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Studies towards the synthesis of the bicyclic 3,8-secotaxane diterpenoid system using a ring closing metathesis strategy

Michela L. Renzulli,[a] Luc Rocheblave,[b] Stanislava I. Avramova,[a] Elena Galletti,[a] Daniele Castagnolo,[a] Andrea Tafi,[a] Federico Corelli[a] and Maurizio Botta[a,*]

[a]*Dipartimento Farmaco Chimico Tecnologico, Università degli Studi di Siena, 53100 Siena, Italy*
[b]*Laboratoire de Stéreochimie Dynamique et Chiralité, Faculté des Sciences de Saint Jérôme, avenue Escadrille Normandie Niemen, 13397 Marseille cedex 20, France*

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Abstract—Molecular modelling studies on the interations between taxanes and tubulins, developed by us, revealed that modified Taxuspines U and X could adopt a conformation similar to that of the bioactive conformation of paclitaxel and could be well accommodated within the proposed model. Accordingly, simplified Taxuspine U and X analogues have been rationally designed and their bicyclic 3,8-secotaxane diterpenoids intermediates have been synthesized through an approach that involves ring closing metathesis (RCM) as the key step for the macrocycle formation. Extensive studies on RCM have been performed using chemically diverse substrates, outlining the influence in the macrocyclization of the presence and position of functionalities, the molecular constraints and the importance of the site of ring closure.

1. Introduction

The remarkable therapeutic potential and challenging structural complexity of taxane diterpenoids have stimulated considerable synthetic efforts worldwide. In spite of numerous synthetic approaches towards Taxol® and Taxotere® (**1** and **2**), including six total syntheses,[1] not enough attention has been paid to bicyclic 3,8-secotaxane diterpenoids Taxuspine U (**3**) and X (**4**). These natural products, whose skeleton has been proposed as biogenetic precursor for taxanes, were isolated from the Japanese yew *Taxus Cuspidata* in very poor yield.[2]

Based on our efforts to find a theoretical quantitative model describing the relationships between the structure and biological activity of microtubules stabilizing anticancer agents (MSAAs), an atomic pseudoreceptor model has been proposed in our previous studies.[3,4] These computational studies have revealed that modified Taxuspines U and X can adopt a shape similar to that of the bioactive conformation of paclitaxel and can be well accommodated within the pseudoreceptor model proposed to predict the microtubule-stabilizing activity for taxanes.

In particular, compound **5** is predicted to be as active as Taxol®, while natural Taxuspine U (**3**) is predicted by the model to be less active. The similarity between the macrocycle conformation of **5** and its orientation inside the binding site suggested us that compound **5** might mimic the ABC ring system of Taxol®. Compound **5** is structurally simpler and synthetically more accessible than paclitaxel and it could be an interesting alternative to the tricyclic taxanes, as a novel lead compound for new microtubule-stabilizing agents (Fig. 1).

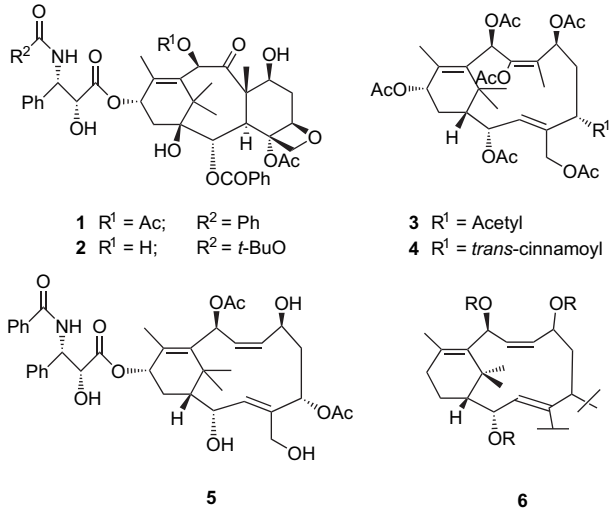

Figure 1.

Keywords: Microtubules-stabilizing anticancer agents (MSAAs); Taxuspines U and X; Minireceptor model; Ring closing metathesis.
* Corresponding author. Tel.: +39 0577 234306; fax: +39 0577 234333; e-mail: botta@unisi.it

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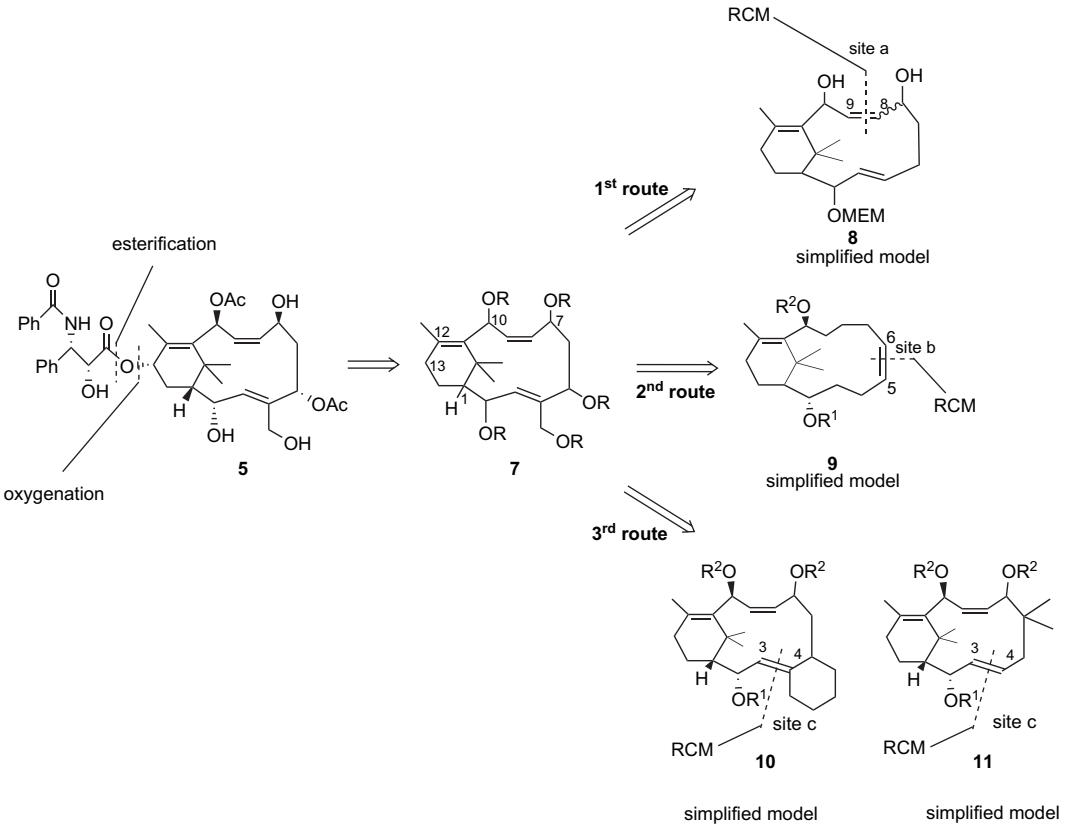


Scheme 1. Retrosynthetic analysis.

On the other hand, if a *trans*-cinnamoyl moiety is introduced on the C-5 oxygen and the β-phenyl isoserine side chain is removed from C-13, **5** could in principle be transformed into Taxuspine X (**4**) analogues, potentially interesting as multidrug resistance (MDR) reversing agents.[5] Accordingly, our project opens a pathway to a variety of taxoids to be tested as anticancer and MDR reversing agents, and represents a preliminary study for the synthesis of Taxuspine U and X analogues.

In our recent communication,[6] we reported the methodology for the synthesis of bicyclic 3,8-secotaxane diterpenoids, involving ring closing methatesis (RCM) as the key step for the macrocycle formation.[7] We now report a full account of our efforts towards the synthesis of **6**, the common bicyclic intermediate of Taxuspine U and X analogues, via RCM; all the trials to obtain the constrained 12-membered macrocycle will be discussed herein, because there is a little information available concerning RCM on related systems. It has been shown, in fact, that RCM works very well when applied to substrates devoid of any conformational constraints and it must be considered to be among the most efficient entries into macrocycles if the sites of ring closure are properly chosen.[8]

2. Results and discussion

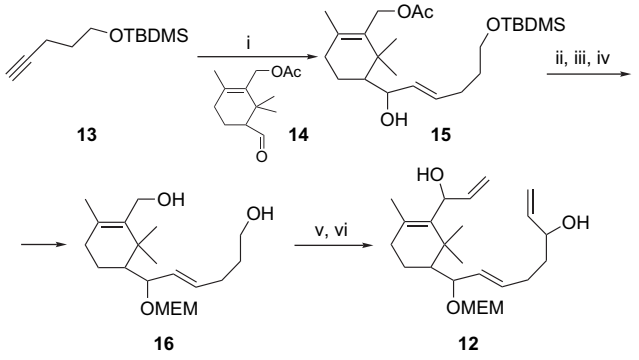
Compound **5** is a challenging target for an original synthesis and no procedures for its preparation have been reported in the literature so far.[9] In the retrosynthetic analysis, **5** offers several points for disconnection; thus, appropriate protections and removal of the phenylisoserine chain and deoxygenation at the C-13 position afforded the naked carbocyclic core 7, which was further simplified, leading to models **8–11**. All these compounds could in principle be obtained by RCM, as outlined in Scheme 1.

Three main routes for the macrocyclization were initially considered. Compound **8** could be obtained from an allylic alcohol precursor, in which the double bonds are activated towards RCM, while the precursor of **9** would display two sterically unencumbered double bonds to be involved in the complexation with ruthenium catalyst. Finally, compound **10** (or **11**) should be obtained from more constrained precursors bearing substituents that in some cases may help the RCM.[8]

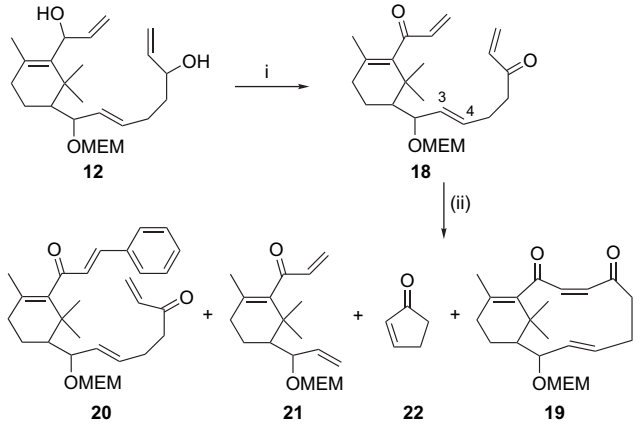
Disconnection at *site a* identified as synthetic precursor the tetraene intermediate **12**, which was readily prepared as described in Scheme 2.

Hydrozirconiation of **13** with the Schwartz reagent (Cp_2ZrHCl)[10a,b] gave the intermediate vinylzirconocene, which was reacted with aldehyde **14** and catalytic silver perchlorate ($AgClO_4$) to afford the secondary alcohol **15** as a mixture of diastereoisomers (*syn–anti* 3:1 ratio, according to the HPLC analysis and confirmed by precedent literature data),[10c] in 80% yield. The mixture of diastereoisomeric alcohols **15** was in turn protected on the secondary alcohol as a methoxyethoxymethyl ether and deprotected at the primary alcohol groups, leading to the diol **16**.

