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# Dienyne Ring-Closing Metathesis Approach for the Construction of Taxosteroids

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**Abstract:** A cascade dienyne ring-closing metathesis approach has been applied to the synthesis of the tetracyclic carbon framework of a new class of hybrid compounds—the taxosteroids—possessing carbon frameworks incorporating moieties characteristic of both taxanes (such as AB rings) and steroids (i.e., CD system and side chain). This tandem cyclization is highly stereoselective, allowing the one-step formation of the bicyclo[5.3.1]undecene system characteristic of taxol. In this work we describe the scope and limitations of such cyclizations.

**Keywords:** medium-ring compounds · metathesis · ring-closing dienyne metathesis (RCDEYM) · steroid analogues · taxosteroids

## Introduction

The creation of molecular entities that blend the structural characteristics of two or more natural products or pharmacophore-derived fragments joined by at least one carbon–carbon bond is one of the most appealing strategies in drug discovery.[1] Conceptually, the objective in this approach is the design of new functional molecules with enhanced or even new types of properties arising from the combination of diverse structural features from two or more functionally active compounds. We have previously reported a molecular hybrid system, in the form of the taxosteroids (**I**, Figure 1),[2] characterized by the presence of the [5.3.1] system (A and B rings) of taxanes (**III**) joined in fusion with the [4.3.0] bicyclic unit (rings C and D) of the steroid system (**II**).[3] Interest in compounds of this type of structure arises both from their structural novelty and from their potential biological activity. The recent discovery that some steroid analogues behave like paclitaxel,[4] increasing tubulin assembly and stabilizing microtubules, further supports this hypothesis with regard to the potential activity of taxosteroids.[5] Additionally, the structure is ideally suited for the development of new methodologies for the construction of fused and bridged polycyclic systems.[6] To this end we envisioned, as an alternative to other lengthy procedures developed so far, the direct preparation of the core system through a cascade[7] metathesis strategy, in which the power of ring-closing metathesis (RCM)[8] would be combined with a sequential bond formation. In particular, we considered a ring-closing dienyne metathesis (RCDEYM)[9] reaction in which the initial first ring formation by ring-closing enyne metathesis

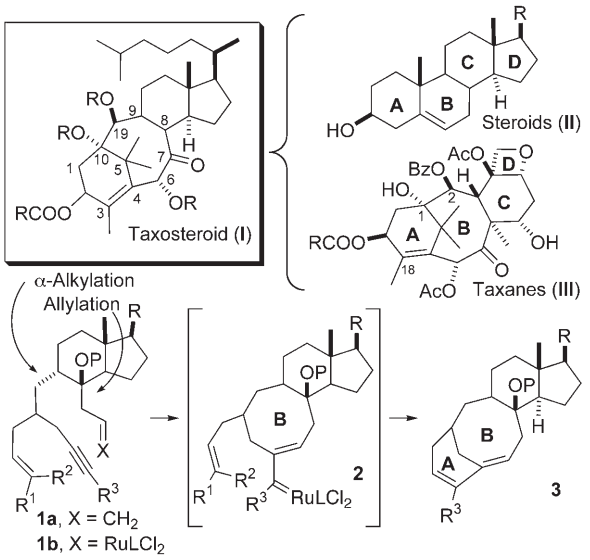


Figure 1. Top: General structure of taxosteroids (**I**), in which the bicyclo[5.3.1]undecene system (rings A and B) of taxol is fused to the [4.3.0] bicycle, rings C and D of the steroid system. Bottom: General strategy for preparation of taxosteroid skeleton.

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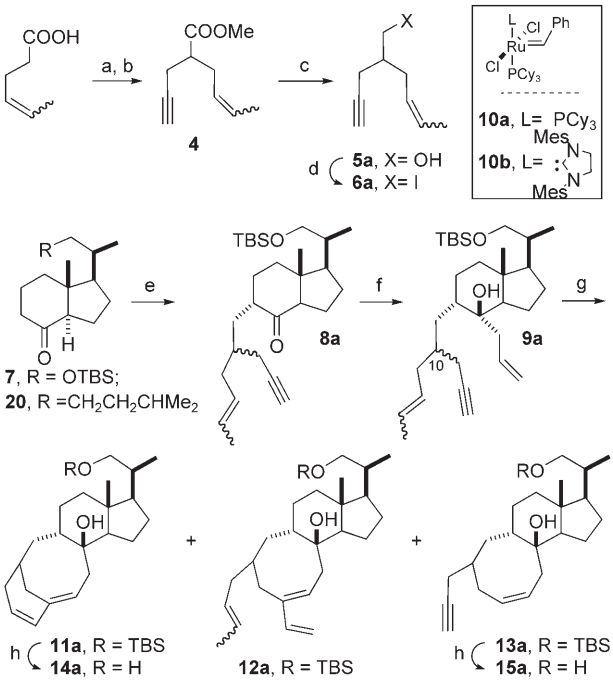
(RCEYM)[10] between the alkyne and the less substituted olefin would provide a metal alkylidene intermediate that would then undergo RCM with the other double bond to give a second ring. This transformation is very useful for the construction of two-ring systems from acyclic starting materials and has even been extended to the construction of three or four rings: the steroid skeleton, for example, has been prepared in one step from a linear dienetriyne in this way.[11] The proposed domino-metathesis approach (RCDEYM) to taxosteroids implies an initial enyne RCM of precursor **1a** that would form ring B[12] and generate intermediate **2**, which would cyclize again to form ring A of **3** (Figure 1). Regiocontrol over the first cyclization would be achieved through appropriate selection of the substituents $R^1$, $R^2$ and/or $R^3$ such as to ensure that the catalyst would initially react with the less substituted olefin to form **1b** and then with the alkynyl moiety, so that the formation of the thermodynamically less stable eight-membered ring would be favored.[13]

Here we report full details of the application of this tandem metathesis to the synthesis of novel taxosteroids, including the preparation of precursors, the structural requirements and the influence of dienyne substituents on the key tandem process, as well as an enantioselective version. The preparation of the appropriate precursors is based, as previously reported, on a combination of enol alkylation and carbonyl allylation of the ketone containing the CD fragment.[2,12] The use of a hydrindanone possessing a methylsilyloxyethyl side chain (**7** in Scheme 1) would both aid formation of the eight-membered ring[2] and provide a CD system on which a modified steroid side chain could be introduced.




Scheme 1. Synthesis of dienyne **9a** and RCM studies. a) MeI, $K_2CO_3$, DMF, 77%. b) LDA, propargyl bromide, THF, −60°C, 43%. c) $LiAlH_4$, $Et_2O$, 94%. d) $I_2$, $PPh_3$, imidazole, 85%. e) 1) KHMDS, toluene/DMF, −78°C, 2) **6a**, 79%. f) AllylMgBr, THF, 95%. g) **10a** (15%), $CH_2Cl_2$, Δ, 44%. h) TBAF, THF, 97%.

## Results and Discussion

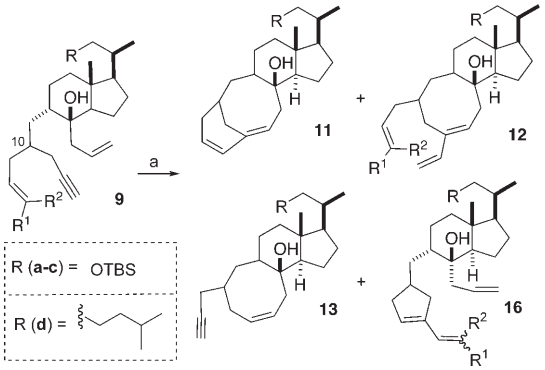
**Synthesis of the taxosteroid skeleton by RCDEYM—structural requirements**: Following the synthetic strategy described above, we initially prepared the alkylating agent **6a** (Scheme 1). This iodide was obtained in four steps from the commercially available hex-4-enoic acid, which was esterified by treatment with methyl iodide in basic DMF. The resulting ester was deprotonated with freshly prepared lithium diisopropylamide (LDA) at −60°C and the generated enolate was trapped with propargyl bromide to afford ester **4** in 43% yield.[14] After reduction with lithium aluminium hydride, the resulting alcohol **5a** was treated with triphenylphosphine, imidazole and iodine to give **6a**.

Treatment of **6a** with the kinetic enolate of **7** (generated with KHMDS in toluene/DMF 1:1), followed by allylation of the resulting ketone (**8a**), gave dienyne **9a** in 75% yield (from **7**) as an inseparable 1:1 mixture of C10-epimers.[15] Treatment of **9a** with Grubbs' catalyst **10a** (15%) provided a 2:2:1 mixture of enyne **13a** (formed by simple diene RCM without involvement of the alkynyl moiety), triene **12a** (the product of simple RCEYM without involvement of the more substituted double bond) and the desired tetracyclic compound **11a**, with a global yield of 44% (Scheme 1 and Table 1, entry 1). Flash chromatography of the crude mixture allowed isolation of compound **12a**. The other two products were easily separated after removal of the *tert*-butyldimethylsilyl group by treatment with tetrabutylammonium fluoride. NMR analysis of the deprotected minor compound **14a** showed it to be a single isomer, suggesting that only one of the C10-epimers of **9a** can undergo the tandem RCDEYM reaction, with the geometric impediments to the second annulation of the other epimer causing it to remain as **12a**.[2,12c,16] This hypothesis was supported by a lack of conversion of triene **12a** into **11a** when treated with RCM catalyst **10a** or the more reactive Grubbs' catalyst **10b**,[17] either in methylene chloride or in benzene.

Although the taxosteroid skeleton had only been obtained as a minor product, the above result had at least demonstrated the feasibility of the proposed strategy. To improve the yield, we first tried using the more reactive Grubbs' catalyst **10b**, which has been employed in previously reported RCDEYM reactions.[9a,10a] However, the use of this catalyst with compound **9a** afforded a complex mixture in which no compound containing an eight-membered ring was observed, the main isolated product being the cyclopentene **16a**, in this case in a 20% yield (Table 1, entry 2). This behavior was attributed to the catalyst initially reacting with the acetylene group and then, presumably because of thermodynamic preference for **16a** over **11a** or **12a**, with the more substituted alkene (vide infra).[18]

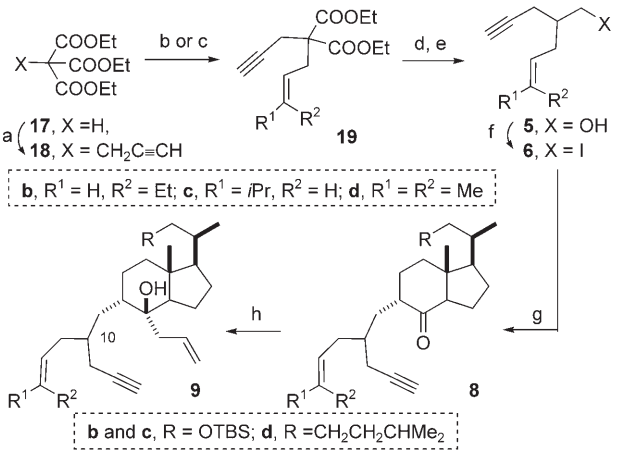
  

Table 1. Results of RCM of dienynes **9a–d**.




| Entry | 9 | $R^1$ | $R^2$ | Cat[a] | Relative ratios[b] 11 | 12 | 13 | 16 | Global yield[c] |
|---|---|---|---|---|---|---|---|---|---|
| 1 | **9a** | Me/H | Me/H | **10a** | 1 | 2 | 2 | 0 | 44 |
| 2 | **9a** | Me/H | Me/H | **10b** | 0 | 0 | 0 | 1 | 20 |
| 3 | $\mathbf{9b}_{10R}$[d] | H | Et | **10a** | 1 | 0 | 1 | 0 | 80 |
| 4 | $\mathbf{9b}_{10S}$[d] | H | Et | **10a** | 0 | 0 | 9 | 1 | 97 |
| 5 | $\mathbf{9c}_{10R}$[d] | *i*Pr | H | **10a** | 9 | 1 | 0 | 0 | 90 |
| 6 | $\mathbf{9c}_{10S}$[d] | *i*Pr | H | **10a** | 0 | 1 | 0 | 0 | 55 |
| 7 | **9d** | Me | Me | **10a** | 0 | 4 | 0 | 1 | 60 |
| 8 | **9d** | Me | Me | **10b** | 0 | 0 | 0 | 1 | 20 |

[a] The amounts of catalysts **10a** or **10b** were not optimized and 15% was routinely used. [b] Approximate relative ratios determined by NMR spectroscopy on the crude mixture. [c] Global yields of products isolated by chromatography on silica gel or aluminum oxide. [d] C10-epimers separated by flash chromatography are differentiated by a subscript (10*R* or 10*S*).




Scheme 2. Synthesis of dienynes **9b–d**. a) 1) NaOEt, EtOH, $Et_2O$, 2) $BrCH_2C{\equiv}CH$, toluene/DMF, Δ, 86%. b) NaOEt, $MeSO_3CH_2CH{=}CR^1R^2$, THF, 35% for **19b** and 85% for **19c**. c) NaOEt, $BrCH_2CH{=}C(CH_3)_2$, THF, 75%. d) NaOEt, EtOH, 32–55%. e) $LiAlH_4$, THF, 89–94%. f) $I_2$, $PPh_3$, imidazole, 85–98%. g) Grundmann's ketone (**20**) or **7**, KHMDS, toluene/DMF, −78 °C, and then **6b–d**, 35–78%. h) AllylMgBr, THF, 70–95%.

Because the use of catalyst **10b** had failed to improve the yield of **11a** afforded by catalyst **10a**, we prepared a series of compounds (**9b–d**) bearing different substituents on the longer olefin chain ($R^1$ and/or $R^2$) in the hope that these substrates would be less likely to support conversion into enynes **13** by diene RCM and/or less likely to give triene intermediates **12** that could not cyclize to **11**. The alkylating agents needed to prepare these substrates, compounds **6b–d**, were obtained from triethyl methanetricarboxylate (**17**) as shown in Scheme 2. Deprotonation of **17** (EtONa, EtOH/$Et_2O$), followed by heating of a toluene/DMF (1:1) solution of the resulting sodium salt at 80 °C in the presence of propargyl bromide, gave the alkyne triester **18**. Decarboxylation with sodium ethoxide and in situ alkylation of the resulting anion with the appropriate allyl electrophilic reagents afforded compounds **19b–d**. Attempted monodecarboxylation of these malonates by heating in acidic aqueous solution ($HCl/H_2O$) gave only very poor yields (in the case of **19d**, zero yield after 3 h at reflux), and no improvement was achieved by treatment with sodium hydroxide followed by heating in water or DMSO in the presence of NaCl. The best yields (32–55%) were achieved by heating a solution of malonate in ethanol containing sodium ethoxide, with subsequent neutralization.[19] Reduction of the resulting esters with lithium aluminium hydride in THF afforded the alcohols **5b–d**, which were transformed into iodides **6b–d** in good yields by treatment with triphenylphosphine, imidazole and iodine. Finally, dienynes **9b–d** were obtained by alkylation either of the kinetic enolate of **7** with **6b** and **6c** or of the enolate of Grundmann's ketone (**20**)[20] (Scheme 1) with iodide **6d**, followed by allylation of the resulting ketones.

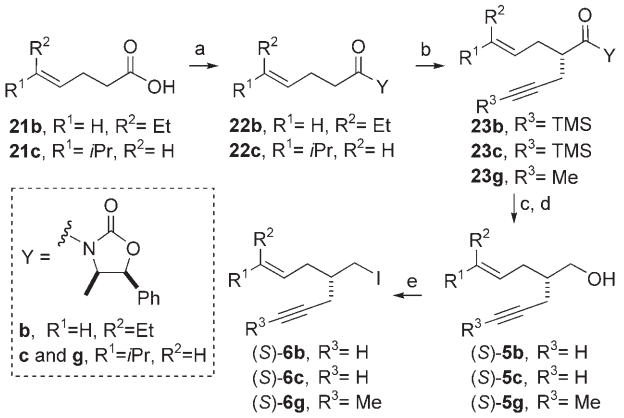
The two C10-epimers of dienynes **9b** and **9c** were separated by flash chromatography. In the case of **9c** they were not obtained in equal amounts: the $\mathbf{9c}_{10S}/\mathbf{9c}_{10R}$ ratio (the elucidation of the stereochemistry is described below) was 10:1 after use of three equivalents of **6c** (overall yield 75%), and 3:1 after use of 1.5 equivalents (overall yield 78%), showing that one of the enantiomers of **6c** [(*R*)-**6c**] reacts more rapidly than the other with the enolate of **7** to give the 10*S* diastereomer of dienyne **9**. Since it turned out to be the other isomers (10*R*) of dienynes **9** that were susceptible to RCDEYM (see below), we later tried to prepare **9c** with the use of fewer than 1.5 equivalents of **6c**, but this reduced the global yield of the reaction significantly. The two C10-epimers of **9d** could not be separated.

Like the reactive isomer of **9a**, which proved to be 10*R*, the same isomers (10*R*) of dienynes **9b** and **9c** both afforded the desired taxosteroid **11a** (R = OTBS) when subjected to RCDEYM conditions with catalyst **10a**. In these cases the yields of the taxosteroid **11** increased with the steric impediment to the diene RCM ($R^1$ or $R^2$ = Me, Et, *i*Pr; entries 1, 3, and 5, Table 1), as did the overall yields.[21] The other isomers (10*S*) of **9b** and **9c**, like the unreactive isomer of **9a**, failed to afford compound **11a**; instead $\mathbf{9b}_{10S}$ gave mainly the diene RCM product **13a** (entry 4, Table 1), whilst $\mathbf{9c}_{10S}$ gave only triene **12c** (entry 6, Table 1). These results confirm that only one of the isomers of dienynes **9** can undergo both annulations, and show that for this isomer the desired annulation sequence can be favored by the presence of appropriate terminal substituents on the longer olefin chain. Disubstitution at this position, however, was counterproductive: when **9d** was used as substrate for the RCDEYM reaction, the major products were triene **12d**

(48%) when the catalyst was **10a** and cyclopentene **16d** (20%) when the catalyst was **10b** (entries 7 and 8, Table 1), although treatment of isolated **12d** with **10b** at reflux in dichloromethane for 12 h did afford a small yield of **11d** (14%).[22] This last finding supports our earlier conclusion that the failure of **10b** to induce RCDEYM of **9** was due to the presence of the alkyne moiety, and also suggests that in the case of **9d** there was not only a total stereochemical impediment to RCDEYM of the 10*S* diastereomer, but also a somewhat less intractable impediment to RCDEYM of the 10*R* diastereomer (presumably involving steric hindrance due to the methyl groups $R^1$ and $R^2$).

**Enantioselective synthesis of (10*R*)-taxosteroids by RCDEYM**: Molecular mechanical calculations suggested that, as anticipated above, it was the 10*R* stereoisomers of compounds **9** that were able to cyclize. To confirm this and to establish the configurations of the taxosteroids at C10, we prepared the enantiopure alkylating agents **6b** and **6c** by use of (4*R*,5*S*)-4-methyl-5-phenyloxazolidin-2-one as chiral auxiliary (Scheme 3).[23] Treatment of (*Z*)-hept-4-enoic acid




Scheme 3. Enantioselective synthesis of iodides (*S*)-**6b**, (*S*)-**6c**, and (*S*)-**6g**. a) 1) Pivaloyl chloride, $Et_3N$, THF, −78°C, 2) (4*R*,5*S*)-4-methyl-5-phenyloxazolidin-2-one, DMPA, room temperature, 59% for **22b**, 80% for **22c**. b) LiHMDS, $BrCH_2C{\equiv}CR^3$, THF, −78°C, 65% ($R^3$=TMS) from **22b**, 70% ($R^3$=Me), 65% ($R^3$=TMS) from **22c**. c) $LiAlH_4$, THF, 0°C, 90% for (*S*)-**5g**. d) TBAF, THF, 80% for (*S*)-**5b**, 90% for (*S*)-**5c** (two steps). e) $I_2$, $PPh_3$, imidazole, 75% for (*S*)-**6b**, 75% for (*S*)-**6c**, 70% for (*S*)-**6g**.

