DOI: 10.1002/ejoc.200700490

Cyclic Allyl Carbamates in Stereoselective *syn* S_E' Processes: Synthetic Approach to Sarcodictyins and Eleutherobin

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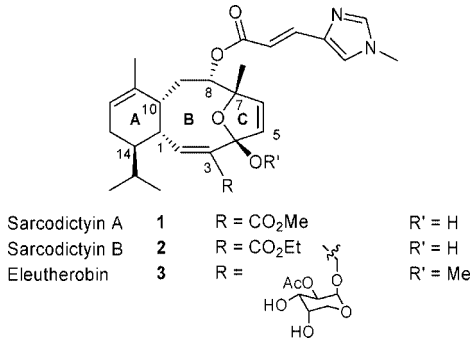
Keywords: Cytotoxic agents / Synthesis / *syn* S_E' / Carbamates / Terpenoids

Our synthetic approach of marine diterpenoids sarcodictyins A and B and eleutherobin relies on the one-step attachment of a C5–C9 side chain at the C10 position. The C1,C10 *cis*-disubstituted cyclohexene derivative is obtained in 86 % yield with total stereoselectivity. The reaction is based on a *syn* S_E' process involving a cyclic (*Z*)-allyl diisopropylcarbamate.

Introduction

Marine diterpenoids sarcodictyin **1** and **2** (Scheme 1) were successively isolated by Pietra in 1987[1] from Mediterranean coral *Sarcodictyon roseum* and by Kashman in 1996 from *Eleutherobia aurea* (South Africa coral).[2] Another member of this family eleutherobin **3** was first identified by Fenical in 1995[3] from soft red-coloured coral *Eleutherobia* cf. *albiflora* in the Indian Ocean, and then by Andersen from *Erythropodium caribaeorum* in the Pacific Ocean in 2000.[4]



Scheme 1. Sarcodictyins and eleutherobin.

These compounds are potent inducers of tubulin polymerization and possess cytotoxic activity against human colon and ovarian carcinoma cell lines (IC50 10.7 and 13.7 nM, respectively); furthermore, they are active against paclitaxel resistant tumour cell lines.[5] Owing to the biological interest of these molecules, much work has been devoted to the total synthesis of sarcodictyins **1** and **2** and eleutherobin **3**. However, to date, only two syntheses of eleutherobin **3** have been described by Nicolaou[6] and Danishefsky,[7] and one synthesis of sarcodictyins **1** and **2** by Nicolaou.[8] In addition, two formal syntheses by Metz and Gennari[9] and several approaches[10] of these compounds were reported.

Results and Discussion

Our strategy (Scheme 2) involved the formation of the 10-membered ring B of **4** by cyclization of the conveniently substituted precursor **5** with the use of the Mukaiyama reaction.

This silyl enol ether could be constructed from diol **6**, which in turn would be obtained from the key intermediate **7** by C7–C8 the Sharpless dihydroxylation reaction,[11] deoxygenation at C9[12] and reduction of the O-enecarbamate functionality [*i*PrMgCl/catalytic $Ni(acac)_2$].[13]

In this paper, we describe a new method for the installation of a C5–C9 side chain at the C10 position of compound **7** starting with allylic carbamate **8**, which can be prepared by the vinylogous Mukaiyama aldol reaction of (*R*)-carvone (**9**) previously described by Gennari.[9b,10a]

The key step for the formation of compound **7** consisted in the S_E' reaction of a stable allyl metal with an electrophile. More specifically, the homoaldol reaction with secondary metallated allyl carbamates reported by Hoppe was considered.[14–16] We already demonstrated the utility of

