride (13.1 mL, 78.2 mmol) through a syringe over 15 min. The resulting pale yellow solution was left at room temperature for 2 h, during which a white precipitate formed. Sat. aq. NH_4Cl (100 mL) was added and stirring was continued for another 30 min. The aqueous layer was separated and extracted with diethyl ether (3× 50 mL). The combined organic phases were washed with water (100 mL), satd. aq. NaCl (100 mL) and dried with $MgSO_4$. After removal of all volatiles a pale yellow oil was obtained that yielded tetrahydrofuran **44** (17.3 g, 91%) as a colorless oil after flash column chromatography (SiO_2, hexane/EtOAc, 20:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.67 (s, 1 H), 4.04 (d, J = 4.4 Hz, 1 H), 3.93 (ddd, J = 9.3, 5.4, 3.9 Hz, 1 H), 3.71 (dd, J = 10.8, 3.8 Hz, 1 H), 3.67–3.55 (m, 3 H), 3.32 (s, 3 H), 2.16–2.09 (m, 1 H), 1.89–1.80 (m, 1 H), 1.61–1.53 (m, 1 H), 0.96 (dt, J = 8.1, 4.3 Hz, 18 H), 0.91 (s, 9 H), 0.65–0.58 (m, 12 H), 0.07 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 109.3, 84.8, 77.3, 66.3, 61.8, 54.5, 40.2, 28.9, 26.1 (3 C), 18.6, 6.9 (6 C), 5.1 (3 C), 4.6 (3 C), –5.2 (2 C) ppm. HRMS (ESI): calcd. for $C_{26}H_{58}O_5Si_3Na$ $[M + Na]^+$ 557.3490; found 557.3477. IR: $\tilde{\nu}$ = 2953, 2877, 1461, 1251, 1102, 1041, 1003, 958, 834, 775 cm^{-1}. $[\alpha]_D^{20}$ = +6.9, ($CHCl_3$, c = 1.2). R_f (hexane/EtOAc, 10:1) 0.36.

2-((2*S*,3*R*,4*R*,5*R*)-2-{[(*tert*-Butyldimethylsilyl)oxy]methyl}-5-methoxy-4-[(triethylsilyl)oxy]tetrahydrofuran-3-yl)acetaldehyde (45): To a solution of oxalyl chloride (2.0 mL, 23.4 mmol) in CH_2Cl_2 (20 mL) in a flame-dried 50 mL round-bottomed flask equipped with a bubbler, dimethyl sulfoxide (3.4 mL, 48.1 mmol) was added dropwise over 5 min at –78 °C. After the evolution of gas had ceased the bubbler was removed and stirring was continued for a further 10 min at –78 °C. Tetrahydrofuran **44** (2.5 g, 4.7 mmol) dissolved in CH_2Cl_2 (20 mL) was added to the resulting reaction mixture through a syringe over 10 min. After 3 h at –78 °C an intermediate formed [TLC, hexane/EtOAc (3:1), R_f = 0.18]. The reaction mixture was dropwise treated with Et_3N (6.5 mL, 46.7 mmol). The turbid solution was quenched by the addition of satd. aq. $NaHCO_3$ (20 mL) after 4 h and warmed to room temperature. The aqueous layer was separated and extracted with diethyl ether (3× 20 mL). The combined organic phases were washed with water (30 mL) and satd. aq. NaCl (30 mL) and dried with $MgSO_4$. Removal of the volatiles under reduced pressure and flash column chromatography (SiO_2, hexane/EtOAc, 20:1) of the remaining residue gave aldehyde **45** (1.9 g, 97%) as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.79 (s, 1 H), 4.69 (s, 1 H), 4.22 (d, J = 4.4 Hz, 1 H), 3.94 (ddd, J = 8.4, 5.5, 0.7 Hz, 1 H), 3.74 (dd, J = 10.3, 4.9 Hz, 1 H), 3.59 (dd, J = 10.3, 6.1 Hz, 1 H), 3.32 (s, 3 H), 2.79 (ddd, J = 17.3, 8.6, 1.0 Hz, 1 H), 2.64–2.76 (m, 1 H), 2.58–2.53 (m, 1 H), 0.94 (t, J = 8.0 Hz, 9 H), 0.89 (s, 9 H), 0.58 (ddd, J = 17.3, 7.5, 0.9 Hz, 6 H), 0.06 (s, 3 H), 0.06 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 201.2, 109.5, 83.3, 77.1, 66.4, 54.7, 41.0, 39.4, 26.1 (3 C), 18.5, 6.9 (3 C), 4.9 (3 C), –5.3 (2 C) ppm. HRMS (ESI): calcd. for $C_{20}H_{42}O_5Si_2Na$ $[M + Na]^+$ 441.2468; found 441.2476. IR: $\tilde{\nu}$ = 2955, 2929, 2879, 1728, 1462, 1254, 1127, 1108, 1039, 837 cm^{-1}. $[\alpha]_D^{20}$ = +1.4, ($CHCl_3$, c = 1.2). R_f (hexane/EtOAc, 8:1) = 0.68.

Butenolide 46: LiHMDS (720 μL, 1.0 M in toluene, 5.6 mmol) was added to a solution of butyrolactone **32** (2.0 g, 4.9 mmol) in THF (22 mL) at –40 °C over 10 min. After 30 min a solution of aldehyde **45** (2.05 mg, 4.9 mmol) in THF (25 mL) was added dropwise over 20 min. After 2 h at –40 °C the reaction mixture was quenched by the addition of satd. aq. NH_4Cl (30 mL) and CH_2Cl_2 (30 mL). The aqueous phase was separated and extracted with CH_2Cl_2 (3× 40 mL). The combined organic phases were washed with water (40 mL) and satd. aq. NaCl (40 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. NMR spectroscopic analysis of the crude pale yellow oil indicated consumption of butyrolactone **32** and showed a complex mixture of four diastereoisomers (4.5 g, 4.9 mmol) and traces of aldehyde **45**.

H_2O_2 (3.7 mL, 32.6 mmol) was added under vigorous stirring to the aforementioned complex mixture in CH_2Cl_2 (50 mL) and pyridine (5 mL) at 0 °C. The resulting biphasic mixture was left at this temperature for 1 h, quenched by the addition of satd. aq. NaS_2O_3 (30 mL) and stirred for an additional 30 min. The aqueous phase was separated and extracted with CH_2Cl_2 (3× 30 mL). After the combined organic phases were washed with water (50 mL) and satd. aq. NaCl (50 mL), $MgSO_4$ was added followed by filtration. Evaporation of the volatiles and flash column chromatography (SiO_2, hexane/EtOAc, 12:1) of the remaining oil yielded desired butenolide **46** as an inseparable 1:1 mixture as a pale yellow oil (3.01 g, 4.5 mmol, 92%). Diastereoisomer A: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.30 (t, J = 1.5 Hz, 1 H), 5.26 (t, J = 6.7 Hz, 1 H), 5.24–5.20 (m, 1 H), 4.84 (d, J = 6.5 Hz, 1 H), 4.69 (s, 1 H), 4.51–4.47 (m, 1 H), 4.16 (d, J = 4.6 Hz, 1 H), 4.12 (d, J = 7.1 Hz, 1 H), 4.06 (dt, J = 8.7, 5.3 Hz, 1 H), 3.77 (t, J = 4.7 Hz, 1 H), 3.72–3.69 (m, 1 H), 3.69–3.65 (m, 1 H), 3.31 (s, 3 H), 2.42–2.35 (m, 1 H), 1.98–1.90 (m, 2 H), 1.81 (dd, J = 14.3, 7.3 Hz, 1 H), 1.69–1.61 (m, 1 H), 1.47 (s, 3 H), 0.95 (t, J = 7.9 Hz, 9 H), 0.91 (s, 9 H), 0.73 (q, J = 7.7 Hz, 6 H), 0.14 (s, 9 H), 0.1 (br. s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.7, 150.1, 136.0, 109.0, 99.7, 83.9, 79.0, 78.6, 78.2, 78.0, 72.8, 66.7, 66.2, 54.7, 47.1, 41.7, 32.1, 27.8, 26.1 (3 C), 18.6, 6.9 (3 C), 5.0 (3 C), 2.4 (3 C), –5.3 (2 C) ppm. Diastereoisomer B: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.31 (t, J = 1.4 Hz, 1 H), 5.26 (t, J = 6.7 Hz, 1 H), 5.24–5.20 (m, 1 H), 4.85 (d, J = 6.7 Hz, 1 H), 4.67 (s, 1 H), 4.51–4.46 (m, 1 H), 4.13 (d, J = 12.6 Hz, 1 H), 4.10 (d, J = 4.4 Hz, 1 H), 4.00 (dt, J = 9.0, 4.8 Hz, 1 H), 3.79 (t, J = 4.8 Hz, 1 H), 3.72–3.68 (m, 1 H), 3.40 (d, J = 5.2 Hz, 1 H), 3.31 (s, 3 H), 2.35–2.29 (m, 1 H), 2.20 (dd, J = 7.9, 2.6 Hz, 1 H), 2.17 (dd, J = 7.9, 2.5 Hz, 1 H), 1.96–1.90 (m, 1 H), 1.79 (dd, J = 14.3, 7.2 Hz, 1 H), 1.47 (s, 3 H), 0.96 (t, J = 7.9 Hz, 9 H), 0.90 (s, 9 H), 0.63 (q, J = 7.8 Hz, 6 H), 0.14 (s, 9 H), 0.1 (br. s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 172.8, 150.2, 135.9, 109.2, 99.7, 83.9, 78.9, 78.6, 78.2, 78.0, 72.8, 66.5, 66.1, 54.8, 47.2, 41.1, 32.3, 27.8, 26.1 (3 C), 18.6, 6.9 (3 C), 5.0 (3 C), 2.4 (3 C), –5.3 (2 C) ppm. HRMS (ESI): calcd. for $C_{33}H_{62}O_8Si_3Na$ $[M + Na]^+$ 693.3650; found 693.3650. R_f (hexane/EtOAc, 3:1) = 0.57.

Cage-Shaped Lactones 49 and 50 (and 47 and 48): A solution of a diastereoisomeric mixture of **46** (*dr* = 1:1, 490 mg, 0.7 mmol) in

freshly degassed cyclohexane (four pump-freeze-thaw cycles, 80 mL) was split in 8 equal parts and transferred to quartz tubes of a diameter of 1 cm and a total height of 16 cm, which were equipped with magnetic stirring bars. These charged quartz vials were placed 0.5 cm in front of a UV-C lamp (*SYLVANIA* G8W T5, 8 W) in a custom-made reactor and irradiated and stirred for 2 h. The contents of all vials were combined and the volatiles were removed under reduced pressure. The remaining slightly yellow oil was subjected to flash column chromatography (SiO_2, hexane/EtOAc, 20:1) yielding undesired [4.2.0]ring systems **47** and **48** (76 mg, 15% combined yield) as well as the desired cleft [2+2]-photocyclization products **49** (170 mg, 35%) and **50** (169 mg, 34%) as colorless oils. Analytic data for **49**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.40 (dd, *J* = 2.7, 1.2 Hz, 1 H), 5.20 (dd, *J* = 2.1, 1.1 Hz, 1 H), 5.16 (td, *J* = 7.9, 5.2 Hz, 1 H), 4.69 (s, 1 H), 4.14 (d, *J* = 4.5 Hz, 1 H), 4.02 (dt, *J* = 9.0, 5.5 Hz, 1 H), 3.98 (dt, *J* = 9.7, 2.9 Hz,1 H), 3.75 (dd, *J* = 10.4, 5.3 Hz, 1 H), 3.71 (d, *J* = 2.2 Hz, 1 H), 3.66 (dd, *J* = 10.4, 5.7 Hz, 1 H), 3.33–3.29 (m, 4 H), 3.14–3.11 (m, 1 H), 2.45 (qd, *J* = 12.4, 1.7 Hz, 1 H), 2.43–2.46 (m, 1 H), 1.94 (dd, *J* = 14.7, 5.3 Hz, 1 H), 1.79–1.67 (m, 2 H), 1.43 (s, 3 H), 0.96 (t, *J* = 7.9 Hz, 9 H), 0.91 (s, 9 H), 0.62 (q, *J* = 8.2 Hz, 6 H), 0.11 (s, 9 H), 0.09 (s, 3 H), 0.08 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 177.7, 144.0, 115.1, 109.0, 84.9, 84.1, 83.7, 77.5, 70.4, 67.0, 57.8, 57.7, 54.6, 49.6, 44.8, 41.4, 27.9, 26.2 (3 C), 23.4, 18.6, 7.0 (3 C), 5.1 (3 C), 2.4 (3 C), –5.2, –5.3 ppm. HRMS (ESI): calcd. for $C_{33}H_{62}O_8Si_3Na$ $[M + Na]^+$ 693.3650; found 693.3629. IR: $\tilde{\nu}$ = 3500, 2954, 1767, 1462, 1375, 1301, 1251, 1186, 1104, 988 cm^{-1}. $[\alpha]_D^{20}$ = –38.7, ($CHCl_3$, *c* = 1.1). R_f (hexane/EtOAc, 4:1) = 0.45. Analytical data for **50**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.27 (dd, *J* = 2.7, 1.4 Hz, 1 H), 5.19 (td, *J* = 8.0, 5.3 Hz, 1 H), 5.15 (dd, *J* = 2.0, 1.5 Hz, 1 H), 4.66 (s, 1 H), 4.17 (d, *J* = 4.8 Hz, 1 H), 4.12 (ddd, *J* = 11.7, 5.7, 2.2 Hz, 1 H), 3.96 (ddd, *J* = 8.1, 5.9, 4.7 Hz, 1 H), 3.79 (dd, *J* = 10.5, 4.6 Hz, 1 H), 3.66 (dd, *J* = 10.6, 6.1 Hz, 1 H), 3.43 (dd, *J* = 8.2, 6.3 Hz, 1 H), 3.31 (s, 3 H), 3.13–3.09 (m, 1 H), 3.05 (d, *J* = 5.7 Hz, 1 H), 2.45 (qd, *J* = 12.4, 1.6 Hz, 1 H), 2.44–2.38 (m, 1 H), 1.93 (dd, *J* = 14.8, 5.3 Hz, 1 H), 1.87 (ddd, *J* = 14.1, 8.7, 2.3 Hz, 1 H), 1.67 (ddd, *J* = 14.0, 11.7, 5.7 Hz, 1 H), 1.42 (s, 3 H), 0.97 (t, *J* = 7.9 Hz, 9 H), 0.91 (s, 9 H), 0.63 (q, *J* = 8.2 Hz, 6 H), 0.12 (s, 9 H), 0.11 (s, 3 H), 0.10 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 176.8, 145.4, 114.5, 109.2, 85.0, 84.0, 83.6, 79.1, 70.2, 67.1, 59.6, 57.7, 54.7, 49.8, 43.5, 41.6, 28.9, 26.2 (3 C), 23.6, 18.7, 6.9 (3 C), 5.1 (3 C), 2.4 (3 C), –5.3 (2 C) ppm. HRMS (ESI): calcd. for $C_{33}H_{62}O_8Si_3Na$ $[M + Na]^+$ 693.3650; found 693.3647. IR: $\tilde{\nu}$ = 3484, 2954, 1768, 1462, 1348, 1251, 1187, 1106, 1040, 991 cm^{-1}. $[\alpha]_D^{20}$ = –26.7, ($CHCl_3$, C = 0.6). R_f (hexane/EtOAc, 4:1) = 0.39.

Analytic Data for 47: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.76–5.74 (m, 1 H), 4.75 (dt, *J* = 8.7, 1.8 Hz, 1 H), 4.66 (s, 1 H), 4.13 (m, 1 H), 4.09 (d, *J* = 4.9 Hz, 1 H), 3.93–3.90 (m, 2 H), 3.84 (dd, *J* = 10.1, 4.5 Hz, 1 H), 3.61 (dd, *J* = 10.1, 7.2 Hz, 1 H), 3.51–3.49 (m, 1 H), 3.29 (s, 3 H), 3.28–3.24 (m, 1 H), 2.74 (dd, *J* = 13.4, 1.1 Hz, 1 H), 2.35–2.27 (m, 1 H), 2.53 (dd, *J* = 15.4, 5.9 Hz, 1 H), 1.95 (dd, *J* = 15.4, 1.8 Hz, 1 H), 1.77 (dd, *J* = 6.0, 4.1 Hz, 2 H), 1.36 (s, 3 H), 0.96 (t, *J* = 7.9 Hz, 9 H), 0.91 (s, 9 H), 0.62 (q, *J* = 7.7 Hz, 6 H), 0.10 (s, 6 H), 0.06 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 179.1, 137.9, 127.9, 108.8, 83.1, 78.3, 76.6, 71.1, 70.1, 67.0, 55.6, 54.5, 47.9, 44.8, 42.8, 38.8, 31.2, 29.2, 25.9 (3 C), 18.4, 6.7 (3 C), 4.8 (3 C), 2.2 (3 C), –5.5 (2 C) ppm. HRMS (ESI): calcd. for $C_{33}H_{62}O_8Si_3Na$ $[M + Na]^+$ 693.3650; found 693.3650. IR: $\tilde{\nu}$ = 3476, 2955, 2930, 1768, 1462, 1251, 1111, 1042, 1005, 839 cm^{-1}. $[\alpha]_D^{20}$ = –44.1, ($CHCl_3$, *c* = 2.0). R_f (hexane/EtOAc, 4:1) = 0.28.