(**21b**) with pivaloyl chloride, followed in situ by Evans' oxazolidinone, afforded compound **22b**, the enolate of which (generated with LiHMDS) was treated at −78°C with 1-bromo-3-trimethylsilylprop-2-yne to give the corresponding propargylated oxazolidinone **23b** in >90% *de*. Reduction of **23b** with lithium aluminium hydride and subsequent desilylation provided alcohol (*S*)-**5b**, and treatment of this alcohol with iodine, triphenylphosphine and imidazole afforded iodide (*S*)-**6b** in 75% yield. The (*E*)-isopropyl derivative (*S*)-**6c** was prepared from (*E*)-6-methylhept-4-enoic acid[23] (**21c**) in similar yield by the same strategy. Alkylation of the kinetic enolate of **7** with (*S*)-**6b** or (*S*)-**6c**, followed by allylation of the resulting ketone, afforded compounds with spectroscopic characteristics identical to those of the reactive isomers of **9b** and **9c**, thus confirming these as $\mathbf{9b_{10R}}$ and $\mathbf{9c_{10R}}$.[24] Subjection of these compounds to RCM conditions gave, as expected, results identical to those obtained with the reactive compounds derived from racemic mixtures of iodides **6b** and **6c** (entries 3 and 5, Table 1). Definitive confirmation of the stereochemistry of the reactive isomers of **9** was obtained by X-ray crystallography of the methyl ether **11e** (P=Me, Figure 2), which was obtained by alkyla-

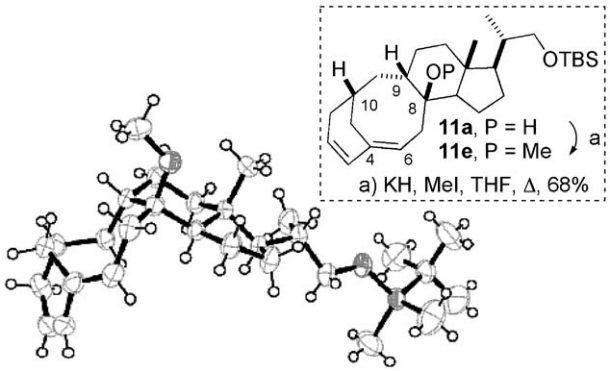
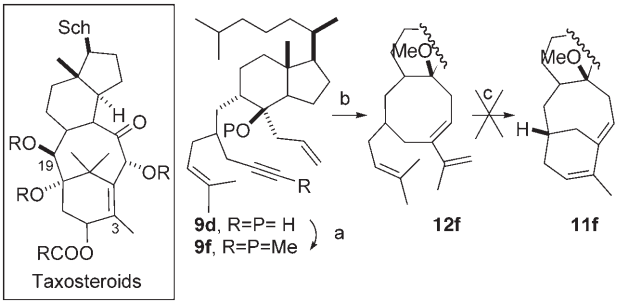



Figure 2. X-ray structure of compound **11e**, confirming the C10-*R* configuration.

tion of **11a** with KH and MeI and then crystallized from chloroform by vapor-phase equilibration with hexane. The structure calculated from the X-ray data showed the expected taxane-like bicyclo[5.3.1]undecadiene system with the bridgehead C4=C6 double bond left untouched by the RCDEYM reaction and with the *R* configuration at C10, as a result of which the C10 hydrogen is *cis* to the C8 methoxy group and C9 hydrogen (Figure 2).

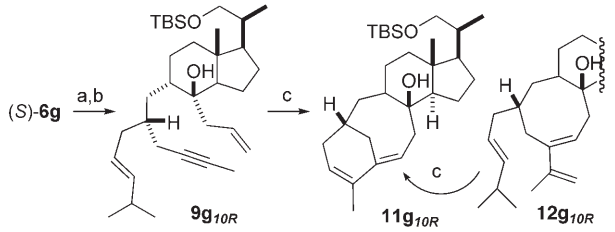
**Enantioselective synthesis of a 3-methyltaxosteroid by RCDEYM**: Our next step was to use an RCDEYM substrate with an alkyne chain terminated by a methyl group that should end up at the position corresponding to the C18-methyl group of taxol (C3 in the taxosteroid skeleton, Scheme 4). Accordingly, compound **9f** was prepared by




Scheme 4. RCDEYM of dienyne **9f** for the synthesis of taxosteroids containing the C18-methyl group of taxol (C3 at taxosteroid skeleton). a) *n*BuLi, MeI, THF, 76%. b) **10b** (15%), $CH_2Cl_2$, Δ, 38%. c) **10b** (15%), benzene, Δ.

treatment of **9d** with two equivalents of *n*BuLi, followed by methyl iodide (Scheme 4). Although RCDEYM of **9f** was expected to suffer from steric hindrance from the geminal methyl groups of the alkene, the formation of **11d** by treatment of triene **12d** with **10b** encouraged us to hope that **9f** might afford a similar result. However, the desired taxosteroid **11f** was obtained neither directly by treatment of **9f** with **10a** or **10b**, nor when the product isolated from that reaction, a 38% yield of triene **12f**, was treated with **10b** in benzene at reflux. Apparently, RCDEYM was impossible for **9f** not only in the case of the 10*S* diastereomer but also in that of its 10R epimer, because of excessive steric hindrance due to the combination of the acetylenic methyl group and the geminal olefinic methyl groups. Unexpectedly, the use of **10b** did not result in the formation of any product containing the cyclopentene present in **16**, although this type of derivative had previously always been obtained when this catalyst had been applied to a dienyne substrate.

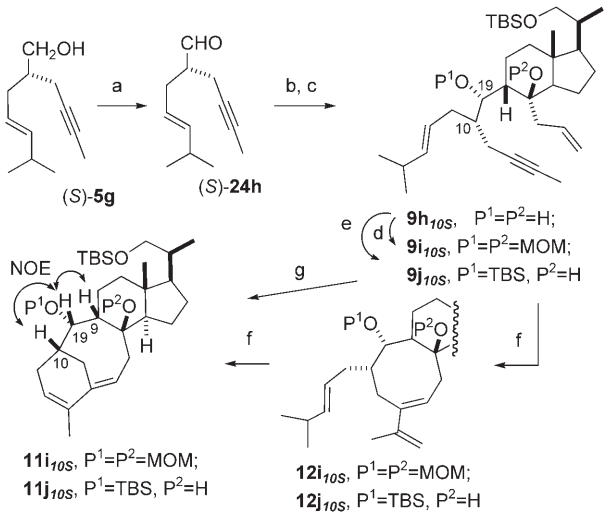
In view of the above results, we decided to reduce the steric hindrance in the substrate by using **6g**, in which $R^1 = i$Pr and $R^2 = H$ (Scheme 3), and at the same time avoid unnecessary production of the 10*S* diastereomer by using only $\mathbf{9g}_{10R}$ (Scheme 5). Accordingly, iodide (*S*)-**6g** was prepared




Scheme 5. Synthesis of a taxosteroid containing the C18-methyl group of taxol (**11g**). a) **7**, KHMDS, toluene/DMF, −78°C, and then (*S*)-**6g**, 70%. b) AllylMgBr, THF, 93%. c) **10b** (10%), benzene, Δ, 69% from $\mathbf{9g}_{10R}$ and 70% from $\mathbf{12g}_{10R}$.

in the same way as (*S*)-**6c** (but with use of 1-bromobut-2-yne instead of 1-bromo-3-trimethylsilylprop-2-yne to alkylate **22c**; Scheme 3). Addition of (*S*)-**6g** to the potassium enolate of **7**, followed by allylation of the resulting ketone, afforded dienyne $\mathbf{9g}_{10R}$ in 70% yield. With this dienyne the steric hindrance problem still persisted, but was no longer insurmountable. Although treatment of $\mathbf{9g}_{10R}$ with **10a** in dichloromethane or benzene afforded $\mathbf{11g}_{10R}$ only as a very minor product (the major product being the triene $\mathbf{12g}_{10R}$), treatment of isolated $\mathbf{12g}_{10R}$ with **10b** (10%) at reflux in benzene for 4 h produced $\mathbf{11g}_{10R}$ almost exclusively (70%). It was then found that treatment of $\mathbf{9g}_{10R}$ directly with **10b** at reflux in benzene also afforded $\mathbf{11g}_{10R}$ as the major product (69%), without any of the cyclopentene formation that we had initially expected.

**Stereoselective synthesis of (19*S*)-hydroxylated taxosteroids by RCDEYM**: In order to increase the structural complexity of the taxosteroid hybrids further, we decided to introduce the taxol C2 hydroxy group (C19 in the taxosteroid skeleton). This group could be generated by aldol condensation of the kinetic enolate of **7** and an aldehyde, such as (*S*)-**24h** (Scheme 6), containing the enyne moiety and the isopropyl group needed for optimal RCDEYM product formation. It was believed that the well known *anti* aldol product selectivity and the enolate axial attack,[25] together with facial selectivity for alkylation of hydrindinone **7**, should preferentially provide only one (19*S*) diastereomer. Aldehyde (*S*)-**24h** was obtained in 72% yield by oxidation of alcohol (*S*)-**5g** with pyridinium dichromate (PDC), and addition of the lithium kinetic enolate of **7** to a cooled (−78°C) solution of aldehyde (*S*)-**24h** in THF, followed by carbonyl allylation of the resulting ketone, provided diol $\mathbf{9h}_{10S}$ in 72% yield (two steps) as a single isomer (Scheme 6).[26] It was not possible at this point to confirm the expected 19*S* configuration by NMR experiments. Unfortunately, treatment of the resulting diol $\mathbf{9h}_{10S}$ with Grubbs' catalysts **10a** or **10b** at reflux in either benzene or dichloromethane did not provide any cyclization products, and the starting dienynediol was not recovered in any of these cases, being completely decomposed. We have attributed this result to the presence of the two unprotected hydroxy groups, which has been claimed to decompose the catalyst.[27]




Scheme 6. Synthesis of taxosteroids **11i,j** (10*S* epimers) containing the C2-hydroxy group of taxol (C19 at taxosteroid skeleton). a) PDC, $CH_2Cl_2$, 72%. b) **7**, LDA, THF, −78°C, and then (*S*)-**24h**, 92%. c) AllylMgBr, THF, 79%. d) MOMCl, DIEA, $CH_2Cl_2$, 80%. e) TBSOTf, Py, $CH_2Cl_2$, 0°C to rt, 75%. f) **10b** (10%), benzene, Δ, 80% for $\mathbf{12j}_{10S}$ and 80% for $\mathbf{11j}_{10S}$. g) **10b** (10%), benzene, Δ, 2 h and then **10b** (10%), Δ, 62%.

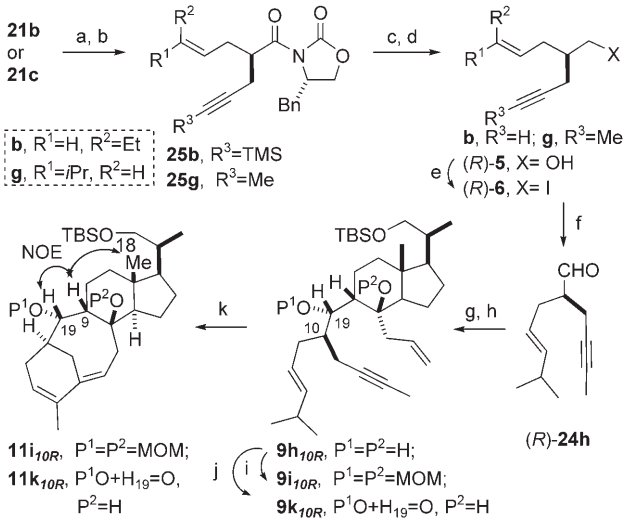
Protection of those hydroxy groups was only possible as MOM acetals, by treatment of diol $\mathbf{9h}_{10S}$ with methoxymethyl chloride and *N*,*N*′-diisopropylethylamine (DIEA), to give compound $\mathbf{9i}_{10S}$ in 80% yield. Treatment of MOM derivative $\mathbf{9i}_{10S}$ under the above optimal RCDEYM conditions (10% **10b** in benzene) afforded a complex mixture of compounds in which the main compound was the triene derivative $\mathbf{12i}_{10S}$ rather than the desired tetracyclic derivative $\mathbf{11i}_{10S}$. Furthermore, the monoprotected silyl ether $\mathbf{9j}_{10S}$

gave mainly triene **12j$_{10S}$** (80%) under the same conditions.[28]

Interestingly, while treatment of isolated **12i$_{10S}$** with **10b** at reflux in benzene had not afforded any **11i$_{10S}$**, the silyl ether **12j$_{10S}$** was transformed into the tetracyclic derivative **11j$_{10S}$** in good yield. The best conditions for the formation of the taxosteroid skeleton from dienyne **9j$_{10S}$** required two additions of catalyst **10b** (10%), the second one being after two hours of heating, when the main product observed by TLC was the triene precursor **12j$_{10S}$**. Under these conditions compound **11j$_{10S}$** was obtained in 62% yield. The observed NOE cross-peaks between the H19 and H9 and H10 in NMR spectra of **11j$_{10S}$** confirm the proposed *19S* configuration.

These results obtained with 19-hydroxylated derivatives (**9i$_{10S}$** and **9j$_{10S}$**) might suggest that the presence of substituents at position C19 and a protecting group on the tertiary hydroxy group produces some conformational modification that might preclude the final cyclization. For that reason we decided also to study the 10*R* isomer, hoping that these conformational changes might now facilitate its cyclization. To this end we prepared alcohol (*R*)-**5g** in the same way as (*S*)-**5c** (Scheme 3) but with use of (*S*)-4-benzyloxazolidin-2-one as chiral auxiliary (Scheme 7).[23,24] Oxidation of alcohol (*R*)-**5g** with PDC afforded the enantiomerically pure aldehyde (*R*)-**24h**, which on condensation with the kinetic enolate of **7** and subsequent allylation produced diol **9h$_{10R}$** in 62% yield as a single isolated isomer at C19 (Scheme 7). Once again, treatment of the resulting diol with Grubbs' catalyst **10b** at reflux in benzene did not provide any cyclization




Scheme 7. Synthesis of taxosteroids **11i** and **11k** (10*R* diastereomer) containing the C2-hydroxy group of taxol (C19). a) 1) Pivaloyl chloride, $Et_3N$, THF, −78°C, 2) (4*S*)-4-benzyloxazolidin-2-one, DMPA, room temperature, 42% from **21b**, 94% from **21c**. b) LiHMDS, $BrCH_2C{\equiv}CR^3$, THF, −78°C, 77% for **25b** and 73% for **25g**. c) $LiAlH_4$, $Et_2O$, 0°C, 87% for (*R*)-**5g**. d) TBAF, THF, 75% for (*R*)-**5b** (two steps). e) $I_2$, $PPh_3$, imidazole, 85% for (*R*)-**6b**. f) PDC, $CH_2Cl_2$, 70%. g) **7**, LDA, THF, −78°C, and then (*R*)-**24h**, 91%. h) AllylMgBr, THF, 68%. i) MOMCl, DIEA, $CH_2Cl_2$, 82%. j) PDC, $CH_2Cl_2$, 46%. k) **10b** (10%), benzene, Δ, 90% for **11i$_{10R}$**, 54% for **11k$_{10R}$**.

product and no starting material was recovered. Now, however, the MOM-protected derivative **9i$_{10R}$** was cyclized to **11i$_{10R}$** under optimal RCDEYM conditions in excellent yield (90%). Interestingly, the ketone **9k$_{10R}$** was also cyclized in good yield under the same conditions, to form the 19-ketotaxosteroid derivative **11k$_{10R}$**. Inspection of the two-dimensional NMR spectra of the two taxosteroids **11i$_{10R}$** and **11k$_{10R}$** showed clear NOE relationships between H9 ($\delta$ = 2.56 ppm and 2.98 ppm, respectively) and Me18 ($\delta$ = 0.98 ppm) that can only be explained by the C ring adopting a boat conformation. Additional structural information was provided by the observed NOE between the neighbouring protons H19 ($\delta$ = 3.99 ppm) and H9 in spectra of **11i$_{10R}$**, which confirms the proposed 19*S* configuration. Definitive confirmation of the stereochemistry of the C19-OH taxosteroid was again obtained by X-ray crystallography, this time of **11i$_{10R}$**, which was obtained by crystallization from methanol. The structure calculated from the X-ray data for **11i$_{10R}$** showed the expected taxane-like bicyclo[5.3.1]undecadiene system fused to a C ring in a boat conformation, together with the *S* configuration at C19 (Figure 3).

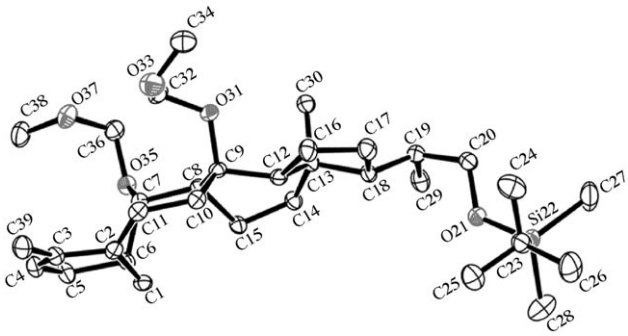
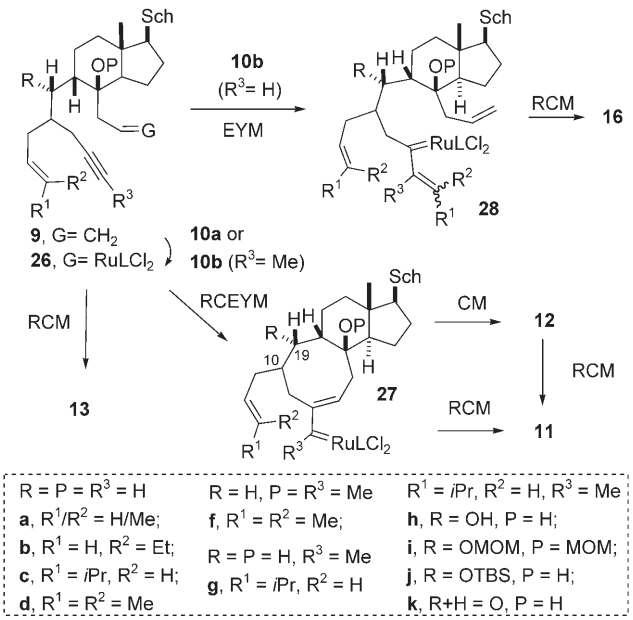



Figure 3. X-ray structure of compound **11i$_{10R}$**, confirming the C10-*R* configuration.

**Mechanistic conclusions**:[18,29] It would appear that, as we had originally envisaged, the first-generation Grubbs' catalyst **10a** initially reacts preferentially with the less substituted double bond in dienynes **9a–k**, forming the corresponding vinylideneruthenium(II) intermediates **26** (Scheme 8). Diene RCM of **26** affords enynes **13**, while RCEYM of **26** gives the secondary vinylideneruthenium(II) intermediates **27**. RCM of **27** produces—if there is not too much steric hindrance—the desired taxosteroids **11**, while cross-metathesis of **27** with another molecule of substrate **9** generates fresh **26** and leaves, as products, the trienes **12**. In the case of the 10*S* diastereomers of **27**, annulation to the taxosteroid is stereochemically impossible if the C ring adopts a chair conformation, but RCM will take place if the conformation of ring C is boat, induced by the presence of a substituent (R ≠ H) at C19 and if there is not too much steric hindrance. On the other hand, the 10*R* epimers of **27** can undergo RCM to afford **11** when the C ring can adopt the chair conformation. Formation of taxosteroids **11** can also take place by RCM of conformationally predisposed trienes




Scheme 8. Mechanistic paths for dienyne metathesis compounds.