Oxidation with Dess–Martin periodinane [11,12] provided the corresponding dialdehyde, which was converted into **12** by



Scheme 2. Synthesis of **12**. Reagents, conditions and yields: (i) Cp_2ZrHCl, **14**, $AgClO_4$, CH_2Cl_2, 0 °C, 80%; (ii) MEMCl, DIPEA, DMAP, CH_2Cl_2, 95%; (iii) TBAF, THF, 90%; (iv) $LiOH{\cdot}H_2O$, CH_3OH/H_2O, 85%; (v) Dess–Martin periodinane, CH_2Cl_2 and (vi) vinylmagnesium bromide, THF, 56% (over two steps).



Scheme 4. Oxidation of allyl alcohols and RCM of **18**. Reagents, conditions and yields: (i) Dess–Martin periodinane, CH_2Cl_2, 75% and (ii) Grubbs' II cat., CH_2Cl_2, rt to reflux, 13% (overall yield).

treatment with vinylmagnesium bromide. The diastereoisomeric ratio was not calculated and **12** was used as a mixture of isomers.

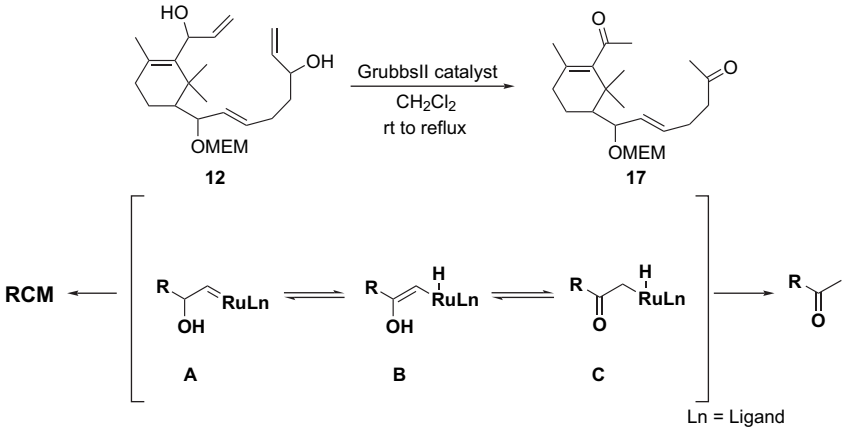
When **12** was treated with Grubbs' catalyst in order to perform a macrocyclization,[13,14] only the methyl ketone **17** was obtained instead of the expected macrocycle **8** (Scheme 3). It is clear that the ruthenium carbene species, coming from the Grubbs' catalyst, was consumed by this side reaction: the use of only 10 mol % and 20 mol % of ruthenium catalyst results in low conversion of **12** and all the ^1H NMR spectroscopic resonances due to the catalyst disappeared. It has been suggested in similar cases [15,16] that the initial metal-complexed carbene A (Scheme 3) undergoes tautomerization to the enolyl ruthenium hydride species B, which can further undergo reductive elimination, either before or after tautomerization to the oxoalkyl ruthenium hydride C, to produce the methyl ketone.

In order to circumvent this side reaction, **12** was subjected to oxidation with Dess–Martin periodinane, affording the ketone derivative **18**, which was treated with 20 mol % of Grubbs' ruthenium catalyst in dry and degassed dichloromethane at room temperature and then at reflux (Scheme 4).

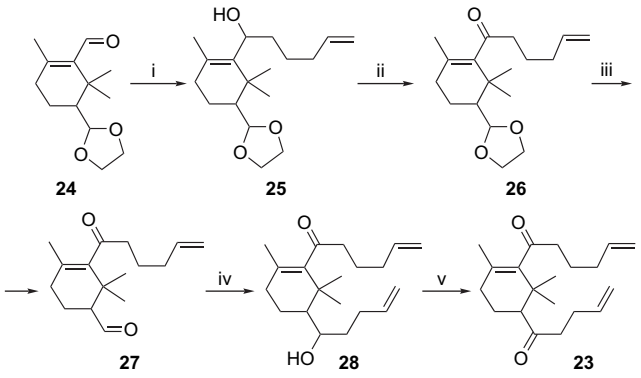
However, only traces of the expected macrocycle **19** were detected, together with compound **20**, resulting from carbene exchange between **18** and the benzylidene ligand of the catalyst as outlined in Scheme 4; compound **21** and cyclopentenone **22**, arising from intramolecular ring closing metathesis between C3–C4 and terminal double bonds. Attempts to perform the RCM reaction on **12** after protection of the allylic alcohol groups as silyl ether or acetate did not afford better results, as only the cyclopentene derivatives and products of fragmentation of type **21** were obtained.

In the meantime, the second route was also explored and the new ω–ω′-diolefin triene **23** was prepared from the aldehyde **24**[17] in an overall yield of 82% (Scheme 5). Treatment of **24** with a small excess of 4-pentenylmagnesium bromide in diethyl ether at room temperature led to a diastereoisomeric mixture of alcohols **25**, which on selective oxidation with TPAP-NMO [18] was then converted into the ketone **26**. After hydrolysis of the acetal group of **26** with CSA in THF/H_2O, the aldehyde **27** was submitted to Grignard reaction with 3-butenylmagnesium bromide in diethyl ether at 0 °C. Oxidation of the resulting mixture of alcohols **28** with TPAP-NMO furnished the diketone **23**.

Triene **23** was submitted to RCM and different results were obtained, according to the reaction conditions (Scheme 6). Thus, a 3 mM solution of **23** in 1,2-dichloroethane (DCE) was treated with 20 mol % of Grubbs' I catalyst at room



Scheme 3. Attempted ring closing metathesis of **12**.



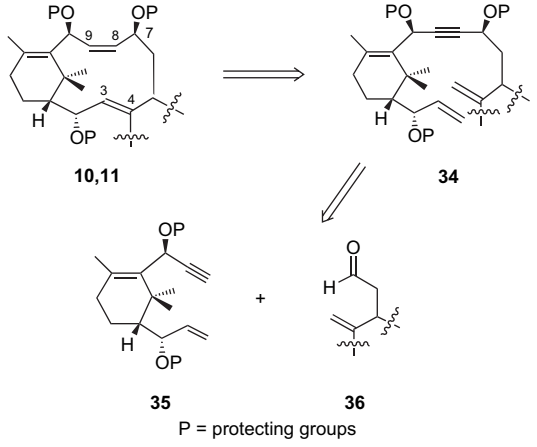
Scheme 5. Synthesis of **23**. Reagents, conditions and yields: (i) pentenylmagnesium bromide, diethyl ether, rt, 92%; (ii) TPAP, MNO, CH_2Cl_2, molecular sieves, 58%; (iii) CSA, THF/H_2O, reflux, 99%; (iv) butenylmagnesium bromide, 0 °C to rt, 63% and (v) TPAP, NMO, CH_2Cl_2, molecular sieves, 99%.

temperature and after one day the presence of four new products was detected, even if 70% of starting material was still present. The HPLC–MS analysis of the crude reaction mixture revealed the presence of two different families of compounds, which were separated: acyclic dimers and 24-membered macrocycles.[19] Concerning the regiochemical outcome of the metathesis, HPLC–MS–MS analysis of the mixture of acyclic dimers revealed the presence of only two compounds (**29** and **30**) instead of the expected three dimers. The analysis of the cyclic dimers confirmed the presence of both compounds **31** and **32** in a 1:1 ratio. The analysis of the MS–MS fragmentation confirmed the structures described in Scheme 6 (vide infra: Supplementary data).

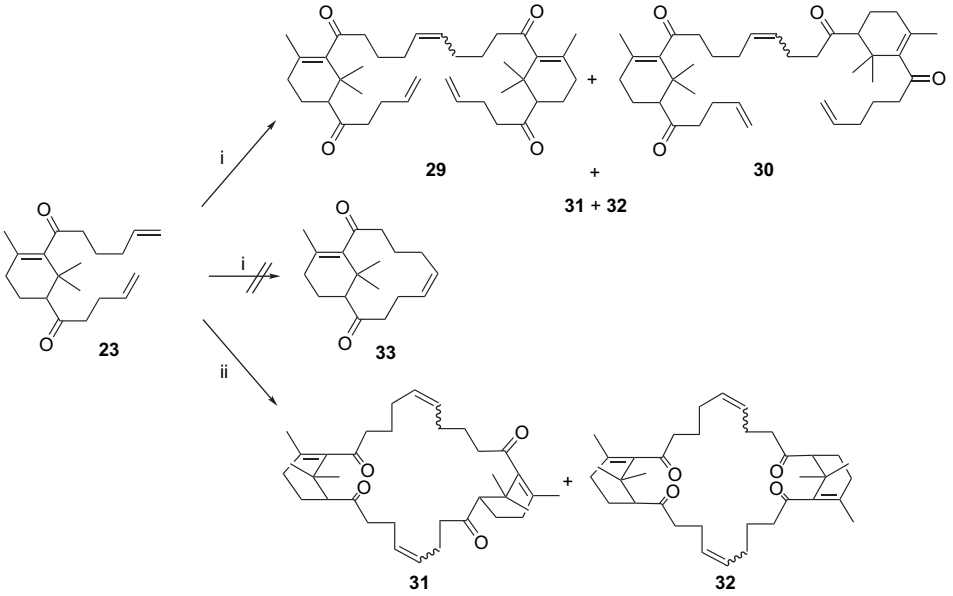
Concerning the stereochemical outcome of the metathesis, the configuration of the newly formed double bonds has not been proved due to the symmetry of the molecules and/or the complexity of the spectral data.

In order to improve the RCM and to obtain the desired macrocycle **33**, this reaction was further investigated using different amounts (5%, 10% and 15%) of Grubbs' II catalyst, higher dilutions (1 mM and 0.75 mM in DCE) and longer reaction time, but in these cases only the acyclic dimers **29** and **30** were obtained. Conversely, after heating the reaction at reflux temperature, even under the same conditions of dilution and catalyst, only the dimers **31** and **32** were isolated. Finally, when the reaction was performed at higher temperature (refluxing toluene) the catalyst decomposition was competitive with the metathesis reaction and no product was obtained. These results showed that probably, due to both entropic and enthalpic reasons[7f] related to the length of the chains as well as to the conformation of the substrate **23** and the products **31** and **32**, the dimerization is favoured. The resistance of these unfunctionalized dienes towards cyclization confirmed that the presence of polar functional groups is a pivotal parameter for successful RCM.[8]

Following the observations described above, a third route was devised, for which the trieneyne **34** was envisaged to be a suitably functionalised and constrained substrate for the key RCM. The disconnection of the B-ring of **10** or **11** (Scheme 7) at the *site c* (Scheme 1) leads to **34**, a further



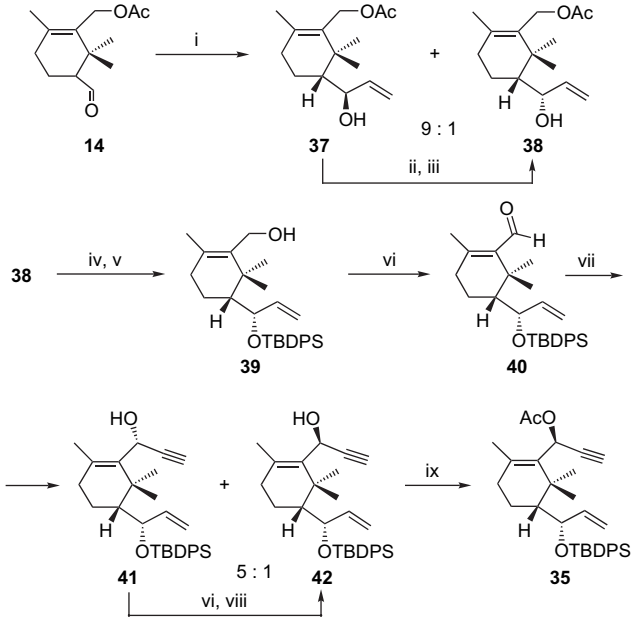
Scheme 7. Disconnection of **10** or **11**.