Oxidation/Reduction Sequence of 50 to 49: At 0 °C crushed molecular sieves (4 Å 100 mg), *N*-methylmorpholine *N*-oxide (NMO; 52 mg, 0.45 mmol) and tetrapropylammonium perruthenate (5 mg, 0.05 mmol) were added sequentially to a solution of **50** (100 mg, 0.15 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was warmed to room temperature and stirred for 18 h. Diethyl ether (10 mL) was added and the resulting mixture was filtered through a pad of Celite. Removal of the volatiles and column chromatography (SiO_2, hexane/EtOAc, 6:1) gave the desired ketone (74 mg, 0.11 mmol, 74%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.52 (t, *J* = 2.4 Hz, 1 H), 5.30 (t, *J* = 2.2 Hz, 1 H), 5.22 (dt, *J* = 8.0, 5.3 Hz, 1 H), 4.69 (s, 1 H), 4.32 (d, *J* = 4.5 Hz, 1 H), 3.93 (dt, *J* = 10.1, 5.2 Hz, 1 H), 3.87 (dd, *J* = 8.2, 6.5 Hz, 1 H), 3.69 (dd, *J* = 10.6, 5.4 Hz, 1 H), 3.64 (dd, *J* = 10.5, 5.1 Hz, 1 H), 3.33 (s, 3 H), 3.22 (dd, *J* = 19.4, 3.4 Hz, 1 H), 3.17–3.13 (m, 1 H), 3.04 (dd, *J* = 19.4, 9.9 Hz, 1 H), 2.54–2.46 (m, 2 H), 1.94 (dd, *J* = 14.8, 5.3 Hz, 1 H), 1.44 (s, 3 H), 0.92 (t, *J* = 8.0 Hz, 9 H), 0.90 (s, 9 H), 0.58 (dd, *J* = 8.0, 2.4 Hz, 3 H), 0.54 (dd, *J* = 8.0, 3.2 Hz, 3 H), 0.11 (s, 9 H), 0.06 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 200.0, 171.7, 144.0, 115.7, 109.5, 84.8, 83.7, 83.4, 76.9, 66.5, 65.1, 57.5, 54.6, 49.5, 44.6, 39.5, 34.9, 26.1 (3 C), 23.5, 18.6, 6.9 (3 C), 5.0 (3 C), 2.4 (3 C), –5.2, –5.3 ppm. HRMS (ESI): calcd. for $C_{33}H_{60}O_8Si_3Na$ $[M + Na]^+$ 691.3494; found 691.3495. IR: $\tilde{\nu}$ = 2955, 2929, 1769, 1714, 1464, 1252, 1149, 1108, 1039, 840 cm^{-1}. $[\alpha]_D^{20}$ = –77.3, ($CHCl_3$, *c* = 0.3). R_f (hexane/EtOAc, 6:1) = 0.66.

To a solution of the ketone (15 mg, 0.02 mmol) and (*S*)-2-methyl-CBS-oxazaborolidine (45 μL, 0.05 mmol, 1.0 M in toluene) in THF (500 μL) was added BH_3·THF (45 μL, 0.05 mmol, 1.0 M in THF) at –78 °C. No reaction was observed by TLC (hexane/EtOAc, 4:1) until 0 °C. The reaction mixture was stirred at 0 °C for 6 h. Sat. aq. NH_4Cl (5 mL) and diethyl ether (5 mL) were added. The aqueous layer was separated and washed with diethyl ether (2× 5 mL). The combined organic phases were washed with satd. aq. NaCl (5 mL), dried with $MgSO_4$, filtered, and concentrated in vacuo to give a 1:2 mixture of **49** and **50** (15 mg) in quantitative yield. For analytic data see above.

Cage Shaped Epoxide 52: At 0 °C, alcohol **49** (10 mg, 0.07 mmol) was dissolved in a freshly prepared solution of DMDO (0.4 mL, 0.08 M, 0.03 mmol) in acetone. The resulting colorless reaction mixture was warmed to room temperature overnight. Additional DMDO (0.4 mL, 0.08 M, 0.03 mmol) was added and the reaction was stirred for an additional 24 h. Because TLC analysis (hexane/EtOAc, 4:1) still indicated remaining starting material, a further portion of DMDO (0.4 mL, 0.08 M, 0.03 mmol) was added and the reaction was stirred for another 24 h. The volatiles were removed under reduced pressure in a cold-water bath (15 °C). The resulting colorless residue was purified by flash column chromatography (SiO_2, hexane/EtOAc, 12:1) yielding desired epoxide **51** (9 mg, 85%) as a colorless oil.

Alternatively: To a solution of **49** (32 mg, 0.05 mmol) in CH_2Cl_2 (1 mL) was added $NaHCO_3$ (12 mg, 0.14 mmol) and *m*CPBA (25 mg, 0.14 mmol) at 0 °C. Prior to use, commercially available *m*CPBA was purified by extraction of a solution in diethyl ether (mL/g) with pH 7.5 buffer (3× mL/g) and evaporation of the organic solvent in a water bath at 20 °C. After 4 h at 0 °C, satd. aq. $NaHCO_3$ (5 mL) and diethyl ether (5 mL) were added, the aqueous phase was separated and extracted with diethyl ether (2× 5 mL). The combined organic phases were washed with satd. aq. NaCl (5 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was subjected to column chromatography (SiO_2, hexane/EtOAc, 8:1) yielding desired epoxide **51** (30 mg, 94%) as a 4:1 diastereoisomeric mixture. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.21–5.15 (m, 1 H), 4.68 (s, 1 H), 4.11 (d, *J* = 4.5 Hz, 1 H), 4.03 (dt, *J* = 8.6, 5.4 Hz, 1 H), 3.95 (t, *J* = 6.6 Hz, 1 H), 3.76

(dd, J = 10.3, 5.2 Hz, 1 H), 3.67 (dd, J = 10.3, 5.7 Hz, 1 H), 3.56 (t, J = 7.7 Hz, 1 H), 3.31 (s, 3 H), 3.25 (s br., OH), 3.07 (dd, J = 7.3, 1.8 Hz, 1 H), 2.97 (d, J = 4.4 Hz, 1 H), 2.78 (d, J = 4.4 Hz, 1 H), 2.57 (ddd, J = 14.7, 7.5, 1.9 Hz, 1 H), 2.40–2.33 (m, 1 H), 1.93 (dd, J = 14.7, 5.1 Hz, 1 H),1.66 (t, J = 6.7 Hz, 2 H), 1.32 (s, 3 H), 0.95 (t, J = 8.0 Hz, 9 H), 0.92 (s, 9 H), 0.63 (q, J = 7.8 Hz, 6 H), 0.11–0.09 (m, 15 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 176.2, 109.1, 83.9, 83.5, 82.9, 77.6, 67.5, 67.0, 62.9, 58.0, 56.9, 54.6, 50.7, 47.7, 42.1, 41.7, 27.9, 26.2 (3 C), 23.4, 18.9, 6.9 (3 C), 5.0 (3 C), 2.4 (3 C), –5.2, –5.3 ppm. HRMS (ESI): calcd. for $C_{33}H_{62}O_9Si_3Na$ [M + Na]$^+$ 709.3555; found 709.3598. IR: $\tilde{\nu}$ = 2955, 2930, 1768, 1462, 1376, 1252, 1143, 1040, 991, 840 cm^{-1}. $[\alpha]_D^{20}$ = –32.0, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 4:1) = 0.53.

A solution of epoxide (21 mg, 0.03 mmol) in CH_2Cl_2 (0.5 mL) was cooled to 0 °C and pyridine (7 μL, 0.09 mmol), acetic anhydride (6 μL, 0.06 mmol) and 4-(dimethylamino)pyridine (DMAP; 1 mg, 0.01 mmol) were sequentially added. The round-bottomed flask was sealed with a stopper and the reaction mixture was warmed to room temperature overnight. Diethyl ether (5 mL) and satd. aq. NH_4Cl (5 mL) were added. The aqueous phase was separated and extracted with diethyl ether (3 × 5 mL). The combined organic phases were washed with satd. aq. $CuSO_4$ (10 mL), water (10 mL) and satd. aq. NaCl (10 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Flash column chromatography (SiO_2, hexane/EtOAc, 12:1) of the residue gave desired acylated epoxide **52** (22 mg, quant.) as needle-shaped crystals that were subjected to X-ray analysis. ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 5.31 (dd, J = 11.1, 3.2 Hz, 1 H), 5.19 (dt, J = 7.9, 5.3 Hz, 1 H), 4.65 (s, 1 H), 4.23 (d, J = 4.2 Hz, 1 H), 3.83 (dt, J = 9.4, 5.1 Hz, 1 H), 3.71 (dd, J = 10.3, 4.9 Hz, 1 H), 3.57 (dd, J = 10.3, 5.8 Hz, 1 H), 3.54 (dd, J = 8.7, 7.4 Hz, 1 H), 3.27 (s, 3 H), 3.02 (dd, J = 7.1, 1.8 Hz, 1 H), 2.88 (d, J = 4.6 Hz, 1 H), 2.70 (d, J = 4.6 Hz, 1 H), 2.58 (dq, J = 2.5, 2.0 Hz, 1 H), 2.14 (s, 3 H), 2.03–1.94 (m, 1 H), 1.91 (dd, J = 14.7, 5.3 Hz, 1 H), 1.84–1.75 (m, 2 H), 1.31 (s, 3 H), 0.97 (t, J = 8.0 Hz, 9 H), 0.92 (s, 9 H), 0.69 (q, J = 8 Hz, 6 H), 0.12 (s, 9 H), 0.08 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 174.9, 170.3, 109.5, 83.5, 83.4, 82.6, 76.4, 68.2, 66.3, 62.2, 57.9, 55.8, 54.6, 50.2, 47.0, 42.4, 40.7, 26.1 (3 C), 25.7, 23.1, 21.3, 18.5, 7.0 (3 C), 4.9 (3 C), 2.4 (3 C), –5.3 (2 C) ppm. HRMS (ESI): calcd. for $C_{35}H_{64}O_{10}Si_3Na$ [M + Na]$^+$ 751.3705; found 751.3704, m.p. 93–95 °C. IR: $\tilde{\nu}$ = 2955, 2928, 1768, 1744, 1231, 1124, 1041, 991, 843, 776 cm^{-1}. $[\alpha]_D^{20}$ = –23.1, ($CHCl_3$, c = 0.4). R_f (hexane/EtOAc, 4:1) = 0.53.

Hemiacetal 53: To a solution of **51b** (5 mg, 0.01 mmol) in THF/DMSO (2:1, 450 μL) was added lithium acetylide ethylenediamine complex (50 mg, 0.54 mmol) at 0 °C. After 15 min diethyl ether (5 mL) and satd. aq. NH_4Cl (5 mL) were added. The aqueous phase was extracted with diethyl ether (2 × 5 mL). The combined organic layers were washed with water (10 mL) and satd. aq. NaCl (5 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography (SiO_2, hexane/EtOAc, 6:1) gave hemiacetal **53** (5 mg, 0.01 mmol) in quantitative yield. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.96 (dd, J = 14.9, 7.5 Hz, 1 H), 4.71 (s, 1 H), 4.53 (dd, J = 10.7, 3.7 Hz, 1 H), 4.19 (d, J = 4.3 Hz, 1 H), 3.93 (dt, J = 8.86, 5.13 Hz, 1 H), 3.72 (dd, J = 10.5, 5.4 Hz, 1 H), 3.62 (dd, J = 10.5, 5.4 Hz, 1 H), 3.40 (t, J = 7.5 Hz, 1 H), 3.29 (s, 3 H), 3.02 (d, J = 4.8 Hz, 1 H), 3.00 (d, J = 4.8 Hz, 1 H), 2.87 (d, J = 15.3 Hz, 1 H), 2.77 (d, J = 15.3 Hz, 1 H), 2.73 (s, OH), 2.70 (dd, J = 7.2, 1.9 Hz, 1 H), 2.36 (dd, J = 13.9, 7.0 Hz, 1 H), 2.32–2.07 (m, 4 H), 1.34 (s, 3 H), 1.00 (t, J = 7.9 Hz, 9 H), 0.89 (s, 9 H), 0.68 (q, J = 7.9 Hz, 6 H), 0.08 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 169.1, 109.1, 108.0, 86.1, 85.7, 84.1, 79.6, 76.9, 66.5, 60.6, 57.7, 54.6, 54.2, 50.6, 49.5, 48.0, 45.4, 41.2, 26.2, 26.1 (3 C), 24.0, 18.4, 7.0 (3 C), 5.2 (3 C), 2.4 (3 C), –5.2 (2 C) ppm. HRMS (ESI): calcd. for $C_{35}H_{64}O_{10}Si_3Na$ [M + Na]$^+$ 751.3705; found 751.3694. IR: $\tilde{\nu}$ = 2955, 2929, 1760, 1413, 1375, 1252, 1146, 1121, 1021, 838 cm^{-1}. $[\alpha]_D^{20}$ = +28.4, ($CHCl_3$, c = 0.25). R_f (hexane/EtOAc, 3:1) = 0.31.

Acetate 57: To a solution of alcohol **49** (250 mg, 0.37 mmol) in CH_2Cl_2 (4.0 mL), pyridine (90 μL, 1.12 mmol), acetic anhydride (70 μL, 0.70 mmol) and DMAP (5 mg, 0.04 mmol) were sequentially added at 0 °C. The reaction mixture was warmed to room temperature overnight. Diethyl ether (20 mL) and satd. aq. NH_4Cl (20 mL) were added. The aqueous phase was separated and extracted with diethyl ether (3 × 20 mL). The combined organic phases were washed with satd. aq. $CuSO_4$ (20 mL), water (20 mL) and satd. aq. NaCl (20 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The desired acetylated product (266 mg, quant.) was isolated as a colorless amorphous solid, that was used without further purification in the next reaction. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.48 (dd, J = 11.0, 3.1 Hz, 1 H), 5.34 (dd, J = 2.6, 1.6 Hz, 1 H), 5.20 (dd, J = 2.2, 1.6 Hz, 1 H), 5.13 (dt, J = 8.0, 5.3 Hz, 1 H), 4.66 (s, 1 H), 4.14 (d, J = 4.1 Hz, 1 H), 3.87 (dt, J = 9.1, 5.1 Hz, 1 H), 3.69 (dd, J = 10.4, 4.8 Hz, 1 H), 3.60 (dd, J = 10.4, 5.4 Hz, 1 H), 3.40 (dd, J = 8.2, 6.5 Hz, 1 H), 3.27 (s, 3 H), 3.14–3.11 (m, 1 H), 2.47 (ddd, J = 14.8, 7.7, 1.7 Hz, 1 H), 2.08 (s, 3 H), 2.01–1.88 (m, 4 H), 1.41 (s, 3 H), 0.99 (t, J = 7.9 Hz, 9 H), 0.92 (s, 9 H), 0.69 (q, J = 7.8 Hz, 6 H), 0.12 (s, 9 H), 0.08 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.2, 170.7, 144.1, 115.8, 109.4, 84.8, 83.7, 82.9, 76.5, 71.0, 66.1, 57.6, 57.2, 54.6, 49.6, 44.7, 40.5, 26.1 (3 C), 25.5, 23.6, 21.0, 18.5, 7.0 (3 C), 5.0 (3 C), 2.4 (3 C), –5.3 (2 C) ppm. HRMS (ESI): calcd. for $C_{35}H_{64}O_9Si_3Na$ [M + Na]$^+$ 735.3756; found 735.3769. IR: $\tilde{\nu}$ = 2954, 1772, 1747, 1462, 1372, 1251, 1150, 1040, 991, 840 cm^{-1}. $[\alpha]_D^{20}$ = –15.8, ($CHCl_3$, c = 0.7). R_f (hexane/EtOAc, 5:1) = 0.52.

The acylated substrate was taken up in an AcOH/THF/H_2O (2:1:1) mixture (2.8 mL) and left at room temperature for 24 h. All volatiles were removed under reduced pressure and the remaining pale yellow residue was subsequently co-evaporated with toluene (3 × 20 mL) until the smell of acetic acid was gone.