**12**. In some cases (such as **11j$_{10S}$**), the formation of tetracyclic compound occurs mainly through the RCEYM/RCM sequence, probably because cross metathesis to give rise to the triene **12** takes place before the ring-closing process, due to conformation restrictions. In any case, success is not guaranteed and may require the use of **10b** and of relatively long reaction times and/or relatively high temperatures.

If the acetylene group of **9** is terminal ($R^3$=H), the second-generation Grubbs' catalyst **10b** appears to react initially with this group (EYM), forming the conjugated metallovinylidenes **28**. Driven by the greater thermodynamic stability of **16**, this intermediate then undergoes RCM to form these cyclopentene derivatives rather than reacting with the less substituted double bond to form the eight-membered ring, even though the formation of the cyclopentene ring requires reaction of the catalyst with the more substituted olefin. However, the lack of formation of cyclopentenes from **9f–k** suggests that if the acetylene group is non-terminal ($R^3$=Me), formation of **28** is blocked and the reaction proceeds via **27**, although steric hindrance due to the blocking methyl group may make it necessary to use relatively long reaction times and/or relatively high temperatures to achieve the second annulation.

## Conclusion

In this work we have successfully used the tandem ring-closing dienyne metathesis (RCDEYM) reaction to prepare hybrid compounds: taxosteroids, combining the AB ring systems of taxanes with the CD ring systems and side chains of steroids. The strategy described here represents an exceptional example of the formation of bridged bicycle systems with a bridgehead double bond produced by dienyne ring-closing metathesis. This RCDEYM is highly stereoselective, can be very efficient and allows the introduction of a variety of substituents characteristic of taxanes (methyl, hydroxy) into the carbon framework. We anticipate that it should also be useful for the construction of complex polycyclic systems from conformationally locked cycloalkanones other than those used in this study (**7** and **20**). Work on the introduction of additional functional groups into the taxosteroid skeleton and on the biological and pharmacological properties of this new class of compounds is currently in progress.

## Experimental Section

**Methyl (*E*,*Z*)-hex-4-enoate**: Hex-4-enoic acid (3.00 g, 26.28 mmol) and MeI (5.0 mL, 28.9 mmol) were added successively to a suspension of $K_2CO_3$ (5.40 g, 39.07 mmol) in DMF (15 mL). After having been stirred for 2 h at room temperature, the mixture was poured into water and extracted with $Et_2O$ (2×10 mL). The organic phases were washed with water (3×10 mL), dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The crude residue was distilled (50 °C at 1 mmHg) to afford the target ester (2.60 g, 77 %, colorless oil); $^1$H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=5.44 (m, 2H), 3.66 (s, 3H), 2.33 (m, 4H), 1.64 ppm (d, $^3J$=4.9 Hz, 3H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=173.0 (CO), 128.9 (*trans* CH), 128.0 (*cis* CH), 125.7 (*trans* CH), 124.9 (*cis* CH), 50.9 ($CH_3$), 33.6 ($CH_2$), 27.5 ($CH_2$), 22.0 (*cis* $CH_3$), 17.4 ppm (*trans* $CH_3$); EM-IQ$^+$: *m*/*z* (%): 128 (11) $[M]^+$, 97 (6) $[M-OMe]^+$, 69 (11) $[M-CO_2Me]^+$; HRMS calcd for $C_7H_{12}O_2$ $[M]^+$: 128.08373; found: 128.08376.

**Methyl (*E*,*Z*)-2-(prop-2-ynyl)hex-4-enoate (4)**: A solution of methyl (*E*,*Z*)-hex-4-enoate (3.09 g, 24.11 mmol) in THF (50 mL) was added at −60 °C to a solution of LDA in THF (1 M, 26.6 mL, 26.6 mmol). The mixture was stirred at that temperature for 30 min, propargyl bromide (80 % w/w solution in toluene, 4.6 mL, 41.0 mmol) was added, stirring was continued at −60 °C for 45 min, and the reaction mixture was poured into $NH_4Cl$ (20 mL) and extracted with $Et_2O$. The organic phases were washed successively with HCl (10 %) and $NaHCO_3$, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/hexanes 5 %) to afford **4** [1.72 g, 43 %, $R_f$=0.5 (EtOAc/hexanes 10 %), colorless oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=5.38 (m, 2H), 3.69 (s, 3H), 3.60 (m, 1H), 2.37 (m, 4H), 1.96 (t, $^3J$=2.6 Hz, 1H), 1.62 ppm (m, 3H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=174.3 (CO), 128.4 (CH), 126.6 (CH), 81.4 (C≡), 70.0 (C≡), 51.7 ($CH_3$), 44.4 (CH), 34.0 ($CH_2$), 28.2 ($CH_2$), 17.9 ppm ($CH_3$); MS: *m*/*z* (%): 167 (8) $[M+H]^+$, 136 (3) $[M+H-OMe]^+$, 108 (9) $[M+H-CO_2Me]^+$; HRMS calcd for $C_{10}H_{15}O_2$ $[M+H]^+$: 167.10720; found: 167.10703.

**(*E*,*Z*)-2-(Prop-2-ynyl)hex-4-en-1-ol (5a)**: $LiAlH_4$ (113 mg, 2.99 mmol) was added at 0 °C to a solution of ester **4** (289 mg, 1.49 mmol) in $Et_2O$ (10 mL). The reaction mixture was stirred at that temperature for 30 min, quenched with $H_2SO_4$ (5 %, 15 mL) and extracted with $Et_2O$, and the organic phase was dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. This concentrate was purified by flash chromatography on silica gel (EtOAc/hexanes 10 %), affording the desired alcohol [213 mg, 94 %, $R_f$=0.3 (EtOAc/hexanes 10 %), pale yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=5.50 (m, 1H), 5.37 (m, 1H), 3.64 (m, 2H), 2.30–2.18 (m, 2H), 2.06 (dd, $^3J$=10.8 and 6.5 Hz, 2H), 1.97 (t, $^3J$=2.6 Hz, 1H), 1.74 (td, $^3J$=12.3 and 6.3 Hz, 1H), 1.63 ppm (d, $^3J$=6.3 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=128.3 (CH), 127.5 (CH), 82.6 (C≡), 69.6 (C≡), 64.9 ($CH_2$), 39.9 (CH), 33.6 ($CH_2$), 19.9 ($CH_2$), 17.9 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3306, 3018, 2920, 2855, 2362, 2116, 1716, 1438, 1378, 1292, 1234, 1067, 1032, 968 cm$^{-1}$; MS: *m*/*z* (%): 139 (5) $[M+H]^+$, 121 (15) $[M+H-H_2O]^+$; HRMS calcd for $C_9H_{15}O$ $[M+H]^+$: 139.11229; found: 139.11241; elemental analysis calcd (%) for $C_9H_{14}O$: C 78.21, H 10.21; found: C 78.35, H 10.42.

**(*Z*)-2-(Prop-2-ynyl)hept-4-en-1-ol (5b)**: This compound was prepared from ethyl (*Z*)-2-(prop-2-ynyl)hept-4-enoate (747 mg, 3.85 mmol, prepared from malonate **19b**) in THF, in the same way as **5a** from **4** [527 mg, 90%, $R_f$=0.4 (EtOAc/hexanes 25%), pale yellow oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.41 (m, 1H), 5.25 (m, 1H), 3.61 (m, 2H), 2.25 (m, 2H), 2.13 (m, 4H), 1.96 (t, $^3J$=2.7 Hz, 1H), 1.75 (m, 1H), 0.93 ppm (t, $^3J$=7.5 Hz, 3H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=133.9 (CH), 126.0 (CH), 82.5 (C≡), 69.7 (C≡), 64.7 ($CH_2$), 40.2 (CH), 28.0 ($CH_2$), 20.6 ($CH_2$), 19.8 ($CH_2$), 14.2 ppm ($CH_3$); MS: *m*/*z* (%): 153 (36) $[M+H]^+$, 135 (51) $[M+H-H_2O]^+$; HRMS calcd for $C_{10}H_{17}O$ $[M+H]^+$: 153.12794; found: 153.12859.

**(2*R*,4*Z*)-2-(Prop-2-ynyl)hept-4-en-1-ol [(*R*)-5b]**: $LiAlH_4$ (0.32 g, 8.43 mmol) was added at 0°C to a solution of oxazolidinone **25b** (1.13 g, 8.43 mmol) in $Et_2O$ (60 mL), and the reaction mixture was stirred for 1 h at this temperature and quenched with $H_2SO_4$ (5%, 20 mL). The aqueous layer was extracted with $Et_2O$, and the combined organic phases were dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The resulting crude product was dissolved in THF (20 mL), treated with TBAF (1M, 7.7 mL, 7.7 mmol) and stirred at room temperature for 30 min. The reaction mixture was poured into water and then extracted with $Et_2O$, the organic phases were dried, filtered and concentrated under reduced pressure, and the resulting residue was purified by flash chromatography on silica gel (EtOAc/hexanes7%), affording alcohol (*R*)-**5b** [324 mg, 75%, $R_f$=0.4 (EtOAc/hexanes 25%), pale yellow oil].

**(2*S*,4*Z*)-2-(Prop-2-ynyl)hept-4-en-1-ol [(*S*)-5b]**: This compound was prepared from oxazolidinone **23b** (9.46 g, 23.83 mmol) in THF, in the same way as (*R*)-**5b** from **25b** [2.90 g, 80%, $R_f$=0.4 (EtOAc/hexanes 25%), pale yellow oil].

**(*E*)-6-Methyl-2-(prop-2-ynyl)hept-4-en-1-ol (5c)**: This compound was prepared from ethyl (*E*)-6-methyl-2-(prop-2-ynyl)hept-4-enoate (878 mg, 4.22 mmol, prepared from malonate **19c**) in THF, in the same way as **5a** from **4** [624 mg, 89%, $R_f$=0.3 (EtOAc/hexanes 15%), pale yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.45 (dd, $^3J$=15.3 and 6.4 Hz, 1H), 5.30 (dt, $^3J$=15.2 and 7.1 Hz, 1H), 3.62 (m, 2H), 2.24 (m, 1H), 1.96 (t, $^3J$=2.6 Hz, 1H), 1.76 (m, 1H), 0.95 ppm (d, $^3J$=6.7 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=140.3 (CH), 124.0 (CH), 82.6 (C≡), 69.7 (C≡), 64.8 ($CH_2$), 40.0 (CH), 33.6 ($CH_2$), 31.0 (CH), 22.6 ($CH_3$), 19.8 ppm ($CH_2$); MS: *m*/*z* (%): 167 (31) $[M+H]^+$, 149 (51) $[M+H-H_2O]^+$; HRMS calcd for $C_{11}H_{19}O$ $[M+H]^+$: 167.14359; found: 167.14431; elemental analysis calcd (%) for $C_{11}H_{18}O$: C 78.99, H 11.45; found: C 78.68, H 11.42.

**(2*S*,4*E*)-6-Methyl-2-(prop-2-ynyl)hept-4-en-1-ol [(*S*)-5c]**: This compound was prepared from oxazolidinone **23c** (5.56 g, 13.52 mmol) in THF, in the same way as (*R*)-**5b** from **25b** [2.02 g, 90%, $R_f$=0.3 (EtOAc/hexanes 15%), pale yellow oil].

**5-Methyl-2-(prop-2-ynyl)hex-4-en-1-ol (5d)**: This compound was prepared from ethyl 5-methyl-2-(prop-2-ynyl)hex-4-enoate (420 mg, 2.17 mmol, prepared from malonate **19d**) in THF, in the same way as **5a** from **4** [310 mg, 94%, $R_f$=0.1 (EtOAc/hexanes 10%), pale yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.22–4.92 (m, 1H), 3.64 (t, $^3J$=5.5 Hz, 2H), 2.27 (ddd, $^3J$=6.3, 4.7, 2.6 Hz, 2H), 2.08 (t, $^3J$=7.1 Hz, 2H), 1.98 (t, $^3J$=2.7 Hz, 1H), 1.77 (dd, $^3J$=12.1, 6.3 Hz, 1H), 1.70 (d, $^3J$=1.1 Hz, 3H), 1.62 ppm (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=133.7 (C), 121.7 (CH), 82.8 (C≡), 69.6 (C≡), 64.9 ($CH_2$), 40.5 (CH), 29.0 ($CH_2$), 25.8 ($CH_3$), 19.9 ($CH_2$), 17.8 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$= 3307, 2961, 2917, 2855, 2116, 1437, 1377, 1226, 1081, 1032 cm$^{-1}$; MS: *m*/*z* (%): 153 (15) $[M+H]^+$, 135 (27) $[M+H-H_2O]^+$; HRMS calcd for $C_{10}H_{17}O$ $[M+H]^+$: 153.12794; found: 153.12803.

**(2*S*,4*E*)-6-Methyl-2-(but-2-ynyl)hept-4-en-1-ol [(*S*)-5g]**: This compound was prepared from oxazolidinone **23g** (1.4 g, 3.97 mmol) in THF, in the same way as (*R*)-**5b** from **25b** [645 mg, 90%, $R_f$=0.4 (20% EtOAc/hexanes), pale yellow oil]; $[\alpha]_D^{20}$: 8.01 (*c*=0.02 in $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.43 (dd, $^3J$=15.5, 6.4 Hz, 1H), 5.32 (dt, $^3J$=15.2, 6.4 Hz, 1H), 3.61 (dd, $^3J$=5.2, 1.8 Hz, 2H), 2.27–2.13 (m, 2H), 2.03 (t, $^3J$=6.7 Hz, 2H), 1.89 (s, 1H), 1.76 (t, $^3J$=2.4 Hz, 3H), 1.75–1.65 (m, 2H), 0.95 ppm (d, $^3J$=6.7 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C, TMS): $\delta$=140.0 (CH), 124.3 (CH), 77.1 (C≡), 65.3 ($CH_2$), 40.3 (CH), 33.8 ($CH_2$), 31.0 (CH), 22.5 ($CH_3$), 20.3 ($CH_2$), 3.4 ppm ($CH_3$); MS: *m*/*z* (%): 181 (8) $[M+H]^+$, 165 (7) $[M+H-Me]^+$, 163 (14) $[M+H-H_2O]^+$, 137 (20) $[M+H-i\mathrm{Pr}H]^+$, 128 (11) $[M+H-CH_2-C\alpha C-CH_3]^+$; HRMS: calcd for $C_{12}H_{21}O$: 181.15924; found: 181.16005.

**(2*S*,4*E*)-6-Methyl-2-(but-2-ynyl)hept-4-en-1-ol [(*R*)-5g]**: This compound was prepared from oxazolidinone **25g** (3.17 g, 8.98 mmol) in the same way as (*R*)-**5b** from **25b** [1.3 g, 87%, $R_f$=0.4 (20% AcOEt/hexanes), yellow oil]; $[\alpha]_D^{20}$: −8.01 (*c*=0.02 in $CHCl_3$).

**(*E*,*Z*)-4-(Iodomethyl)oct-6-en-1-yne (6a)**: Triphenylphosphine (2.85 g, 10.87 mmol), imidazole (1.85 g, 27.17 mmol) and iodine (2.53 g, 9.96 mmol) were successively added at 0°C to a solution of alcohol **5a** (1.25 g, 9.06 mmol) in THF (45 mL). The resulting mixture was stirred at that temperature for 30 min, and for 30 minutes more at room temperature, and was then poured into water (30 mL) and extracted with $Et_2O$. The combined organic phases were dried over $Na_2SO_4$ and concentrated under reduced pressure, and the crude residue was purified by flash chromatography on silica gel (hexanes), to yield the desired iodide [1.91 g, 85%, $R_f$=0.8 (EtOAc/hexanes 10%), colorless oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.56 (m, 1H), 5.31 (m, 1H), 3.33 (m, 2H), 2.23 (m, 4H), 1.99 (t, $^3J$=2.6 Hz, 1H), 1.65 (m, 3H), 1.55 ppm (m, 1H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=128.3 (*trans* CH), 127.3 (*trans* CH),126.9 (*cis* CH), 126.6 (*cis* CH), 81.4 (C≡), 70.1 (C≡), 38.9 (CH), 36.6 ($CH_2$), 23.4 ($CH_2$), 18.0 ($CH_3$), 13.2 ($CH_2$).

**(*Z*)-4-(Iodomethyl)non-6-en-1-yne (6b)**: This compound was prepared from **5b** (351 mg, 2.31 mmol) in the same way as **6a** from **5a** [520 mg, 86%, $R_f$=0.8 (EtOAc/hexanes 10%), colorless oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.49 (m, 1H), 5.23 (m, 1H), 3.34 (m, 2H), 2.35 (m, 2H), 2.27 (dd, $^3J$=6.7, 2.6 Hz, 2H), 2.17 (m, 2H), 2.00 (t, $^3J$=2.6 Hz, 1H), 1.55 (m, 1H), 0.96 ppm (t, $^3J$=7.5 Hz, 3H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=134.7 (CH), 125.0 (CH), 81.4 (C≡), 70.2 (C≡), 39.3 (CH), 31.3 ($CH_2$), 23.5 ($CH_2$), 20.8 ($CH_2$), 14.1 ($CH_3$), 13.0 ppm ($CH_2$); IR (KBr): $\tilde{\nu}$=3302, 3006, 2962, 2929, 2871, 2850, 2360, 2118, 1457, 1426, 1230, 1178, 1069, 968 cm$^{-1}$; MS: *m*/*z* (%): 263 (0.1) $[M+H]^+$, 136 (11) $[M+H-I]^+$, 121 (15), 107 (55); HRMS calcd for $C_{10}H_{16}$ [M+H−I]: 136.12520; found: 136.12467.

**(4*R*,6*Z*)-4-(Iodomethyl)non-6-en-1-yne [(*R*)-6b]**: This compound was prepared from (*R*)-**5b** (361 mg, 2.37 mmol) in the same way as **6a** from **5a** [529 mg, 85% yield].

**(4*S*,6*Z*)-4-(Iodomethyl)non-6-en-1-yne [(*S*)-6b]**: This compound was prepared from (*S*)-**5b** (685 mg, 4.50 mmol) in the same way as **6a** from **5a** (884 mg, 75%).

**(*E*)-4-(Iodomethyl)-8-methylnon-6-en-1-yne (6c)**: This compound was prepared from **5c** (933 mg, 5.62 mmol) in the same way as **6a** from **5a** [1.32 g, 85%, $R_f$=0.9 (EtOAc/hexanes 10%), colorless oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.45 (tdd, $^3J$=15.3, 6.6, 1.1 Hz, 1H), 5.18 (dtd, $^3J$=15.3, 7.1, 7.1, 1.1 Hz, 1H), 3.27 (ddd, $^3J$=15.7, 9.8, 5.3 Hz, 2H), 2.3–2.0 (m, 5H), 1.94 (t, $^3J$=2.7 Hz, 1H), 1.48 (td, $^3J$=11.5, 5.8 Hz, 1H), 0.91 ppm (d, $^3J$=6.7 Hz, 6H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=141.1 (CH), 122.8 (CH), 81.4 (C≡), 70.1 (C≡), 38.9 (CH), 36.5 ($CH_2$), 31.0 (CH), 23.3 ($CH_2$), 22.5 (2×$CH_3$), 13.1 ppm ($CH_2$); MS: *m*/*z* (%): 277 (2) $[M+H]^+$, 150 (2) $[M+H-I]^+$.

**(4*S*,6*E*)-4-(Iodomethyl)-8-methylnon-6-en-1-yne [(*S*)-6c]**: This compound was prepared from (*S*)-**5c** (1.69 g, 10.15 mmol) in the same way as **6a** from **5a** (2.1 g, 75%).