Scheme 6. Ring closing metathesis of **23**. Reagents, conditions and yields: (i) Grubbs' I or II cat., DCE, rt, 64% and (ii) Grubbs' I or II cat., DCE, reflux, 75%.

diolefin intermediate, while the cis-C8–C9 double bond is expected to result from selective reduction of the corresponding triple bond. The second bond disconnection was planned between C7 and C8 to provide a highly convergent approach to the Taxuspine nucleus from the suitably functionalized ring A building block **35** and aldehyde **36**.

The alkyne **35** was obtained according to Scheme 8. Treatment of aldehyde **14**[1b,17] with a small excess of vinylmagnesium bromide, led to a mixture of **37** and **38** with high diastereoselectivity, 9:1 ratio in favour of the *syn* compound **37**, previously assigned by Fallis et al.[22] and confirmed by us.[6]

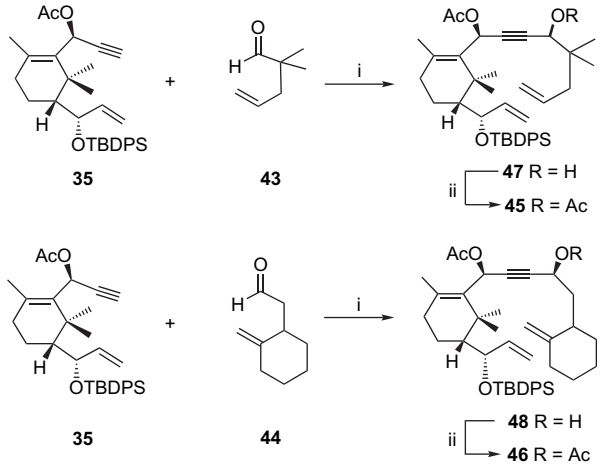


Scheme 8. Synthesis of alkyne **35**. Reagents, conditions and yields: (i) vinylmagnesium bromide, THF, −78 °C to rt, 84%; (ii) Dess–Martin periodinane, CH_2Cl_2, 90%; (iii) L-Selectride, THF, −78 °C to rt, 84%; (iv) TBDPSCl, imidazole, DMAP, DMF, rt, 85%; (v) K_2CO_3, CH_3OH, quantitative; (vi) TPAP, MNO, molecular sieves, CH_2Cl_2, rt, 91%; (vii) ethynylmagnesium bromide, THF, −78 °C to rt, 85%; (viii) 9-BBN, THF, 0 °C, 90% and (ix) Ac_2O, Et_3N, DMAP, CH_2Cl_2, rt, quantitative.

The most abundant isomer **37** was converted into **38** by oxidation with Dess–Martin periodinane followed by reduction with L-Selectride.[21] The orthogonal protection of the allylic alcohol **38** as TBDPS ether, followed by removal of the *O*-acetyl group, produced the corresponding alcohol **39**, which was oxidized with TPAP-NMO to the aldehyde **40** in 95% yield. When the latter compound was reacted with ethynylmagnesium bromide, a mixture of two diastereoisomers **41** and **42** was obtained in a 5:1 ratio.[20,22]

The resulting propargylic alcohols **41** and **42** were separated by flash chromatography and **41** was converted into the diastereoisomer **42** by oxidation with TPAP-NMO, followed by reduction with 9-BBN.[23] The propargyl alcohol **42** was finally acetylated providing the intermediate **35**.

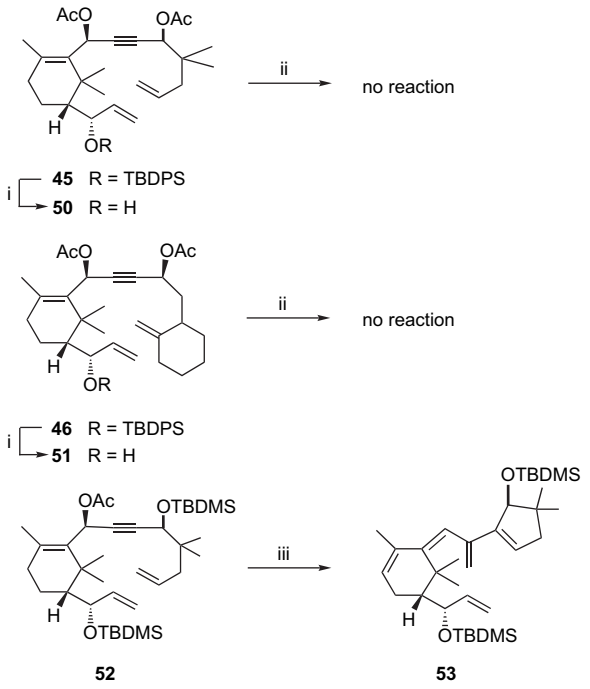
For establishing the C7–C8 bond (numbering referred to the target compound) we chose the commercially available 2,2-dimethyl-4-pentenaldehyde **43** and the easily obtainable 2-(2-methylenecyclohexyl)acetaldehyde **44**.[6] As outlined in Scheme 9, the macrocycle precursors **45** and **46** were prepared from the lithium derivative of **35** and aldehydes **43** and **44**, respectively, followed by acetylation of the newly formed alcohols **47** and **48**. In both cases, HPLC analysis revealed the presence of one major isomer. The C-7 relative stereochemistry of the major isomer **48** was tentatively assigned on the basis of the NOESY analysis and later confirmed by the analysis of the cyclized compounds **58** and **60** (vide infra) for comparison with the literature data relative to Taxuspine U and X.[2d,e,6] The C-7 relative stereochemistry of **47** has been assumed based on very similar spectroscopic data and chemical behaviour of the alkynylation.[24]



Scheme 9. Synthesis of macrocycle precursors. Reagents, conditions and yields: (i) LHMDS, THF, −78 °C to rt, 65–72% and (ii) Ac_2O, Et_3N, DMAP, CH_2Cl_2, rt, quantitative.

Conformational analysis has been performed on **46** and on its partially hydrogenated derivative **49**, in order to evaluate possible problems in terms of hindrance and conformational strains of the 12-membered macrocycle, that could limit the success of RCM reaction.[25,26] Calculations suggested that both alkyne- and alkene-linked dienes should be viable substrates for the RCM macrocyclization reaction (vide infra: Supplementary data).

Different RCM assays were performed on the intermediates **45** and **46** but in no case intramolecular cyclization occurred and the starting material was consistently recovered, either varying the RCM conditions and the ruthenium catalysts used (Grubbs' I or Grubbs' II catalyst). In order to reduce the steric hindrance of the double bond and to help the complexation between the catalyst and the substrate, the silyl ether in the allylic position was cleaved, giving the corresponding alcohols **50** and **51**, and another macrocycle precursor **52** was prepared as well (by protection of the diasteromeric mixture of **47** as a TBS ether), but olefin metathesis always failed on all these substrates (Scheme 10). However, while **50** and **51** were recovered unaltered, compound **52** underwent a smooth transformation to **53**, through intramolecular ene–yne metathesis involving the terminal unhindered double bond and the more electron-rich alkyne moiety, followed by elimination of acetic acid and rearrangement of the double bond, resulting in a more stable conjugated system (Scheme 10).[27]



Scheme 10. Studies of RCM. Reagents, conditions and yields: (i) TBAF, THF, 40 °C, 62%; (ii) RCM conditions and (iii) Grubbs' II ruthenium cat., CH_2Cl_2, 66%.

We reasoned that the alkyne function could affect the catalyst, interfering our plan of RCM. Aside from the undesired ene–yne metathesis, the cyclization could be further complicated by the linear character of the acetylene group and by the non-productive coordination of the triple bond to the RCM catalytic machinery.[28] To the best of our knowledge, in fact, no example of carbo-macrocycle bearing an endocyclic triple bond has been obtained by olefin RCM.

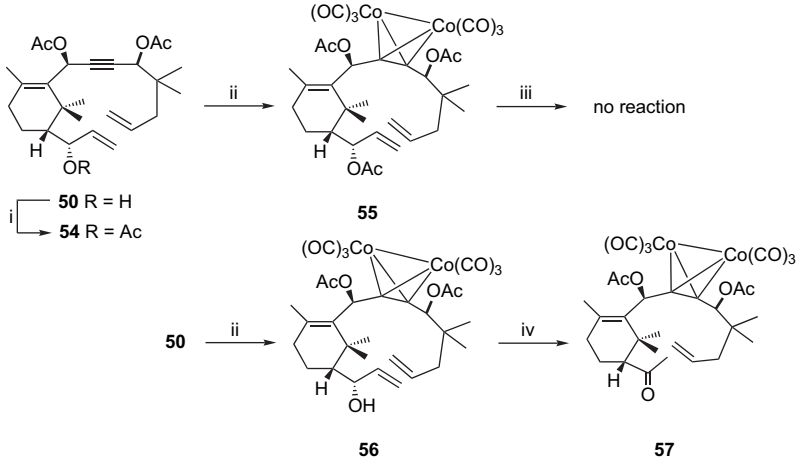
Accordingly, we thought that protection of the alkyne might be necessary. It is well known that reactions of dicobalt carbonyl with acetylene can lead to stable complexes.[28–30] Moreover, the geometry of these cobalt-complexed alkynes optimizes at approximately 140° and such a departure from linearity could well favour cyclization.[31]

To test this hypothesis, the fully acetylated compound **54** was treated with cobalt dicarbonyl (Scheme 11). Complex formation proceeded readily at room temperature in DCM even if the reaction did not go to completion, probably because of the steric hindrance around the triple bond. The complexation provided the stable compound **55**, which was isolated after silica gel chromatography in 70% yield.

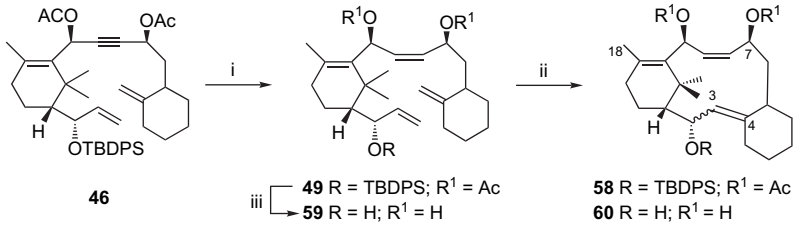
Unfortunately, when **55** was subjected to the conditions of RCM with 10% and 15% Grubbs' II catalyst in DCM and high dilution, no cyclization reaction occurred and starting compound was largely recovered. Also **50** was subjected to the complexation with cobalt dicarbonyl under the same conditions, to afford **56** (Scheme 11). When this cobalt-complexed diolefin was treated with Grubbs' catalyst, a smooth reaction occurred, providing the methyl ketone **57**, instead of the desired 12-membered macrocycle, in analogy to our previous data observed for the metathesis on substrate **12**.