To a solution of the resulting crude colorless amorphous solid (144 mg) and imidazole (600 mg, 8.75 mmol) in CH_2Cl_2 (4.0 mL) was added chlorotriethylsilane (650 μL, 3.85 mmol) through a syringe under vigorous stirring over 5 min. After 16 h, diethyl ether (20 mL) and satd. aq. NH_4Cl (20 mL) were added to the resulting suspension. The aqueous layer was separated and extracted with diethyl ether (3 × 20 mL). The combined organic phases were washed with water (20 mL) and satd. aq. NaCl (20 mL) before being dried with $MgSO_4$. The solids were removed by filtration and the filtrate was concentrated under reduced pressure. Flash column chromatography (SiO_2, hexane/EtOAc, 10:1) gave desired globally triethylsilyl (TES)-protected acetate **57** (265 mg, 94%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.48 (dd, J = 10.2, 3.6 Hz, 1 H), 5.34 (dd, J = 2.6, 1.6 Hz, 1 H), 5.19 (dd, J = 2.1, 1.6 Hz, 1 H), 5.14 (dt, J = 8.0, 5.3 Hz, 1 H), 4.64 (s, 1 H), 4.14 (d, J = 3.8 Hz, 1 H), 3.89 (dt, J = 8.6, 5.2 Hz, 1 H), 3.69 (dd, J = 10.3, 5.2 Hz, 1 H), 3.60 (dd, J = 10.3, 5.4 Hz, 1 H), 3.39 (dd, J = 8.2, 6.5 Hz, 1 H), 3.28 (s, 3 H), 3.11–3.08 (m, 1 H), 2.44 (ddd, J = 14.7, 7.8, 1.6 Hz, 1 H), 2.08 (s, 3 H), 1.97–1.87 (m, 4 H), 1.41 (s, 3 H), 1.01–0.90 (m, 27 H), 0.69 (q, J = 8.0 Hz, 6 H), 0.65–0.55 (m, 12 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.3, 170.6, 144.3, 115.7, 109.4, 84.4, 83.7, 83.0, 76.5, 71.0, 66.1, 57.8, 57.2, 54.6, 49.7, 44.8, 40.8, 25.5, 23.4, 21.0, 7.1 (3 C), 7.0 (3 C), 6.9 (3 C), 6.6 (3 C), 5.1 (3 C), 4.5 (3 C) ppm. HRMS (ESI): calcd. for $C_{38}H_{70}O_9Si_3Na$ [M + Na]$^+$ 777.4225; found 777.4195. IR: $\tilde{\nu}$ = 2954, 2877, 1772, 1371, 1230, 1150, 1040, 991, 807, 743 cm^{-1}. $[\alpha]_D^{22}$ = –17.8, ($CHCl_3$, c = 0.7). R_f (hexane/EtOAc, 3:1) = 0.59.

Acetate 58: Alcohol **50** (284 mg, 0.42 mmol) was subjected to the procedure as for alcohol **49** (see above, **57**) giving corresponding globally TES-protected acetate **58** (278 mg, 87%) as a colorless oil.

Analytic Data for the Intermediate: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.48 (dd, J = 11.1, 2.4 Hz, 1 H), 5.32 (dd, J = 2.7, 1.6 Hz, 1 H), 5.22 (dd, J = 2.1, 1.7 Hz, 1 H), 5.18 (dt, J = 8.1, 5.4 Hz, 1 H), 4.67 (s, 1 H), 3.96 (d, J = 4.5 Hz, 1 H), 3.93–3.89 (m, 1 H), 3.73 (dd, J = 10.9, 3.7 Hz, 1 H), 3.62 (dd, J = 10.9, 6.0 Hz, 1 H), 3.42 (dd, J = 8.3, 6.4 Hz, 1 H), 3.30 (s, 3 H), 3.16–3.13 (m, 1 H), 2.47 (ddd, J = 14.7, 7.8, 1.7 Hz, 1 H), 2.11 (dd, J = 14.2, 6.0 Hz, 1 H), 2.07 (m, 1 H), 2.03 (s, 3 H), 1.92 (dd, J = 14.7, 5.4 Hz, 1 H), 1.84 (m, 1 H), 1.42 (s, 3 H), 0.98 (t, J = 7.9 Hz, 9 H), 0.91 (s, 9 H), 0.63 (q, J = 8.13 Hz, 6 H), 0.11 (s, 9 H), 0.08 (s, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.7, 170.1, 144.4, 115.6, 109.2, 85.1, 84.9, 83.1, 77.9, 71.9, 66.8, 58.1, 58.0, 54.8, 49.4, 44.2, 40.9, 26.2 (3 C), 26.1, 23.4, 21.2, 18.6, 6.9 (3 C), 5.1 (3 C), 2.4 (3 C), –5.1, –5.2 ppm. HRMS (ESI): calcd. for $C_{35}H_{64}O_9Si_3Na$ [M + Na]$^+$ 735.3756; found 735.3759. IR: $\tilde{\nu}$ = 2954, 2878, 1774, 1748, 1461, 1372, 1250, 1149, 1040, 991 cm^{-1}. $[\alpha]_D^{20}$ = –46.6, ($CHCl_3$, c = 1.5). R_f (hexane/EtOAc, 5:1) = 0.48.

Analytic Data for Acetate 58: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.49 (dd, J = 11.2, 2.2 Hz, 1 H), 5.32 (dd, J = 2.6, 1.6 Hz, 1 H), 5.22 (dd, J = 2.1, 1.6 Hz, 1 H), 5.19 (dt, J = 8.1, 5.4 Hz, 1 H), 4.67 (s, 1 H), 3.95 (d, J = 4.4 Hz, 1 H), 3.93–3.89 (m, 1 H), 3.73 (dd, J = 10.8, 3.7 Hz, 1 H), 3.60 (dd, J = 10.8, 6.4 Hz, 1 H), 3.42 (dd, J = 8.2, 6.4 Hz, 1 H), 3.30 (s, 3 H), 3.12 (m, 1 H), 2.45 (ddd, J = 14.7, 7.9, 1.6 Hz, 1 H), 2.12–2.05 (m, 1 H), 2.03 (s, 3 H), 2.05–2.01 (m, 1 H), 1.92 (dd, J = 14.7, 5.4 Hz, 1 H), 1.85 (ddd, J = 14.4, 5.4, 2.4 Hz, 1 H), 1.42 (s, 3 H), 0.98 (t, J = 7.9 Hz, 9 H), 0.97 (t, J = 7.8 Hz, 9 H), 0.94 (t, J = 7.9 Hz, 9 H), 0.63 (q, J = 7.9 Hz, 12 H), 0.58 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.7, 170.1, 144.5, 115.5, 109.2, 85.2, 84.6, 83.2, 76.9, 72.0, 66.6, 58.19, 58.16, 54.7, 49.5, 44.2, 41.1, 26.1, 23.3, 21.2, 7.1 (3 C), 6.9 (3 C), 6.9 (3 C), 6.6 (3 C), 5.1 (3 C), 4.5 (3 C) ppm. HRMS (ESI): calcd. for $C_{38}H_{70}O_9Si_3Na$ [M + Na]$^+$ 777.4225; found 777.4232. IR: $\tilde{\nu}$ = 2955, 2877, 1775, 1749, 1229, 1150, 1108, 1077, 1042, 1001 cm^{-1}. $[\alpha]_D^{23}$ = –45.9, ($CHCl_3$, c = 0.7). R_f (hexane/EtOAc, 3:1) = 0.52.

Aldehyde 59: To a solution of oxalyl chloride (660 μL, 7.7 mmol) in CH_2Cl_2 (8 mL) in a flame-dried 50 mL round-bottomed flask equipped with a bubbler, dimethyl sulfoxide (1.1 mL, 15.5 mmol) was added dropwise over 5 min at –78 °C. After the evolution of gas had ceased the bubbler was removed and stirring was continued for a further 10 min at –78 °C. Acetate **57** (1.16 g, 1.5 mmol) dissolved in CH_2Cl_2 (8 mL) was added to the resulting reaction mixture through a syringe over 10 min. After 3 h at –78 °C an intermediate formed [TLC, hexane/EtOAc (2:1), R_f = 0.23]. The reaction mixture was dropwise treated with Et_3N (2.2 mL, 15.5 mmol). The turbid solution was quenched by the addition of satd. aq. $NaHCO_3$ (15 mL) after 4 h and warmed to room temperature. The aqueous layer was separated and extracted with diethyl ether (3× 15 mL). The combined organic phases were washed with water (20 mL) and satd. aq. NaCl (20 mL) and dried with $MgSO_4$. Removal of the volatiles under reduced pressure and flash column chromatography (SiO_2, hexane/EtOAc, 8:1) of the remaining residue gave aldehyde **59** [666 mg, 67%, 89% based on recovered starting material (brsm)] as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.57 (d, J = 3.1 Hz, 1 H), 5.50 (dd, J = 11.6, 2.4 Hz, 1 H), 5.31 (dd, J = 2.7, 1.7 Hz, 1 H), 5.19 (dd, J = 3.8, 2.0 Hz, 1 H), 5.17 (dt, J = 7.9, 5.4 Hz, 1 H), 4.81 (s, 1 H), 4.21 (d, J = 4.2 Hz, 1 H), 4.05 (dd, J = 9.7, 3.0 Hz, 1 H), 3.43 (dd, J = 8.2, 6.4 Hz, 1 H), 3.39 (s, 3 H), 3.10–3.07 (m, 1 H), 2.45 (ddd, J = 14.7, 7.8, 1.7 Hz, 1 H), 2.20–2.13 (m, 1 H), 2.07 (s, 3 H), 1.98–1.79 (m, 3 H), 1.41 (s, 3 H), 1.00 (t, J = 7.9 Hz, 9 H), 0.94 (t, J = 7.9 Hz, 9 H), 0.71 (q, J = 7.8 Hz, 6 H), 0.58 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 202.4, 174.2, 170.7, 144.3, 115.6, 110.6, 86.5, 84.4, 83.2, 75.7, 70.6, 58.0, 57.4, 55.2, 49.7, 44.5, 40.4, 25.2, 23.5, 21.0, 7.1 (3 C), 6.9 (3 C), 6.6 (3 C), 5.0 (3 C) ppm. HRMS (ESI): calcd. for $C_{33}H_{53}O_{10}Si_2Na$ [M + MeOH + Na]$^+$ 693.3466; found 693.3467. IR: $\tilde{\nu}$ = 2955, 2877, 1770, 1745, 1459, 1373, 1231, 1151, 1038, 808 cm^{-1}. $[\alpha]_D^{20}$ = –39.3, ($CHCl_3$, c = 0.6). R_f (hexane/EtOAc, 2:1) = 0.50.

Aldehyde 60: Aldehyde **60** (310 mg, 87%, 97% brsm) was prepared according to the procedure for **59**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.57 (d, J = 3.1 Hz, 1 H), 5.38 (t, J = 6.4 Hz, 1 H), 5.36 (dd, J = 2.7, 1.7 Hz, 1 H), 5.26 (t, J = 2.0 Hz, 1 H), 5.20 (td, J = 8.1, 5.4 Hz, 1 H), 4.80 (s, 1 H), 4.11 (dd, J = 8.7, 3.0 Hz, 1 H), 4.00 (d, J = 4.6 Hz, 1 H), 3.42 (dd, J = 8.3, 6.3 Hz, 1 H), 3.39 (s, 3 H), 3.15–3.11 (m, 1 H), 2.50–2.42 (m, 2 H), 2.04 (s, 3 H), 2.03 (t, J = 6.6 Hz, 2 H), 1.92 (dd, J = 14.7, 5.4 Hz, 1 H), 1.42 (s, 3 H), 0.98 (t, J = 8.0 Hz, 9 H), 0.94 (t, J = 8.2 Hz, 9 H), 0.64 (q, J = 8.2 Hz, 6 H), 0.58 (q, J = 8.3 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 201.4, 174.6, 170.3, 144.1, 116.0, 110.3, 87.2, 84.7, 83.3, 77.6, 71.4, 58.2 58.1, 55.2, 49.5, 44.1, 40.6, 26.5, 23.3, 21.1, 7.1 (3 C), 6.9 (3 C), 6.6 (3 C), 5.02 (3 C) ppm. HRMS (ESI): calcd. for $C_{33}H_{53}O_{10}Si_2Na$ [M + MeOH + Na]$^+$ 693.3466; found 693.3458. IR: $\tilde{\nu}$ = 2955, 2912, 2877, 1773, 1748, 1231, 1150, 1106, 1040, 1017 cm^{-1}. $[\alpha]_D^{23}$ = –50.0, ($CHCl_3$, c = 0.6). R_f (hexane/EtOAc, 3:1) = 0.43.

Alkyne 61: A solution of **59** (72 mg, 0.11 mmol) in THF (1 mL) was treated with a 0.5 M solution of ethynylmagnesium bromide (340 μL, 0.17 mmol) in THF at –78 °C. The resulting solution was warmed to –20 °C over 4 h and left at this temperature for 16 h. Sat. aq. NH_4Cl (5 mL) and diethyl ether (5 mL) were added. The aqueous phase was separated and extracted with diethyl ether (2× 5 mL). The combined organic phases were washed with satd. aq. NaCl (10 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the residue by column chromatography (SiO_2, hexane/EtOAc, 8:1) gave desired propargylic alcohol **61** (45 mg, 0.07 mmol, 93% brsm) as a single diastereoisomer. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.47 (dd, J = 11.7, 2.4 Hz, 1 H), 5.34 (dd, J = 2.7, 1.7 Hz, 1 H), 5.20 (dd, J = 2.2, 1.7 Hz, 1 H), 5.16 (dt, J = 8.0, 5.3 Hz, 1 H), 4.68 (s, 1 H), 4.51 (dt, J = 3.7, 2.3 Hz, 1 H), 4.20 (d, J = 4.4 Hz, 1 H), 4.07 (dd, J = 9.0, 3.4 Hz, 1 H), 3.39 (dd, J = 6.3, 2.0 Hz, 1 H), 3.36 (s, 3 H), 3.12–3.09 (m, 1 H), 2.69 (d, J = 4.1 Hz, 1 H, 1 H), 2.50–2.42 (m, 1 H), 2.48 (d, J = 2.2 Hz, 1 H, 1 H), 2.34–2.27 (m, 1 H), 2.17–2.13 (m, 1 H), 2.11 (s, 3 H), 2.03–1.97 (m, 1 H), 1.90 (dd, J = 14.7, 5.3 Hz, 1 H), 1.41 (s, 3 H), 1.00 (t, J = 7.9 Hz, 9 H), 0.94 (t, J = 7.9 Hz, 9 H), 0.70 (q, J = 8.0 Hz, 6 H), 0.58 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.2, 170.9, 144.3, 115.6, 109.7, 85.9, 84.5, 83.1, 81.4, 76.5, 74.8, 71.0, 63.4, 57.7, 57.2, 55.5, 49.7, 44.8, 38.1, 26.1, 23.5, 21.1, 7.1 (3 C), 7.0 (3 C), 6.6 (3 C), 5.0 (3 C) ppm. HRMS (ESI): calcd. for $C_{34}H_{56}O_9Si_2Na$ [M + Na]$^+$ 687.3361; found 687.3366. IR: $\tilde{\nu}$ = 3484, 2955, 2877, 1770, 1745, 1459, 1231, 1151, 1039, 991 cm^{-1}. $[\alpha]_D^{20}$ = –9.04, ($CHCl_3$, c = 0.37). R_f (hexane/EtOAc, 3:1) = 0.28.

Dibromide 65: *N*-Bromosuccinimide (NBS; 4 mg, 0.02) was added as a solid to a solution of **61** (11 mg, 0.02 mmol) in CH_2Cl_2 (0.5 mL). The round-bottomed flask was sealed with a stopper and heated to 50 °C for 5 h. The volatiles were removed under reduced pressure and the remaining residue was subjected to column chromatography (SiO_2, hexane/EtOAc, 12:1). *trans*-Dibromo compound **65** (4 mg, 0.01 mmol, 30%, 66% brsm) was obtained as a

colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.66 (s, 1 H), 5.50 (dd, J = 11.4, 2.4 Hz, 1 H), 5.31 (dd, J = 2.5, 1.8 Hz, 1 H), 5.19 (t, J = 1.8 Hz, 1 H), 5.16 (dt, J = 8.0, 5.3 Hz, 1 H), 4.75 (s, 1 H), 4.61 (d, J = 8.9 Hz, 1 H), 4.21 (d, J = 4.32 Hz, 1 H), 3.45 (dd, J = 8.1, 6.5 Hz, 1 H), 3.25 (s, 3 H), 3.11–3.08 (m, 1 H), 2.61–2.54 (m, 1 H), 2.45 (ddd, J = 14.7, 7.8, 1.6 Hz, 1 H), 2.09 (s, 3 H), 1.96–1.87 (m, 2 H), 1.83–1.76 (m, 1 H), 1.40 (s, 3 H), 1.00 (t, J = 7.9 Hz, 9 H), 0.95 (t, J = 7.9 Hz, 9 H), 0.72 (q, J = 7.9 Hz, 6 H), 0.58 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 189.9, 174.3, 170.8, 144.4, 131.6, 130.8, 115.5, 110.6, 84.6, 84.4, 83.3, 75.9, 70.6, 57.9, 57.5, 55.5, 49.7, 44.5, 40.9, 25.9, 23.5, 21.0, 7.2 (3 C), 7.0 (3 C), 6.6 (3 C), 4.9 (3 C) ppm. HRMS (ESI): calcd. for $C_{34}H_{54}Br_2O_9Si_2Na$ $[M + Na]^+$ 845.1550; found 845.1547. IR: $\tilde{\nu}$ = 2955, 2877, 2349, 1770, 1702, 1460, 1373, 1232, 1151, 1042 cm^{-1}. $[\alpha]_D^{20}$ = –11.1, ($CHCl_3$, c = 0.02). R_f (hexane/EtOAc, 4:1) = 0.48.