**4-(Iodomethyl)-7-methyloct-6-en-1-yne (6d)**: This compound was prepared from **5d** (190 mg, 1.25 mmol) in the same way as **6a** from **5a** [320 mg, 98%, $R_f$=0.8 (EtOAc/hexanes 10%), colorless oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.00 (t, $^3J$=6.8 Hz, 1H), 3.29 (m, 2H), 2.23 (m, 2H), 2.05 (dd, $^3J$=12.3, 6.8 Hz, 2H), 1.95 (t, $^3J$=2.6 Hz, 1H), 1.65 (s, 3H), 1.59 (s, 3H), 1.51 ppm (m, 1H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=134.4 (C), 120.8 (CH), 81.5 (C≡), 70.05 (C≡), 39.6 (CH), 32.15 ($CH_2$), 25.8 ($CH_3$), 23.5 ($CH_2$), 18.1 ($CH_3$), 13.2 ppm ($CH_2$); MS: *m*/*z* (%): 263 (0.2) $[M+H]^+$, 136 (2) $[M+H-I]^+$; HRMS calcd for $C_{10}H_{16}I$ $[M+H]^+$: 263.02968; found: 263.03099.

**(5*S*,6*E*)-5-(Iodomethyl)-9-methyldec-6-en-2-yne [(*S*)-6g]**: This compound was prepared from (*S*)-**5g** (152 mg, 0.84 mmol) in the same way as **6a** from **5a** [170 mg, 70%, $R_f$=0.9 (EtOAc/hexanes 10%), colorless oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.49 (dd, $^3J$=15.2 and

6.7 Hz, 1H), 5.24 (dt, $^3J$=15.5 and 7.0 Hz, 1H), 3.38–3.24 (m, 2H), 2.30–2.00 (m, 5H), 1.77 (t, $^3J$=2.4 Hz, 3H), 1.46 (m, 1H), 0.96 ppm (d, $^3J$=6.7 Hz, 1H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=140.8 (CH), 123.2 (CH), 77.3 (C≡), 76.1 (C≡), 39.4 (CH), 36.6 ($CH_2$), 31.0 (CH), 23.7 ($CH_2$), 22.5 ($CH_3$), 13.8 ($CH_2$), 3.5 ($CH_3$); MS (IQ+): *m/z* (%): 291 (2) $[M+H]^+$, 164 (3) $[M+H-I]^+$, 163 (9) $[M+H-HI]^+$, 247 (3) $[M+H-i\mathrm{Pr}H]^+$, 149 (100) $[M+H-I-CH_3]^+$.

**Ketone 8a**: A solution of ketone **7**[30] (498 mg, 1.54 mmol) in DMF (3 mL) was slowly added at −78°C to a mixture of KHMDS (0.5 M in toluene, 9.3 mL, 4.6 mmol) and DMF (4 mL), the resulting mixture was stirred for 0.5 h, and a solution of alkylating agent **6a** (1.14 g, 4.61 mmol) in DMF (2 mL) was added. After 2 h, a saturated solution of $NH_4Cl$ was added and the aqueous layer was extracted with $Et_2O$. The combined organic extracts were washed with brine, dried over $Na_2SO_4$ and concentrated under reduced pressure, giving a residue that, when flash chromatographed on silica gel (EtOAc/hexanes 2%), afforded ketone **8a** [540 mg, 79%, $R_f$=0.5 (EtOAc/hexanes 10%), pale yellow oil]. $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.46 (m, 1H), 5.30 (m, 1H), 3.56 (dd, $^3J$=9.5 and 2.6 Hz, 1H), 3.33 (dd, $^3J$=9.5 and 5.9 Hz, 1H), 1.94 (t, $^3J$=2.6 Hz, 1H), 1.02 (d, $^3J$=6.2 Hz, 3H), 0.90 (s, 9H), 0.65 (s, 3H), 0.04 ppm (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=214.8 (CO), 128.2 (CH), 127.5 (CH), 82.2 (C≡), 69.7 (C≡), 67.6 ($CH_2$), 57.7 (CH), 53.3 (CH), 50.3 (C), 47.3 (CH), 38.7 (CH), 36.5 ($CH_2$), 35.9 ($CH_2$), 35.4 ($CH_2$), 35.0 (CH), 29.3 ($CH_2$), 27.1 ($CH_2$), 26.0 ($CH_3$), 21.4 ($CH_2$), 19.2 ($CH_2$), 18.5 (C), 18.0 ($CH_3$), 17.1 ($CH_3$), 12.9 ($CH_3$), −5.2 ($CH_3$), −5.3 ppm ($CH_3$); IR ($CHCl_3$): $\tilde{\nu}$=3307, 3020, 2956, 2929, 2957, 1699, 1603, 1472, 1386, 1214, 1088, 1006 cm$^{-1}$; MS: *m/z* (%): 445 (29) $[M+H]^+$, 314 (15) $[M+H-OTBS]^+$, 312 (5) $[M+H-TBS-H_2O]^+$, 296 (17) $[M+H-OTBS-H_2O]^+$, 294 (2); HRMS calcd for $C_{28}H_{49}O_2Si$ $[M+H]^+$: 445.35018; found: 445.35036.

**Ketone 8b**: This compound was prepared from **7** (309 mg, 0.95 mmol) and **6b** (386 mg, 1.47 mmol) in the same way as **8a** from **7** and **6a** [153 mg, 35%, $R_f$=0.2 (EtOAc/hexanes 5%), pale yellow oil]. $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.43 (m, 1H), 5.19 (m, 1H), 3.54 (dd, $^3J$=9.7, 2.3 Hz, 1H), 3.29 (dd, $^3J$=9.6, 6.2 Hz, 1H), 2.56 (dd, $^3J$=11.3, 7.3 Hz, 1H), 0.87 (s, 9H), 0.62 (s, 3H), 0.01 ppm (s, 6H); $^{13}$C NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=214.9 (CO), 133.9 (CH), 126.1 (CH), 82.0 (C≡), 69.7 (C≡), 67.5 ($CH_2$), 57.6 (CH), 53.2 (CH), 50.2 (C), 47.6 (CH), 38.6 (CH), 36.3 ($CH_2$), 35.3 ($CH_2$), 35.1 (CH), 31.05 ($CH_2$), 29.2 ($CH_2$), 27.0 ($CH_2$), 25.9 (3×$CH_3$), 21.3 ($CH_2$), 20.6 ($CH_2$), 19.0 ($CH_2$), 18.3 (C), 17.0 ($CH_3$), 14.2 ($CH_3$), 12.8 ($CH_3$), −5.4 ($CH_3$), −5.5 ppm ($CH_3$); IR ($CHCl_3$): $\tilde{\nu}$=3307, 3012, 2958, 2930, 2858, 2117, 1701, 1463, 1386, 1254, 1089, 1006 cm$^{-1}$; MS: *m/z* (%): 459 (23) $[M+H]^+$, 328 (2) $[M+H-OTBS]^+$, 310 (3) $[M+H-OTBS-H_2O]^+$; HRMS calcd for $C_{29}H_{51}O_2Si$ $[M+H]^+$: 459.36584; found: 459.36641.

**Ketone 8b$_{10S}$**: This compound was prepared from **7** (271 mg, 0.84 mmol) and (*R*)-**6b** (340 mg, 1.30 mmol) in the same way as **8a** from **7** and **6a** [296 mg, 77%, $R_f$=0.5 (EtOAc/hexanes 5%), pale yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.43 (m, 1H), 5.20 (m, 1H), 3.55 (dd, $^3J$=9.6, 2.7 Hz, 1H), 3.31 (dd, $^3J$=9.6, 6.2 Hz, 1H), 2.57 (dd, $^3J$=11.2, 7.1 Hz, 1H), 0.88 (s, 9H), 0.63 (s, 3H), 0.01 ppm (s, 6H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=214.8 (CO), 133.9 (CH), 126.1 (CH), 82.0 (C≡), 69.7 (C≡), 67.5 ($CH_2$), 57.6 (CH), 53.2 (CH), 50.2 (C), 47.2 (CH), 38.6 (CH), 36.0 ($CH_2$), 35.4 ($CH_2$), 35.2 (CH), 31.1 ($CH_2$), 29.2 ($CH_2$), 27.0 ($CH_2$), 25.9 ($CH_3$), 21.4 ($CH_2$), 20.6 ($CH_2$), 19.0 ($CH_2$), 17.8 (C), 17.0 ($CH_3$), 14.2 ($CH_3$), 12.8 ($CH_3$), −5.4 ($CH_3$), −5.5 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3311, 2957, 2929, 2857, 2362, 2116, 1708, 1462, 1385, 1359, 1251, 1217, 1091, 1040, 1006 cm$^{-1}$; MS: *m/z* (%): 459 (38) $[M+H]^+$, 328 (10) $[M+H-OTBS]^+$, 310 (11) $[M+H-OTBS-H_2O]^+$; HRMS calcd for $C_{29}H_{51}O_2Si$ $[M+H]^+$: 459.36584; found: 459.36504.

**Ketone 8b$_{10R}$**: This compound was prepared from **7** (270 mg, 0.83 mmol) and (*S*)-**6b** (338 mg, 1.29 mmol) in the same way as **8a** from **7** and **6a** [264 mg, 69%, $R_f$=0.5 (EtOAc/hexanes 5%), pale yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.43 (m, 1H), 5.20 (m, 1H), 3.55 (dd, $^3J$=9.6, 2.7 Hz, 1H), 3.31 (dd, $^3J$=9.6, 6.2 Hz, 1H), 2.57 (m, 1H), 0.88 (s, 9H), 0.63 (s, 3H), 0.01 ppm (s, 6H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=214.9 (CO), 133.9 (CH), 126.1 (CH), 82.0 (C≡), 69.7 (C≡), 67.6 ($CH_2$), 57.6 (CH), 53.3 (CH), 50.2 (C), 47.2 (CH), 38.6 (CH), 36.0 ($CH_2$), 35.4 ($CH_2$), 35.2 (CH), 31.1 ($CH_2$), 29.2 ($CH_2$), 27.0 ($CH_2$), 25.9 ($CH_3$), 21.4 ($CH_2$), 20.6 ($CH_2$), 19.0 ($CH_2$), 18.3 (C), 17.0 ($CH_3$), 14.3 ($CH_3$), 12.8 ($CH_3$), −5.4 ($CH_3$), −5.5 ppm ($CH_3$); IR ($CHCl_3$): $\tilde{\nu}$=3307, 3008, 2961, 2930, 2868, 2116, 1700, 1462, 1386, 1254, 1213, 1089, 1040, 1006, 972 cm$^{-1}$; MS: *m/z* (%): 459 (21) $[M+H]^+$, 328 (6) $[M+H-OTBS]^+$, 310 (8) $[M+H-OTBS-H_2O]^+$; HRMS calcd for $C_{29}H_{51}O_2Si$ $[M+H]^+$: 459.36584; found: 459.36415.

**Ketone 8c**: This compound was prepared from **7** (607 mg, 1.87 mmol) and **6c** (775 mg, 2.81 mmol) in the same way as **8a** from **7** and **6a** [690 mg, 78%, $R_f$=0.3 (EtOAc/hexanes 5%), pale yellow oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.41 (dd, $^3J$=15.3, 6.4 Hz, 1H), 5.22 (m, 1H), 3.53 (dd, $^3J$=9.7, 2.3 Hz, 1H), 3.30 (dd, $^3J$=9.5, 5.8 Hz, 1H), 2.56 (dd, $^3J$=11.2, 7.3 Hz, 1H), 0.87 (s, 9H), 0.62 (s, 3H), 0.01 ppm (s, 6H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=214.6 (CO), 140.4 (CH), 124.1 (CH), 82.2 (C≡), 69.7 (C≡), 67.5 ($CH_2$), 57.6 (CH), 53.2 (CH), 50.3 (C), 47.2 (CH), 38.5 (CH), 36.4 ($CH_2$), 35.7 ($CH_2$), 35.4 ($CH_2$), 34.9 (CH), 31.1 (CH), 29.3 ($CH_2$), 27.0 ($CH_2$), 25.9 ($CH_3$), 22.6 ($CH_3$), 21.3 ($CH_2$), 19.0 ($CH_2$), 18.3 (C), 17.0 ($CH_3$), 12.8 ($CH_3$), −5.4 ppm ($CH_3$); MS: *m/z* (%): 473 (100) $[M+H]^+$, 342 (6) $[M+H-OTBS]^+$, 341 (28), 323 (12); HRMS calcd for $C_{30}H_{53}O_2Si$ $[M+H]^+$: 473.38149; found: 473.38379.

**Ketone 8c$_{10R}$**: This compound was prepared from **7** (1.37 g, 4.23 mmol) and (*S*)-**6c** (1.75 g, 6.35 mmol) in the same way as **8a** from **7** and **6a** [1.40 g, 70%, $R_f$=0.3 (EtOAc/hexanes 5%), pale yellow oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.41 (dd, $^3J$=15.3 and 6.4 Hz, 1H), 5.27 (m, 1H), 3.54 (dd, $^3J$=9.7, 2.3 Hz, 1H), 3.31 (dd, $^3J$=9.7, 6.1 Hz, 1H), 0.87 (s, 9H), 0.63 (s, 3H), 0.01 ppm (s, 6H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=214.8 (CO), 140.5 (CH), 124.0 (CH), 82.1 (C≡), 69.5 (C≡), 67.5 ($CH_2$), 57.6 (CH), 53.2 (CH), 50.2 (C), 47.4 (CH), 38.5 (CH), 36.3 ($CH_2$), 35.6 ($CH_2$), 35.4 ($CH_2$), 34.9 (CH), 31.0 (CH), 29.2 ($CH_2$), 27.0 ($CH_2$), 25.9 (2×$CH_3$), 22.6 (3×$CH_3$), 21.3 ($CH_2$), 19.0 ($CH_2$), 18.3 (C), 17.0 ($CH_3$), 12.8 ($CH_3$), −5.4 ppm (2×$CH_3$); IR (KBr): $\tilde{\nu}$=3312, 2956, 2928, 2858, 2117, 1709, 1463, 1384, 1362, 1252, 1091, 1040, 1006, 972 cm$^{-1}$; MS: *m/z* (%): 473 (13) $[M+H]^+$, 342 (7) $[M+H-OTBS]^+$, 341 (28), 323 (33); HRMS calcd for $C_{30}H_{53}O_2Si$ $[M+H]^+$: 473.38148; found: 473.38269.

**Ketone 8d**: This compound was prepared from **20**[19] (509 mg, 1.93 mmol) and **6d** (1.52 g, 5.78 mmol) in the same way as **8a** from **7** and **6a** [530 mg, 69%, $R_f$=0.6 (EtOAc/hexanes 10%), pale yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.03 (t, $^3J$=6.8 Hz, 1H), 1.70 (s, 6H), 1.14 (d, $^3J$=5.7 Hz, 3H), 0.87 (d, $^3J$=6.6 Hz, 6H), 0.64 ppm (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=215.1 (CO), 133.6 (C), 121.9 (CH), 82.3 (C≡), 69.5 (C≡), 57.8 (CH), 56.8 (CH), 50.2 (C), 47.2 (CH), 39.3 ($CH_2$), 36.0 ($CH_2$), 35.9 ($CH_2$), 35.5 (CH), 35.4 ($CH_2$), 31.9 ($CH_2$), 29.3 ($CH_2$), 27.9 (CH), 27.5 ($CH_2$), 25.8 (CH), 23.7 ($CH_2$), 22.7 ($CH_3$), 22.5 ($CH_3$), 21.3 ($CH_2$), 18.9 ($CH_2$), 18.6 ($CH_3$), 17.9 ($CH_3$), 12.6 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3312, 2952, 2928, 2869, 2113, 1708, 1450, 1383, 1261, 1238, 1121, 969 cm$^{-1}$; MS: *m/z* (%): 399 (94) $[M+H]^+$, 381 (52) $[M+H-H_2O]^+$; HRMS calcd for $C_{28}H_{47}O$ $[M+H]^+$: 399.36269; found: 399.36200.

**Ketone 8g$_{10R}$**: This compound was prepared from **7** (107 mg, 0.33 mmol) and (*S*)-**6g** (144 mg, 0.50 mmol) in the same way as **8a** from **7** and **6a** [110 mg, 69%, $R_f$=0.3 (EtOAc/hexanes 5%), pale yellow oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.40 (dd, $^3J$=15.2, 6.0 Hz, 1H), 5.25 (dt, $^3J$=15.2, 6.7 Hz, 1H), 3.54 (dd, $^3J$=9.4, 2.1 Hz, 1H), 3.33 (dd, $^3J$=9.7, 5.5 Hz, 1H), 1.76 (t, $^3J$=2.4 Hz, 3H), 1.01 (d, $^3J$=5.8 Hz, 3H), 0.95 (d, $^3J$=6.7 Hz, 6H), 0.88 (s, 9H), 0.63 (s, 3H), 0.02 ppm (s, 6H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=215.2 (CO), 140.2 (CH), 124.1 (CH), 77.5 (C≡), 76.6 (C≡), 67.5 ($CH_2$), 57.5 (CH), 53.3 (CH), 50.2 (C), 47.6 (CH), 38.5 (CH), 36.1 ($CH_2$), 35.9 (CH), 35.8 ($CH_2$), 35.3 ($CH_2$), 31.1 (CH), 29.2 ($CH_2$), 27.0 ($CH_2$), 25.9 (2×$CH_3$), 23.0 ($CH_2$), 22.6 ($CH_3$), 19.0 ($CH_2$), 18.3 (C), 17.1 ($CH_3$), 12.8 ($CH_3$), 3.4 ($CH_3$), −5.5 ppm ($CH_3$); MS: *m/z* (%): 487 (20) $[M+H]^+$, 355 (6) $[M+H-HOTBS]^+$, 430 (39), 403 (14); HRMS calcd for $C_{31}H_{55}O_2Si$ $[M+H]^+$: 487.39714; found: 487.39763.

**Compound 8h$_{10S}$**: A solution of ketone **7** (79 mg, 0.23 mmol) in THF (1.4 mL) was added dropwise at −78°C to a freshly prepared solution of LDA (1 M, 0.7 mL, 0.7 mmol). After having been stirred for 30 min, the

solution of the enolate was added at −78 °C to a solution of the aldehyde (*S*)-**24h** (123 mg, 0.69 mmol) in THF (1.4 mL). The resulting mixture was stirred at that temperature for 3 h and the reaction was quenched by addition of $NH_4Cl$ (sat., 3 mL). The aqueous layer was extracted with $Et_2O$ and the combined organic extracts were dried over $Na_2SO_4$ and concentrated under reduced pressure to give an oil, which was purified by flash chromatography (AcOEt/hexanes 3%), yielding the desired compound [106 mg, 91%, $R_f$=0.4 (10% AcOEt/hexanes), yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=5.45 (dd, $^3J$=15.3, 6.5 Hz, 1H), 5.33 (dt, $^3J$=15.3, 6.8 Hz, 1H), 4.14 (ddd, $^3J$=9.3, 5.8, 2.2 Hz, 1H), 3.62 (m, 1H), 3.54 (dd, $^3J$=5.8, 2.2 Hz, 1H), 3.33 (dd, $^3J$=9.6, 6.3 Hz, 1H), 2.75 (dd, $^3J$=11.4, 7.4 Hz, 1H), 2.46 (m, 1H), 2.32–2.10 (m, 6H), 2.04 (t, $^3J$= 7.00 Hz, 1H), 1.97–1.83 (m, 3H), 1.77 (dd, $^3J$=4.0, 2.5 Hz, 1H), 0.99 (d, $^3J$=6.4 Hz, 3H), 0.95 (d, $^3J$=6.7 Hz, 6H), 0.87 (s, 9H), 0.66 (s, 3H), 0.01 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=214.0 (CO), 140.3 (CH), 124.7 (CH), 77.7 (C), 77.4 (C), 74.0 (CH), 67.5 ($CH_2$), 65.5 ($CH_2$), 59.1 (CH), 53.4 (CH), 49.0 (CH), 40.6 (C), 38.6 (CH), 33.9 (CH), 31.0 ($CH_2$), 30.2 ($CH_2$), 27.1 ($CH_2$),25.9 ($CH_3$), 25.6 ($CH_2$), 22.5 ($CH_3$), 20.9 ($CH_2$), 20.5 ($CH_2$), 19.1 (C), 18.3 (C), 17.0 ($CH_3$), 13.9 ($CH_3$), 3.5 ($CH_3$), −5.4 ppm ($CH_3$); MS: *m*/*z* (%): 503 (94) $[M+H]^+$, 485 (100) $[M+H-H_2O]^+$, 445 (44) $[M+H-t\mathrm{Bu}H]^+$; HMRS: calcd for $C_{31}H_{55}O_3Si$: 503.39205; found: 503.39222.