Subsequently, the conversion of the triple bonds of **45** and **46** to the corresponding *cis*-alkenes was investigated. Hydrogenation of **45** and **47** to the corresponding *cis*-alkenes with Lindlar/quinoline was unsatisfactory,[32] while the use of Rosenmund's catalyst/quinoline did afford the cis-C8–C9 alkene derivatives of **45** and **47**, but with concomitant hydrogenation of the ω–ω′-double bonds. Conversely, the partial hydrogenation of **46** to the corresponding *cis*-alkene, in the presence of Lindlar catalyst and quinoline proved to be effective and the new macrocycle precursor **49** was obtained in high yield, as outlined in Scheme 12.

Finally, RCM using 10% Grubbs' II catalyst in dry and degassed DCM at room temperature, starting from the ω–ω′-diolefin **49** gave in 20% yield the desired macrocycle **58**, a 3,8-secotaxane diterpenoid, simplified analogue of taxuspine U and the first target of this work (Scheme 12). Similar result was obtained in the macrocyclization of **59**, the fully deprotected derivative of **49**, and **60** was isolated in the same yield. NOESY correlation peaks of H7/$H_3$18 and H10/$H_3$18 revealed that H7 and H10 have the same relative configuration.[2d,e] It was not possible to determine the geometry of the C3–C4 double bond on the basis of the NMR data



Scheme 11. Protection of the alkyne moiety with cobalt complex and RCM. Reagents, conditions and yields: (i) Ac_2O, Et_3N, DMAP, CH_2Cl_2, rt, quantitative; (ii) $Co_2(CO)_8$, CH_2Cl_2, rt, 65–70%; (iii) 15% Grubbs' II cat. CH_2Cl_2 (1 mM), rt or reflux; (iv) 15% Grubbs' II cat. CH_2Cl_2 (1 mM), rt, 55%.



Scheme 12. Synthesis of the target compounds. Reagents, conditions and yields: (i) H_2, Lindlar cat., quinoline, petrol ether, 90%; (ii) Grubbs' II ruthenium cat., CH_2Cl_2, 20 and 25% and (iii) a: TBAF, THF, 40 °C, 75%; b: K_2CO_3, CH_3OH, quantitative.

available. However, MM (Molecular Mechanic) calculations revealed that the *E* isomer is the most stable one.

Attempts to increase the efficiency of the RCM reaction met with little success due to the formation of intractable side products. The macrocycles **58** and **60** represent the first examples of a highly constrained 6/12 bicyclic system obtained by RCM.

3. Conclusions

In conclusion, as part of a wider project aimed at the design and synthesis of new antimitotic agents stabilizing microtubules and MDR reversing agents, we have set up a new methodology for the synthesis of simplified Taxuspines U analogues. This synthetic pathway involves macrocyclization via RCM to give fused 6/12 bicyclic 3,8-secotaxane diterpenoids, the first examples of a highly constrained macrocycle prepared via metathesis. Extensive studies towards RCM have been performed using chemically different substrates. These experiments outlined the influence on the macrocyclization of several different factors, such as the presence and position of functionalities as well as molecular constraints.[33] Although the target compounds have been obtained in low to moderate yield, this route led to an interesting and important result in the synthesis of highly functionalized and complex macrocycle and represents an example of a systematic approach to constrained and hindered systems.

4. Experimental section

4.1. General methods

Unless otherwise stated, all reactions were carried out under nitrogen or argon atmosphere. Reagents were obtained from commercial suppliers and used without further purifications. Merck silica gel 60 was used for both column chromatography (70–230 mesh) and flash chromatography (230–400 mesh). NMR spectra were recorded on a Bruker AC200 (200 MHz) or Bruker Avance DPX400 (400 MHz). The numbers for the peak assignments are referred to the bicyclic systems, described in Scheme 1. The HPLC analysis was recorded by reverse phase liquid chromatography on Agilent series 1100 LC/MSD with an UV detector at λ=254 nm and an electrospray ionization source (ESI) with an electron beam of 70 eV. The LC elution methods (using Zorbax Eclipse XDB®, 4.6×150 mm, 5 μm C8 column) were as following: method 1: 25 min, flow rate 1.15 mL/min, A 50%, B 50%; method 2: 25 min, flow rate 1 mL/min, A 15%, B 85% (solvents were HPLC grade; A: water; B: methanol). FTIR spectra were recorded on a Perkin–Elmer 1600 spectrophotometer. Elemental analyses (C, H and N) were performed in house. All the analytical and spectral data are referred to the major isomer.

4.1.1. [5-((*E*)-6-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-1-hydroxy-2-hexenyl)-2,6,6-trimethyl-1-cyclohexenyl]-methyl acetate (15). To a cooled (0 °C) solution of 4-(*tert*-butyldimethylsilyloxy)-1-pentyne (**13**) (1.35 g, 6.8 mmol) in dichloromethane (13 mL), the freshly prepared Schwartz reagent (1.75 g, 6.3 mmol), in three portions during 20 min, was added. The ice bath was removed, the flask protected from light, and the mixture was stirred for 15 min. After 10 min the complete dissolution of the reagent was observed. The solution was recooled to 0 °C, before adding the aldehyde **14** (1.27 g, 5.67 mmol), dissolved in dichloromethane (2 mL), and then $AgClO_4$ (36 mg, 0.175 mmol). After 30 min the brown mixture was treated with saturated aqueous $NaHCO_3$. The aqueous phase was separated and extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and evaporated. The resulting residue was purified by flash chromatography (light petroleum ether/ethyl acetate, 9:1), affording the two diastereoisomers of **15** as colourless oils (1.91 g, 80% overall yield) in a ratio of 3:1. The ^{1}H NMR spectral data are referred to the major isomer. IR (film): ν 3502, 1736, 1250 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.64–5.57 (m, 2H, C*H*=C*H*), 4.58 (s, 2H, CH_2OAc), 4.20 (pseudo t, *J*=5.60 Hz, 1H, H-2), 3.60 (t, *J*=6.6 Hz, 2H, H-7), 2.09–1.97 (m, 2H, H-14, H-5), 2.02 (s, 3H, COCH_3), 1.77–1.51 (m, 6H, H-13, H-5, C=CCH_3), 1.37–1.22 (m, 4H, H-1, H-14, H-6), 1.19 (s, 3H, CH_3CCH_3), 1.14 (s, 3H, CH_3CCH_3), 0.87 (s, 9H, (CH_3)$_3$C), 0.03 (s, 6H, Si(CH_3)$_2$). ESIMS (*m*/*z*): 447 [M+Na]$^+$. Anal. Calcd for $C_{24}H_{44}O_4Si$: C, 67.87; H, 10.44. Found: C, 67.89; H, 10.54.

4.1.2. (6*E*)-8-[3-(1-Hydroxyallyl)-2,2,4-trimethyl-3-cyclohexenyl]-8-[(2-methoxyethoxy)methoxy]-1,6-octadien-3-ol (12). Compound **16** (79 mg, 0.22 mmol) in dry CH_2Cl_2 at 0 °C was treated with Dess–Martin periodinane (DMP, 328 mg, 0.77 mmol). The mixture was stirred at 0 °C for 5 min and for further 1 h at room temperature. Pentane was then added, the mixture was stirred for 10 min and then filtered through a pad of silica gel (diethyl ether 100%) affording the dialdehyde, as revealed by HPLC–MS analysis, which was used directly without further purification. The dialdehyde was dissolved in dry THF and the mixture was cooled at 0 °C; vinylmagnesium bromide (0.54 mL of

a 1 M solution in THF) was added dropwise and the mixture was stirred at room temperature for 1 h. The reaction was quenched with NH_4Cl and the aqueous phase was extracted twice with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The resulting residue was purified by chromatography (diethyl ether/light petroleum ether 2:1), affording the mixture of diasteroisomers of **12**, as colourless oils (50 mg, 56%, two steps). IR (film): ν 3502, 1250, 890 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 6.09–5.78 (m, 2H, COHC*H*=CH_2, COHC*H*=CH_2), 5.66–5.47 (m, 3H, H-3, H-4, CC*H*OHCH), 5.40–5.02 (m, 4H, COCH=CH_2, C(OMEM)CH=CH_2), 4.78–4.76 (m, 1H, CH_2C*H*OHCH), 4.72 (d, J=6.4 Hz, 1H, OHC*H*O), 4.56 (d, J=6.4 Hz, 1H, OHC*H*O), 4.08 (d, J=7.4 Hz, 1H, H-2), 3.71–3.49 (m, 4H, ($CH_2O)_2$), 3.35 (s, 3H, OCH_3), 2.14–1.84 (m, 2H, H-14, H-5), 1.71 (s, 3H, C=CCH_3), 1.63–1.52 (m, 3H, H-13, H-5), 1.29 (s, 3H, CH_3CCH_3), 1.23 (s, 3H, CH_3CCH_3), 1.20–1.08 (m, 4H, H-1, H-14, H-6). ESIMS (m/z): 431 $[M+Na]^+$. Anal. Calcd for $C_{24}H_{40}O_5$: C, 70.55; H, 9.87. Found: C, 70.67; H, 9.78.

4.1.3. (*E*)-7-(3-Acetyl-2,2,4-trimethyl-3-cyclohexenyl)-7-[(2-methoxyethoxy)methoxy]-5-hepten-2-one (17). Compound **12** (20 mg, 0.049 mmol) was dissolved in 5 mL of dry and degassed CH_2Cl_2 and the mixture was heated at reflux. Grubbs' catalyst (30 mol %) was added via syringe pump over 5 h. After 12 h the mixture was cooled, the solvent was removed and the crude product was purified by flash chromatography (diethyl ether/light petroleum ether 1:3), affording **17** (3.7 mg, 0.0098 mmol). The unreacted starting material was recovered. IR (film): ν 1670, 1250, 890 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 5.57–5.42 (m, 2H, H-3, H-4), 4.86 (d, J=6.4 Hz, 1H, OHC*H*O), 4.64 (d, J=6.4 Hz, 1H, OHC*H*O), 4.04–3.99 (m, 1H, H-2), 3.70–3.66 (m, 4H, ($CH_2O)_2$), 3.35 (s, 3H, OCH_3), 2.67 (m, 2H, H-6), 2.32 (m, 2H, H-14, H-5), 2.20 (s, 3H, CH_2COCH_3), 1.93 (s, 3H, CCOCH_3), 1.83–1.67 (m, 1H, H-5), 1.52 (s, 3H, C=CCH_3), 1.50–1.29 (m, 4H, H-1, H-14, H-13), 1.10 (s, 3H, CH_3CCH_3), 0.99 (s, 3H, CH_3CCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ 139.3, 136.5, 133.9, 132.4, 128.2, 126.0, 116.1, 116.0, 92.5, 80.8, 73.2, 71.8, 66.5, 61.0, 58.3, 54.0, 38.5, 37.7, 30.7, 28.4, 26.3, 26.2, 17.5, 17.4. ESIMS (m/z): 403 $[M+Na]^+$. Anal. Calcd for $C_{24}H_{36}O_5$: C, 69.44; H, 9.54. Found: C, 69.35; H, 9.41.