Carboxylic Acid 67: A solution of $NaClO_2$ (34 mg, 0.37 mmol) and NaH_2PO_4 (62 mg, 0.45 mmol) in water (450 μL) were added through a Pasteur pipette to a solution of aldehyde **59** (24 mg, 0.04 mmol) in 2-methyl-2-butene (300 μL) and *t*BuOH (800 μL) at 0 °C. The resulting solution was warmed to room temperature and stirred for 16 h. Sat. aq. NH_4Cl (5 mL) and diethyl ether (10 mL) were added. The aqueous phase was separated and extracted with diethyl ether (2 × 10 mL). The combined organic layers were washed with water (10 mL) and satd. aq. NaCl (10 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (SiO_2, hexane/EtOAc, 1:1) afforded desired acid **67** (24 mg, 0.37 mmol, 98%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.6 (br. s, 1 H), 5.50 (dd, J = 11.6, 2.5 Hz, 1 H), 5.30 (dd, J = 2.6, 1.8 Hz, 1 H), 5.22–5.17 (m, 2 H), 4.82 (s, 1 H), 4.30 (d, J = 10.1 Hz, 1 H), 4.27 (d, J = 4.0 Hz, 1 H), 3.49 (dd, J = 8.2, 6.5 Hz, 1 H), 3.44 (s, 3 H), 3.40–3.30 (m, 1 H), 3.10–3.08 (m, 1 H), 2.44 (qd, J = 12.4, 1.7 Hz, 1 H), 2.28–2.20 (m, 1 H), 2.10–1.88 (m, 4 H), 2.08 (s, 1 H), 1.41 (s, 3 H), 1.00 (t, J = 7.9 Hz, 9 H), 0.95 (t, J = 7.9 Hz, 9 H), 0.73 (q, J = 8.2 Hz, 6 H), 0.58 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.3, 173.4, 170.9, 144.5, 115.4, 111.0, 84.4, 83.3, 80.7, 75.6, 70.4, 58.1, 57.5, 49.7, 44.4, 42.9, 29.9, 25.6, 23.5, 21.0, 7.15 (3 C), 6.89 (3 C), 6.62 (3 C), 4.95 (3 C) ppm. HRMS (ESI): calcd. for $C_{32}H_{54}NaO_{10}Si_2$ $[M + Na]^+$ 677.3153; found 677.3135. IR: $\tilde{\nu}$ = 3218, 2922, 2853, 1769, 1743, 1460, 1374, 1231, 1137, 990 cm^{-1}. $[\alpha]_D^{20}$ = –14.7, ($CHCl_3$, c = 0.5). R_f (hexane/EtOAc, 1:1) = 0.14.

(3a*R*,5*S*,6*R*,6a*R*)-5-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-2,2-dimethyl-6-vinyltetrahydrofuro[2,3-*d*][1,3]dioxole (73): To a suspension of freshly powdered lithium aluminium hydride (LAH; 911 mg, 24 mmol) in diethyl ether (150 mL) was added a solution of ester **72** (7.6 g, 24 mmol) in diethyl ether (100 mL) at 0 °C over 15 min. After 1 h at that temperature, satd. aq. NH_4Cl (100 mL) was carefully added followed by satd. aq. Na/K tartrate (100 mL). The resulting biphasic mixture was stirred at room temperature for 1 h. The aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with satd. aq. NaCl (100 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. The alcohol was isolated as a colorless gum (6.31 g, 21.9 mmol, 91%) and used without purification in the next reaction.

To a solution of the alcohol (6.3 g, 21.9 mmol), triphenylphosphine (17.2 g, 65.7 mmol) and imidazole (4.5 g, 65.7 mmol) in CH_3CN/benzene (1:2, 210 mL) was added iodine (16.7 g, 65.6 mmol) in 6 portions over 30 min at 0 °C. The resulting mixture was stirred for 1 h before satd. aq. $Na_2S_2O_3$ (50 mL) was added. The organic phase was separated, washed with water (50 mL) and satd. aq. NaCl (50 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Filtration (hexane/EtOAc, 3:1) through a short pad of silica gave the desired iodide (8.5 g, 21.3 mmol, 97%) as a pale yellow oil, which was used without further purification in the next step. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.77 (d, J = 3.7 Hz, 1 H), 4.66 (t, J = 3.9 Hz, 1 H), 4.09 (dd, J = 8.2, 6.3 Hz, 1 H), 4.02 (dd, J = 6.7, 5.3 Hz, 1 H), 3.91 (dd, J = 8.2, 5.3 Hz, 1 H), 3.79 (dd, J = 9.1, 7.0 Hz, 1 H), 3.43–3.38 (m, 1 H), 3.25 (dt, J = 9.4, 6.3 Hz, 1 H), 2.31 (dt, J = 9.5, 7.3 Hz, 1 H), 2.15–2.04 (m, 2 H), 1.50 (s, 3 H), 1.42 (s, 3 H), 1.34 (s, 3 H), 1.31 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 112.1, 109.8, 105.1, 81.5, 80.8, 77.7, 67.6, 49.0, 29.2, 26.9, 26.8, 26.6, 25.4, 4.9 ppm. HRMS (ESI): calcd. for $C_{14}H_{23}IO_5Na$ $[M + Na]^+$ 421.0488; found 421.0485. IR: $\tilde{\nu}$ = 2986, 2934, 1454, 1380, 1256, 1214, 1171, 1065, 1017, 847 cm^{-1}. $[\alpha]_D^{20}$ = +76.5, ($CHCl_3$, c = 0.9). R_f (hexane/EtOAc, 1:1) = 0.67.

To a solution of the iodide (11.7 g, 29 mmol) in THF (300 mL) was added *t*BuOK (9.9 g, 88 mmol) in three portions at 0 °C over 30 min. The resulting mixture was stirred at that temperature for 2 h. Sat. aq. NH_4Cl (100 mL) was added and the layers were separated. The aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with water (100 mL) and satd. aq. NaCl (100 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude residue by column chromatography (SiO_2, hexane/EtOAc, 6:1) gave desired diacetonide **73** (7.7 g, 28.5 mmol, 97%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.87 (dd, J = 10.3, 8.8 Hz, 1 H), 5.82 (d, J = 3.6 Hz, 1 H), 5.28 (ddd, J = 17.3, 1.6, 0.7 Hz, 1 H), 5.22 (dd, J = 10.3, 1.6 Hz, 1 H), 4.62 (dd, J = 4.5, 3.8 Hz, 1 H), 4.26 (dt, J = 4.0, 6.7 Hz, 1 H), 4.10 (dd, J = 10.1, 3.9 Hz, 1 H), 3.99 (dd, J = 8.2, 6.8 Hz, 1 H), 3.89 (dd, J = 8.2, 6.6 Hz, 1 H), 2.62 (dt, J = 4.8, 9.5 Hz, 1 H), 1.54 (s, 3 H), 1.43 (s, 3 H), 1.35 (s, 3 H), 1.32 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 132.5, 119.2, 112.0, 109.7, 104.9, 83.9, 80.0, 76.3, 65.5, 50.7, 26.9, 26.6, 26.4, 25.4 ppm. HRMS (ESI): calcd. for $C_{14}H_{22}O_5Na$ $[M + Na]^+$ 293.1365; found 293.1362. IR: $\tilde{\nu}$ = 2986, 2935, 1372, 1251, 1214, 1167, 1102, 1065, 1015, 848 cm^{-1}. $[\alpha]_D^{22}$ = +94.5, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 2:1) = 0.38.

Triethyl({(2*S*,3*R*,4*R*,5*R*)-5-methoxy-4-[(triethylsilyl)oxy]-3-vinyltetrahydrofuran-2-yl}methoxy)silane (74): To a solution of diacetonide **73** (330 mg, 1.22 mmol) in MeOH (13 mL) was added acetyl chloride (260 μL, 3.66 mmol) at 0 °C. The resulting solution was warmed to room temperature and stirred for 3 h. Et_3N (1 mL) was added and the volatiles were removed under reduced pressure. The remaining white residue was subjected to column chromatography (SiO_2, EtOAc) giving the desired triol (170 mg, 0.83 mmol, 68%) as a colorless gum. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.91 (ddd, J = 17.9, 9.9, 8.1 Hz, 1 H), 5.35–5.32 (m, 1 H), 5.30 (d, J = 0.8 Hz, 1 H), 4.83 (s, 1 H), 4.24 (dd, J = 9.0, 4.5 Hz, 1 H), 4.10 (t, J = 4.3 Hz, 1 H), 3.87–3.83 (m, 1 H), 3.67 (t, J = 4.8 Hz, 1 H), 3.40 (s, 3 H), 3.08 (td, J = 8.6, 4.5 Hz, 1 H), 2.71 (d, J = 3.7 Hz, 1 H), 2.28 (t, J = 5.6 Hz, 1 H), 2.09 (d, J = 4.3 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 133.2, 120.2, 109.2, 83.0, 78.4, 73.8, 63.6, 55.5, 47.0 ppm. HRMS (ESI): calcd. for $C_9H_{16}O_5Na$ $[M + Na]^+$ 227.0895; found 227.0891. IR: $\tilde{\nu}$ = 3363, 2926, 1438, 1420, 1306, 1195, 1154, 1103, 1033, 943 cm^{-1}. $[\alpha]_D^{22}$ = +10.5, ($CHCl_3$, c = 0.6). R_f (EtOAc) 0.29.

Glycol cleavage of the vicinal diol (11.0 g, 53 mmol) was achieved according to the procedure for **42** giving the desired diol (8.1 g, 46.5 mmol, 86%) as a colorless gum. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.89 (ddd, J = 17.2, 10.5, 8.1 Hz, 1 H), 5.30–5.28 (m, 1 H), 5.27–5.24 (m, 1 H), 4.84 (s, 1 H), 4.24 (ddd, J = 9.3, 4.2, 2.7 Hz, 1 H), 4.11 (t, J = 4.4 Hz, 1 H), 3.79 (ddd, J = 11.9, 4.3, 2.7 Hz, 1 H), 3.53–3.46 (m, 1 H), 3.41 (s, 3 H), 2.97 (td, J = 8.8, 4.4 Hz, 1

H), 2.10 (dd, J = 7.8, 4.6 Hz, 1 H), 2.03 (d, J = 4.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 132.3, 120.1, 109.2, 83.1, 78.2, 63.2, 55.8, 46.3 ppm. HRMS (ESI): calcd. for $C_8H_{14}O_4Na$ [M + Na]$^+$ 197.0790; found 197.0783. IR: $\tilde{\nu}$ = 3397, 2924, 1640, 1451, 1352, 1305, 1248, 1092, 1035, 970 cm^{-1}. $[\alpha]_D^{22}$ = +14.6, ($CHCl_3$, c = 0.7). R_f (EtOAc) = 0.5.

To a solution of the crude diol (8.1 g, 46.5 mmol) in CH_2Cl_2 (500 mL) was added imidazole (19.0 g, 279.0 mmol). Triethylsilyl chloride (19.5 mL, 117.5 mmol) was added through a syringe over 10 min. The resulting suspension was stirred for 6 h. Water (100 mL) was added and the separated aqueous phase was extracted with diethyl ether (3× 50 mL). The combined organic layers were washed with satd. aq. NaCl (100 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (SiO_2, hexane/EtOAc, 30:1) afforded **74** (17.8 g, 44.2 mmol, 96%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.86 (dt, 1 H, J = 18.0, 9.3 Hz), 5.15 (dd, J = 5.1, 2.0 Hz, 1 H), 5.12–5.11 (m, 1 H), 4.70 (br. s, 1 H), 4.11 (ddd, J = 9.7, 6.0, 2.8 Hz, 1 H), 4.04 (d, J = 4.2 Hz, 1 H), 3.73 (dd, J = 10.9, 2.9 Hz, 1 H), 3.55 (dd, J = 10.9, 6.1 Hz, 1 H), 3.34 (s, 3 H), 2.67 (td, J = 9.4, 4.2 Hz, 1 H), 0.96 (t, J = 7.9 Hz, 9 H), 0.95 (t, J = 7.9 Hz, 9 H), 0.61 (q, J = 8.0 Hz, 6 H), 0.60 (q, J = 7.8 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 134.3, 118.4, 109.5, 83.8, 79.4, 65.0, 54.5, 48.6, 6.89 (3 C), 6.87 (3 C), 4.9 (3 C), 4.5 (3 C) ppm. HRMS (ESI): calcd. for $C_{20}H_{42}O_4Si_2Na$ [M + Na]$^+$ 425.2519; found 425.2518. IR: $\tilde{\nu}$ = 2954, 2912, 2877, 1459, 1415, 1239, 1120, 1042, 1004, 917 cm^{-1}. $[\alpha]_D^{20}$ = +12.1, ($CHCl_3$, c = 1.2). R_f (hexane/EtOAc, 2:1) = 0.89.

(2*S*,3*R*,4*R*,5*R*)-5-Methoxy-4-[(triethylsilyl)oxy]-3-vinyltetrahydrofuran-2-carbaldehyde (75): Compound **74** (5.0 g, 12.4 mmol) was subjected to the same Swern-oxidation procedure as **57** (to **59**) giving desired aldehyde **75** (3.3 g, 11.4 mmol, 92%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.56 (d, J = 2.9 Hz, 1 H), 5.88 (ddd, J = 17.1, 10.3, 8.8 Hz, 1 H), 5.23–5.21 (m, 1 H), 5.20–5.17 (m, 1 H), 4.82 (s, 1 H), 4.30 (dd, J = 9.7, 2.8 Hz, 1 H), 4.10 (d, J = 4.2 Hz, 1 H), 3.43 (s, 3 H), 2.93 (dt, J = 9.2, 4.2 Hz, 1 H), 0.96 (t, J = 7.9 Hz, 9 H), 0.61 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 201.0, 131.9, 119.9, 110.6, 85.9, 78.6, 55.1, 48.8, 6.8 (3 C), 4.9 (3 C) ppm. HRMS (ESI): calcd. for $C_{14}H_{26}O_4SiNa$ [M + Na]$^+$ 309.1498; found 309.1479. IR: $\tilde{\nu}$ = 2955, 2832, 1737, 1460, 1415, 1314, 1239, 1120, 1002, 836 cm^{-1}. $[\alpha]_D^{20}$ = +10.8, ($CHCl_3$, c = 0.65). R_f (hexane/EtOAc, 3:1) = 0.45.

Triethyl[((2*R*,3*R*,4*R*,5*S*)-4-(iodomethyl)-2-methoxy-5-{[(triethylsilyl)oxy]methyl}tetrahydrofuran-3-yl)oxy]silane (76): Through a solution of **74** (1.3 g, 3.2 mmol) in CH_2Cl_2/MeOH (3:1, 40 mL) was bubbled an ozone/air mixture at –78 °C until the color of the solution turned blue (10 min). The resulting solution was degassed with a stream of air until colorless and $NaBH_4$ (490 mg, 12.9 mmol) was added. The reaction mixture was warmed to 0 °C and stirred for 1 h. Water (30 mL) and diethyl ether (30 mL) were added and the aqueous phase was extracted with diethyl ether (3× 20 mL). The combined organic layers were washed with satd. aq. NaCl (30 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the residue by column chromatography (SiO_2, hexane/EtOAc, 10:1) gave the desired alcohol (1.0 g, 2.5 mmol, 76%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.64 (s, 1 H), 4.21 (d, J = 4.8 Hz, 1 H), 4.20 (dt, J = 8.3, 4.7 Hz, 1 H), 3.86 (dd, J = 9.6, 4.8 Hz, 1 H), 3.78 (t, J = 5.7 Hz, 2 H), 3.46 (dd, J = 9.3, 8.5 Hz, 1 H), 3.30 (s, 3 H), 3.23 (t, J = 5.72 Hz, 1 H), 2.30–2.24 (m, 1 H), 0.96 (t, J = 7.9 Hz, 9 H), 0.95 (t, J = 7.9 Hz, 9 H), 0.63 (q, J = 7.9 Hz, 6 H), 0.61 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 109.3, 82.8, 79.0, 66.2, 61.0, 54.6, 48.9, 6.8 (3), 6.7 (3 C), 4.8 (3 C), 4.3 (3 C) ppm. HRMS (ESI): calcd. for $C_{19}H_{42}O_5Si_2Na$ [M + Na]$^+$ 465.3180; found 465.3172. IR: $\tilde{\nu}$ = 3471, 2954, 2912, 2877, 1460, 1240, 1113, 1006, 957, 810 cm^{-1}. $[\alpha]_D^{20}$ = –27.9, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 6:1) = 0.43.