**Compound $8h_{10R}$**: This compound was prepared from **7** (75 mg, 0.23 mmol) and (*R*)-**24h** (122 mg, 0.69 mmol) in the same way as $8h_{10S}$ from **7** and (*S*)-**24h** [107 mg, 92%, $R_f$=0.4 (15% AcOEt/hexanes), yellow oil]; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=5.51 (dd, $^3J$= 15.4, 6.5 Hz, 1H), 5.34 (dt, $^3J$=15.5, 7.0 Hz, 1H), 3.93 (ddd, $^3J$=9.8, 7.4, 2.8 Hz, 1H), 3.55 (dd, $^3J$=9.6, 2.8 Hz, 1H), 3.34 (dd, $^3J$=9.6, 6.1 Hz, 1H), 2.71 (dd, $^3J$=11.3, 7.4 Hz, 1H), 2.57 (ddd, $^3J$=9.1, 6.1, 2.6 Hz, 1H), 2.46 (d, $^3J$=7.3 Hz, 1H), 2.33–2.12 (m, 5H), 2.0–1.80 (m, 2H), 1.78 (t, $^3J$= 2.6 Hz, 3H), 1.60–1.45 (m,2H), 1.39–1.25 (m, 2H), 1.00 (d, $^3J$=6.3 Hz, 3H), 0.98 (d, $^3J$=6.0 Hz, 6H), 0.89 (s, 9H), 0.67 (s, 3H), 0.02 ppm (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=213.8 (CO), 140.6 (CH), 124.6 (CH), 77.9 (C), 77.5 (C), 73.7 (CH), 67.4 ($CH_2$), 59.1 (CH), 53.3 (CH), 52.8 (CH), 49.0 (C), 40.0 (CH), 38.5 (CH), 35.8 ($CH_2$), 34.4 ($CH_2$), 31.1 (CH), 27.1 ($CH_2$), 25.9 ($CH_3$), 25.7 ($CH_2$), 22.6 (CH), 19.0 ($CH_2$), 18.3 (C), 17.3 ($CH_2$), 17.0 (CH), 13.8 ($CH_3$), 3.5 ($CH_3$), −5.4 ppm ($CH_3$); MS: *m*/*z* (%): 503 (16) $[M+H]^+$, 485 (8) $[M+H-H_2O]^+$; HRMS: calcd for $C_{31}H_{55}O_3Si$: 503.39205; found: 503.39202.

**Dienyne 9a**: A solution of allylMgBr (1 M in $Et_2O$, 0.75 mL, 0.75 mmol) was added dropwise at −78 °C to a solution of ketone **8a** (115 mg, 0.26 mmol) in THF (2 mL). After the mixture had been stirred for 2 h at this temperature, a saturated solution of $NH_4Cl$ was added, and the resulting mixture was extracted with $Et_2O$. The combined organic extracts were washed with brine, dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude alcohol was purified by flash chromatography (EtOAc/hexanes 2%), yielding dienyne **9a** [120 mg, 95%, $R_f$=0.5 (EtOAc/hexanes 10%), pale yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=5.90 (m, 1H), 5.39 (m, 2H), 5.13 (m, 2H), 3.54 (m, 1H), 3.24 (m, 1H), 0.95 (d, $^3J$=6.3 Hz, 3H), 0.87 (s, 9H), 0.01 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=133.2 (CH), 128.3 (CH), 127.4 (CH), 119.4 ($CH_2$), 83.3 (C≡), 76.0 (C), 67.3 (C≡), 67.7 ($CH_2$), 53.6 (CH), 51.1 (CH), 43.4 ($CH_2$), 43.3 (C), 39.5 (CH), 38.5 (CH), 35.2 (CH), 34.8 ($CH_2$), 34.5 ($CH_2$), 31.2 ($CH_2$), 26.7 ($CH_2$), 26.0 ($CH_3$), 23.8 ($CH_2$), 20.3 ($CH_2$), 20.2 ($CH_2$), 18.3 (C), 18.0 ($CH_3$), 16.7 ($CH_3$), 13.5 ($CH_3$), −5.4 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3564, 3525, 3311, 3075, 2943, 2931, 2856, 2116, 1637, 1471, 1386, 1362, 1254, 1128, 1087, 1005 cm$^{-1}$; MS: *m*/*z* (%): 487 (19) $[M+H]^+$, 355 (47), 337 (100); HRMS calcd for $C_{31}H_{55}O_2Si$ $[M+H]^+$: 487.39714; found: 487.39624.

**Dienyne $9b_{10S}$**: This compound was prepared from $8b_{10S}$ or **8b** (345 mg, 0.75 mmol) in the same way as **9a** from **8a** [132 mg, 35%, $R_f$=0.42 (EtOAc/hexanes 10%), pale yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=5.86 (m, 1H), 5.45 (m, 1H), 5.28 (m, 1H), 5.16 (m, 2H), 3.56 (dd, $^3J$=9.6, 3.3 Hz, 1H), 3.26 (dd, $^3J$=9.5, 7.2 Hz, 1H), 0.88 (s, 9H), 0.02 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=133.8 (CH), 133.2 (CH), 126.2 (CH), 119.5 ($CH_2$), 83.3 (C≡), 76.1 (C≡), 69.3 ($CH_2$), 67.7 (C), 53.7 (CH), 51.2 (CH), 43.5 ($CH_2$), 43.4 (C), 39.7 (CH), 38.5 (CH), 35.6 (CH), 34.6 ($CH_2$), 31.6 ($CH_2$), 29.7 ($CH_2$), 26.7 ($CH_2$), 26.0 ($CH_3$), 23.8 ($CH_2$), 20.7 ($CH_2$), 20.5 ($CH_2$), 20.3 ($CH_2$), 18.4 (C), 16.7 ($CH_3$), 14.3 ($CH_3$), 13.5 ($CH_3$), −5.3 ($CH_3$), −5.4 ppm ($CH_3$); IR ($CHCl_3$): $\tilde{\nu}$=3565, 3311, 2961, 2929, 2856, 1729, 1462, 1386, 1363, 1255, 1127, 1089, 1004 cm$^{-1}$; MS: *m*/*z* (%): 501 (22) $[M+H]^+$, 370 (7) $[M+H-OTBS]^+$, 352 (31) $[M+H-OTBS-H_2O]^+$; HRMS calcd for $C_{32}H_{57}O_2Si$ $[M+H]^+$: 501.41278; found: 501.41329.

**Dienyne $9b_{10R}$**: This compound was prepared from $8b_{10R}$ or **8b** (345 mg, 0.75 mmol) in the same way as **9a** from **8a** [131 mg, 35%, $R_f$=0.37 (EtOAc/hexanes 10%), pale yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=5.98 (m, 1H), 5.46 (m, 1H), 5.29 (m, 1H), 5.15 (m, 2H), 3.56 (dd, $^3J$=9.6, 3.2 Hz, 1H), 3.25 (dd, $^3J$=9.5, 7.5 Hz, 1H), 0.88 (s, 9H), 0.02 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=133.6 (CH), 133.3 (CH), 126.8 (CH), 119.7 ($CH_2$), 82.5 (C), 75.8 (C), 69.8 ($CH_2$), 67.7 (C), 53.7 (CH), 51.2 (CH), 43.5 ($CH_2$), 43.3 (C), 39.8 (CH), 38.5 (CH), 34.8 (CH), 34.6 ($CH_2$), 32.2 ($CH_2$), 30.8 ($CH_2$), 26.7 ($CH_2$), 26.0 ($CH_3$), 21.1 ($CH_2$), 20.7 ($CH_2$), 20.35 ($CH_2$), 20.3 ($CH_2$), 18.4 (C), 16.7 ($CH_3$), 14.3 ($CH_3$), 13.5 ($CH_3$), −5.3 ($CH_3$), −5.4 ppm ($CH_3$); MS: *m*/*z* (%): 501 (0.05) $[M+H]^+$, 352 (2) $[M+H-OTBS-H_2O]^+$; HRMS calcd for $C_{32}H_{57}O_2Si$ $[M+H]^+$: 501.41278; found: 501.41308.

**Dienyne $9c_{10R}$**: This compound was prepared from $8c_{10R}$ or **8c** (1.99 g, 4.20 mmol) in the same way as **9a** from **8a** [477 mg, 22%, $R_f$=0.29 (EtOAc/hexanes 10%), pale yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=5.86 (m, 1H), 5.44 (dd, $^3J$=15.4, 6.3 Hz, 1H), 5.29 (m, 1H), 5.16 (m, 2H), 3.56 (dd, $^3J$=9.6, 3.4 Hz, 1H), 3.25 (dd, $^3J$=9.6, 7.3 Hz, 1H), 1.95 (t, $^3J$=2.6 Hz, 1H), 0.89 (s, 9H), 0.03 ppm (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=140.1 (CH), 133.3 (CH), 124.8 (CH), 119.6 ($CH_2$), 82.6 (C), 75.8 (C), 69.7 (C), 67.7 ($CH_2$), 53.7 (CH), 51.2 (CH), 43.5 ($CH_2$), 43.3 (C), 39.8 (CH), 38.4 (CH), 37.5 ($CH_2$), 34.7 (CH), 34.6 ($CH_2$), 31.0 (CH), 30.4 ($CH_2$), 26.6 ($CH_2$), 26.0 ($CH_3$), 22.7 ($CH_3$), 21.3 ($CH_2$), 20.3 ($CH_2$), 20.2 ($CH_2$), 18.4 (C), 16.6 ($CH_3$), 13.5 ($CH_3$), −5.4 ppm (2×$CH_3$); IR ($CHCl_3$): $\tilde{\nu}$=3565, 3312, 2954, 2930, 2857, 1731, 1634, 1463, 1384, 1352, 1254, 1089, 1004, 972 cm$^{-1}$; MS: *m*/*z* (%): 515 (14) $[M+H]^+$, 384 (1) $[M+H-OTBS]^+$, 364 (0.3) $[M+H-TBS-2H_2O]^+$; HRMS calcd for $C_{33}H_{59}O_2Si$ $[M+H]^+$: 515.42844; found: 515.42937.

**Dienyne $9c_{10S}$**: This compound was prepared from $8c_{10S}$ or **8c** (1.99 g, 4.20 mmol) in the same way as **9a** from **8a** [3.77 g, 68%, $R_f$=0.35 (EtOAc/hexanes 5%), pale yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=5.88 (m, 1H), 5.48 (dd, $^3J$=15.2, 6.1 Hz, 1H), 5.32 (m, 1H), 5.20 (m, 2H), 3.60 (m, 1H), 3.29 (m, 1H), 1.95 (t, $^3J$=2.5 Hz, 1H), 0.86 (s, 9H), 0.06 ppm (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=140.3 (CH), 133.2 (CH), 123.9 (CH), 119.5 ($CH_2$), 83.5 (C), 69.3 (C), 76.0 (C), 67.7 ($CH_2$), 53.6 (CH), 51.1 (CH), 43.5 ($CH_2$), 43.3 (C), 39.5 (CH), 38.5 (CH), 35.3 (CH), 34.9 ($CH_2$), 34.5 ($CH_2$), 31.3 ($CH_2$), 31.1 (CH), 26.7 ($CH_2$), 26.0 (2$CH_3$), 23.7 ($CH_2$), 22.6 ($CH_3$), 20.4 ($CH_2$), 20.3 ($CH_2$), 18.4 (C), 16.7 ($CH_3$), 13.5 ($CH_3$), −5.4 ppm ($CH_3$); MS: *m*/*z* (%): 515 (22) $[M+H]^+$, 497 (9) $[M+H-H_2O]^+$, 384 (10) $[M+H-OTBS]^+$, 383 (41), 365 (100), 323(38); HRMS calcd for $C_{33}H_{59}O_2Si$ $[M+H]^+$: 515.42844; found: 515.42810.

**Dienyne 9d**: This compound was prepared from **8d** (362 mg, 0.91 mmol) in the same way as **9a** from **8a** [320 mg, 80%, $R_f$=0.5 (EtOAc/hexanes 10%), pale yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=5.83 (m, 1H), 5.03 (m, 3H), 0.88 ppm (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=133.3 (C), 133.2 (CH), 121.1 (CH), 119.3 ($CH_2$), 83.5 (C≡), 76.0 (C), 69.2 (C≡), 57.1 (CH), 51.3 (CH), 43.3 (C), 43.4 ($CH_2$), 39.6 (CH), 39.5 ($CH_2$), 35.85 (CH), 35.8 ($CH_2$), 35.2 (CH), 34.6 ($CH_2$), 33.0 ($CH_2$), 31.5 ($CH_2$), 30.25 ($CH_2$), 28.0 (CH), 27.2 ($CH_2$), 25.8 ($CH_3$), 23.7 ($CH_2$), 22.8 ($CH_3$), 22.5 ($CH_3$), 20.4 ($CH_2$), 20.0 ($CH_2$), 18.3 ($CH_3$), 17.8 ($CH_3$), 13.4 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3565, 3311, 3074, 2957, 2931, 2872, 2116, 1731, 1636, 1456, 1382, 1268, 1222, 1168, 1122, 993 cm$^{-1}$; MS: *m*/*z* (%): 441 (44) $[M+H]^+$, 423 (100) $[M+H-H_2O]^+$; HRMS calcd for $C_{31}H_{53}O$ $[M+H]^+$: 441.40964; found: 441.40945.

**Dienyne 9f**: A solution of *n*BuLi in THF (0.13 mL, 2.15 M, 0.28 mmol) was added to a solution of dienyne **9d** (50 mg, 0.11 mmol) in THF (2 mL), the mixture was stirred for 2 h, and MeI (0.02 mL, 0.34 mmol) was added. The reaction mixture was stirred for 4 h at room temperature and poured into water. The aqueous layer was extracted with $Et_2O$ and the combined organic phases were dried over $Na_2SO_4$, filtered and con-

centrated under reduced pressure. This crude product was purified by flash chromatography on silica gel (EtOAC/hexanes 2%), yielding **9e** [39 mg, 76%, $R_f$=0.5 (EtOAc/hexanes 10%), yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.94–5.77 (m, 1H), 5.15 (m, 2H), 5.09 (t, $^3J$=6.7 Hz, 1H), 0.94 (s, 3H), 0.89 (d, $^3J$=6.5 Hz, 3H), 0.87 (d, $^3J$=6.5 Hz, 3H), 0.86 ppm (d, $^3J$=6.5 Hz, 3H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=133.3 (C=), 133.0 (CH=), 122.1 (CH=), 119.3 ($CH_2$=), 85.5 (C≡), 78.4 (C≡), 62.2 (C), 57.2 (CH), 51.3 (CH), 43.4 ($CH_2$), 39.7 (CH), 39.5 ($CH_2$), 36.4 (CH), 35.9 ($CH_2$), 35.2 (CH), 34.6 ($CH_2$), 31.6 ($CH_2$), 30.7 ($CH_2$), 30.3 (C), 28.0 (CH), 27.2 ($CH_2$), 25.8 ($CH_3$), 24,2 ($CH_2$), 23.7 ($CH_2$), 22.8 ($CH_3$), 22.5 ($CH_3$), 20.4 ($CH_2$), 20.0 ($CH_2$), 18.4 ($CH_3$), 17.8 ($CH_3$), 13.4 ($CH_3$), 3.5 ppm ($CH_3$); MS: *m/z* (%): 455 (1) $[M+H]^+$, 437 (3) $[M+H-H_2O]^+$; HRMS calcd for $C_{32}H_{55}O$ $[M+H]^+$: 455.42529; found: 455.42609.

**Compound 9g$_{10R}$**: This compound was prepared from **8g$_{10R}$** (143 mg, 0.29 mmol) in the same way as **9a** from **8a** [144 mg, 93%, $R_f$=0.4 (EtOAc/hexanes 10%), pale yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=6.00 (m, 1H), 5.45 (dd, $^3J$=15.2 and 6.1 Hz, 1H), 5.31 (dt, $^3J$=15.2, 6.7 Hz, 1H), 5.15 (m, 2H), 3.57 (dd, $^3J$=9.4, 3.3 Hz, 1H), 3.25 (dd, $^3J$=9.4, 7.3 Hz, 1H), 1.78 (t, $^3J$=2.4 Hz, 3H), 0.97 (d, $^3J$=9.7 Hz, 3H), 0.95 (d, $^3J$=5.8 Hz, 6H), 0.89 (s, 9H), 0.02 ppm (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=139.7 (CH), 133.3 (CH), 125.1 (CH), 119.6 ($CH_2$), 77.2 (C≡), 75.9 (C≡), 67.7 ($CH_2$), 53.7 (CH), 51.1 (CH), 43.5 (C), 43.3 ($CH_2$), 39.7 (CH), 38.4 (CH), 37.7 ($CH_2$), 35.0 (CH), 34.6 ($CH_2$), 31.1 (CH), 30.5 ($CH_2$), 26.6 ($CH_2$), 26.0 ($CH_3$), 22.7 ($CH_3$), 21.6 ($CH_2$), 20.2 ($CH_2$), 18.4 (C), 16.6 ($CH_3$), 13.5 ($CH_3$), 3.4 ($CH_3$), −5.4 ppm (2×$CH_3$); IR (KBr): $\tilde{\nu}$=3563, 2954, 2930, 2857, 1727, 1637, 1463, 1383, 1361, 1254, 1123, 1090, 1043, 1004, 971 cm$^{-1}$; MS: *m/z* (%): 529 (1) $[M+H]^+$, 511 (2) $[M+H-H_2O]^+$, 453 (9), 355 (16), 337 (21).

**Compound 9h$_{10S}$**: This compound was prepared from **8h$_{10S}$** (37 mg, 0.07 mmol) in the same way as **9a** from **8a** [31 mg, 79%, $R_f$=0.4 (10% AcOEt/hexanes), white solid]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=6.00 (m, 1H), 5.50 (dd, $^3J$=15.3, 6.5 Hz, 1H), 5.37 (dt, $^3J$=15.3, 7.3 Hz, 1H), 5.10 (m, 2H), 3.88 (dd, $^3J$=9.7, 4.5 Hz, 1H), 3.57 (dd, $^3J$=9.6, 3.2 Hz, 1H), 3.24 (dd, $^3J$=9.4, 7.4 Hz, 1H), 2.50 (s, 1H), 2.39–2.10 (m, 7H), 1.79 (t, $^3J$=2.2 Hz, 3H), 1.65–1.48 (m, 7H), 1.34–1.13 (m, 5H), 1.00 (s, 3H), 0.97 (d, $^3J$=6.7 Hz, 6H), 0.93 (d, $^3J$=6.5 Hz, 3H), 0.89 (s, 9H), 0.02 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C, TMS): $\delta$=140.2 (CH), 135.6 (CH), 126.0 (CH), 118.0 ($CH_2$), 78.4 (C), 75.9 (C), 73.0 (CH), 67.6 ($CH_2$), 54.1 (CH), 51.8 (CH), 46.0 (CH), 42.4 (C), 39.9 (CH), 38.6 (CH), 36.9 ($CH_2$), 34.7 ($CH_2$), 31.1 (CH), 30.3 ($CH_3$), 29.7 ($CH_2$), 27.4 ($CH_2$), 26.0 ($CH_3$), 22.6 ($CH_3$), 21.7 ($CH_2$), 20.2 ($CH_2$), 18.4 (C), 16.7 ($CH_2$), 16.6 ($CH_3$), 3.7 ($CH_3$), −5.3 ppm ($CH_3$); MS: *m/z* (%): 545 (2) $[M+H]^+$, 528 (12) $[M+H-CH_4]^+$, 418 (46) $[M+H-OTBS-H_2O]^+$; HRMS: calcd for $C_{34}H_{61}O_3Si$: 545.43900; found: 545.43891.