4.1.4. (6*E*)-8-(3-Acryloyl-2,2,4-trimethyl-3-cyclohexenyl)-8-[(2-methoxyethoxy)methoxy]-1,6-octadien-3-one (18). Compound **12** (50 mg, 0.12 mmol) in dry CH_2Cl_2 at 0 °C was treated with Dess–Martin periodinane (DMP, 182 mg, 0.42 mmol). The mixture was stirred at 0 °C for 5 min and for further 1 h at room temperature. Pentane was then added, the mixture was stirred for 10 min and then filtered through a pad of silica gel (diethyl ether/light petroleum ether 1:1) affording **18** (colourless oils 36.4 mg, 75%), as mixture of diasteroisomers. IR (film): ν 1665, 1250, 890 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 6.30–6.20 (m, 2H, CCOC*H*=CH_2, CH_2COC*H*=CH_2), 6.12–5.76 (m, 4H, CCOCH=CH_2, CH_2COCH=CH_2), 5.64–5.36 (m, 2H, H-3, H-4), 4.67 (d, J=6.6 Hz, 1H, OHC*H*O), 4.53 (d, J=6.6 Hz, 1H, OHC*H*O), 4.14 (dd, J=2.5, 7.5 Hz, 1H, H-2), 3.59–3.43 (m, 4H, ($CH_2O)_2$), 3.32 (s, 3H, OCH_3), 2.63 (t, J=7.4 Hz, 2H, H-6), 2.35 (m, 2H, H-14, H-5), 1.75–1.70 (m, 1H, H-5), 1.46 (s, 3H, C=CCH_3), 1.41–1.16 (m, 4H, H-1, H-14, H-13), 1.07 (s, 3H, CH_3CCH_3), 0.96 (s, 3H, CH_3CCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ 202.2, 195.0, 153.1, 141.3, 138.6, 137.9, 136.9, 134.2, 128.8, 127.9, 94.1, 82.0, 73.9, 66.7, 60.8, 54.7, 40.2, 31.70, 29.5, 26.8, 26.4, 26.3, 17.5, 17.0. ESIMS (m/z): 427 $[M+Na]^+$. Anal. Calcd for $C_{24}H_{36}O_5$: C, 71.26; H, 8.97. Found: C, 71.12; H, 8.79.

4.1.5. Compounds 19 and 20. Compound **18** (30 mg, 0.07 mmol) was dissolved in 7 mL of dry and degassed CH_2Cl_2 and the mixture was heated at reflux. Grubbs' catalyst (20 mol %) was added via syringe pump over 5 h. After 12 h the mixture was cooled, the solvent was removed and the crude reaction mixture was purified by flash chromatography (diethyl ether/light petroleum ether 1:3), affording **21** (2 mg) and **20** (4 mg), **22** and traces of **19**. Overall yield: 13%.

4.1.5.1. (3*Z*,8*E*)-10-((2-Methoxyethoxy)methoxy)-14,15,15-trimethylbicyclo[9.3.1]pentadeca-1(14),3,8-triene-2,5-dione (19). IR (film): ν 1665, 1250, 890 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 6.77 (d, J=11.7 Hz, 1H, C*H*=CH), 6.36 (d, J=11.7 Hz, 1H, CH=C*H*), 5.64–5.36 (m, 2H, H-3, H-4), 4.79 (d, J=6.4 Hz, 1H, OHC*H*O), 4.64 (d, J=6.4 Hz, 1H, OHC*H*O), 4.11–4.08 (m, 1H, H-2), 3.60–3.46 (m, 4H, ($CH_2O)_2$), 3.37 (s, 3H, OCH_3), 2.65 (t, J=7.3 Hz, 2H, H-6), 2.17 (m, 2H, H-14, H-5), 2.01–1.95 (m, 1H, H-5), 1.71 (s, 3H, C=CCH_3), 1.83–1.58 (m, 4H, H-1, H-14, H-13), 1.08 (s, 3H, CH_3CCH_3), 0.98 (s, 3H, CH_3CCH_3). ESIMS (m/z): 399 $[M+Na]^+$. Anal. Calcd for $C_{22}H_{32}O_5$: C, 70.18; H, 8.57. Found: C, 70.05; H, 8.44.

4.1.5.2. (6*E*)-8-[(2-Methoxyethoxy)methoxy]-8-2,2,4-trimethyl-3-[(*E*)-3-phenyl-2-propenoyl]-3-cyclohexenyl-1,6-octadien-3-one (20). IR (film): ν 1665, 1250, 890, 810 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.57–7.36 (m, 5H, Ph), 7.44 (d, J=16.0 Hz, 1H, PhC*H*=CH), 6.7 (d, J=16.0 Hz, 1H, COC*H*=CHPh), 6.33 (dd, J=17.5, 10.6 Hz, 1H, COC*H*=CH_2), 6.7 (d, J=17.5 Hz, 1H, COCH=CH_2), 5.90 (d, J=10.6 Hz, 1H, COCH=CH_2), 5.67–5.41 (m, 2H, H-3, H-4), 4.70 (d, J=6.8 Hz, 1H, OHC*H*O), 4.53 (d, J=6.8 Hz, 1H, OHC*H*O), 4.19–4.14 (m, 1H, H-2), 3.70–3.40 (m, 4H, ($CH_2O)_2$), 3.34 (s, 3H, OCH_3), 2.73 (t, J=7.6 Hz, 2H, H-6), 2.40 (m, 2H, H-14, H-5), 2.04–1.97 (m, 1H, H-5), 1.47 (s, 3H, C=CCH_3), 1.36–1.15 (m, 4H, H-1, H-14, H-13), 1.09 (s, 3H, CH_3CCH_3), 0.99 (s, 3H, CH_3CCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 195.0, 153.1, 152.8, 141.3, 138.6, 136.9, 135.5, 134.2, 129.3, 129.1, 128.8, 128.7, 128.2, 126.7, 126.6, 94.1, 82.0, 73.9, 66.7, 60.8, 54.7, 40.2, 31.70, 29.5, 26.8, 26.4, 26.3, 17.5, 17.0. ESIMS (m/z): 530 $[M+Na]^+$. Anal. Calcd for $C_{30}H_{40}O_5$: C, 74.97; H, 8.39. Found: C, 74.88; H, 8.24.

4.1.6. 1-[5-(1-Hydroxy-4-pentenyl)-2,6,6-trimethyl-1-cyclohexenyl]-5-hexen-1-one (28). Magnesium turnings (44 mg, 2.16 mmol) in 5 mL of dry diethyl ether were treated with 1-butenyl bromide (243 mg, 1.8 mmol). The mixture was refluxed for 30 min and then cooled to 0 °C. The aldehyde **27** (224 mg, 0.9 mmol) in 5 mL of ether was added dropwise to the clear solution of the Grignard's reagent and the mixture was stirred at room temperature overnight. The mixture was cooled to 0 °C and 5 mL of saturated NH_4Cl solution was added. The aqueous phase was

extracted three times with diethyl ether; the combined organic phases were washed with saturated $NaHCO_3$ and NaCl, dried over Na_2SO_4 anhydrous and evaporated in vacuo. The residue was purified by flash chromatography (45% diethyl ether in light petroleum ether) to give the diastereoisomeric mixture of alcohols **28** (171 mg, 63%) as a colourless oil. IR (film): ν 3425, 1675, 910 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 5.75 (m, 2H, C*H*=CH_2, C*H*=CH_2), 4.9 (m, 4H, CH=CH_2, CH=CH_2), 3.87–3.82 (m, 1H, C*H*OH), 2.46 (m, 2H, CH_2C=O), 2.2–1.8 (m, 9H, H-1, H-13, H-14, CH_2CH=CH_2, CH_2CH=CH_2), 1.8–1.5 (m, 4H, $CH_2CH_2CH_2$, CHCH_2CH_2), 1.44 (s, 3H, CH_3C=C), 1.04 (s, 3H, C$H_3$$CCH_3$), 0.92 (s, 3H, CH_3CCH_3). ESIMS (*m*/*z*): 305 $[M+1]^+$, 327 $[M+Na]^+$. Anal. Calcd for $C_{20}H_{32}O_2$: C, 79.90; H, 10.59. Found: C, 79.95; H, 10.48.

4.1.7. 1-[2,6,6-Trimethyl-5-(4-pentenoyl)-1-cyclohexenyl]-5-hexen-1-one (23). Tetra(*n*-propyl)ammonium perruthenate (5 mg, 0.015 mmol) was added portionwise to a stirred suspension of the alcohol **28** (88 mg, 0.29 mmol) in dry dichloromethane (5 mL), 4 Å molecular sieves and 4-methylmorpholine *N*-oxide (41 mg, 0.348 mmol). The resulting suspension was stirred for 1 h at room temperature and then filtered through Celite. After evaporation of the solvent in vacuo, the residue was purified directly by flash chromatography (40% diethyl ether in light petroleum ether) affording 86 mg (99% yield) of compound **23** as a colourless oil. IR (film): ν 1690, 1675, 883 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.75 (m, 2H, C*H*=CH_2, C*H*=CH_2), 4.96 (m, 4H, CH=CH_2, CH=CH_2), 2.58 (m, 5H, H-1, CH_2C=O, CH_2C=O), 2.2–1.92 (m, 4H, H-13, H-14), 1.9–1.78 (m, 4H, CH_2CH=CH_2, CH_2CH=CH_2), 1.8–1.5 (m, 2H, $CH_2CH_2CH_2$), 1.57 (s, 3H, CH_3C=C), 1.09 (s, 3H, C$H_3$$CCH_3$), 1.05 (s, 3H, CH_3CCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 214.0, 201.8, 144.6, 142.5, 134.8, 134.3, 116.7, 115.9, 63.5, 41.0, 40.7, 34.0, 30.1, 29.8, 25.6, 24.7, 24.6, 24.1, 20.3, 17.4. ESIMS (*m*/*z*): 303 $[M+1]^+$, 325 $[M+Na]^+$. Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.32; H, 10.18.

4.1.8. Acyclic dimers 29 and 30. 1-[3-(5-Hexenoyl)-2,2,4-trimethyl-3-cyclohexenyl]-9-[2,6,6-trimethyl-5-(4-pentenoyl)-1-cyclohexenyl]-4-nonene-1,9-dione. To a 1 mM solution of **23** (40 mg, 0.132 mmol) in dry and degassed dichloroethane (132 mL) Grubbs' I ruthenium catalyst (32 mg, 0.039 mmol), or Grubbs' II catalyst (11 mg, 0.0132 mmol), was added. The reaction was stirred for 24 h at room temperature, then the solvent was removed in vacuo. Purification of the residue by flash chromatography (30% diethyl ether in light petroleum ether) afforded the non-separable mixture of acyclic dimers **29** and **30**, as colourless oil (48 mg, 64% yield). IR (film): ν 1690, 1675, 883 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.9–5.62 (m, 1H, C*H*=CH_2), 5.4–5.25 (m, 1H, C*H*=CH), 4.98 (br d, *J*=13.9 Hz, 1H, CH=CH_2), 4.92 (br d, *J*=9.6 Hz, 1H, CH=CH_2), 2.56–2.48 (m, 5H, H-1, CH_2C=O, CH_2C=O), 2.45–2.15 (m, 2H, H-13), 2.12–1.92 (m, 4H, CH_2CH=CH_2, CH_2CH=CH_2), 1.88–1.55 (m, 4H, H-14, $CH_2CH_2CH_2$), 1.52 (s, 3H, CH_3C=C), 1.07 (s, 3H, C$H_3$$CCH_3$), 1.04 (s, 3H, CH_3CCH_3). ESIMS (*m*/*z*): 599 $[M+Na]^+$, 615 $[M+K]^+$. Anal. Calcd for $C_{38}H_{56}O_4$: C, 79.12; H, 9.78. Found: C, 79.32; H, 9.65. HPLC method 1 t_R=7.52 min and 8.02 min.