At 0 °C, to a solution of the alcohol (112 mg, 0.28 mmol), polymer-bound triphenylphosphine (1.6 mmol/g, 344 mg, 0.55 mmol) and imidazole (56 mg, 0.83 mmol) in CH_2Cl_2 (5.5 mL) was added a solution of freshly sublimated and crushed iodine (140 mg, 0.55 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was warmed to room temp. and stirred for 6 h. Sat. aq. NH_4Cl solution (10 mL) and satd. aq. $Na_2S_2O_3$ solution (5 mL) were added and the aqueous layer was extracted with diethyl ether (3× 50 mL). The combined organic layers were washed with brine (20 mL) and dried with $MgSO_4$. After removal of the solvent the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 20:1) delivering iodide **76** (115 mg, 0.20 mmol, 81%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.68 (s, 1 H), 4.17 (d, J = 4.0 Hz, 1 H), 3.84 (dt, J = 9.0, 5.7 Hz, 1 H), 3.74 (dd, J = 10.1, 5.3 Hz, 1 H), 3.59 (dd, J = 10.1, 6.2 Hz, 1 H), 3.31 (s, 3 H), 3.32–3.23 (m, 2 H), 2.57–2.50 (m, 1 H), 0.99 (t, J = 8.0 Hz, 9 H), 0.97 (t, J = 8.0 Hz, 9 H), 0.69 (q, J = 8.1 Hz, 6 H), 0.62 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 108.5, 82.6, 77.8, 66.3, 54.6, 49.8, 7.0 (3 C), 6.9 (3 C), 5.2 (3 C), 4.50 (3 C), 0.64 ppm. HRMS (ESI): calcd. for $C_{19}H_{41}O_4Si_2Na$ [M + Na]$^+$ 539.1486; found 539.1487. IR: $\tilde{\nu}$ = 2954, 2876, 1459, 1415, 1237, 1186, 1119, 1071, 1005, 888 cm^{-1}. $[\alpha]_D^{20}$ = +21.9, ($CHCl_3$, c = 0.75). R_f (hexane/EtOAc, 5:1) = 0.84.

2-((2S,3R,4R,5R)-5-Methoxy-4-[(triethylsilyl)oxy]-2-{[(triethylsilyl)oxy]methyl}tetrahydrofuran-3-yl)acetaldehyde (77): To a solution of **74** (250 mg, 0.62 mmol) in THF (6 mL) was added BH_3·THF (1.9 mL, 1.9 mmol) over 10 min at 0 °C. After 4 h satd. aq. $NaHCO_3$ (6 mL) and H_2O_2 (170 µL, 1.49 mmol) were added. The resulting biphasic mixture was vigorously stirred for 1 h at 0 °C before satd. aq. NaS_2O_3 (10 mL) was added. The aqueous phase was separated and extracted with diethyl ether (3× 10 mL). The combined organic phases were washed with water (10 mL) and satd. aq. NaCl (10 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (SiO_2, hexane/EtOAc, 12:1) yielded the desired alcohol (200 mg, 0.48 mmol, 76%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.66 (s, 1 H), 4.08 (d, J = 4.6 Hz, 1 H), 4.03–3.99 (m, 1 H), 3.72 (ddd, J = 10.4, 5.2, 1.1 Hz, 1 H), 3.68–3.60 (m, 3 H), 3.30 (s, 3 H), 2.30–2.17 (m, 2 H), 1.90–1.81 (m, 1 H), 1.70–1.61 (m, 1 H), 0.96 (t, J = 7.9 Hz, 9 H), 0.96 (t, J = 8.0 Hz, 9 H), 0.66–0.58 (m, 12 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 109.2, 84.0, 78.1, 66.6, 61.6, 54.5, 41.6, 29.5, 6.9 (3 C), 6.8 (3 C), 5.0 (3 C), 4.4 (3 C) ppm. HRMS (ESI): calcd. for $C_{20}H_{44}O_5Si_2Na$ [M + Na]$^+$ 443.2625; found 443.2622. IR: $\tilde{\nu}$ = 3458, 2954, 2912, 2877, 1459, 1415, 1239, 1128, 1041, 1005 cm^{-1}. $[\alpha]_D^{20}$ = –9.7, ($CHCl_3$, c = 1.50). R_f (hexane/EtOAc, 6:1) = 0.33.

At 0 °C, SO_3·py (170 mg, 1.07 mmol) was added in one portion to a solution of the alcohol (150 mg, 0.36 mmol) and Et_3N (250 µL, 1.78 mmol) in CH_2Cl_2/DMSO (4:1, 4.0 mL) at 0 °C. The resulting mixture was warmed to room temperature and stirred for further 16 h. Sat. aq. NaS_2O_3 (5 mL) and diethyl ether (5 mL) were added. The aqueous phase was separated and extracted with diethyl ether (3× 5 mL). The combined organic phases were washed with water (5 mL) and satd. aq. NaCl (5 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (SiO_2, hexane/EtOAc, 6:1) gave desired aldehyde **77** (139 mg, 0.33 mmol, 93%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.78 (br. s, 1 H), 4.68 (s, 1 H), 4.21 (d, J = 4.2 Hz, 1 H), 3.94

(t, J = 8.7, 5.7 Hz, 1 H), 3.74 (dd, J = 10.2, 5.3 Hz, 1 H), 3.57 (dd, J = 10.2, 6.1 Hz, 1 H), 3.32 (s, 3 H), 2.82–2.74 (m, 1 H), 2.61–2.53 (m, 2 H), 0.95 (t, J = 8.0 Hz, 9 H), 0.93 (t, J = 7.9 Hz, 9 H), 0.63–0.54 (m, 12 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 201.2, 109.5, 83.3, 77.1, 66.3, 54.6, 41.1, 39.6, 6.84 (6 C), 4.9 (3 C), 4.5 (3 C) ppm. HRMS (ESI): calcd. for $C_{20}H_{42}O_5Si_2Na$ $[M + Na]^+$ 441.2468; found 441.2469. IR: $\tilde{\nu}$ = 2955, 2912, 2877, 1728, 1458, 1386, 1239, 1107, 1007, 958 cm^{-1}. $[\alpha]_D^{20}$ = +7.0, ($CHCl_3$, c = 1.45). R_f (hexane/EtOAc, 6:1) = 0.67.

Aldehyde 81: To a solution of alcohol **80** (40 mg, 0.12 mmol) in MeOH (4.1 mL) was added AcCl (35 μL, 0.49 mmol) at 0 °C. The mixture was warmed to room temperature and stirred for further 4 h, the volatiles were removed under reduced pressure and the residue was dried under high vacuum for 2 h to yield 23 mg (89%) of the diol as a pale pink solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.36 (br. s, 1 H), 5.32–5.25 (m, 1 H), 5.22 (br. s, 1 H), 4.01 (d, J = 11.6 Hz, 1 H), 3.87 (d, J = 11.6 Hz, 1 H), 3.53 (t, J = 6.2 Hz, 1 H), 3.21 (br. s, 1 H), 2.48 (dd, J = 7.7, 15.1 Hz, 1 H), 2.04 (dd, J = 4.7, 15.0 Hz, 1 H), 1.73 (br. s, 2 H), 1.45 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 176.8, 144.4, 115.0, 83.7, 82.7, 63.3, 56.8, 55.9, 48.6, 44.8, 24.1 ppm. HRMS (ESI): calcd. for $C_{11}H_{14}O_4Na$ $[M + Na]^+$: 233.0790; found 233.0781. IR: $\tilde{\nu}$ = 3370, 2925, 1743, 1352, 1158, 1056, 995, 906, 729, 647 cm^{-1}. $[\alpha]_D^{21}$ = –26.7 ($CHCl_3$, c = 1.1). R_f (hexane/EtOAc, 1:1) = 0.15, m.p. 110–112 °C.

The crude diol (15 mg, 0.07 mmol) was dissolved in CH_2Cl_2 (1.4 mL) and cooled to 0 °C. 2,6-Lutidine (50 μL, 0.43 mmol), followed by TESOTf (64 μL, 0.29 mmol) were rapidly added to the reaction vessel and the mixture was stirred at 0 °C for 45 min. The reaction was quenched by addition of $NaHCO_3$ (10 mL), diluted with water (10 mL) and diethyl ether (30 mL). The phases were separated and the aqueous phase was extracted with diethyl ether (2× 15 mL). The organic layers were washed with satd. aq. NaCl (15 mL), dried with Na_2SO_4, filtered, and concentrated under vacuum. The residue was purified by column chromatography (SiO_2, hexane/EtOAc, 15:1) furnishing 30 mg (96%) of the desired TES protected diol as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.22–5.16 (m, 2 H), 5.12 (dd, J = 1.5, 2.2 Hz, 1 H), 4.01 (d, J = 10.6 Hz, 1 H), 3.77 (d, J = 10.5 Hz, 1 H), 3.47 (dd, J = 6.2, 8.3 Hz, 1 H), 3.18–3.14 (m, 1 H), 2.45 (ddd, J = 1.8, 7.8, 14.7 Hz, 1 H), 1.92 (dd, J = 5.5, 14.6 Hz, 1 H), 1.41 (s, 3 H), 0.95 (t, J = 8.0 Hz, 9 H), 0.94 (t, J = 7.9 Hz, 9 H), 0.63–0.54 (m, 12 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 176.3, 145.7, 113.6, 84.7, 83.5, 62.9, 57.4, 56.4, 49.9, 44.8, 23.6, 7.1 (3 C), 6.8 (3 C), 6.6 (3 C), 4.5 (3 C) ppm. HRMS (ESI): calcd. for $C_{23}H_{42}O_4Si_2Na$ $[M + Na]^+$ 461.2519; found 461.2517. IR: $\tilde{\nu}$ = 2954, 2876, 1773, 1458, 1239, 1146, 1107, 991, 805, 742 cm^{-1}. $[\alpha]_D^{24}$ = –12.7 ($CHCl_3$, c = 1.5). R_f (hexane/EtOAc, 10:1) 0.54.

The TES-protected diol (18 mg, 0.04 mmol) was subjected to the same Swern-oxidation procedure as for **59**. Purification by flash chromatography (SiO_2, hexane/EtOAc, 3:1) furnished 11 mg (83%) of aldehyde **81** as an amorphous white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.83 (s, 1 H), 5.44 (t, J = 2.5 Hz, 1 H), 5.30 (t, J = 2.3 Hz, 1 H), 5.26 (dd, J = 5.7, 8.0 Hz, 1 H), 3.80 (dd, J = 6.2, 8.1 Hz, 1 H), 3.25–3.21 (m, 1 H), 2.52 (ddd, J = 1.8, 7.8, 14.8 Hz, 1 H), 1.96 (dd, J = 5.6, 14.8 Hz, 1 H), 1.43 (s, 3 H), 0.93 (t, J = 7.9 Hz, 9 H), 0.61 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 192.5, 171.8, 142.7, 116.2, 84.8, 84.2, 63.6, 57.8, 49.3, 42.7, 7.1 (3 C), 23.1, 6.6 (3 C) ppm. HRMS (ESI): calcd. for $C_{17}H_{26}O_4SiNa$ $[M + Na]^+$: 345.1498; found 345.1490. IR: $\tilde{\nu}$ = 2931, 2856, 1768, 1721, 1253, 1145, 1047, 987, 836, 775 cm^{-1}. $[\alpha]_D^{22}$ = –87.6 ($CHCl_3$, c = 0.7). R_f (hexane/EtOAc, 3:1) = 0.28.

Cage-Shaped Cyclobutane 82: To a solution of **76** (48 mg, 0.09 mmol) in THF (700 μL) was added dropwise *t*BuLi (120 μL, 1.7 M in THF, 0.20 mmol) at –78 °C. After 30 min a solution of crude aldehyde **81** (30 mg, 0.09 mmol) in THF (700 μL) was added over 5 min. The resulting mixture was warmed to 0 °C over 3 h. Sat. aq. NH_4Cl (5 mL) and diethyl ether (5 mL) were added. The aqueous phase was separated and extracted with diethyl ether (3× 5 mL). The combined organic phases were washed with water (5 mL) and satd. aq. NaCl (5 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography (SiO_2, hexane/EtOAc, 6:1) provided **82** with a *dr* of 4:1 (8 mg, 0.01 mmol, 12%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.39 (dd, J = 2.7, 1.2 Hz, 1 H), 5.20 (dd, J = 1.9, 1.4 Hz, 1 H), 5.17 (td, J = 8.1, 5.6 Hz, 1 H), 4.69 (s, 1 H), 4.13 (d, J = 4.5 Hz, 1 H), 4.05 (dt, J = 8.8, 5.7 Hz, 1 H), 3.98 (dt, J = 9.8, 2.9 Hz, 1 H), 3.83 (d, J = 2.4 Hz, 1 H), 3.74 (dd, J = 10.3, 5.7 Hz, 1 H), 3.64 (dd, J = 10.3, 5.8 Hz, 1 H), 3.32 (dd, J = 8.2, 6.2 Hz, 1 H), 3.31 (s, 3 H), 3.12–3.09 (m, 1 H), 2.45 (ddd, J = 14.6, 7.9, 1.7 Hz, 1 H), 2.39–2.32 (m, 1 H), 1.94 (dd, J = 14.6, 5.4 Hz, 1 H), 1.79–1.67 (m, 2 H), 1.42 (s, 3 H), 0.97 (t, J = 7.8 Hz, 9 H), 0.96 (t, J = 8.0 Hz, 9 H), 0.93 (t, J = 7.7 Hz, 9 H), 0.63 (q, J = 8.0 Hz, 12 H), 0.57 (q, J = 8.8 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 177.6, 144.3, 114.9, 109.1, 84.6, 84.1, 83.8, 77.6, 70.5, 67.0, 58.0, 57.8, 54.6, 49.6, 44.8, 41.7, 28.2, 23.3, 7.1 (3 C), 6.93 (3 C), 6.88 (3 C), 6.6 (3 C), 5.1 (3 C), 4.4 (3 C) ppm. HRMS (ESI): calcd. for $C_{36}H_{68}O_8Si_3Na$ $[M + Na]^+$ 735.4120; found 735.4125. IR: $\tilde{\nu}$ = 2954, 2876, 1767, 1460, 1376, 1300, 1240, 1104, 990, 906 cm^{-1}. $[\alpha]_D^{20}$ = –38.7, ($CHCl_3$, c = 0.55). R_f (hexane/EtOAc, 4:1) = 0.42.

(5S)-5-{(*S*)-2-Methyl-2-[(triethylsilyl)oxy]penta-3,4-dien-1-yl}-3-(phenylselanyl)dihydrofuran-2(3*H*)-one (83): Alcohol **37** was subjected to the same procedure as for **32** with TESOTf for protection instead of TMSOTf. The use of Allenic alcohol (5.4 g, 29.6 mmol), 2,6-lutidine (10 mL, 88.9 mmol), TESOTf (10 mL, 44.5 mmol), CH_2Cl_2 (150 mL) gave TES-protected allenic alcohol (8.2 g, 27.6 mmol, 93%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.26 (t, J = 6.6 Hz, 1 H), 4.83 (d, J = 0.6 Hz, 1 H), 4.82 (br. s, 1 H), 4.80–4.74 (m, 1 H), 2.51 (br. d, J = 10.1 Hz, 1 H), 2.49 (d, J = 9.8 Hz, 1 H), 2.39–2.31 (m, 1 H), 2.00–1.85 (m, 3 H), 1.40 (s, 3 H), 0.94 (t, J = 7.9 Hz, 9 H), 0.59 (q, J = 8.0 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 206.4, 177.4, 99.9, 78.1, 77.9, 72.4, 49.7, 29.9, 29.1, 27.7, 7.1 (3 C), 6.6 (3 C) ppm. HRMS (ESI): calcd. for $C_{16}H_{28}O_3SiNa$ $[M + Na]^+$ 319.1705; found 319.1708. IR: $\tilde{\nu}$ = 2953, 2876, 1957, 1777, 1459, 1379, 1155, 1110, 1003, 917 cm^{-1}. $[\alpha]_D^{20}$ = –36.1, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 2:1) = 0.21.