**Compound 9h$_{10R}$**: This compound was prepared from **8h$_{10R}$** (103 mg, 0.20 mmol) in the same way as **9a** from **8a** [74 mg, 68%, $R_f$=0.2 (AcOEt/hexanes 10%), white solid]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=6.05 (m, 1H), 5.46 (dd, $^3J$=15.3, 6.4 Hz, 1H), 5.35 (dt, $^3J$=15.3, 6.5 Hz, 1H), 5.13 (t, $^3J$=13.1 Hz, 2H), 4.16 (dd, $^3J$=10.0, 2.8 Hz, 1H), 3.58 (dd, $^3J$=9.6, 3.3 Hz, 1H), 3.27 (dd, $^3J$=9.6, 7.2 Hz, 1H), 2.37 (s, 1H), 2.40 (s, 1H), 2.33–2.16 (m, 4H), 1.98 (m, 1H), 1.80 (t, $^3J$=2.5 Hz, 3H), 1.71–1.46 (m, 4H), 1.44 (s, 1H), 1.38–1.21 (m, 4H), 1.01 (s, 3H), 0.98 (d, $^3J$=6.7 Hz, 6H), 0.96 (d, $^3J$=6.5 Hz, 3H), 0.90 (s, 9H), 0.03 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C, TMS): $\delta$=139.9 (CH), 135.8 (CH), 125.1 (CH), 118.3 ($CH_2$), 77.9 (C), 75.8 (C), 73.4 (CH), 67.7 ($CH_2$), 54.1 (C), 51.7 (CH), 45.9 (CH), 44.1 (CH), 42.8 ($CH_2$), 40.2 (CH), 38.6 (CH), 36.9 ($CH_2$), 31.0 (CH), 30.4 ($CH_3$), 29.8 ($CH_2$), 27.3 ($CH_2$), 26.0 ($CH_3$), 22.5 ($CH_3$), 21.4 ($CH_2$), 20.8 ($CH_2$), 20.2 ($CH_2$), 18.5 (C), 16.6 ($CH_3$), 3.6 ($CH_3$), −5.3 ppm ($CH_3$); MS: *m/z* (%): 545 (3) $[M+H]^+$, 527 (46) $[M+H-H_2O]^+$, 509 (100) $[M+H-2H_2O]^+$; HRMS: calcd for $C_{34}H_{61}O_3Si$: 545.43900; found: 545.43876.

**Compound 9i$_{10R}$**: DIEA (1.3 mL, 7.44 mmol) and ClMOM (0.56 mL, 7.44 mmol) were added to a solution of dienyne **9h$_{10R}$** (338 mg, 0.62 mmol) in $CH_2Cl_2$ (21 mL). The reaction was stirred at room temperature for 15 h and then $NH_4Cl$ (sat, 15 mL) was added. The aqueous layer was extracted with $CH_2Cl_2$ and the organic extracts were dried over $Na_2SO_4$ and concentrated under reduced pressure, giving a residue that, when flash chromatographed (AcOEt/hexanes 2%), afforded compound **9i$_{10R}$** [320 mg, 82%, $R_f$=0.5 (10% AcOEt/hexanes), yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=6.06 (m, 1H), 5.41 (dd, $^3J$=15.3, 6.2 Hz, 1H), 5.31 (dt, $^3J$=15.3, 7.5 Hz, 1H), 5.02 (dd, $^3J$=16.9, 2.7 Hz, 1H), 4.98 (dd, $^3J$=10.0, 1.8 Hz, 1H), 4.82 (d, $^3J$=6.6 Hz, 1H), 4.67 (d, $^3J$=6.5 Hz, 1H), 4.61 (d, $^3J$=6.5 Hz, 1H), 4.58 (d, $^3J$=6.5 Hz, 1H), 3.99 (d, $^3J$=8.1 Hz, 1H), 3.58 (dd, $^3J$=9.6, 3.3 Hz, 1H), 3.41 (s, 3H), 3.37 (s, 3H), 3.25 (dd, $^3J$=9.6, 7.2 Hz, 1H), 2.72 (dd, $^3J$=16.1, 6.6 Hz, 1H), 2.37 (dd, $^3J$=16.1, 6.5 Hz, 1H), 2.30–2.05 (m, 7H), 1.78 (t, $^3J$=2.4 Hz, 3H), 1.00 (s, 3H), 0.97 (d, $^3J$=6.7 Hz, 6H), 0.96 (d, $^3J$=6.7 Hz, 3H), 0.08 (s, 9H), 0.02 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C, TMS): $\delta$=139.7 (CH), 136.8 (CH), 125.4 (CH), 115.7 ($CH_2$), 99.2 ($CH_2$), 91.4 ($CH_2$), 82.7 (C), 82.6 (CH), 79.0 (C), 76.6 (C), 67.9 ($CH_2$), 56.6 ($CH_3$), 56.0 ($CH_3$), 53.9 (CH), 53.8 (CH), 44.1 (CH), 43.5(C), 41.6 ($CH_2$), 41.3 (CH), 38.3 (CH), 36.0 ($CH_2$), 32.0 ($CH_2$), 31.1 (CH), 26.8 ($CH_2$), 26.0 ($CH_3$), 22.6 ($CH_3$), 22.1 ($CH_2$), 21.7 ($CH_2$), 20.5 ($CH_2$), 18.4 (C), 16.8 ($CH_3$), 14.1 ($CH_3$), 3.6 ($CH_3$), −5.3 ppm ($CH_3$); MS: *m/z* (%): 655 (8) $[M+Na]^+$; HRMS: calculated for $C_{38}H_{68}NaO_5Si$: 655.47282; found: 655.47536.

**Compound 9i$_{10S}$**: This compound was prepared from **9h$_{10S}$** (34 mg, 0.06 mmol) in the same way as **9i$_{10R}$** from **9h$_{10R}$** [30 mg, 80%, $R_f$=0.5 (10% AcOEt/hexanes), yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=6.01 (m, 1H), 5.48 (dd, $^3J$=15.4, 6.3 Hz, 1H), 5.30 (dt, $^3J$=7.9, 5.4 Hz, 1H), 4.97 (t, $^3J$=13.4 Hz, 2H), 4.79 (d, $^3J$=6.5 Hz, 1H), 4.61 (d, $^3J$=6.4 Hz, 1H), 4.55 (d, $^3J$=6.5 Hz, 2H), 3.65 (d, $^3J$=7.8 Hz, 1H), 3.57 (dd, $^3J$=9.6, 3.2 Hz, 1H), 3.39 (s, 3H), 3.35 (s, 3H), 3.21 (dd, $^3J$=9.3, 7.8 Hz, 1H), 2.64 (dd, $^3J$=16.1, 6.9 Hz, 1H), 2.40–2.04 (m, 8H), 1.78 (t, $^3J$=2.1 Hz, 3H), 0.97 (d, $^3J$=8.1 Hz, 3H), 0.88 (s, 9H), 0.87 (s, 3H), 0.85 (d, $^3J$=6.6 Hz, 6H), 0.02 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C, TMS): $\delta$=140.5 (CH), 136.7 (CH), 125.7 (CH), 115.8 ($CH_2$), 98.9 ($CH_2$), 91.5 ($CH_2$), 81.3 (CH), 78.9 (C), 76.2 (C), 67.7 ($CH_2$), 56.6 ($CH_3$), 56.1 ($CH_3$), 53.9 (CH), 44.3 (CH), 43.5 (C), 42.2 (CH), 41.7 ($CH_2$), 38.5 (CH), 36.1 ($CH_2$), 34.1 ($CH_2$), 31.6 ($CH_2$), 31.1 (CH), 29.1 ($CH_2$), 26.8 ($CH_2$), 26.0 ($CH_3$), 22.6 (CH), 22.1 ($CH_2$), 19.3 ($CH_2$), 18.7 ($CH_3$), 18.4 (C), 16.6 ($CH_3$), 14.1 ($CH_3$), 11.1 ($CH_3$), 3.6 ($CH_3$), −5.4 ppm ($CH_3$); MS: *m/z* (%): 655 (8) $[M+Na]^+$; HRMS: calcd for $C_{38}H_{68}NaO_5Si$: 655.47282; found: 655.47328.

**Compound 9j$_{10S}$**: Pyridine (15 μL, 0.2 mmol) and TBSOTf (39 μL, 0.17 mmol) were added dropwise at 0°C to a solution of dienyne **9h$_{10S}$** (30 mg, 0.05 mmol) in $CH_2Cl_2$ (1.7 mL). The final solution was stirred at that temperature for 30 min and was then allowed to reach room temperature and stirred for another 5 h. The reaction was quenched by addition of water (2 mL) and the aqueous layer was extracted with $CH_2Cl_2$, dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography (1% AcOEt/hexanes) to provide the protected compound [27 mg, 75%, $R_f$=0.6 (10% AcOEt/hexanes), yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.97 (m, 1H), 5.42 (dd, $^3J$=15.3, 6.4 Hz, 1H), 5.26 (dt, $^3J$=13.9, 6.9 Hz, 1H), 5.10 (d, $^3J$=4.0 Hz, 1H), 5.05 (s, 1H), 4.22 (dd, $^3J$=9.9, 3.9 Hz, 1H), 3.55 (dd, $^3J$=9.6, 3.3 Hz, 1H), 3.22 (dd, $^3J$=9.5, 7.4 Hz, 1H), 2.44–2.13 (m, 5H), 1.75 (t, $^3J$=2.3 Hz, 3H), 0.95 (d, $^3J$=3.2 Hz, 6H), 0.93 (d, $^3J$=6.4 Hz, 3H), 0.93 (s, 3H), 0.88 (s, 9H), 0.86 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H), −0.01 ppm (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=140.2 (CH), 135.2 (CH), 125.3 (CH), 118.2 ($CH_2$), 99.9 (C), 78.7 (C), 75.2 (C), 67.7 ($CH_2$), 54.2 (CH), 51.8 (CH), 47.6 (CH), 44.8 (CH), 42.2 (C), 43.7 ($CH_2$), 38.6 (CH), 37.1 ($CH_2$), 31.1 (CH), 30.3 (CH), 29.7 ($CH_2$), 27.2 ($CH_2$), 26.2 ($CH_3$), 26.0 ($CH_3$), 22.6 ($CH_3$), 22.5 ($CH_3$), 21.3 ($CH_2$), 20.8 ($CH_2$), 20.4 ($CH_2$), 18.4 (C), 3.5 ($CH_3$), −3.4 ($CH_3$), −3.8 ($CH_3$), −5.4 ppm ($CH_3$); MS: *m/z* (%): 659 (4) $[M+H]^+$, 641 (5) $[M+H-H_2O]^+$, 527 (15) $[M+H-OTBS]^+$; HRMS: calculated for $C_{40}H_{75}O_3Si_2$: 659.52548; found: 659.52374.

**Compound 9k$_{10R}$**: PDC (29 mg, 0.08 mmol) was added to a solution of dienyne **9h$_{10R}$** (28 mg, 0.05 mmol) in $CH_2Cl_2$ (1.5 mL) and the suspension was stirred at rt. After 6 h the reaction mixture was filtered through a short pad of $SiO_2$/celite (1:1) and washed with $Et_2O$ to give a residue that, upon flash chromatography, afforded the ketone **9k$_{10R}$** [13 mg, 46%, $R_f$=0.4 (10% AcOEt/hexanes), white solid]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.78 (m, 1H), 5.42 (dd, $^3J$=15.3, 6.4 Hz, 1H), 5.20 (dt, $^3J$=15.1, 7.3 Hz, 1H), 5.08 (ddd, $^3J$=18.6, 13.7, 1.8 Hz, 1H), 3.57 (dd,

$^3J$=9.6, 3.5 Hz, 1H), 3.18 (dd, $^3J$=9.5, 8.0 Hz, 1H), 2.86 (tt, $^3J$=9.3, 4.7 Hz, 1H), 2.72 (dd, $^3J$=6.5, 1.2 Hz, 1H), 2.44 (dd, $^3J$=14.1, 7.7 Hz, 1H), 1.69 (t, $^3J$=2.5 Hz, 3H), 0.94 (d, $^3J$=6.5 Hz, 6H), 0.91 (d, $^3J$=6.6 Hz, 3H), 0.87 (s, 9H), 0.87 (s, 3H), 0.00 ppm (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=212.4 (CO), 141.1 (CH), 133.3 (CH), 122.9 (CH), 119.7 ($CH_2$), 77.3 (C), 74.0 (C), 67.7 ($CH_2$), 54.8 (CH), 53.1 (CH), 51.4 (CH), 50.3 (CH), 43.5 ($CH_2$), 43.0 (C), 38.5 (CH), 35.8 ($CH_2$), 34.9 ($CH_2$), 31.0 (CH), 26.7 ($CH_2$), 26.0 ($CH_3$), 22.4 ($CH_3$), 20.8 ($CH_2$), 20.3 ($CH_2$), 19.4 ($CH_2$), 18.4 (C), 16.5 ($CH_3$), 13.1 ($CH_3$), 3.4 ($CH_3$), −5.3 ppm ($CH_3$); MS: *m/z* (%): 543 (25) $[M+H]^+$, 525 (75) $[M+H-H_2O]^+$; HRMS: calcd for $C_{34}H_{59}O_3Si$ 543.42280; found: 543.42164.

**RCDEYM cyclization—general conditions: Compound 11a**: Grubbs' catalyst **10a** (0.006 mmol) was added to a solution of dienyne **9c$_{10R}$** (220 mg, 0.43 mmol) in $CH_2Cl_2$ (100 mL). The reaction mixture was heated at reflux for 4 h, allowed to come to room temperature and concentrated under reduced pressure. The crude residue was purified by chromatography on aluminium oxide (8% $H_2O$) to yield **11a** [152 mg, 80%, $R_f$=0.27 (EtOAc/hexanes 10%), yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=6.18 (d, $^3J$=10.1 Hz, 1H), 5.43 (m, 1H), 5.34 (t, $^3J$=8.1 Hz, 1H), 3.61 (dd, $^3J$=3.5, 9.6 Hz, 1H), 3.20 (m, 1H), 2.87 (dd, $^3J$=11.4, 3.9 Hz, 1H), 2.01 (d, $^3J$=11.4 Hz, 1H), 0.91 (s, 9H), 0.05 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C, TMS): $\delta$=139.7 (C), 130.5 (CH), 125.8 (CH), 119.1 (CH), 81.2 (C), 67.8 ($CH_2$), 53.8 (CH), 48.5 (CH), 45.2 (CH), 43.7 (C), 40.5 ($CH_2$), 38.6 (CH), 35.6 ($CH_2$), 35.1 ($CH_2$), 34.9 (CH), 33.3 ($CH_2$), 30.4 ($CH_2$), 29.9 ($CH_2$), 26.5 ($CH_2$), 26.0 ($CH_3$), 20.6 ($CH_2$), 18.4 (C), 16.4 ($CH_3$), 14.0 ($CH_3$), −5.3 ppm (2×$CH_3$); IR (KBr): $\tilde{\nu}$=2952, 2927, 2855, 1712, 1462, 1377, 1252, 1091, 1007, 984 cm$^{-1}$; MS: *m/z* (%): 445 (4) $[M+H]^+$, 313 (4), 295 (83); HRMS calcd for $C_{28}H_{49}O_2Si$ $[M+H]^+$: 445.35018; found: 445.35141.

**Compound 11d**: This compound was prepared from **12d** (25 mg, 0.056 mmol) in the same way as **11a** from **9c$_{10R}$**, with use of **10b** and final chromatography on silica gel to yield **11d** [3 mg, 14%, $R_f$=0.5 (EtOAc/hexanes 10%), yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=6.19 (d, $^3J$=9.7 Hz, 1H), 5.43 (m, 1H), 5.34 (m, 1H), 2.86 (dd, $^3J$=11.5 and 4.2 Hz, 1H), 1.99 (d, $^3J$=11.5 Hz, 1H), 0.85 (d, $^3J$=6.6 Hz, 6H), 0.85 ppm (s, 3H); IR ($CHCl_3$): $\tilde{\nu}$=3020, 2929, 2870, 1603, 1457, 1215, 996 cm$^{-1}$; MS: *m/z* (%): 385 (5) $[M+H]^+$, 367 (37) $[M+H-H_2O]^+$; HRMS calcd for $C_{27}H_{45}O$ $[M+H]^+$: 385.34704; found: 385.34682.

**Compound 11e**: KH (35% dispersion in mineral oil, 10 mg, 0.09 mmol), crown ether (2 mg) and MeI (10 mL, 0.16 mmol) were added to a solution of alcohol **11a** (20 mg, 0.04 mmol) in THF (2 mL) and the resulting mixture was heated at reflux for 12 h. The reaction was quenched by addition of $H_2O$ and the resulting mixture was extracted with hexanes. The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated under reduced pressure, giving a residue that was flash chromatographed (hexanes) to afford compound **11e** [14 mg, 68%, $R_f$=0.80 (EtOAc/hexanes 5%), colorless oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=6.18 (d, $^3J$=9.6 Hz, 1H), 5.42 (m, 1H), 5.38 (t, $^3J$=8.0 Hz, 1H), 3.60 (dd, $^3J$=9.6, 3.5 Hz, 1H), 3.23 (s, 3H), 3.17 (m, 1H), 2.81 (m, 1H), 1.95 (m, 1H), 0.93 (d, $^3J$=6.5 Hz, 3H), 0.89 (s, 9H), 0.03 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C, TMS): $\delta$=138.7 (C), 130.7 (CH), 125.6 (CH), 119.9 (CH), 84.8 (C), 67.9 ($CH_2$), 54.0 (CH), 49.0 ($CH_3$), 47.5 (CH), 43.5(C), 38.6 (CH), 37.8 (CH), 35.4 ($CH_2$), 35.2 ($CH_2$), 35.1 (CH), 33.3 ($CH_2$), 32.3 ($CH_2$), 30.2 ($CH_2$), 29.8 ($CH_2$), 26.6 ($CH_2$), 26.0 (3×$CH_3$), 20.8 ($CH_2$), 18.4 (C), 16.5 ($CH_3$), 14.3 ($CH_3$), −5.3 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3312, 3019, 2928, 2856, 1738, 1470, 1381, 1361, 1253, 1088, 1036, 1005, 987 cm$^{-1}$; EM-IQ$^+$: *m/z* (%): 459 (11) $[M+H]^+$, 411 (11), 369 (5), 295 (7); HRMS calcd for $C_{29}H_{51}O_2Si$ $[M+H]^+$: 459.36584; found: 459.36413.