4.1.9. Cyclic dimers 31 and 32. To a 1 mM solution of **23** (38 mg, 0.125 mmol) in dry dichloroethane (125 mL) was added Grubbs' I ruthenium catalyst (31 mg, 0.037 mmol) or Grubbs' II catalyst (10 mg, 0.0125 mmol). The reaction was refluxed for 24 h, then cooled and the solvent was removed in vacuo. Purification of the residue by flash chromatography (30% diethyl ether in light petroleum ether) afforded a non-separable mixture of dimers **31** and **32** as colourless oil (50 mg, 75% yield). IR (film): ν 1690, 1675, 883 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.4–5.25 (m, 2H, C*H*=CH, C*H*=CH), 2.56–2.48 (m, 5H, H-1, CH_2C=O, CH_2C=O), 2.45–2.15 (m, 2H, H-13), 2.12–1.92 (m, 4H, CH_2CH=CH_2, CH_2CH=CH_2), 1.88–1.55 (m, 4H, H-14, $CH_2CH_2CH_2$), 1.52 (s, 3H, CH_3C=C), 1.21 (s, 3H, C$H_3$$CCH_3$), 1.07 (s, 3H, CH_3CCH_3). ESIMS (*m*/*z*): 297 $[C_{18}H_{26}O_2+Na]^+$, 379 $[C_{24}H_{36}O_2+Na]^+$, 571 $[M+Na]^+$. Anal. Calcd for $C_{36}H_{52}O_4$: C, 78.79; H, 9.55. Found: C, 78.85; H, 9.42. HPLC method 1 t_R=4.98 min and 6.15 min.

4.1.10. 1-[5-(1-{[1-(*tert*-Butyl)-1,1-diphenylsilyl]oxy}-allyl)-2,6,6-trimethyl-1-cyclohexenyl]-2-propyn-1-ol (41). A 0.5 M solution of ethynylmagnesium bromide in THF (17.46 mL, 8.73 mmol) was added dropwise over 5 min to a stirred solution of the aldehyde **40** (1.3 g, 2.91 mmol) in dry THF (15 mL) at 0 °C under nitrogen atmosphere. The mixture was stirred for 45 min at 0 °C, allowed to warm to room temperature and stirred for 2 h. The clear solution was cooled to 0 °C and then quenched with saturated aqueous NH_4Cl (10 mL) and diethyl ether (20 mL). The organic layer was separated and the aqueous layer was re-extracted with ether (3×20 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford a yellow oil. Purification by chromatography on silica gel (25% diethyl ether in light petroleum ether) gave 1.11 g (85%) of the diastereoisomeric propargyl alcohols **42** (17%) and **41** (83%). IR (film): ν 3442, 3085, 2129, 1613, 979 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.68–7.63 (m, 5H, Ph), 7.37–7.24 (m, 5H, Ph), 5.9 (ddd, *J*=17, 9.7, 6.5 Hz, 1H, C*H*=CH_2), 5.03–4.89 (m, 3H, CH=CH_2, C*H*OH), 4.37 (br d, *J*=6.5 Hz, 1H, C*H*OSi), 2.45 (d, *J*=2 Hz, 1H, C≡C*H*), 2.03 (app t, *J*=4 Hz, 2H, H-13), 1.94 (s, 3H, CH_3C=C), 1.62–1.52 (m, 1H, H-1), 1.41–1.25 (m, 2H, H-14), 1.05 (s, 9H, $(CH_3)_3C$), 0.81 (s, 3H, CH_3CCH_3), 0.68 (s, 3H, CH_3CCH_3). ESIMS (*m*/*z*): 495 $[M+Na]^+$. Anal. Calcd for $C_{31}H_{40}O_2Si$: C, 78.76; H, 8.53. Found: C, 78.81; H, 8.73.

4.1.11. 1-[5-(1-{[1-(*tert*-Butyl)-1,1-diphenylsilyl]oxy}-allyl)-2,6,6-trimethyl-1-cyclohexenyl]-2-propyn-1-ol (42). Tetra(*n*-propyl)ammonium perruthenate (33 mg, 0.095 mmol) was added portionwise to a stirred suspension of the alcohol **41** (900 mg, 1.9 mmol) in dry dichloromethane (15 mL), 4 Å molecular sieves and 4-methylmorpholine *N*-oxide (266 mg, 2.28 mmol). The resulting suspension was stirred for 50 min at room temperature and then filtered through Celite. The oil residue, obtained for evaporation of the solvent in vacuo, was used without further purification. To a THF (3 mL) solution of the previously described ketone (1.9 mmol) was added 9-BBN (0.5 M in THF, 15.2 mL, 7.6 mmol). The mixture was stirred at 0 °C overnight, then 10 mL of aqueous solution of $NaHCO_3$ and 2 mL of H_2O_2 (30% v/v) were added and the solution was stirred for further 30 min. The organic layer was separated

and the aqueous layer was re-extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated in vacuo affording a yellow oil. Purification by flash chromatography (25% diethyl ether in light petroleum ether) gave the allyl alcohol **42** (807 mg, 90% over two steps). IR (film): ν 3442, 3085, 2129, 1613, 979 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.68–7.63 (m, 5H, Ph), 7.37–7.24 (m, 5H, Ph), 5.9 (ddd, J=17, 9.7, 6.5 Hz, 1H, C*H*=CH_2), 5.03–4.89 (m, 3H, CH=CH_2, C*H*OH), 4.37 (br d, J=6.5 Hz, 1H, C*H*OSi), 2.45 (d, J=2 Hz, 1H, C≡C*H*), 2.03 (app t, J=4 Hz, 2H, H-13), 1.94 (s, 3H, CH_3C=C), 1.62–1.52 (m, 1H, H-1), 1.41–1.25 (m, 2H, H-14), 1.05 (s, 9H, (CH_3)$_3$C), 0.81 (s, 3H, CH_3CCH_3), 0.68 (s, 3H, CH_3CCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 138.8, 134.4, 134.3, 132.6 (4C), 130.8 (2C), 129.0 (4H), 127.5, 114.5, 84.0, 77.3, 71.2, 56.0, 49.7, 36.6, 32.1, 25.6 (2C), 25.3 (3H), 19.6, 17.0. ESIMS (*m*/*z*): 495 $[M+Na]^+$. Anal. Calcd for $C_{31}H_{40}O_2Si$: C, 78.76; H, 8.53. Found: C, 78.83; H, 8.70.

4.1.12. 1-[5-(1-{[1-(*tert*-Butyl)-1,1-diphenylsilyl]oxy}-allyl)-2,6,6-trimethyl-1-cyclohexenyl]-2-propynyl acetate (35). To a dry CH_2Cl_2 (6 mL) solution of propargyl alcohol **42** (715 mg, 1.5 mmol) was added dry TEA (192 μL, 1.38 mmol), DMAP (cat.) and acetic anhydride (165 μL, 1.74 mmol). The resulting yellow solution was stirred overnight at room temperature, then was diluted with dichloromethane and washed with HCl 1 M (4 mL), water (2×5 mL), brine (5 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by flash chromatography (20% diethyl ether in light petroleum ether) affording 763 mg (99%) of desired acetyl derivative **35** as pale yellow oil. IR (film): ν 3085, 2129, 1745, 1613, 979 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.67–7.64 (m, 5H, Ph), 7.37–7.33 (m, 5H, Ph), 5.9 (ddd, J=17, 10.6, 6.5 Hz, 1H, C*H*=CH_2), 5.86 (d, J=2 Hz, 1H, C*H*OAc), 5.04 (br d, J=10.6 Hz, 1H, CH=CH_2), 5 (br d, J=17 Hz, 1H, CH=CH_2), 4.36 (br d, J=6.5 Hz, 1H, C*H*OSi), 2.44 (s, 1H, C≡C*H*), 2.03 (s, 3H, CH_3C=O), 1.92–1.8 (m, 4H, H-13, H-14), 1.87 (s, 3H, CH_3C=C), 1.59–1.50 (m, 1H, H-1), 1.25 (s, 3H, CH_3CCH_3), 1.04 (s, 9H, (CH_3)$_3$C), 0.99 (s, 3H, CH_3CCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 139.2, 138.8, 134.4, 134.3, 132.6 (4C), 130.8 (2C), 129.0 (4H), 127.5, 114.5, 84.0, 77.3, 71.2, 63.4, 56.0, 36.6, 32.1, 25.6 (2C), 25.3 (3H), 21.0, 19.6, 17.0. ESIMS (*m*/*z*): 537 $[M+Na]^+$. Anal. Calcd for $C_{33}H_{42}O_3Si$: C, 77.00; H, 8.22. Found: C, 77.81; H, 8.73.

4.1.13. 4-(Acetyloxy)-1-[5-(1-{[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}allyl)-2,6,6-trimethyl-1-cyclohexenyl]-5,5-dimethyl-7-octen-2-ynyl acetate (45). The alkyne **35** (160 mg, 0.311 mmol) in dry THF (2 mL) at −78 °C was treated with a 1 M solution of LiHMSA (317 μL, 0.317 mmol) and stirred at low temperature for 30 min. A solution of the aldehyde **43** (85 μL, 0.622 mmol) in dry THF (1 mL) was then added, via *cannula*, to the solution of the lithiated alkyne at −78 °C. The mixture was stirred overnight then, after partial evaporation of the THF, it was diluted with diethyl ether and washed with a saturated solution of NH_4Cl (2×3 mL), H_2O (2×3 mL), brine (2 mL) and dried over anhydrous Na_2SO_4. The yellow-brown oil obtained for evaporation of the solvent was acetylated, without purification. HPLC method 2 t_R=16.23 min.