The phenylselenyl group was introduced according to the procedure for **32**. TES-protected allenic alcohol (2.5 g, 8.4 mmol), LiHMDS (8.9 mL, 1.0 M in toluene, 8.9 mmol), TMSCl (1.2 mL, 9.3 mmol), PhSeCl (1.9 g, 9.7 mmol). Phenylseleno lactone **83** (3.31 g, 7.3 mmol, 87%) with a *dr* of 1:1 as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.69–7.65 (m, 4 H), 7.40–7.29 (m, 6 H), 5.21 (dt, J = 8.8, 6.7 Hz, 2 H), 4.82–4.80 (m, 4 H), 4.72–4.62 (m, 2 H), 4.02 (dd, J = 10.2, 9.1 Hz, 1 H), 3.93 (dd, J = 6.3, 4.0 Hz, 1 H), 2.75 (ddd, J = 13.6, 9.1, 6.4 Hz, 1 H), 2.39–2.36 (m, 2 H), 2.06–1.93 (m, 2 H), 1.87–1.79 (m, 2 H), 1.74–1.69 (m, 1 H), 1.35 (s, 3 H), 1.34 (s, 3 H), 0.93 (t, J = 7.9 Hz, 9 H), 0.91 (t, J = 7.9 Hz, 9 H), 0.57 (q, J = 7.5 Hz, 6 H), 0.55 (q, J = 7.6 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 206.3, 136.0, 135.8, 129.5, 129.5, 129.2, 128.9, 127.3, 127.1, 99.8, 78.0, 77.2, 76.8, 76.5, 72.4, 72.3, 49.6, 49.3, 38.5, 37.9, 37.9, 37.3, 27.6, 7.18 (3 C), 7.15 (3 C), 6.62 (3CH), 6.59 (3CH) ppm. HRMS (ESI): calcd. for $C_{22}H_{32}O_3SeSiNa$ $[M + Na]^+$ 475.1184; found 475.1190. IR: $\tilde{\nu}$ = 2954, 2875, 1956, 1770, 1458, 1414, 1354, 1180, 1112, 1003 cm^{-1}. $[\alpha]_D^{20}$ = –23.7, ($CHCl_3$, c = 1.0). R_f (hexane/EtOAc, 6:1) = 0.36.

Butenolide 84: Phenylseleno lactone **83** (842 mg, 1.86 mmol) was coupled with aldehyde **77** (820 mg, 1.96 mmol) according to the

procedure for **46**. A mixture of four diastereoisomers (1.63 g) was obtained as a colorless oil that was used without further purification in the next reaction. The oxidative elimination of the phenylselenide was carried out according to the procedure for **22**. A mixture of four diastereoisomers (1.63 g) gave desired butenolide **84** (1.1 g, 1.54 mmol, 83% over 2 steps) with a *dr* of 3:1 as a colorless gum that was used directly in the next reaction. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.30 (t, J = 1.5 Hz, 1 H), 7.29 (t, J = 1.5 Hz, 3 H), 5.28–5.23 (m, 8 H), 4.84–4.83 (m, 8 H), 4.68–4.66 (m, 4 H), 4.52–4.46 (m, 4 H), 4.16 (d, J = 4.6 Hz, 3 H), 4.12–4.07 (m, 4 H), 3.90 (d, J = 4.3 Hz, 3 H), 3.81–3.76 (m, 4 H), 3.66–3.61 (m, 4 H), 3.53 (d, J = 5.1 Hz, 1 H), 3.31 (s, 9 H), 3.30 (s, 3 H), 2.39–2.28 (m, 4 H), 2.23–2.17 (m, 3 H), 1.99–1.85 (m, 6 H), 1.83–1.75 (m, 4 H), 1.67–1.60 (m, 4 H), 1.46 (br. s, 12 H), 0.99–0.93 (m, 108 H), 0.67–0.58 (m, 72 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 206.42, 206.41, 172.7, 172.6, 150.1, 150.0, 136.2, 136.1, 109.2, 109.0, 99.7, 83.8, 83.7, 78.94, 78.87, 78.7, 78.17, 78.15, 77.2, 72.39, 72.37, 66.8, 66.5, 66.4, 66.0, 54.7, 54.6, 47.4, 47.2, 42.5, 41.5, 32.5, 32.5, 27.9, 27.8, 7.1, 6.9, 6.8, 6.6, 5.0, 4.4, 4.3 ppm. HRMS (ESI): calcd. for $C_{36}H_{68}O_8Si_3Na$ [M + Na]$^+$ 735.4120; found 735.4128. R_f (hexane/EtOAc, 6:1) = 0.30.

Cage-Shaped Cyclobutanes 82 and 85: A diastereoisomeric mixture of **84** (153 mg, 0.21 mmol) was treated with UV-C light according to the procedure for **47/48** giving **82** (78 mg, 0.11 mmol) and **85** (38 mg, 0.05 mmol) as colorless gums. For analytic data of **82** see above. Analytic data for **85**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.26 (dd, J = 2.7, 1.3 Hz, 1 H), 5.20 (td, J = 8.0, 5.3 Hz, 1 H), 5.14 (dd, J = 2.0, 1.5 Hz, 1 H), 4.66 (s, 1 H), 4.18–4.12 (m, 2 H), 4.02–3.96 (m, 1 H), 3.78 (dd, J = 10.3, 4.8 Hz, 1 H), 3.59 (dd, J = 10.3, 6.8 Hz, 1 H), 3.54–3.49 (m, 1 H), 3.45 (dd, J = 8.2, 6.3 Hz, 1 H), 3.31 (s, 3 H), 3.22 (d, J = 5.6 Hz, 1 H), 3.09–3.06 (m, 1 H), 2.48–2.38 (m, 2 H), 1.95–1.87 (m, 1 H), 1.71–1.61 (m, 1 H), 1.54 (s, 3 H), 0.99–0.91 (m, 27 H), 0.68–0.53 (m, 18 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 176.8, 145.5, 114.4, 109.3, 84.7, 83.9, 83.7, 79.1, 69.9, 66.9, 59.6, 58.0, 54.6, 49.8, 43.4, 41.9, 29.2, 23.5, 7.1 (3 C), 6.92 (3 C), 6.86 (3 C), 6.6 (3 C), 5.0 (3 C), 4.3 (3 C) ppm. HRMS (ESI): calcd. for $C_{36}H_{68}O_8Si_3Na$ [M + Na]$^+$ 735.4120; found 735.4123. IR: $\tilde{\nu}$ = 2955, 2912, 2877, 1769, 1459, 1414, 1240, 1107, 1042, 1006 cm^{-1}. $[\alpha]_D^{20}$ = –107.1, ($CHCl_3$, c = 0.2). R_f (hexane/EtOAc, 4:1) = 0.35.

Formate 89: The acylation of **82** (246 mg, 0.34 mmol) was performed according to the procedure for **57** giving the desired acetate (260 mg, quant.) as a colorless oil. For the preparation of aldehyde **59** and for the analytic data see above.

To a suspension of aldehyde **59** (207 mg, 0.3 mmol) and $NaHCO_3$ (82 mg, 0.1 mmol) in CH_2Cl_2 (3.5 mL) was added *m*CPBA (111 mg, 0.7 mmol), which was purified by extraction of a solution in diethyl ether with pH 7.5 buffer prior to use, in one portion under vigorous stirring at 0 °C. After 2 h the reaction was quenched by the addition of dimethyl sulfide (300 μL, 4 mmol). After an additional 30 min diethyl ether (10 mL) and satd. aq. NH_4Cl (10 mL) were added at 0 °C. The aqueous phase was separated and extracted with diethyl ether (3× 10 mL). The combined organic extracts were washed with satd. aq. $NaHCO_3$ (15 mL), water (15 mL) and satd. aq. NaCl (15 mL). After drying with $MgSO_4$ and filtration, the volatiles were removed under reduced pressure. Purification of the remaining residue by flash column chromatography (SiO_2, hexane/EtOAc, 8:1) gave desired formate **89** (169 mg, 79%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.11 (s, 1 H), 6.14 (d, J = 4.6 Hz, 1 H), 5.49 (dd, J = 10.5, 3.1 Hz, 1 H), 5.33 (dd, J = 2.6, 1.8 Hz, 1 H), 5.21 (dd, J = 2.1, 1.8 Hz, 1 H), 5.17 (dt, J = 8.0, 5.4 Hz, 1 H), 4.79 (s, 1 H), 4.26 (dd, J = 5.0, 0.3 Hz, 1 H), 3.40 (dd, J = 8.2, 6.4 Hz, 1 H), 3.35 (s, 3 H), 3.11–3.09 (m, 1 H), 2.45 (ddd, J = 14.7, 7.8, 1.7 Hz, 1 H), 2.39–2.33 (m, 1 H), 2.08 (s, 3 H), 2.04–1.94 (m, 2 H), 1.90 (dd, J = 14.6, 5.3 Hz, 1 H), 1.41 (s, 3 H), 0.98 (t, J = 7.9 Hz, 9 H), 0.94 (t, J = 7.9 Hz, 9 H), 0.67 (q, J = 7.9 Hz, 6 H), 0.58 (q, J = 7.9 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.3, 170.7, 160.7, 144.1, 115.9, 110.9, 102.4, 84.5, 83.2, 76.2, 71.2, 57.8, 57.4, 55.6, 49.6, 44.9, 44.7, 25.0, 23.4, 21.1, 7.1 (3 C), 6.9 (3 C), 6.6 (3 C), 4.9 (3 C) ppm. HRMS (ESI): calcd. for $C_{32}H_{54}O_{10}Si_2Na$ [M + Na]$^+$ 677.3153; found 677.3136. IR: $\tilde{\nu}$ = 2955, 2877, 1769, 1740, 1227, 1152, 1111, 1039, 1017, 990 cm^{-1}. $[\alpha]_D^{25}$ = –9.3, ($CHCl_3$, c = 0.8). R_f (hexane/EtOAc, 3:1) = 0.55.

Aldehyde 60: Secondary alcohol **85** (284 mg, 0.42 mmol) was subjected to the identical acylation procedure as **57** (see above) giving acetate **58** (300 mg, quant.) as a colorless oil (for analytical data see there). For the preparation of aldehyde **60** and for analytical data see above.

Vinyl Bromide 86: To a slightly turbid mixture of formate **89** (186 mg, 0.28 mmol) and bromoallylsilane **90** (112 μL, 0.65 mmol) in CH_2Cl_2 (5.6 mL) was added dropwise $SnCl_4$ (454 μL, 0.45 mmol) through a syringe at –78 °C. The reaction was stirred until TLC analysis (hexane/EtOAc, 6:1) indicated full consumption of the starting aldehyde. Thereafter, a mixture of MeOH and satd. aq. $NaHCO_3$ 2:1 (6 mL) and diethyl ether (6 mL) were sequentially added. The resulting heterogenic mixture was warmed to room temperature and water was added until all solids were dissolved. The resulting clear aqueous phase was extracted with diethyl ether (3× 10 mL). The combined organic extracts were washed with Na/K tartrate (15 mL), water (15 mL) and satd. aq. NaCl (15 mL). After drying with $MgSO_4$ the solids were removed by filtration and the filtrate was concentrated under reduced pressure giving a colorless oil. The residue was taken up in a minimum amount of hexane/EtOAc (6:1) and purified by filtration through a short pad of silica (hexane/EtOAc, 6:1) yielding desired vinyl bromide **86** (194 mg, 94%) after removal of the volatiles as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.64 (s, 1 H), 5.52 (dd, J = 11.5, 2.7 Hz, 1 H), 5.50 (s, 1 H), 5.33 (dd, J = 2.5, 1.8 Hz, 1 H), 5.21 (dd, J = 1.9, 1.8 Hz, 1 H), 5.17 (dt, J = 8.0, 5.4 Hz, 1 H), 4.72 (s, 1 H), 4.40 (ddd, J = 10.3, 8.5, 2.6 Hz, 1 H), 4.07 (d, J = 4.2 Hz, 1 H), 3.39 (dd, J = 8.2, 6.5 Hz, 1 H), 3.31 (s, 3 H), 3.12–3.09 (m, 1 H), 2.79 (dd, J = 14.6, 10.5 Hz, 1 H), 2.48–2.36 (m, 3 H), 2.11 (s, 3 H), 1.90 (dd, J = 14.8, 5.3 Hz, 1 H), 1.89–1.77 (m, 2 H), 1.41 (s, 3 H), 0.98 (t, J = 7.9 Hz, 9 H), 0.94 (t, J = 7.8 Hz, 9 H), 0.66 (q, J = 7.9 Hz, 6 H), 0.58 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.4, 170.7, 144.2, 131.8, 118.7, 115.8, 108.5, 84.4, 83.2, 77.9, 77.1, 71.5, 57.7, 57.3, 55.0, 49.6, 45.5, 44.8, 40.0, 23.8, 23.4, 21.1, 7.1 (3 C), 6.9 (3 C), 6.6 (3 C), 4.9 (3 C) ppm. HRMS (ESI): calcd. for $C_{36}H_{64}BrN_2O_8Si_2$ [M + H_3CCN+NH_4]$^+$ 789.3364; found 789.3349. IR: $\tilde{\nu}$ = 2954, 2877, 1770, 1747, 1459, 1372, 1226, 1151, 1049, 990 cm^{-1}. $[\alpha]_D^{25}$ = –50.1, ($CHCl_3$, c = 1.5). R_f (hexane/EtOAc, 3:1) = 0.55.

Macrocycle 91: To a solution of vinyl bromide **86** (14 mg, 0.02 mmol) in freshly degassed toluene (0.8 mL) were added $Pd(OAc)_2$ (0.5 mg, 0.002 mmol), triphenylphosphine (1 mg, 0.004 mmol), Ag_2CO_3 (16 mg, 0.058 mmol) and crushed molecular sieves (4 Å 100 mg). After stirring at 80 °C for 3 d the reaction mixture was cooled to room temperature at which diethyl ether (5 mL) and water (5 mL) were added. The resulting heterogeneous mixture was filtered through a short pad of Celite. The aqueous phase was separated and extracted with diethyl ether (3× 5 mL). The combined organic phases were washed with water (5 mL) and satd. aq. NaCl (5 mL) followed by drying with $MgSO_4$. Filtration

of the solids, removal of the volatiles under reduced pressure and flash column chromatography (SiO_2, hexane/EtOAc, 8:1) of the residue and mass analysis of the collected fractions indicated the formation of desired macrocycle **91**. HRMS (ESI): calcd. for $C_{36}H_{63}N_2O_8Si_2$ $[M+CH_3CN+NH_4]^+$ 707.4117; found 707.4108.

Macrocycle 92: A suspension of vinyl bromide **86** (20 mg, 0.027 mmol), NaOAc (11 mg, 0.13 mmol), Bu_4NCl (15 mg, 0.053 mmol) and crushed molecular sieves (4 Å, 150 mg) in freshly degassed dimethylformamide (DMF; 2.7 mL) was added $Pd(OAc)_2$ (0.6 mg, 0.003 mmol) as a solid at room temperature. The flask was sealed and immediately heated to 85 °C in an oil bath under vigorous stirring. After 1.5 h the starting material was consumed. The reaction mixture was cooled to room temperature followed by the addition of diethyl ether (5 mL) and water (5 mL). The resulting heterogeneous mixture was filtered through a short pad of Celite. The aqueous phase was separated and extracted with diethyl ether (3 × 5 mL). The combined organic phases were washed with water (5 mL) and satd. aq. NaCl (5 mL) followed by drying with $MgSO_4$. Filtration of the solids, removal of the volatiles under reduced pressure and flash column chromatography (SiO_2, hexane/EtOAc, 8:1) of the residue resulted in isolation of carbooxygenation product **92** (10 mg, 55%) and vinyl nitrile **93** (4 mg, 22%). Analytic data for **92**: ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 5.50 (dd, J = 11.3, 2.6 Hz, 1 H), 5.33 (dd, J = 2.7, 1.8 Hz, 1 H), 5.21 (t, J = 1.92 Hz, 1 H), 5.18 (dt, J = 5.4, 8.0 Hz, 1 H), 4.83 (s, 2 H), 4.73 (s, 1 H), 4.25 (ddd, J = 10.8, 8.3, 2.7 Hz, 1 H), 4.09 (d, J = 4.3 Hz, 1 H), 3.40 (dd, J = 8.2, 6.5 Hz, 1 H), 3.31 (s, 3 H), 3.11–3.09 (m, 1 H), 2.55 (dd, J = 15.1, 10.8 Hz, 1 H), 2.45 (ddd, J = 14.7, 7.8, 1.7 Hz, 1 H), 2.36–2.34 (m, 1 H), 2.34–2.32 (m, 1 H), 2.15 (s, 3 H), 2.08 (s, 3 H), 1.90 (dd, J = 14.6, 5.4 Hz, 1 H), 1.88–1.79 (m, 2 H), 1.41 (s, 3 H), 0.99 (t, J = 8.0 Hz, 9 H), 0.94 (t, J = 7.9 Hz, 9 H), 0.67 (q, J = 8.0 Hz, 6 H), 0.58 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 174.4, 170.6, 169.3, 154.0, 144.2, 115.8, 108.8, 103.4, 84.4, 83.2, 77.6, 76.8, 71.4, 57.7, 57.3, 55.1, 49.6, 44.8, 40.1, 37.7, 23.7, 23.4, 21.3, 21.0, 7.2 (3 C), 6.9 (3 C), 6.6 (3 C), 6.4 (3 C) ppm. HRMS (ESI): calcd. for $C_{36}H_{60}NaO_{10}Si_2$ $[M + H_3CCN+NH_4]^+$ 731.3623; found 731.3628. IR: $\tilde{\nu}$ = 2955, 2915, 1769, 1371, 1226, 1207, 1101, 1051, 1018, 990 cm^{-1}. $[\alpha]_D^{15}$ = –50.8, ($CHCl_3$, c = 0.4). R_f (hexane/EtOAc, 4:1) = 0.27.