**Compound 11g$_{10R}$**: Grubbs' catalyst **10b** (2.8 mg, $3.8\times10^{-3}$ mmol) was added to a solution of dienyne **9g$_{10R}$** (20 mg, 0.038 mmol) in benzene (8 mL). The reaction mixture was heated at reflux for 2 h, allowed to reach room temperature and concentrated under reduced pressure. The crude product was purified by chromatography on aluminium oxide (8% $H_2O$) to yield **11g$_{10R}$** [12 mg, 69%, $R_f$=0.2 (EtOAc/hexanes 10%), yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.41 (m, 1H), 5.17 (m, 1H), 3.62 (dd, $^3J$=9.5, 3.7 Hz, 1H), 3.20 (dd, $^3J$=9.5, 8.1 Hz, 1H), 2.90 (dd, $^3J$=11.0, 4.0 Hz, 1H), 1.80 (s, 3H), 0.97 (s, 3H), 0.91 (s, 9H), 0.05 ppm (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=142.2 (C), 136.1 (C), 121.0 (CH), 117.3 (CH), 80.9 (C), 67.8 ($CH_2$), 53.9 (CH), 48.5 (CH), 45.3 (CH), 43.7 (C), 40.6 ($CH_2$), 38.6 (CH), 35.8 ($CH_2$), 35.2 ($CH_2$), 34.6 (CH), 33.0 ($CH_2$), 30.5 (CH), 30.4 ($CH_2$), 29.8 ($CH_2$), 26.6 ($CH_2$), 26.1 ($CH_3$), 20.7 ($CH_2$), 18.5 ($CH_3$), 16.6 ($CH_3$), 14.1 ($CH_3$), −5.2 ppm (2×$CH_3$); IR ($CHCl_3$): $\tilde{\nu}$=3012, 2952, 2929, 2850, 1718, 1603, 1464, 1365, 1255, 1214, 1149, 1086, 1038 cm$^{-1}$; MS: *m/z* (%): 459 (2) $[M+H]^+$, 459 (1) $[M+H-H_2O]^+$, 383 (8), 307 (3); HRMS calcd for $C_{29}H_{50}O_2Si$ $[M+H]^+$: 458.35801; found: 458.35637.

**Compound 11i$_{10R}$**: This compound was prepared from **9i$_{10R}$** (25 mg, 0.04 mmol) in the same way as **11g$_{10R}$** from **9g$_{10R}$** [20 mg, 90%, $R_f$=0.4 (10% AcOEt/hexanes), white solid]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.68 (t, $^3J$=7.6 Hz, 1H), 5.24 (s, 1H), 4.87 (d, $^3J$=6.6 Hz, 1H), 4.73 (d, $^3J$=6.6 Hz, 1H), 4.73 (d, $^3J$=6.6 Hz, 1H), 4.55 (d, $^3J$=6.6 Hz, 1H), 3.99 (d, $^3J$=9.6 Hz, 1H), 3.56 (dd, $^3J$=9.6, 3.3 Hz, 1H), 3.38 (s, 3H), 3.35 (s, 3H), 3.27 (dd, $^3J$=9.6, 7.0 Hz, 1H), 2.83 (dd, $^3J$=11.8, 3.7 Hz, 1H), 2.56 (d, $^3J$=7.9 Hz, 2H), 2.23 (m, 1H), 2.16 (m, 1H), 1.77 (d, $^3J$=1.5 Hz, 3H), 0.98 (s, 3H), 0.95 (d, $^3J$=6.6 Hz, 6H), 0.93 (d, $^3J$=7.5 Hz, 3H), 0.89 (s, 9H), 0.03 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C, TMS): $\delta$=141.9 (CH), 135.7 (CH), 121.4 (CH), 119.5 (CH), 96.1 ($CH_2$), 91.7 ($CH_2$), 85.8 (C), 78.7 (CH), 67.6 ($CH_2$), 56.6 (CH), 55.9 ($CH_3$), 55.0 ($CH_3$), 54.2 (CH), 50.3 (CH), 41.6 (C), 38.9 ($CH_2$), 38.8 (CH), 38.1 (CH), 33.7($CH_2$), 29.4 ($CH_2$), 27.2 ($CH_2$), 26.0 ($CH_2$), 26.9 ($CH_3$), 21.4 ($CH_2$), 19.5 ($CH_2$), 19.1 ($CH_3$),18.4 ($CH_3$), 16.7 ($CH_3$), −5.3 ppm ($CH_3$); MS: *m/z* (%): 563 (6) $[M+H]^+$, 502 (15) $[M+H-OMOM]^+$, 441 (32) $[M+H-2\times OMOM]^+$.

**Compound 11j$_{10S}$**: Grubbs' catalyst **10b** (2 mg, $2.7\times10^{-3}$ mmol) was added to a solution of dienyne **9j$_{10S}$** (18 mg, 0.027 mmol) in benzene (5.5 mL). The reaction mixture was heated at reflux for 2 h and then another 2 mg of catalyst were added. After having been stirred for 2 h more at the same temperature, the solution was allowed to reach room temperature and concentrated under reduced pressure. The crude product was purified by chromatography on aluminium oxide (8% $H_2O$) to yield **11j$_{10S}$** [10 mg, 62%, $R_f$=0.5 (10% AcOEt/hexanes), white solid]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.39 (dd, $^3J$=11.1, 5.1 Hz, 1H), 5.10 (s, 1H), 4.13 (dd, $^3J$=4.7, 2.6 Hz, 1H), 3.60 (dd, $^3J$=9.7, 3.4 Hz, 1H), 3.26 (dd, $^3J$=9.7, 7.4 Hz, 1H), 2.76 (dd, $^3J$=12.2, 1.2 Hz, 1H), 2.65 (td, $^3J$=9.5, 4.7 Hz, 1H), 2.55 (t, $^3J$=11.8 Hz, 1H), 2.45 (dt, $^3J$=20.1, 2.4 Hz, 1H), 2.27 (dd, $^3J$=12.3, 5.1 Hz, 1H), 2.20 (dt, $^3J$=15.2, 2.1 Hz, 1H), 2.10 (dd, $^3J$=20.9, 10.2 Hz, 1H), 1.99 (dd, $^3J$=12.3, 6.0 Hz, 1H), 1.88 (dd, $^3J$=12.6, 7.7 Hz, 1H), 1.81 (d, $^3J$=1.6 Hz, 3H), 1.76 (ddd, $^3J$=12.9, 8.3, 1.6 Hz, 1H), 1.71–1.61 (m, 4H), 1.57 (m, 3H), 0.94 (s, 3H), 0.93 (d, $^3J$=5.4 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H), 0.04 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C, TMS): $\delta$=144.4 (C), 137.5 (C), 121.7 (CH), 117.6 (CH), 79.2 (C), 73.8 (C), 67.7 ($CH_2$), 55.6 (CH), 54.6 (CH), 51.4 (CH), 43.4 (CH), 41.2 (C), 38.8 (CH), 38.5 ($CH_2$), 38.0 ($CH_2$), 30.7 ($CH_2$), 30.3 (CH), 29.7 ($CH_2$), 27.3 ($CH_2$), 26.0 ($CH_3$), 25.7 ($CH_3$), 24.8 ($CH_2$), 19.6 ($CH_3$), 19.3 ($CH_2$), 18.4 (C), 18.3 ($CH_3$), 17.9 (C), 16.5 ($CH_3$), −4.8 ($CH_3$), −5.3 ppm ($CH_3$); MS: *m/z* (%): 589 (7) $[M+H]^+$, 571 (23) $[M+H-H_2O]^+$, 527 (66) $[M+H-OTBS]^+$; HRMS: calcd for $C_{35}H_{65}O_3Si_2$: 589.44723; found: 589.44705.

**Compound 11k$_{10R}$**: This compound was prepared from **9k$_{10R}$** (30 mg, 0.055 mmol) in the same way as **11g$_{10R}$** from **9g$_{10R}$** [14 mg, 54%, $R_f$=0.3 (10% AcOEt/hexanes), white solid]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.51 (t, $^3J$=6.9 Hz, 1H), 5.23 (s, 1H), 3.55 (dd, $^3J$=9.6, 3.2 Hz, 1H), 3.28 (dd, $^3J$=9.5, 6.9 Hz, 1H), 3.20 (s, 1H), 2.98 (d, $^3J$=11.6 Hz, 1H), 2.40 (m, 2H), 2.13 (m, 2H), 1.74 (brs, 3H), 0.98 (s, 3H), 0.93 (d, $^3J$=6.6 Hz, 3H), 0.88 (s, 9H), 0.02 ppm (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C, TMS): $\delta$=120.5 (CH), 120.1 (CH), 77.0 (CH), 67.4 ($CH_2$), 65.8 ($CH_2$), 58.7 (C), 54.4 (CH), 38.6 (CH), 37.3 (C), 29.4 (CH), 27.3 ($CH_2$), 26.0 ($CH_3$), 22.1 ($CH_2$), 19.6 ($CH_2$), 18.7 ($CH_3$), 18.4 (C), 16.6 ($CH_3$), 15.2 ($CH_3$), −5.4 ppm ($CH_3$); MS: *m/z* (%): 495 (2) $[M+Na^+]^+$, 307 (100) $[M-2H_2O-OTBS]^+$; HRMS: calcd for $C_{29}H_{48}NaO_3Si$: 495.32649; found: 495.32604.

**Triethyl but-3-yne-1,1,1-tricarboxylate (18)**: A solution of NaOEt (1.93 g, 28.42 mmol) in EtOH (24 mL) was added to a solution of triethyl methanetricarboxylate (6.00 g, 25.84 mmol) in $Et_2O$ (20 mL), cooled in an ice

bath. The white sodium salt that precipitated was collected, washed with $Et_2O$ and dried in vacuo, affording triethyl sodium methanetricarboxylate (5.78 g, 22.73 mmol) as a white powder that was dissolved in a toluene/DMF mixture (1:1, 50 mL) and treated with propargyl bromide (80% w/w solution in toluene, 5.1 mL, 45.5 mmol). The mixture was stirred at 80°C for 1.5 h, cooled and filtered, and the residue was washed with toluene. The combined filtrates were washed with water, dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. Distillation of the crude product (97°C at 0.2 mmHg) afforded triethyl but-3-yne-1,1,1-tricarboxylate [6.03 g, 86%, $R_f$=0.2 (EtOAc/hexanes 10%), pale yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=4.25 (q, $^3J$=7.1 Hz, 6H), 2.98 (d, $^3J$=2.6 Hz, 2H), 2.01 (t, $^3J$=2.6 Hz, 1H), 1.26 ppm (t, $^3J$=7.1 Hz, 9H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=165.6 (CO), 78.6 (C≡), 70.6 (C≡), 64.4 (C), 62.4 ($CH_2$), 23.1 ($CH_2$), 13.75 ppm ($CH_3$); MS: *m/z* (%): 271 (100) $[M+H]^+$, 197 (35), 125 (24); HRMS calcd for $C_{13}H_{19}O_6$ $[M+H]^+$: 271.11816; found: 271.11868.

**Malonate 19b**: A solution of **18** (3.00 g, 11.10 mmol) in THF (3 mL) was added by cannula to a suspension of sodium ethoxide (980 mg, 14.4 mmol) in THF (35 mL) and the mixture was stirred at room temperature for 1.5 h. (*Z*)-Pent-2-enynyl methanesulfonate (3.64 g, 22.2 mmol) was added, and stirring was continued for 3 h, after which the mixture was poured into brine (30 mL) and extracted with $Et_2O$. The combined organic phases were dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (EtOAc/hexanes 4%), affording the dialkylmalonate **19b** [1.03 g, 35%, $R_f$=0.4 (EtOAc/hexanes 10%), yellow oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.48 (m, 1H), 4.97 (m, 1H), 4.11 (m, 4H), 2.70 (m, 4H), 2.07 (m, 2H), 1.94 (t, $^3J$=2.7 Hz, 1H), 1.18 (t, $^3J$=7.2 Hz, 6H), 0.88 ppm (t, $^3J$=7.5 Hz, 3H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=169.7 (CO), 136.4 (CH), 121.6 (CH), 78.9 (C≡), 71.1 (C≡), 61.4 ($CH_2$), 61.1 ($CH_2$), 56.5 (C), 29.5 ($CH_2$), 22.2 ($CH_2$), 20.5 ($CH_2$), 14.0 ($CH_3$), 13.9 ($CH_3$), 13.6 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3285, 2979, 2936, 2875, 1736, 1465, 1447, 1367, 1325, 1289, 1243, 1208, 1188, 1137, 1096, 1070, 1054, 1016 cm$^{-1}$; MS: *m/z* (%): 267 (100) $[M+H]^+$, 194 (5) $[M+H-CO_2Et]^+$, 121 (5) $[M+H-(CO_2Et)_2]^+$; HRMS calcd for $C_{15}H_{23}O_4$ $[M+H]^+$: 267.15963; found: 267.16007.

**Malonate 19c**: This compound was prepared in the same way as **19b** with (*E*)-4-methylpent-2-enyl methanesulfonate[31] (3.18 g, 17.85 mmol) to afford **19c** [2.2 g, 88%, $R_f$=0.5 (EtOAc/hexanes 15%), yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.52 (dd, $^3J$=15.2, 6.9 Hz, 1H), 5.15 (m, 1H), 4.17 (q, $^3J$=7.1 Hz, 4H), 2.75 (d, $^3J$=2.6 Hz, 2H), 2.70 (d, $^3J$=7.5 Hz, 2H), 2.21 (m, 1H), 1.98 (t, $^3J$=2.6 Hz, 1H), 1.23 (t, $^3J$=7.1H, z6H), 0.92 ppm (d, $^3J$=6.8 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=169.8 (CO), 143.2 (CH), 119.7 (CH), 79.1 (C≡), 71.2 (C≡), 61.5 ($CH_2$), 57.0 (C), 35.0 ($CH_2$), 31.1 (CH), 22.0 ($CH_3$), 21.7 ($CH_2$), 14.1 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3202, 3006, 2962, 2929, 2871, 2850, 2360, 2118, 1457, 1426, 1230, 1178, 1069 cm$^{-1}$; MS: *m/z* (%): 281 (58) $[M+H]^+$, 207 (25), 133 (17); HRMS calcd for $C_{16}H_{25}O_4$ $[M+H]^+$: 281.17528; found: 281.17564.

**Malonate 19d**:[32] This compound was prepared in the same way as **19b** with 1-bromo-3-methylbut-2-ene (3.90 g, 26.15 mmol) to afford **19d** [2.61 g, 75%, $R_f$=0.4 (EtOAc/hexanes 15%), yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=4.89 (t, $^3J$=1.4 Hz, 1H), 4.17 (m, 4H), 2.75 (m, 4H), 1.97 (t, $^3J$=2.7 Hz, 1H), 1.65 (s, 3H), 1.64 (s, 3H), 1.23 ppm (t, $^3J$=7.1 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=170.0 (CO), 136.6 (C), 117.1 (CH), 71.1 (C≡), 79.4 (C≡), 61.5 (2×$CH_2$), 57.0 (C), 30.6 ($CH_2$), 26.0 ($CH_3$), 22.4 ($CH_2$), 18.0 ($CH_3$), 14.0 ppm (2×$CH_3$); MS: *m/z* (%): 267 (1) $[M+H]^+$, 205 (5); HRMS calcd for $C_{15}H_{23}O_4$ $[M+H]^+$: 267.15963; found: 267.15882.

**Ethyl (*Z*)-2-(prop-2-ynyl)hept-4-enoate**: A solution of malonate **19b** (3.20 g, 12.01 mmol) and NaOEt (1.23 g, 18.07 mmol) in EtOH (50 mL) was heated at reflux for 2 days, allowed to come to rt, poured into NaCl (40 mL) and treated with HCl (10%, 20 mL). The aqueous layer was extracted with $Et_2O$, and the combined organic phases were dried over $Na_2SO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (EtOAc/hexanes, 1%), yielding ethyl (*Z*)-2-(prop-2-ynyl)hept-4-enoate [1.30 g, 55%, $R_f$=0.6 (EtOAc/hexanes 10%), yellow oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.44 (m, 1H), 5.19 (m, 1H), 4.11 (q, $^3J$=7.1 Hz, 2H), 2.51 (m, 1H), 2.35 (m, 4H), 2.01 (m, 3H), 1.21 (t, $^3J$=7.1 Hz, 3H), 0.90 ppm (t, $^3J$=7.5 Hz, 3H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=173.8 (CO), 134.6 (CH), 124.3 (CH), 81.4 (C≡), 69.8 (C≡), 60.5 ($CH_2$), 44.4 (CH), 28.5 ($CH_2$), 20.5 ($CH_2$), 20.3 ($CH_2$), 14.2 ($CH_3$), 14.1 ppm ($CH_3$); MS: *m/z* (%): 195 (53) $[M+H]^+$, 167 (27), 149 (17), 121 (100); HRMS calcd for $C_{12}H_{19}O_2$ $[M+H]^+$: 195.13850; found: 195.13884.

**Ethyl (*E*)-6-methyl-2-(prop-2-ynyl)hept-4-enoate**: Malonate **19c** (4.2 g, 14.99 mmol) was decarboxylated in 50% yield in the same way as **19b** [$R_f$=0.5 (EtOAc/hexanes 15%), yellow oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.47 (dd, $^3J$=15.5, 6.3 Hz, 1H), 5.27 (dtd, $^3J$=15.2, 6.9, 1.0 Hz, 1H), 4.15 (q, $^3J$=7.1 Hz, 2H), 2.56 (m, 1H), 2.33 (m, 5H), 1.98 (t, $^3J$=2.6 Hz, 1H), 1.26 (t, $^3J$=7.1 Hz, 3H), 0.94 ppm (d, $^3J$=6.8 Hz, 6H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25°C, TMS): $\delta$=173.5 (CO), 140.7 (CH), 122.3 (CH), 81.2 (C≡), 69.6 (C≡), 60.1 ($CH_2$), 44.3 (CH), 33.8 ($CH_2$), 30.8 (CH), 22.2 ($CH_3$), 19.9 ($CH_2$), 14.0 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3311, 2959, 2930, 2871, 1736, 1466, 1440, 1259, 1177, 1041, 972 cm$^{-1}$; MS: *m/z* (%): 209 (29) $[M+H]^+$, 136 (2) $[M+H-CO_2Et]^+$; HRMS calcd for $C_{13}H_{21}O_2$ $[M+H]^+$: 209.15416; found: 209.15432.

**Ethyl 5-methyl-2-(prop-2-ynyl)hex-4-enoate**: Malonate **19d** (7.34 g, 27.59 mmol) was decarboxylated in the same way as **19b** [32%, $R_f$=0.6 (EtOAc/hexanes 10%), yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=5.04 (t, $^3J$=1.4 Hz, 1H), 4.15 (q, $^3J$=7.1 Hz, 2H), 2.54 (m, 1H), 2.39 (m, 4H), 1.96 (t, $^3J$=2.6 Hz, 1H), 1.68 (s, 3H), 1.61 (s, 3H), 1.24 ppm (t, $^3J$=7.1 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=174.1 (CO), 134.6 (C), 120.1 (CH), 81.7 (C≡), 69.7 (C≡), 60.5 ($CH_2$), 44.7 (CH), 29.6 ($CH_2$), 25.8 ($CH_3$), 20.3 ($CH_2$), 17.8 ($CH_3$), 14.2 ppm ($CH_3$); MS: *m/z* (%): 195 (1) $[M+H^+]^+$.