To a dry CH_2Cl_2 (2 mL) solution of the crude alcohol derivative **47** (0.311 mmol) was added dry TEA (56 μL, 0.404 mmol), DMAP (cat.) and acetic anhydride (35 μL, 0.373 mmol). The resulting yellow solution was stirred for 45 min at room temperature, then was diluted with dichloromethane and washed with HCl 1 M (2 mL), water (2× 2 mL), brine (3 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by flash chromatography (20% diethyl ether in light petroleum ether) affording 170 mg (82% over two steps) of the acetylated product **45** as pale yellow oil. IR (film): ν 3080, 2129, 1745, 1613, 979 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.69–7.62 (m, 5H, Ph), 7.55–7.24 (m, 5H, Ph), 6.02 (s, 1H, C=CC*H*OAc), 5.92–5.65 (m, 2H, CHC*H*=CH_2, CH_2C*H*=CH_2), 5.17 (s, 1H, (CH_3)$_2$CC*H*OAc), 5.04 (dd, J=10, 1.5 Hz, 1H, CH_2CH=CH_{cis}H), 5.02 (dd, J=18.7, 1.5 Hz, 1H, CH_2CH=CH_{trans}H), 4.6 (d, J=10 Hz, 1H, CHCH=C*H*H), 4.51 (d, J=17 Hz, 1H, CHCH=C*H*H), 4.34 (d, J=8.5 Hz, 1H, C*H*OSi), 2.35–2.18 (m, 4H, H-13, CH_2=CHCH_2), 2.06 (s, 3H, CH_3C=O), 2.02 (s, 3H, CH_3C=O), 1.87 (s, 3H, CH_3C=C), 1.81–1.42 (m, 3H, H-1, H-13), 1.25 (s, 3H, (CH_3)$_2$CCH_2), 1.02 (s, 3H, (CH_3)$_2$CCH_2), 0.99 (s, 9H, (CH_3)$_3$C), 0.94 (s, 3H, CH_3CCH_3), 0.89 (s, 3H, CH_3CCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 169.5, 139.2, 138.8, 135.1, 134.4, 134.3, 132.6 (4C), 130.8 (2C), 129.0 (4H), 127.5, 115.3, 114.5, 91.7, 89.4, 79.2, 71.2, 60.4, 56.0, 41.1, 39.8, 36.6, 32.1, 25.6 (2C), 25.3 (3C), 20.2, 20.1, 19.8 (2C), 19.6, 17.04, 16.9. ESIMS (*m*/*z*): 707 $[M+K]^+$, 691 $[M+Na]^+$. Anal. Calcd for $C_{42}H_{56}O_5Si$: C, 75.41; H, 8.44. Found: C, 75.35; H, 8.48.

4.1.14. 1-[5-(1-{[1-(*tert*-Butyl)-1,1-diphenylsilyl]oxy}-allyl)-2,6,6-trimethyl-1-cyclohexenyl]-4-hydroxy-5-(2-methylenecyclohexyl)-2-pentynyl acetate (48). The alkyne **35** (250 mg, 0.486 mmol) in dry THF (3 mL) at −78 °C was treated with a 1 M solution of LiHMSA (496 μL, 0.496 mmol) and stirred at low temperature for 30 min. A solution of the aldehyde **44** (80 mg, 0.583 mmol) in dry THF was then added, via *cannula*, to the solution of the lithiated alkyne at −78 °C. The mixture was stirred overnight then, after partial evaporation of the solvent, it was diluted with diethyl ether and washed with a saturated solution of NH_4Cl (2×3 mL), H_2O (2×3 mL), brine (2 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by flash chromatography (30% diethyl ether in light petroleum ether) affording two diastereoisomeric alcohols **48** (total yield of 75%, ratio 3:1) as yellow pale oils. The data are referred to the major compound, whose structure is described in Scheme 9. IR (film): ν 3442, 3080, 2230, 1740, 1613, 979 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.65–7.55 (m, 5H, Ph), 7.48–7.32 (m, 5H, Ph), 6.06 (s, 1H, C=CC*H*OAc), 5.85 (ddd, J=17, 12, 8.5 Hz, 1H, C*H*=CH_2), 4.70–4.40 (m, 6H, CH=CH_2, CH_2=C, C*H*OH, C*H*OSi), 2.35–2.18 (m, 4H, H-13, CH_2=CC$H_2$$CH_2$), 2.06 (s, 3H, C$H_3$C=O), 1.97–1.87 (m, 3H, H-5, H-6), 1.85 (s, 3H, CH_3C=C), 1.70–1.65 (m, 5H, H-1, H-14, CH_2=CCHCH_2), 1.30–1.20 (m, 4H, CH_2CH_2C$H_2$$CH_2$), 1.1 (s, 3H, CH_3CCH_3), 1.02 (s, 9H, (CH_3)$_3$C), 0.97 (s, 3H, CH_3CCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 148.2, 138.8, 134.4, 134.3, 132.6 (4C), 130.8 (2C), 129.0 (4C), 127.5, 110.5, 91.7, 89.4, 79.2, 71.2, 62.0, 60.8, 56.0, 38.5, 36.8, 36.6, 35.2, 35.1, 32.1,

30.9, 28.1, 26.0, 25.6 (2C), 25.3 (3C), 19.8, 19.6, 17.04, 16.9. ESIMS (*m/z*): 675 $[M+Na]^+$. Anal. Calcd for $C_{42}H_{56}O_4Si$: C, 77.25; H, 8.64. Found: C, 77.20; H, 8.69. HPLC method 1 t_R=9.17 min.

4.1.15. 4-(Acetyloxy)-4-[5-(1-{[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}allyl)-2,6,6-trimethyl-1-cyclohexenyl]-1-[(2-methylenecyclohexyl)methyl]-2-butynyl acetate (46). To a dry CH_2Cl_2 (3 mL) solution of alcohol **48** (190 mg, 0.3 mmol) was added dry TEA (54 μL, 0.39 mmol), DMAP (cat.) and acetic anhydride (34 μL, 0.36 mmol). The resulting yellow solution was stirred for 45 min at room temperature, then was diluted with dichloromethane and washed with HCl 1 M (2 mL), water (2×2 mL), brine (3 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the oil residue was purified by flash chromatography (20% diethyl ether in light petroleum ether) affording 206 mg (99%) of the acetylated product **46** as pale yellow oil. IR (film): ν 3080, 2230, 1740, 1613, 979 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.69–7.61 (m, 5H, Ph), 7.40–7.28 (m, 5H, Ph), 6 (s, 1H, C=CC*H*OAc), 5.83 (ddd, *J*=17, 12, 8.5 Hz, 1H, C*H*=CH_2), 5.44–3.99 (m, 1H, CH_2CHOAc), 4.66 (br s, 1H, CH_2=C), 4.62 (br s, 1H, CH_2=C), 4.53 (br d, *J*=12 Hz, 1H, CH=CH_{cis}H), 4.49 (br d, *J*=17 Hz, 1H, CH=CH_{trans}H), 4.33 (br d, *J*=8.5 Hz, 1H, C*H*OSi), 2.35–2.18 (m, 4H, H-13, CH_2=CCH_2CH_2), 2.06 (s, 3H, CH_3C=O), 2.02 (s, 1H, CH_3C=O), 1.97–1.87 (m, 3H, H-5, H-6), 1.85 (s, 3H, CH_3C=C), 1.70–1.65 (m, 5H, H-1, H-14, CH_2=CCHCH_2), 1.30–1.20 (m, 4H, $CH_2CH_2CH_2CH_2$), 1.1 (s, 3H, CH_3CCH_3), 1.02 (s, 9H, $(CH_3)_3C$), 0.97 (s, 3H, CH_3CCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 169.5, 148.2, 138.8, 134.4, 134.3, 132.6 (4C), 130.8 (2C), 129.0 (4C), 127.5, 110.5, 91.7, 89.4, 79.2, 71.2, 64.2, 63.0, 56.0, 38.5, 36.8, 36.6, 35.2, 35.1, 32.1, 30.9, 28.1, 26.0, 25.6 (2C), 25.3 (3C), 19.8 (2C), 19.6, 17.04, 16.9. ESIMS (*m/z*): 733 $[M+K]^+$, 717 $[M+Na]^+$. Anal. Calcd for $C_{44}H_{58}O_5Si$: C, 76.04; H, 8.41. Found: C, 75.95; H, 8.5.

4.1.16. 4-(Acetyloxy)-1-[5-(1-hydroxyallyl)-2,6,6-trimethyl-1-cyclohexenyl]-5,5-dimethyl-7-octen-2-ynyl acetate (50). A dry THF (2 mL) solution of the silyl ether **45** (33.5 mg, 0.05 mmol) was treated with a 1 M solution of TBAF (1.5 mL, 1.5 mmol) and stirred at 40 °C for 20 h. The reaction mixture was then cooled to room temperature and evaporated to give a yellow-brown oil. The crude material was purified by flash chromatography (50% ethyl acetate in light petroleum ether) affording 13.5 mg (62%) of the desilylated product **50** as pale yellow oil. IR (film): ν 3440, 3080, 2129, 1745, 1613, 979 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.01 (s, 1H, C=CC*H*OAc), 5.95–5.68 (m, 2H, CHC*H*=CH_2, CH_2CH=CH_2), 5.22 (br d, *J*=17.5 Hz, 1H, CHCH=CH_2), 5.14 (s, 1H, $(CH_3)_2$CC*H*OAc), 5.11 (br d, *J*=10 Hz, 1H, CHCH=CH_2), 5.03 (dd, *J*=8, 1.5 Hz, 1H, CH_2CH=CH_2), 4.97 (dd, *J*=20, 1.5 Hz, 1H, CH_2CH=CH_2), 4.46 (br s, 1H, C*H*OH), 2.35–2.18 (m, 4H, H-13, CH_2=CHCH_2), 2.06 (s, 3H, CH_3C=O), 2.02 (s, 3H, CH_3C=O), 1.87 (s, 3H, CH_3C=C), 1.81–1.42 (m, 3H, H-1 H-14), 1.25 (s, 3H, $(CH_3)_2CCH_2$), 1.02 (s, 3H, $(CH_3)_2CCH_2$), 0.94 (s, 3H, CH_3CCH_3), 0.89 (s, 3H, CH_3CCH_3). ESIMS (*m/z*): 469 $[M+K]^+$, 453 $[M+Na]^+$. Anal. Calcd for $C_{26}H_{38}O_5$: C, 72.53; H, 8.90. Found: C, 72.49; H, 8.96.

4.1.17. *tert*-Butyl[(1-5-[(*E*)-2-(5-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-4,4-dimethyl-1-cyclopentenyl)-2-propenylidene]-4-methyl-3-cyclohexenylallyl)oxy]dimethylsilane (53). To a 1 mM solution of **52** (14 mg, 0.023 mmol) in dry dichloromethane (23 mL) Grubbs' II ruthenium catalyst (2 mg, 0.0023 mmol) was added. The reaction was stirred for 24 h at room temperature, then the solvent was removed in vacuo. Purification of the residue by flash chromatography (15% diethyl ether in light petroleum ether) afforded **53**, as colourless oil (8.5 mg, 66% yield). IR (film): ν 3090, 1655, 883 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.92–5.72 (m, 4H, H-13, H-10, C=C*H*CH_2, CHC*H*=CH_2), 5.12–4.93 (m, 4H, CHCH=CH_2, C=CH_2), 4.39 (br d, *J*=7.6 Hz, 1H, CHC*H*OSi), 4.16 (s, 1H, CC*H*OSi), 2.18–2.03 (m, 3H, H-1, C=CHCH_2), 1.66 (s, 3H, CH_3C=C), 1.62–1.41 (m, 2H, H-14), 1.51 (s, 3H, CH_3CCH_3), 1.49 (s, 3H, CH_3CCH_3), 0.99 (s, 3H, $(CH_3)_2CCH_2$), 0.92 (s, 3H, $(CH_3)_2CCH_2$), 0.89 (s, 9H, $(CH_3)_3C$), 0.86 (s, 9H, $(CH_3)_3C$), 0.12 (s, 3H, CH_3Si), 0.09 (s, 3H, CH_3Si), 0.04 (s, 3H, CH_3Si), −0.01 (s, 3H, CH_3Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7, 142.7, 135.4, 135.2, 131.8, 129.5, 116.9, 113.5, 101.6, 85.2, 73.0, 71.6, 51.4, 42.7, 39.8, 39.2, 29.7, 27.8, 26.0, 25.9 (2C), 25.8, 25.7, 24.0, 22.8, 22.7, 21.2, 18.1, 18.0, 17.4, −3.4, −4.2, −4.5, −5.2. ESIMS (*m/z*): 595 $[M+K]^+$, 579 $[M+Na]^+$, 557 $[M+1]^+$. Anal. Calcd for $C_{34}H_{60}O_2Si_2$: C, 73.31; H, 10.86. Found: C, 73.15; H, 10.92.