Vinyl Nitrile 93: A round-bottomed flask was charged with vinyl bromide **86** (15 mg, 0.021 mmol) in freshly degassed DMF (5.3 mL). $Pd(OAc)_2$ (2.0 mg, 0.009 mmol), triphenylphosphine (5 mg, 0.021 mmol), K_2CO_3 (28 mg, 0.21 mmol) and crushed molecular sieves (4 Å 100 mg) were added. The reaction was stirred at 125 °C for 3 h and cooled to room temperature at which diethyl ether (10 mL) and water (10 mL) were added. The resulting heterogeneous mixture was filtered through a short pad of Celite. The aqueous phase was separated and extracted with diethyl ether (3 × 10 mL). The combined organic phases were washed with water (10 mL) and satd. aq. NaCl (10 mL) followed by drying with $MgSO_4$. Filtration of the solids, removal of the volatiles under reduced pressure and flash column chromatography (SiO_2, hexane/EtOAc, 8:1) of the residue gave vinyl nitrile **93** (7 mg, 50%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.92 (s, 1 H), 5.76 (s, 1 H), 5.52 (dd, J = 11.4, 2.6 Hz, 1 H), 5.33 (br. s, 1 H), 5.22 (s br., 1 H), 5.18 (dt, J = 5.5, 7.9 Hz, 1 H), 4.72 (s, 1 H), 4.29 (ddd, J = 10.8, 8.6, 2.2 Hz, 1 H), 4.08 (d, J = 4.1 Hz, 1 H), 3.40 (dd, J = 7.9, 6.7 Hz, 1 H), 3.30 (s, 3 H), 3.13–3.10 (m, 1 H), 2.58 (dd, J = 14.1, 11.2 Hz, 1 H), 2.46 (ddd, J = 14.8, 7.9, 0.8 Hz, 1 H), 2.41–2.37 (m, 1 H), 2.34 (br. d, J = 14.8 Hz, 1 H), 2.12 (s, 3 H), 1.91 (dd, J = 14.3, 5.3 Hz, 1 H), 1.88–1.79 (m, 2 H), 1.42 (s, 3 H), 0.98 (t, J = 7.9 Hz, 9 H), 0.95 (t, J = 7.8 Hz, 9 H), 0.67 (q, J = 7.9 Hz, 6 H), 0.58 (q, J = 7.8 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.4, 170.7, 144.2, 132.4, 120.8, 118.9, 115.8, 108.6, 84.5, 83.2, 78.1, 77.0, 71.4, 57.7, 57.3, 55.0, 49.6, 44.8, 40.2, 39.1, 23.7, 23.4, 21.1, 7.1 (3 C), 6.9 (3 C), 6.6 (3 C), 4.9 (3 C) ppm. HRMS (ESI): calcd. for $C_{37}H_{64}N_3O_8Si_2$ $[M + H_3CCN+NH_4]^+$ 734.4226; found 734.4215. IR: $\tilde{\nu}$ = 2955, 2914, 2877, 2259, 1769, 1747, 1373, 1227, 1152, 1050 cm^{-1}. $[\alpha]_D^{18}$ = –69.4, ($CHCl_3$, c = 0.35). R_f (hexane/EtOAc, 4:1) = 0.58.

General Procedure for the Tin Mediated Allylation; Homoallylic Alcohol 97: To a solution of aldehyde **59** (25 mg, 0.04 mmol) and (*Z*)-crotylsilane (**94**; 41 µL, 0.23 mmol) in CH_2Cl_2 (800 µL) was added dropwise $SnCl_4$ (120 µL, 1.0 M in CH_2Cl_2, 0.12 mmol) at –78 °C. The reaction mixture was stirred at his temperature for 4 h. A suspension of satd. aq. $NaHCO_3$/MeOH (1:2, 3 mL) was rapidly added at –78 °C. The cooling bath was removed and diethyl ether (5 mL) and water (2 mL) were added. The separated aqueous phase was extracted with diethyl ether (3 × 5 mL). The combined organic phases were washed with satd. aq. Na/K tartrate (5 mL) and satd. aq. NaCl (5 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (SiO_2, hexane/EtOAc, 8:1) gave homoallylic alcohol **97** (27 mg, 0.039 mmol, 98%) as a mixture of diastereoisomers, which was used directly in the next reaction. Major diastereoisomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.75 (ddd, J = 17.2, 10.3, 8.3 Hz, 1 H), 5.47 (dt, J = 11.7, 2.1 Hz, 1 H), 5.34 (dd, J = 4.3, 2.3 Hz, 1 H), 5.20 (dd, J = 3.5, 1.7 Hz, 1 H), 5.17 (td, J = 8.0, 5.4 Hz, 1 H), 5.11 (ddd, J = 17.3, 1.8, 1.0 Hz, 1 H), 5.04 (dd, J = 10.3, 1.8 Hz, 1 H), 4.67 (d, J = 1.4 Hz, 1 H), 4.14 (d, J = 4.2 Hz, 1 H), 4.02 (t, J = 10.2 Hz, 1 H), 3.40–3.32 (m, 2 H), 3.36 (s, 3 H), 3.18–3.09 (m, 2 H), 2.48–2.42 (m, 1 H), 2.25–2.13 (m, 2 H) 2.09 (s, 3 H), 1.92–1.87 (m, 2 H), 1.75–1.65 (m, 1 H), 1.41 (s, 3 H), 1.14 (d, J = 6.8 Hz, 3 H), 1.01–0.92 (m, 18 H), 0.73–0.67 (m, 6 H), 0.61–0.55 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.3, 170.9, 144.3, 141.2, 116.0, 109.9, 84.4, 84.3, 83.1, 76.1, 73.5, 73.1, 70.9, 57.7, 57.2, 55.6, 49.7, 44.8, 43.1, 38.4, 24.9, 23.4, 21.9, 17.0, 7.2 (3 C), 6.9 (3 C), 6.6 (3 C), 5.0 (3 C) ppm. HRMS (ESI): calcd. for $C_{36}H_{62}O_9Si_2Na$ $[M + Na]^+$ 717.3830; found 717.3833. IR: $\tilde{\nu}$ = 2958, 2933, 2909, 1775, 1752, 1238, 1147, 1101, 1015, 988 cm^{-1}. $[\alpha]_D^{20}$ = –43.3, ($CHCl_3$, c = 0.4). R_f (hexane/EtOAc, 2:1) = 0.48.

Homoallylic Alcohol 95: Aldehyde **59** (26 mg, 0.04 mmol) and allyltrimethylsilane (26 µL, 0.16 mmol) were treated with $SnCl_4$ (81 µL, 0.08 mmol) according to the general procedure for the tin mediated allylation giving **95** (25 mg, 0.04 mmol, 93%) as a mixture of diastereoisomers. Major diastereoisomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.96–5.82 (m, 1 H), 5.50–5.44 (m, 1 H), 5.35–5.29 (m, 1 H), 5.21,–5.20 (m, 1 H), 5.19–5.08 (m, 3 H), 4.68–4.66 (m, 1 H), 4.21–4.15 (m, 1 H), 3.89–3.85 (m, 1 H), 3.50–3.43 (m, 1 H), 3.41–3.27 (m, 4 H), 3.10 (br. d, J = 5.4 Hz, 1 H), 2.47–2.29 (m, 3 H), 2.27–2.14 (m, 1 H), 2.10–1.96 (m, 5 H), 1.94–1.87 (m, 2 H), 1.41 (br. s, 3 H), 1.01–0.92 (m, 18 H), 0.73–0.67 (m, 6 H), 0.61–0.55 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 175.2, 171.0, 144.8, 135.2, 117.2, 115.7, 110.3, 87.1, 84.8, 83.6, 78.2, 71.6 (2 C), 58.3, 58.2, 55.9, 49.6, 44.0, 39.6, 39.5, 27.7, 22.9, 20.8, 7.2 (3 C), 6.9 (3 C), 6.5 (3 C), 5.0 (3 C) ppm. HRMS (ESI): calcd. for $C_{37}H_{67}N_2O_9Si_2$ $[M+CH_3CN+NH_4Cl]^+$ 739.4385; found 739.4388. IR: $\tilde{\nu}$ = 2962, 2946, 2928, 1781, 1741, 1243, 1178, 1119, 1024, 998 cm^{-1}. $[\alpha]_D^{20}$ = –11.7, ($CHCl_3$, c = 0.2). R_f (hexane/EtOAc, 2:1) = 0.50.

Homoallylic Alcohol 96: Aldehyde **60** (30 mg, 0.05 mmol) and allyltrimethylsilane (26 µL, 0.16 mmol) were treated with $SnCl_4$ (71 µL, 0.07 mmol) according to the general procedure for the tin mediated allylation giving **96** (30 mg, 0.04 mmol, 94%) as a mixture of dia-

stereoisomers. Major diastereoisomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.91 (ddt, J = 17.2, 10.1, 7.0 Hz, 1 H), 5.45 (dd, J = 11.1, 2.1 Hz, 1 H), 5.32 (dd, J = 2.7, 1.7 Hz, 1 H), 5.24 (t, J = 1.9 Hz, 1 H), 5.21 (td, J = 8.0, 5.4 Hz, 1 H), 5.14 (ddd, J = 17.1, 3.4, 1.4 Hz, 1 H), 5.09 (br. d, J = 10.2 Hz, 1 H), 4.69 (s, 1 H), 4.13 (d, J = 5.5 Hz, 1 H), 3.98 (dd, J = 6.6, 2.1 Hz, 1 H), 3.62–3.56 (m, 1 H), 3.43 (dd, J = 8.3, 6.3 Hz, 1 H), 3.39 (s, 3 H), 3.15–3.11 (m, 1 H), 2.50 (d, J = 8.8 Hz, 1 H), 2.45 (ddd, J = 14.7, 7.9, 1.7 Hz, 1 H), 2.38–2.28 (m, 3 H), 2.04 (s, 3 H), 2.09–2.01 (m, 1 H), 1.92 (dd, J = 14.7, 5.4 Hz, 1 H), 1.85 (ddd, J = 14.8, 8.6, 2.2 Hz, 1 H), 1.42 (s, 3 H), 0.98 (t, J = 7.8 Hz, 9 H), 0.94 (t, J = 7.8 Hz, 9 H), 0.64 (q, J = 7.7 Hz, 6 H), 0.58 (q, J = 7.8 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.8, 170.4, 144.5, 135.4, 117.2, 115.6, 110.1, 87.3, 84.7, 83.4, 78.5, 71.3 (2 C), 58.23, 58.17, 55.7, 49.5, 44.2, 39.6, 39.5, 27.1, 23.3, 21.1, 7.1 (3 C), 6.9 (3 C), 6.6 (3 C), 5.0 (3 C) ppm. HRMS (ESI): calcd. for $C_{37}H_{67}N_2O_9Si_2$ $[M+CH_3CN+NH_4Cl]^+$ 739.4385; found 739.4388. IR: $\tilde{\nu}$ = 2955, 2935, 2912, 1773, 1748, 1231, 1153, 1105, 1040, 1017 cm^{-1}. $[\alpha]_D^{20}$ = –44.0, ($CHCl_3$, c = 0.2). R_f (hexane/EtOAc, 2:1) = 0.37.

Homoallylic Alcohol 98: Aldehyde **60** (30 mg, 0.05 mmol) and (*Z*)-crotylsilane (**94**) (26 μL, 0.16 mmol) were treated with $SnCl_4$ (71 μL, 0.07 mmol) according to the general procedure for the tin-mediated allylation giving **98** (30 mg, 0.04 mmol, 94%) as a mixture of diastereoisomers. Major diastereoisomer: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.94–5.88 (s, 1 H), 5.67 (d, J = 11.0 Hz, 1 H), 5.35 (br. d, J = 1.4 Hz, 1 H), 5.25–5.19 (m, 2 H), 5.15 (br. d, J = 3.3 Hz, 1 H), 5.12 (br. s, 1 H), 4.67 (br. s, 1 H), 4.08 (d, J = 5.6 Hz, 1 H), 3.82 (dd, J = 8.6, 5.5 Hz, 1 H), 3.43 (t, J = 7.3 Hz, 1 H), 3.39–3.35 (m, 1 H), 3.32 (s, 3 H), 3.12 (br. d, J = 4.1 Hz, 1 H), 2.71 (d, J = 6.4 Hz, 1 H), 2.63 (td, J = 10.7, 3.1 Hz, 1 H), 2.45 (dd, J = 14.7, 7.9 Hz, 1 H), 2.28–2.24 (m, 1 H), 2.07–2.02 (m, 4 H), 1.92 (dd, J = 14.7, 5.4 Hz, 1 H), 1.87 (dd, J = 14.9, 8.6 Hz, 1 H), 1.41 (s, 3 H), 1.13 (d, J = 7.0 Hz, 3 H), 0.97 (t, J = 7.9 Hz, 9 H), 0.94 (t, J = 7.9 Hz, 9 H), 0.63 (q, J = 7.8 Hz, 6 H), 0.57 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 175.0, 171.6, 144.2, 139.2, 116.3, 115.8, 109.7, 85.6, 84.6, 83.4, 78.8, 77.7, 72.1, 58.3, 58.2, 55.2, 49.5, 44.0, 41.7, 40.0, 27.8, 23.3, 21.3, 17.5, 7.1 (3 C), 6.9 (3 C), 6.6 (3 C), 4.9 (3 C) ppm. HRMS (ESI): calcd. for $C_{36}H_{62}O_9Si_2Na$ $[M + Na]^+$ 717.3830; found 717.3836. IR: $\tilde{\nu}$ = 3490, 2956, 2877, 1774, 1459, 1373, 1236, 1150, 1106, 997 cm^{-1}. $[\alpha]_D^{24}$ = –35.6, ($CHCl_3$, c = 0.25). R_f (hexane/EtOAc, 3:1) = 0.57.

Dimer 109: To a degassed solution of **97** (42 mg, 0.06 mmol) in toluene (120 mL) at reflux temperatures was added catalyst **103** (8 mg, 0.01 mmol) as a solid in one portion. After 20 h, air was bubbled through the solution for 15 min to destroy the active catalyst. The volatiles were removed and the residue was subjected to column chromatography, and dimer **109** (10 mg, 0.02 mmol, 25%) was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.58–5.54 (m, 1 H), 5.43 (dd, J = 11.7, 2.1 Hz, 1 H), 5.33 (dd, J = 2.5, 1.6 Hz, 1 H), 5.20 (t, J = 1.8 Hz, 1 H), 5.16 (td, J = 8.0, 5.4 Hz, 1 H), 4.69 (s, 1 H), 4.16 (d, J = 4.2 Hz, 1 H), 3.89 (dd, J = 8.8, 5.0 Hz, 1 H), 3.77 (t, J = 4.7 Hz, 1 H), 3.39–3.32 (m, 4 H), 3.11–3.08 (m, 1 H), 2.57 (d, J = 5.1 Hz, 1 H), 2.45 (ddd, J = 14.7, 7.8, 1.6 Hz, 1 H), 2.09 (s, 3 H), 2.04–1.98 (m, 1 H), 1.94–1.87 (m, 2 H), 1.76–1.70 (m, 1 H), 1.66 (br. s, 4 H), 1.41 (s, 3 H), 0.99 (t, J = 7.9 Hz, 9 H), 0.94 (t, J = 8.0 Hz, 9 H), 0.69 (q, J = 7.8 Hz, 6 H), 0.58 (q, J = 7.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.2, 170.8, 144.2, 135.2, 122.1, 115.8, 109.7, 85.4, 84.5, 83.0, 78.6, 76.2, 70.9, 57.7, 57.0, 55.3, 49.7, 44.8, 39.6, 25.0, 23.4, 21.0, 13.2, 7.12 (3 C), 6.98 (3 C), 6.60 (3 C), 5.01 (3 C) ppm. HRMS (ESI): calcd. for $C_{70}H_{120}O_{18}Si_4Na$ $[M + Na]^+$ 1383.7449; found 1383.7454. IR: $\tilde{\nu}$ = 2956, 2914, 2877, 2369, 1771, 1746, 1373, 1222, 1151, 1043 cm^{-1}. $[\alpha]_D^{20}$ = –5.0, ($CHCl_3$, c = 0.2). R_f (hexane/EtOAc, 3:1) = 0.29.