**(4*R*,5*S*)-3-[(*Z*)-Hept-4-enoyl]-4-methyl-5-phenyloxazolidin-2-one (22b)**: Pivaloyl chloride (3.3 mL, 27.2 mmol) was slowly added at −78°C to a flask containing (*Z*)-hept-4-enoic acid[33] (**21b**, 2.09 g, 16.3 mmol) and $Et_3N$ (3.8 mL, 27.1 mmol) in THF (8 mL). The thick white paste was stirred at 0°C for 1 h. In a separate flask, a solution of (4*R*,5*S*)-(+)-4-methyl-5-phenyloxazolidin-2-one (4.37 g, 24.66 mmol) in THF (11 mL) was treated at room temperature with a catalytic amount of DMAP (10 mol%, 302 mg, 2.46 mmol), followed by $Et_3N$ (3.4 mL, 24.6 mmol). This solution was then added at −78°C over 5 min to the above mixed anhydride, and the mixture was stirred for 12 h at room temperature to ensure complete reaction. Volatiles were removed in vacuo, and the resulting white paste was dissolved in $CH_2Cl_2$ (11 mL) and NaOH (1 M, 6 mL). The aqueous phase was removed and the organic phase was washed with brine and then dried, filtered and concentrated under reduced pressure. This concentrate was purified by flash chromatography on silica gel (12% EtOAc/hexanes), yielding **22b** [4.18 g, 59%, $R_f$=0.5 (EtOAc/hexanes 15%), pale yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25°C, TMS): $\delta$=7.35 (m, 5H), 5.64 (d, $^3J$=7.3 Hz, 1H), 5.40 (m, 2H), 4.75 (m, 1H), 2.99 (m, 2H), 2.42 (m, 2H), 2.09 (m, 2H), 0.96 (t, $^3J$=7.6 Hz, 3H), 0.85 ppm (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25°C, TMS): $\delta$=172.4 (CO), 152.9 (CO), 133.3 (C), 133.1 (CH), 128.64 (CH), 128.60 (CH), 126.7 (CH), 125.5 (CH), 78.9 (CH), 54.6 (CH), 35.6 ($CH_2$), 22.0 ($CH_2$), 20.4 ($CH_2$), 14.5 ($CH_3$), 14.2 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3063, 2965, 2934, 2874, 1784, 1700, 1456, 1369, 1345, 1279, 1218, 1195, 1145, 1122, 1067, 1031, 990 cm$^{-1}$; MS: *m/z* (%): 288 (96) $[M+H]^+$, 273 (4), 178 (62); HRMS calcd for $C_{17}H_{22}NO_3$ $[M+H]^+$: 288.15997; found: 288.16074; elemental analysis calcd (%) for $C_{17}H_{21}NO_3$: C 70.81, H 7.69, N 4.86; found: C 70.68, H 7.75, N 5.18.

**(4*R*,5*S*)-3-[(*E*)-6-Methylhept-4-enoyl]-4-methyl-5-phenyloxazolidin-2-one (22c)**: This compound was prepared from (*E*)-6-methylhept-4-enoic acid (**21c**, 1.83 g, 12.87 mmol of crude mixture)[23] in the same way as **22b** from **21b** [3.1 g, 80%, $R_f$=0.75 (30% EtOAc/hexanes), pale yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25°C, TMS): $\delta$=7.36 (m, 5H), 5.65 (d, $^3J$=7.3 Hz, 1H), 5.43 (m, 2H), 4.75 (m, 1H), 3.01 (m, 2H), 2.35 (m, 2H), 2.22 (m, 1H), 0.95 (d, $^3J$=6.7 Hz, 6H), 0.87 ppm (d, $^3J$=6.5 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25°C, TMS): $\delta$=172.5 (CO), 153.0 (CO), 133.3 (C), 138.9 (CH), 128.7 (CH), 128.6 (CH), 125.6 (CH), 124.8 (CH), 78.9 (CH), 54.7 (CH), 35.6 ($CH_2$), 30.9 (CH), 27.2 ($CH_2$), 22.4 ($CH_3$), 14.5 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3526, 3383, 3066, 3035, 2957, 2869, 1777, 1700, 1498, 1457, 1382, 1345, 1197, 1146, 1120, 1091, 1067, 1032, 970 cm$^{-1}$;

MS: *m/z* (%): 302 (28) $[M+H]^+$, 206 (28), 178 (43), 134 (100); HRMS calcd for $C_{18}H_{24}NO_3$ $[M+H]^+$: 302.17562; found: 302.17632.

**(4*R*,5*S*)-3-{(2*S*,4*Z*)-2-[3-(Trimethylsilyl)prop-2-ynyl]hept-4-enoyl}-4-methyl-5-phenyloxazolidin-2-one (23b)**: LiHMDS (1 M, 4.3 mL, 4.3 mmol) was added at −78 °C to a solution of oxazolidinone **22b** (1.14 g, 3.99 mmol) in THF (25 mL), the resulting mixture was stirred for 0.5 h, and a solution of 3-bromo-1-trimethylsilylprop-2-yne (2.29 g, 11.97 mmol) in toluene (5 mL) was added. The reaction mixture was stirred at 0 °C for 3 h, poured into $NH_4Cl$ (30 mL) and extracted with $CH_2Cl_2$. The combined organic phases were dried over $Na_2SO_4$, filtered and concentrated under reduced pressure, and the concentrate was purified by flash chromatography on silica gel (EtOAc/hexanes 5%), affording the desired product [1.03 g, 65%, $R_f$=0.55 (EtOAc/hexanes 15%), pale yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.37 (m, 5H), 5.64 (d, $^3J$=7.3 Hz, 1H), 5.47 (m, 1H), 5.27 (m, 1H), 4.78 (m, 1H), 4.01 (m, 1H), 2.47 (m, 4H), 2.04 (m, 2H), 0.93 (t, $^3J$=7.5 Hz, 3H), 0.86 (d, $^3J$=6.6 Hz, 3H), 0.06 ppm (s, 9H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=173.8 (CO), 152.5 (CO), 134.75 (CH), 133.3 (C), 128.6, 125.5 (CH), 124.3 (CH), 103.6 (C≡), 86.2 (C≡), 78.7 (CH), 54.8 (CH), 42.3 (CH), 28.7 ($CH_2$), 21.7 ($CH_2$), 20.4 ($CH_2$), 14.5 ($CH_3$), 14.1 ($CH_3$), −0.1 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3520, 3400, 3061, 3006, 2960, 2874, 2177, 1765, 1708, 1456, 1346, 1250, 1225, 1198, 1148, 1125, 1032, 979 cm$^{-1}$; MS: *m/z* (%): 398 (3) $[M+H]^+$, 382 (10), 354 (14), 250 (70), 221 (17), 206 (38); HRMS calcd for $C_{23}H_{32}NO_3Si$ $[M+H]^+$: 398.21515; found: 398.21396.

**(4*R*,5*S*)-3-{(2*S*,4*E*)-6-Methyl-2-[3-(trimethylsilyl)prop-2-ynyl]hept-4-enoyl}-4-methyl-5-phenyloxazolidin-2-one (23c)**: This compound was prepared from **22c** (3.77 g, 12.52 mmol) in the same way as **23b** from **22b** [3.45 g, 67%, $R_f$=0.6 (EtOAc/hexanes 15%), pale yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.36 (m, 5H), 5.61 (d, $^3J$=7.3 Hz, 1H), 5.47 (dd, $^3J$=15.3, 6.6 Hz, 1H), 5.32 (m, 1H), 4.77 (m, 1H), 4.05 (m, 1H), 2.52 (m, 2H), 2.38 (m, 1H), 2.25 (m, 2H), 0.95 (d, $^3J$=6.8 Hz, 6H), 0.89 (d, $^3J$=6.6 Hz, 3H), 0.08 ppm (s, 9H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=174.1 (CO), 152.6 (CO), 141.2 (CH), 133.3 (C), 128.7, 125.6 (CH), 122.6 (CH), 103.9 (C≡), 86.1 (C≡), 78.8 (CH), 54.9 (CH), 42.5 (CH), 34.6 ($CH_2$), 31.0 (CH), 22.5 ($CH_3$), 21.7 ($CH_2$), 14.6 ($CH_3$), 0.01 ppm ($CH_3$); IR ($CHCl_3$): $\tilde{\nu}$=3673, 3549, 3032, 3009, 2961, 2871, 2457, 2363, 2175, 1779, 1699, 1456, 1385, 1344, 1250, 1195, 1145, 1121, 975 cm$^{-1}$; MS: *m/z*: 412 $[M+H]^+$ (10), 397 (12), 250 (100); HRMS calcd for $C_{24}H_{34}NO_3Si$ $[M+H]^+$: 412.23080; found: 412.23204.

**(4*R*,5*S*)-3-[(2*S*,4*E*)-2-(But-2-ynyl)-6-methylhept-4-enoyl]-4-methyl-5-phenyloxazolidin-2-one (23g)**: This compound was prepared from **22c** (1.5 g, 4.8 mmol) and 1-bromobut-2-yne (1.75 mL, 19.2 mmol) in the same way as **23b** from **22b** [1.2 g, 70%, $R_f$=0.5 (EtOAc/hexanes 15%), pale yellow oil]; $^1$H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.38–7.26 (m, 5H), 5.58 (d, $^3J$=7.4 Hz, 1H), 5.45 (dd, $^3J$=15.2, 6.2 Hz, 1H), 5.30 (dt, $^3J$=15.6, 7.0 Hz, 1H), 4.75 (m, 1H), 3.98 (m, 1H), 2.48–2.16 (m, 5H), 1.67 (s, 3H), 0.92 (d, $^3J$=6.6 Hz, 6H), 0.86 ppm (d, $^3J$=6.6 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=174.4 (CO), 152.6 (CO), 140.9 (CH), 133.3 (C), 128.6 (CH), 125.5 (CH), 122.8 (CH), 78.7 (CH), 77.0 (C≡), 75.9 (C≡), 54.7 (CH), 42.7 (CH), 34.4 ($CH_2$), 30.9 (CH), 22.5 ($CH_3$), 22.4 ($CH_3$), 20.8 ($CH_2$), 14.4 ($CH_3$), 3.3 ppm ($CH_3$); MS: *m/z* (%): 354 (88) $[M+H]^+$, 338 (16) $[M+H-CH_4]^+$, 310 (70) $[M+H-i\mathrm{PrH}]^+$, 177 (100); HRMS calcd for $C_{22}H_{28}NO_3$ $[M+H]^+$: 354.20692; found: 354.20777.

**(4*S*)-4-Benzyl-3-[(4*E*)-methylhept-4-enoyl]oxazolidin-2-one**: This compound was prepared from **21c** (2.55 g, 17.93 mmol) in the same way as **22b** from **21b** but with use of (4*S*)-4-benzyloxazolidin-2-one [4.98 g, 94%, $R_f$=0.6 (30% AcOEt/hexanes), pale yellow oil]; $^1$H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.35–7.19 (m, 5H), 5.52–5.36 (m, 2H), 4.66 (tdd, $^3J$=10.3, 6.9, 3.5 Hz, 1H), 4.21–4.12 (m, 2H), 3.28 (dd, $^3J$=13.4, 3.1 Hz, 1H), 3.11–2.89 (m, 2H), 2.76 (dd, $^3J$=13.3, 9.6 Hz, 1H), 2.41–2.34 (m, 2H), 2.24 (dc, $^3J$=13.1, 6.6 Hz, 1H), 0.96 ppm (d, $^3J$=6.8 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=172.6 (CO), 153.3 (CO), 138.9 (CH), 135.2 (C), 129.3 (CH), 128.8 (CH), 127.2 (CH), 124.7 (CH), 66.0 ($CH_2$), 55.0 (CH), 37.8 ($CH_2$), 35.5 ($CH_2$), 30.8 (CH), 27.1 ($CH_2$), 22.4 ppm ($CH_3$); MS: *m/z* (%): 302 (61) $[M+H]^+$, 286 (6) $[M+H-CH_4]^+$, 178 (100) $[M+H-CHO(CH_2)_2(CH)_2CH(CH_3)_2]^+$; HRMS: calcd for $C_{18}H_{24}NO_3$: 302.17562; found: 302.17544.

**(4*S*)-4-Benzyl-3-[(4*Z*)-hept-4-enoyl]oxazolidin-2-one**: This compound was prepared from (*Z*)-hept-4-enoic acid (**21b**, 6.14 g, 48.01 mmol) in the same way as **22b** from **21b** but with use of (4*S*)-4-benzyloxazolidin-2-one (8.68 g, 48.97 mmol) [5.79 g, 42%, $R_f$=0.4 (20% EtOAc/hexanes), pale yellow oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.29 (m, 5H), 5.42 (m, 2H), 4.67 (m, 1H), 4.15 (m, 2H), 3.29 (dd, $^3J$=13.4, 3.2 Hz, 1H), 3.01 (m, 2H), 2.79 (dd, $^3J$=13.3, 9.5 Hz, 1H), 2.43 (m, 2H), 2.09 (m, 2H), 0.99 ppm (t, $^3J$=7.5 Hz, 3H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=172.7 (CO), 153.4 (CO), 135.2 (C), 133.1 (CH), 129.3 (CH), 128.8 (CH), 127.2 (CH), 126.7 (CH), 66.1 ($CH_2$), 55.0 (CH), 37.8 ($CH_2$), 35.5 ($CH_2$), 21.9 ($CH_2$), 20.4 ($CH_2$), 14.2 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3527, 3383, 3085, 3029, 3007, 2962, 2903, 2871, 1979, 1784, 1696, 1604, 1496, 1458, 1391, 1359, 1251, 1210, 1126, 1110, 1065, 988 cm$^{-1}$; MS: *m/z* (%): 288 (100) $[M+H]^+$, 206 (46), 178 (74); HRMS calcd for $C_{17}H_{22}NO_3$ $[M+H]^+$: 288.15997; found: 288.16032; elemental analysis calcd (%) for $C_{17}H_{21}NO_3$: C 70.81, H 7.69, N 4.86; found: C 70.94; H 7.58, N 4.99.

**Compound (*R*)-24h**: PDC (3.1 g) and molecular sieves (4 Å, 0.5 g, 8.34 mmol) were added to a solution of alcohol (*R*)-**5g** (1.0 g, 5.56 mmol) in $CH_2Cl_2$ (55 mL). The suspension was stirred at room temperature for 6 h and then filtered through a pad of silica gel/celite (1:1) and washed with $Et_2O$. The crude was flash chromatographed to give a yellow oil that upon distillation (95 °C, 0.2 mbar) afforded the aldehyde (*R*)-**24h** [692 mg, 70%, $R_f$=0.8 (AcOEt/hexanes 20%), colorless oil]; $[\alpha]_D^{20}$: −7.9 ($c$=0.02 in $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=9.69 (s, 1H), 5.49 (dd, $^3J$=15.3 and 6.6 Hz, 1H), 5.29 (dt, $^3J$=15.3 and 6.6 Hz, 1H), 2.45–2.24 (m, 6H), 1.79 (t, $^3J$=2.6 Hz, 3H), 0.97 ppm (d, $^3J$=7.0 Hz, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=203.5 (CO), 141.1 (CH), 122.2 (CH), 77.7 (C), 75.5 (C), 50.7 (CH), 31.2 ($CH_2$), 30.4 (CH), 22.5 ($CH_3$), 17.9 ($CH_2$), 3.6 ppm ($CH_3$); MS: *m/z* (%): 179 (17) $[M+H]^+$, 163 (12) $[M+H-CH_4]^+$, 161 (23) $[M+H-H_2O]^+$, 149 (62) $[M+H-CH_2O]^+$; HRMS: calcd for $C_{12}H_{19}O$ 179.14359; found: 179.14375.

**Compound (*S*)-24h**: This compound was prepared from alcohol (*S*)-**5g** (960 mg, 5.33 mmol) in the same way as (*R*)-**24h** from (*R*)-**5g** [682 mg, 72%, $R_f$=0.8 (20% AcOEt/hexanes), colorless oil]; $[\alpha]_D^{20}$: 7.9 ($c$=0.02 in $CHCl_3$).

**(4*S*)-4-Benzyl-3-{(2*R*,4*Z*)-2-[3-(trimethylsilyl)prop-2-ynyl]hept-4-enoyl}oxazolidin-2-one (25b)**: This compound was prepared from (4*S*)-4-benzyl-3-((*Z*)-hept-4-enoyl)oxazolidin-2-one (4.70 g, 16.37 mmol) in the same way as **23b** from **22b** [5.02 g, 77%, $R_f$=0.4 (EtOAc/hexanes 15%), pale yellow oil]; $^1$H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.28 (m, 5H), 5.49 (m, 1H), 5.28 (m, 1H), 4.68 (td, $^3J$=6.2 and 3.5 Hz, 1H), 4.16 (m, 2H), 3.98 (m, 1H), 3.30 (dd, $^3J$=13.4 and 2.9 Hz, 1H), 2.76 (dd, $^3J$=13.4 and 9.5 Hz, 1H), 2.59 (d, $^3J$=6.5 Hz, 2H), 2.44 (m, 2H), 2.07 (m, 2H), 0.95 (t, $^3J$=7.5 Hz, 3H), 0.12 ppm (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=173.9 (CO), 152.9 (CO), 135.2 (C), 134.8 (CH), 134.7 (CH), 129.3 (CH), 128.8 (CH), 127.2 (CH), 124.4 (CH), 124.3 (CH), 103.6 (C≡), 86.5 (C≡), 65.9 ($CH_2$), 55.2 (CH), 42.3 (CH), 37.9 ($CH_2$), 28.4 ($CH_2$), 21.8 ($CH_2$), 20.5 ($CH_2$), 14.1 ($CH_3$), −0.1 ppm ($CH_3$); IR (KBr): $\tilde{\nu}$=3010, 2962, 2925, 2868, 2358, 2176, 1782, 1699, 1456, 1387, 1350, 1288, 1250, 1208, 1105, 1053, 1011 cm$^{-1}$; MS: *m/z* (%): 398 (28) $[M]^+$, 206 (49), 222 (9), 178 (68); HRMS calcd for $C_{23}H_{32}NO_3Si$ $[M]^+$: 398.21515; found: 398.21645.

**(4*S*)-4-Benzyl-3-[(2*R*,4*E*)-2-(but-2-ynyl)-6-methylhept-4-enoyl]oxazolidin-2-one (25g)**: This compound was prepared from (4*S*)-4-benzyl-3-[(*E*)-methylhept-4-enoyl]oxazolidin-2-one (4.98 g, 16.54 mmol) and 1-bromobut-2-yne (3.0 mL, 33.08 mmol) in the same way as **23b** from **22b** to yield compound **25g** [4.28 g, 73%, $R_f$=0.5 (20% AcOEt/hexanes), yellow oil]; $^1$H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=7.31 (m, 6H), 5.47 (dd, $^3J$=15.4, 6.31 Hz, H), 5.32 (dt, $^3J$=15.4, 6.6 Hz, 1H), 4.70 (m, 1H), 4.20 (d, $^3J$=5.2 Hz, 2H), 4.00 (q, $^3J$=7.0 Hz, 1H), 3.28 (dd, $^3J$=13.3, 3.2 Hz, 1H), 2.80 (dd, $^3J$=13.4, 9.2 Hz, 1H), 2.53–2.16 (m, 5H), 1.76 (t, $^3J$=2.5 Hz, 3H), 1.40 (s, 2H), 0.94 ppm (d, $^3J$=6.7 Hz, 6H); $^{13}$C NMR (63 MHz, $CDCl_3$, 25 °C, TMS): $\delta$=174.6 (CO), 153.0 (CO), 141.0 (CH), 135.2 (C), 129.4 (CH), 128.9 (CH), 127.3 (CH), 122.8 (CH), 77.2 (C), 76.1 (C), 65.9 ($CH_2$), 55.2 (CH), 42.8 (CH), 37.8 ($CH_2$), 34.5 ($CH_2$), 30.9 (CH), 26.3 ($CH_3$), 22.5 ($CH_3$), 20.8 ($CH_2$), 3.5 ppm ($CH_3$); MS: *m/z* (%): 150 (1)

$[M+H]^+$, 91 (100) $[M+H-Bn]^+$; HRMS: calcd for $C_{21}H_{28}NO_3$: 354.20692; found: 354.20704.

CCDC-282836 (**11e**) and CCDC-624627 (**11i$_{10R}$**) contain 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.

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