4.1.18. (*Z*)-4-(Acetyloxy)-4-[5-(1-{[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}allyl)-2,6,6-trimethyl-1-cyclohexenyl]-1-[(2-methylenecyclohexyl)methyl]-2-butenyl acetate (49). A degassed mixture of **46** (30 mg, 0.043 mmol), Lindlar's catalyst (15 mg), quinoline (5 mol %) in light petrol ether (4 mL) with few drops of ethyl acetate was shaken under H_2 for 2 h. The catalyst was filtered off through Celite and the mixture was washed with aqueous 5% $KHSO_4$ (2×2 mL), water (1×2 mL), brine (1×2 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the oil residue was purified by flash chromatography (30% diethyl ether in light petroleum ether) affording 29 mg (99%) of the partially reduced product **49** as pale yellow oil. IR (film): ν 3440, 3080, 1740, 1660, 979 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.69–7.61 (m, 5H, Ph), 7.40–7.28 (m, 5H, Ph), 6.32 (d, *J*=5 Hz, 1H, C=CC*H*OAc), 5.82 (dd, *J*=5, 11 Hz, 1H, C*H*=CH), 5.83 (ddd, *J*=17, 12, 8.5 Hz, 1H, C*H*=CH_2), 5.45 (dd, *J*=8, 11 Hz, 1H, CH=C*H*), 5.22 (dt, *J*=8, 11 Hz, 1H, CH_2CHOAc), 4.66 (br s, 1H, CH_2=C), 4.62 (br s, 1H, CH_2=C), 4.53 (br d, *J*=12 Hz, 1H, CH=CH_{cis}H), 4.49 (br d, *J*=17 Hz, 1H, CH=CH_{trans}H), 4.33 (br d, *J*=8.5 Hz, 1H, C*H*OSi), 2.35–2.18 (m, 4H, H-13, CH_2=CCH_2CH_2), 2.06 (s, 3H, CH_3C=O), 2.02 (s, 3H, CH_3C=O), 1.97–1.87 (m, 3H, H-5, H-6), 1.85 (s, 3H, CH_3C=C), 1.70–1.65 (m, 5H, H-1, H-14, CH_2=CCHCH_2), 1.30–1.20 (m, 4H, $CH_2CH_2CH_2CH_2$), 1.1 (s, 3H, CH_3CCH_3), 1.02 (s, 9H, $(CH_3)_3C$), 0.97 (s, 3H, CH_3CCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ 172.5 (2C), 149.0, 138.9, 135.0 (2C), 133.7, 133.3, 132.2 (4C), 131.3, 130.3 (2C), 129.0 (4C), 127.2, 115.8, 109.9, 72.7, 59.9, 55.9, 38.4, 37.7, 37.6, 36.9, 33.8, 31.2, 28.8, 26.5 (2C), 25.6 (3C), 25.1, 21.2, 21.1 (2C), 19.6, 18.1, 17.2. ESIMS (*m/z*): 735 $[M+K]^+$, 719 $[M+Na]^+$, 697 $[M+1]^+$. Anal. Calcd for $C_{44}H_{60}O_5Si$: C, 75.82; H, 8.68. Found: C, 75.70; H, 8.74.

4.1.19. (2*Z*)-1-(5-(1-Hydroxyallyl)-2,6,6-trimethylcyclohex-1-enyl)-5-(2-methylenecyclohexyl)pent-2-ene-1,4-diol (59). A dry THF (1.5 mL) solution of the silyl ether **49** (50 mg, 0.07 mmol) was treated with a 1 M solution of TBAF (700 μL, 0.7 mmol) and stirred at 40 °C for 20 h. The reaction mixture was then cooled to room temperature and evaporated to give a yellow-brown oil, which was then dissolved in CH_3OH (2 mL) and treated with K_2CO_3 (30 mg, 0.21 mmol). The resulting mixture was stirred for 24 h and the residue obtained after evaporation of the solvent in vacuo was purified by flash chromatography (40% ethyl acetate in light petroleum ether) affording 19 mg (75% over two steps) of desired product **59** as colourless oil. IR (film): ν 3392, 3084, 1750, 1367, 1092, 986 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.88 (ddd, J=17, 11, 4.8 Hz, 1H, C*H*=CH$_2$), 5.71–5.66 (m, 1H, CH=C*H*), 5.47–5.41 (m, 1H, CH=C*H*), 5.22 (d, J=17 Hz, 1H, CH=C*H*$_{trans}$H), 5.1 (d, J=11 Hz, 1H, CH=C*H*$_{cis}$H), 5.09 (d, J=6.7 Hz, 1H, C=CC*H*OH), 4.7–4.65 (m, 3H, C*H*$_2$=C, CH$_2$C*H*OH), 4.45 (d, J=3.8 Hz, 1H, C*H*OH), 2.30–2.1 (m, 2H, CH$_2$=CC*H*$_2$CH$_2$), 1.9–1.5 (m, 10H, H-1, H-5, H-6, H-13, H-14, CH$_2$=CCHC*H*$_2$), 1.8 (s, 3H, C*H*$_3$C=C), 1.43–0.8 (m, 4H, CH$_2$C*H*$_2$C*H*$_2$CH$_2$), 0.86 (s, 3H, *CH*$_3$CCH$_3$), 0.83 (s, 3H, CH$_3$CC*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 139.2, 133.8, 133.0, 128.2, 126.4, 115.9, 109.4, 68.8, 65.8, 63.9, 56.7, 40.6, 37.9, 37.2, 36.5, 34.2, 31.9, 29.1, 26.4, 26.3, 25.2, 18.0, 17.8. ESIMS (*m*/*z*): 397 $[M+Na]^+$. Anal. Calcd for $C_{24}H_{38}O_3$: C, 76.96; H, 10.23. Found: C, 76.81; H, 10.24.

4.1.20. 3,8-Secotaxane diterpenoid 58. To a solution of **49** (35 mg, 0.05 mmol) in dry dichloromethane (15 mL), Grubbs' II ruthenium catalyst (4.5 mg, 0.005 mmol) was added. The reaction was stirred for 36 h at room temperature, then the solvent was removed in vacuo. Purification of the residue by flash chromatography (30% diethyl ether in light petroleum ether) afforded **58**, as colourless oil (7 mg, 20% yield). IR (film): ν 3080, 1740, 1660, 979 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.69–7.61 (m, 5H, Ph), 7.40–7.28 (m, 5H, Ph), 6.32 (d, J=5 Hz, 1H, C=CC*H*OAc), 5.74 (dd, J=5, 7 Hz, 1H, C*H*=CH), 5.55 (dd, J=6, 7 Hz, 1H, CH=C*H*), 5.47–5.41 (m, 1H, CH$_2$C*H*OAc), 5.1 (d, J=10 Hz, 1H, CHC*H*=C), 4.32 (dd, J=2.5, 10 Hz, 1H, C*H*OSi), 2.35–2.18 (m, 4H, H-13, CH$_2$=CC*H*$_2$CH$_2$), 2.06 (s, 3H, C*H*$_3$C=O), 2.02 (s, 3H, C*H*$_3$C=O), 1.97–1.87 (m, 3H, H-5, H-6), 1.85 (s, 3H, C*H*$_3$C=C), 1.70–1.65 (m, 5H, H-1, H-14, CH$_2$=CCHC*H*$_2$), 1.30–1.20 (m, 4H, CH$_2$C*H*$_2$C*H*$_2$CH$_2$), 1.1 (s, 3H, C*H*$_3$CCH$_3$), 1.02 (s, 9H, (C*H*$_3$)$_3$C), 0.97 (s, 3H, CH$_3$CC*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5 (2C), 140.1, 135.0 (2C), 133.7, 133.3, 132.2 (4C), 131.3, 130.3 (2C), 129.0 (4C), 127.2, 122.3, 65.5, 59.9, 55.9, 38.4, 37.6, 36.9, 33.8, 31.8, 31.2, 28.8, 26.5 (2C), 25.6 (3C), 25.1, 21.2, 21.1 (2C), 19.6, 18.1, 17.2. ESIMS (*m*/*z*): 707 $[M+K]^+$, 691 $[M+Na]^+$, 669 $[M+H]^+$. Anal. Calcd for $C_{42}H_{56}O_5Si$: C, 75.41; H, 8.44. Found: C, 75.15; H, 8.76.

4.1.21. 3,8-Secotaxane diterpenoid 60. To a solution of **59** (20 mg, 0.053 mmol) in dry dichloromethane (15 mL), Grubbs' II ruthenium catalyst (4.5 mg, 0.005 mmol) was added. The reaction was stirred for 20 h at room temperature, then the solvent was removed in vacuo. Purification of the residue by flash chromatography (40% ethyl acetate in light petroleum ether) afforded **60**, as colourless oil (4.5 mg, 25% yield). IR (film): ν 3440, 3080, 1660, 979 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.6 (dd, J=5, 7 Hz, 1H, C*H*=CH), 5.5 (d, J=6 Hz, 1H, CH=C*H*), 5.45 (dd, J=7, 7.5 Hz, 1H, C=CC*H*OH), 5.15 (d, J=10 Hz, 1H, CHC*H*=C), 4.45 (br d, J=10 Hz, 1H, C*H*OHCH=C), 4.38 (dd, J=6, 7.5 Hz, 1H, CH$_2$C*H*OH), 2.35–2.18 (m, 4H, H-13, CH$_2$=CC*H*$_2$CH$_2$), 1.97–1.87 (m, 3H, H-5, H-6), 1.85 (s, 3H, C*H*$_3$C=C), 1.70–1.65 (m, 5H, H-1, H-14, CH$_2$=CCHC*H*$_2$), 1.30–1.20 (m, 4H, CH$_2$C*H*$_2$C*H*$_2$CH$_2$), 1.1 (s, 3H, C*H*$_3$CCH$_3$), 0.97 (s, 3H, CH$_3$CC*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.1, 133.8, 133.0, 128.2, 126.4, 122.8, 68.8, 65.8, 63.9, 56.7, 40.6, 37.2, 36.5, 34.2, 31.9, 31.7, 29.1, 26.4, 26.3, 25.2, 18.0, 17.8. ESIMS (*m*/*z*): 385 $[M+K]^+$, 369 $[M+Na]^+$, 347 $[M+H]^+$. Anal. Calcd for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89. Found: C, 75.81; H, 10.54.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2006.10.058.

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