Diene 111: A solution of **96** (32 mg, 0.05 mmol) and 2,6-lutidine (27 μL, 0.23 mmol) in CH_2Cl_2 (700 μL) was treated with TMSOTf (27 μL, 0.15 mmol) at 0 °C. The resulting mixture was stirred for 3 h, satd. aq. NH_4Cl (5 mL) and diethyl ether (5 mL) were added. The separated aqueous layer was extracted with diethyl ether (2× 5 mL). The combined organic layers were washed with satd. aq. NaCl (5 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the residue by column chromatography (SiO_2, hexane/EtOAc, 6:1) gave TMS-protected allylic alcohol **111** (27 mg, 0.04 mmol, 76%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.87–5.77 (m, 1 H), 5.56 (dd, J = 11.3, 2.7 Hz, 1 H), 5.33 (dd, J = 2.6, 1.6 Hz, 1 H), 5.22–517 (m, 1 H), 5.10 (dd, J = 17.1, 2.0 Hz, 1 H), 5.06–5.03 (m, 1 H), 4.64 (s, 1 H), 3.94 (d, J = 4.0 Hz, 1 H), 3.82 (dd, J = 8.1, 3.1 Hz, 1 H), 3.76–3.72 (m, 1 H), 3.43 (dd, J = 8.3, 6.3 Hz, 1 H), 3.31 (s, 3 H), 3.15–3.12 (m, 1 H), 2.45 (ddd, J = 14.7, 7.9, 1.7 Hz, 1 H), 2.40–2.33 (m, 1 H), 2.25–2.15 (m, 2 H), 2.14–2.07 (m, 1 H), 2.04 (s, 3 H), 1.92 (dd, J = 14.7, 5.5 Hz, 1 H), 1.84 (dt, J = 14.3, 3.1 Hz, 1 H), 1.58 (br. d, J = 3.1 Hz, 1 H), 1.42 (s, 3 H), 0.98 (t, J = 8.0 Hz, 9 H), 0.94 (t, J = 8.0 Hz, 9 H), 0.64 (q, J = 8.0 Hz, 6 H), 0.58 (q, J = 7.9 Hz, 6 H), 0.11 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.8, 170.1, 144.5, 135.9, 117.1, 115.5, 108.7, 85.5, 84.7, 83.3, 77.4, 73.2, 72.2, 58.23, 58.1, 54.7, 49.4, 44.2, 39.7, 38.1, 24.9, 23.3, 21.2, 7.10 (3 C), 6.91 (3 C), 6.61 (3 C), 5.16 (3 C), 0.62 (3 C) ppm. HRMS (ESI): calcd. for $C_{38}H_{68}O_9Si_3$ $[M + Na]^+$ 775.4069; found 775.4050. IR: $\tilde{\nu}$ = 2955, 2877, 1775, 1747, 1372, 1229, 1150, 1107, 1041, 993 cm^{-1}. $[\alpha]_D^{20}$ = –51–8, ($CHCl_3$, c = 0.8). R_f (hexane/EtOAc, 3:1) = 0.56.

(3*S*,5*S*)-3-(Methoxymethoxy)-3-methyl-5-(prop-2-yn-1-yloxy)cyclopent-1-ene (115): A solution of alcohol **117** (150 mg, 0.95 mmol) in THF (6 mL) was added dropwise to a suspension of NaH (164 mg, 3.80 mmol) in THF (9 mL) at 0 °C. After 1 h propargyl bromide (310 μL, 2.80 mmol) was added through a syringe and the resulting mixture was warmed to room temperature. After 16 h satd. aq. NH_4Cl (10 mL) was added and the aqueous phase was separated and extracted with diethyl ether (3× 10 mL). The combined organic phases were washed with satd. aq. NaCl (10 mL), dried with $MgSO_4$, filtered and concentrated under reduced pressure. Column chromatography (SiO_2, hexane/EtOAc, 3:1) of the residue afforded desired propargyl ether **115** (184 mg, 0.94 mmol, 99%) as a colorless oil. ^{1}H NMR ([D$_6$]DMSO, 400 MHz): δ = 6.05 (dd, J = 5.6, 2.0 Hz, 1 H), 5.89 (J = 5.6, 1.2 Hz, 1 H), 4.72–4.69 (m, 1 H), 4.54 (d, J = 7.2 Hz, 1 H), 4.49 (d, J = 7.2 Hz, 1 H), 4.15 (dd, J = 16.0, 2.4 Hz, 1 H), 4.11 (dd, J = 13.7, 2.4 Hz, 1 H), 3.39 (t, J = 2.4 Hz, 1 H), 3.21 (s, 3 H), 2.33 (dd, J = 14.1, 7.0 Hz, 1 H), 1.66 (dd, J = 14.1, 3.7 Hz, 1 H), 1.36 (s, 3 H) ppm. ^{13}C NMR ([D$_6$]DMSO, 100 MHz): δ = 139.3, 133.7, 91.2, 86.6, 82.1, 80.8, 76.8, 55.8, 54.4, 43.9, 27.1 ppm. HRMS (EI): calcd. for $C_{10}H_{13}O_3$ $[M – CH_3]^+$ 181.0865; found 181.0862. IR: $\tilde{\nu}$ = 3290, 2930, 1632, 1444, 1361, 1270, 1142, 1095, 1031, 916 cm^{-1}. $[\alpha]_D^{20}$ = –88.7, ($CHCl_3$, c = 0.54). R_f (hexane/EtOAc, 3:1) = 0.42.

Poly-cycle 119: To a solution of propargyl ether **115** (66 mg, 0.34 mmol) in CH_2Cl_2 (3.5 mL) was added $Co_2(CO)_8$ (133 mg, 0.37 mmol) at 0 °C. The resulting mixture was warmed to room temperature and stirring was continued for 16 h. The volatiles were removed under reduced pressure and the crude residue was used without purification in the next reaction.

To a solution of the crude cobalt complex (12 mg, 0.03 mmol) in THF (0.5 mL) was added trimethylamine *N*-oxide (TMANO; 6 mg, 0.08 mmol) at –21 °C. The resulting mixture was warmed to room

temperature and stirred for 1 h. The precipitate was removed by filtration through a short pad of Celite that was rinsed with diethyl ether (5 mL). The volatiles were removed and the remaining residue was subjected to column chromatography (SiO_2, hexane/EtOAc, 3:1) leading to the isolation of dimer **119** (10 mg, 0.02 mmol, 90%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.47 (t, J = 1.6 Hz, 1 H), 6.03 (dd, J = 5.7, 1.9 Hz, 1 H), 5.94 (dd, J = 5.5, 1.2 Hz, 1 H), 4.88–4.83 (m, 1 H), 4.72–4.69 (m, 1 H), 4.67–4.63 (m, 3 H), 4.55 (d, J = 7.3 Hz, 1 H), 4.19–4.11 (m, 2 H), 4.00 (d, J = 9.6 Hz, 1 H), 3.98 (d, J = 9.5 Hz, 1 H), 3.50–3.45 (m, 1 H), 3.34 (s, 3 H), 3.34 (s, 3 H), 3.26 (s, 1 H), 3.04 (d, J = 8.4 Hz, 1 H, 1 H), 2.46 (dd, J = 14.2, 6.8 Hz, 1 H), 2.41 (ddd, J = 14.3, 6.6, 1.5 Hz, 1 H), 1.77 (dd, J = 14.2, 3.8 Hz, 1 H), 1.68 (dd, J = 14.3, 5.2 Hz, 1 H), 1.48 (s, 3 H), 1.46 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 205.5, 196.1, 158.1, 143.8, 139.9, 133.8, 91.9, 91.4, 90.4, 85.8, 84.2, 77.9, 68.9, 63.04, 62.95, 60.38, 58.0, 55.74, 55.68, 55.1, 46.7, 44.3, 27.2, 20.5 ppm. HRMS (ESI): calcd. for $C_{24}H_{32}O_8Na$ $[M + Na]^+$ 471.1995; found 471.2006. IR: $\tilde{\nu}$ = 2923, 2852, 1747, 1700, 1466, 1366, 1270, 1145, 1081, 1030 cm^{-1}. $[\alpha]_D^{22}$ = –75.9, ($CHCl_3$, c = 0.25). R_f (hexane/EtOAc, 1:1) = 0.17.

Supporting Information (see footnote on the first page of this article): Details on the Heck-macrocyclization conditions

Acknowledgments

Financial support from the University of Vienna (doctoral program, Initiativkolleg Functional Molecules IK I041-N) and from the Austrian Science Fund (FWF) (project number P22180) is gratefully acknowledged. The authors thank H. Kählig, L. Brecker, and S. Felsinger for NMR assistance and A. Roller and V. Arion (University of Vienna) for X-ray analysis.

[1] J. Marrero, A. D. Rodríguez, P. Baran, R. G. Raptis, J. A. Sanchez, E. Ortega-Barria, T. L. Capson, *Org. Lett.* **2004**, *6*, 1661–1664.
[2] J. Marrero, A. D. Rodríguez, P. Baran, R. G. Raptis, *Org. Lett.* **2003**, *5*, 2551–2554.
[3] a) B. Doroh, G. A. Sulikowski, *Org. Lett.* **2006**, *8*, 903–906; b) R. Miao, S. G. Gramani, M. J. Lear, *Tetrahedron Lett.* **2009**, *50*, 1731–1733; c) K. C. Nicolaou, V. A. Adsool, C. R. H. Hale, *Angew. Chem.* **2011**, *123*, 5255–5258; *Angew. Chem. Int. Ed.* **2011**, *50*, 5149–5152; d) A. Jana, S. Mondal, Md. F. Hossain, S. Ghosh, *Tetrahedron Lett.* **2012**, *53*, 6830–6833; e) M. E. Meyer, J. H. Phillips, E. M. Ferreira, B. M. Stoltz, *Tetrahedron* **2013**, *69*, 7627–7635; f) A. P. G. Macabeo, C. W. Lehmann, O. Reiser, *Synlett* **2012**, *23*, 2909–2912; g) A. Saitman, S. D. E. Sullivan, E. A. Theodorakis, *Tetrahedron Lett.* **2013**, *54*, 1612–1615; h) J.-B. Farcet, M. Himmelbauer, J. Mulzer, *Org. Lett.* **2012**, *14*, 2195–2197; i) J.-B. Farcet, M. Himmelbauer, J. Mulzer, *Eur. J. Org. Chem.* **2013**, 4379–4398; j) M. Himmelbauer, J.-B. Farcet, J. Gagnepain, J. Mulzer, *Org. Lett.* **2013**, *15*, 3098–3101.
[4] a) P. A. Roethle, D. Trauner, *Org. Lett.* **2006**, *8*, 345–347; b) P. A. Roethle, P. T. Hernandez, D. Trauner, *Org. Lett.* **2006**, *8*, 5901–5904; c) P. A. Roethle, D. Trauner, *Nat. Prod. Rep.* **2008**, *25*, 298–317; d) Y. Li, G. Pattenden, *Nat. Prod. Rep.* **2011**, *28*, 1269–1310.
[5] J.-B. Farcet, M. Himmelbauer, J. Mulzer, *Eur. J. Org. Chem.* DOI:10.1002/ejoc.201300870; see the next paper in this issue.
[6] a) T. Bach, *Synthesis* **1998**, 683–703; b) For a review on photochemical reactions in total syntheses, see: T. Bach, J. P. Hehn, *Angew. Chem.* **2011**, *123*, 1032–1077; *Angew. Chem. Int. Ed.* **2011**, *50*, 1000–1054.
[7] a) A. Stephen, K. Hashmi, M. Rudolph, *Chem. Soc. Rev.* **2008**, *37*, 1766–1775; b) V. Belting, N. Krause, *Org. Biomol. Chem.* **2009**, *7*, 1221–1225; c) M. H. Suhre, M. Reif, S. F. Kirsch, *Org. Lett.* **2005**, *7*, 3925–3927; d) C. Nieto-Oberhuber, M. P. Muñoz, S. López, E. Jiménez-Núñez, C. Nevado, E. Herrero-Gómez, M. Raducan, A. M. Echavarren, *Chem. Eur. J.* **2006**, *12*, 1677–1693; e) C. Nieto-Oberhuber, M. P. Muñoz, E. Buñuel, C. Nevado, D. J. Cárdenas, A. M. Echavarren, *Angew. Chem.* **2004**, *116*, 2456–2460; *Angew. Chem. Int. Ed.* **2004**, *43*, 2402–2406; f) L. Zhang, J. Sun, S. A. Kozmin, *Adv. Synth. Catal.* **2006**, *348*, 2271–2296.
[8] K. Sonogashira, *J. Organomet. Chem.* **2002**, *653*, 46–49.
[9] a) C. R. Schmid, J. D. Bryant, *Org. Synth.* **1995**, *72*, 6; b) J. Mann, A. C. Weymouth-Wilson, *Org. Synth.* **1998**, *75*, 139; c) W. Felzmann, V. B. Arion, J. L. Mieusset, J. Mulzer, *Org. Lett.* **2006**, *8*, 3849–3851.
[10] a) G. Deguest, L. Bischoff, C. Fruit, F. Marsais, *Org. Lett.* **2007**, *9*, 1165–1167; b) K. Maruoka, A. B. Concepcion, N. Murase, M. Oishi, N. Hirayama, H. Yamamoto, *J. Am. Chem. Soc.* **1993**, *115*, 3943–3949.
[11] T. Gaich, H. Weinstabl, J. Mulzer, *Synlett* **2009**, *9*, 1357–1366.
[12] P. A. Krapcho, J. F. Weimaster, J. M. Eldridge, E. G. E. Jahngen Jr., A. J. Lovey, W. P. Stephens, *J. Org. Chem.* **1978**, *43*, 138–147.
[13] S. Searles, Y. Li, B. Nassim, M.-T. R. Lopes, P. T. Tran, P. Crabbé, *J. Chem. Soc. Perkin Trans. 1* **1984**, 747.
[14] a) A. Rosenthal, L. B. Nguyen, *J. Org. Chem.* **1969**, *34*, 1029–1034; b) M. Xie, D. A. Berges, M. Robins, *J. Org. Chem.* **1996**, *61*, 5178–5179 and references cited therein.
[15] CCDC-943950 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[16] J.-P. Dulcère, J. Crandall, R. Faure, M. Santelli, V. Agati, M. N. Mihoubi, *J. Org. Chem.* **1993**, *58*, 5702–5708.
[17] For a review, see: E. M. Becalli, G. Broggini, M. Martinelli, S. Sottocornola, *Chem. Rev.* **2007**, *107*, 5318–5365.
[18] a) L. E. Overman, *Pure Appl. Chem.* **1994**, *66*, 1423–1430; b) A. B. Dounay, L. E. Overman, *Chem. Rev.* **2003**, *103*, 2945–2963.
[19] For a review, see: K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem.* **2005**, *117*, 4564–4601; *Angew. Chem. Int. Ed.* **2005**, *44*, 4490–4527.
[20] U. S. Racherla, H. C. Brown, *J. Org. Chem.* **1991**, *56*, 401–404.
[21] A. Hafner, R. O. Duthaler, R. Marti, G. Rihs, P. Rothe-Streit, F. Schwarzenbach, *J. Am. Chem. Soc.* **1992**, *114*, 2321–2336.
[22] T. M. Trnka, R. H. Grubbs, *Acc. Chem. Res.* **2001**, *34*, 18–29 and references cited therein.
[23] I. C. Stewart, T. Ung, A. A. Pletnev, J. M. Berlin, R. H. Grubbs, Y. Schrodi, *Org. Lett.* **2007**, *9*, 1589–1592.
[24] K. Grela, S. Harutyunyan, A. Michrowska, *Angew. Chem.* **2002**, *114*, 4210–4212; *Angew. Chem. Int. Ed.* **2002**, *41*, 4038–4040.
[25] C. Samojlowicz, M. Bieniek, A. Zarecki, R. Kadyrov, K. Grela, *Chem. Commun.* **2008**, *47*, 6282–6284.
[26] A. K. Chatterjee, T.-L. Choi, D. P. Sanders, R. H. Grubbs, *J. Am. Chem. Soc.* **2003**, *125*, 11360–11370.
[27] a) I. Khand, G. R. Knox, P. L. Pauson, *J. Chem. Soc. Perkin Trans. 1* **1973**, 977–981; b) P. L. Pauson, *Tetrahedron* **1985**, *41*, 5855–5860.
[28] For a review see: A. S. Kende, *Org. React.* **1960**, *11*, 261–316.
[29] For a review see: H. Meier, K. P. Zeller, *Angew. Chem.* **1975**, *87*, 52–63.
[30] a) T. T. Curran, D. A. Hay, *Tetrahedron: Asymmetry* **1996**, *7*, 2791–2792; b) A. Roy, S. W. Schneller, *J. Org. Chem.* **2003**, *68*, 9269–9273; c) M. W. Gilbert, A. Galkina, J. Mulzer, *Synlett* **2004**, *14*, 2558–2562.

Received: June 13, 2013
Published Online: November 19, 2013