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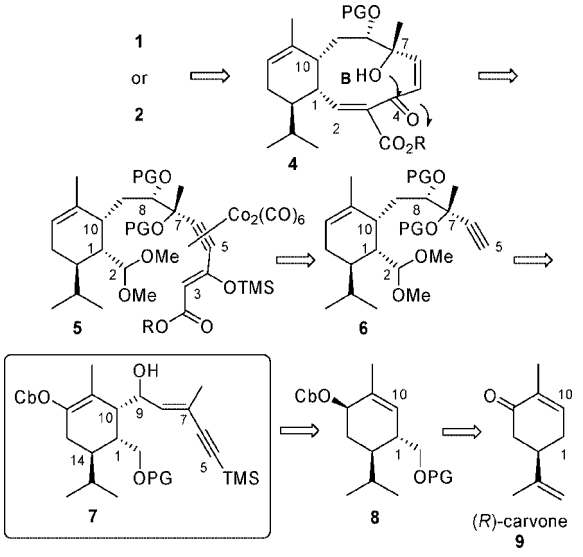
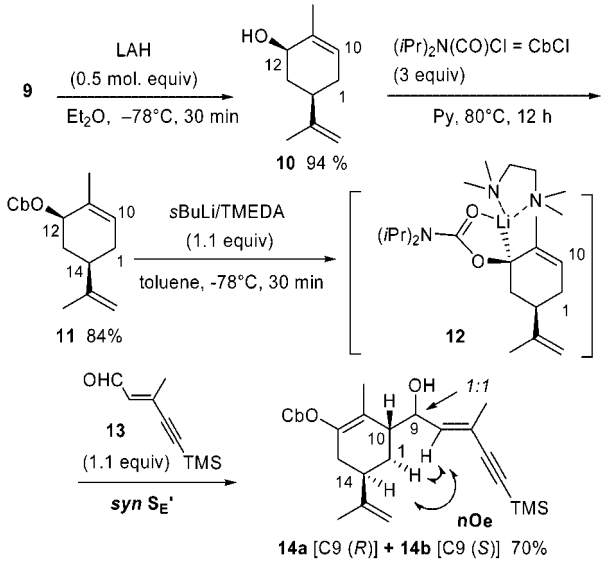
Supporting information for this article is available on the WWW under http://www.eurjoc.org/ or from the author.



Scheme 2. Synthetic strategy.

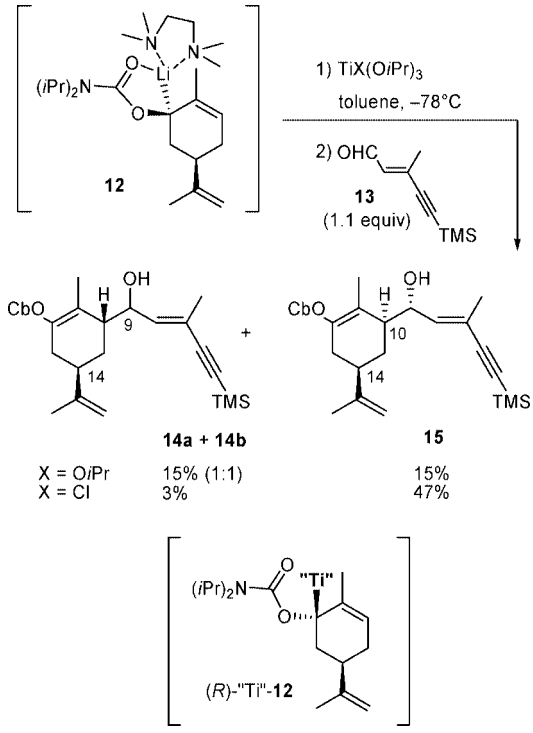
homoaldol reactions from acyclic secondary carbamates in total syntheses,[17] and Hoppe and coworkers described the homoaldol reaction of a C12–C14[18] *cis*-carveyl carbamate similar to **11** with acetone (Scheme 3).[14b,19]



Scheme 3. Formation of C10–C14 *trans* carveyl alcohols **14a** and **14b**.

C12–C14 *cis*-carveyl diisopropylcarbamate **11** was prepared by reduction of **9** and carbamoylation and then deprotonated with *s*BuLi/TMEDA (1.1 equiv., toluene, –78 °C, 30 min); reaction of this lithio compound with enynal **13**[20] delivered a 1:1 C9 diastereomeric mixture of adducts **14a** and **14b** in 70% yield. The configuration at the C10 centre, created with total stereoselectivity, of these two separable products was assigned from ^{1}H NMR spectroscopic analysis and nOe experiments.[21]

To improve the diastereoselectivity of this reaction at C9, a lithium/titanium exchange was then performed. Transmetallation of lithiated **12** with Ti(O*i*Pr)$_4$ led to a 1:1:2 mixture of adducts **14a**, **14b** and **15** (the epimer of **14a** at C10) in 30% yield (Scheme 4).[22] However, switching to TiCl(O*i*Pr)$_3$, the C10–C14 *cis* carveyl enynol **15** was produced in 47% yield (along with 3% of a mixture of **14a** and **14b**, and 31% of recovered starting material **11**).[21] Under the latter conditions, transmetallation occurred with inversion of configuration to afford the titanium intermediate (*R*)-"Ti"-**12**,[23] and this intermediate underwent a *syn* S_E' reaction to produce C10–C14 *cis* compound **15**. The *Re* face selectivity [(*S*)-C9] in this case is excellent, but cannot be explained by a typical Zimmerman–Traxler transition state. The stereochemistry of the side chain at C10 of compound **15** was inferred from NMR spectroscopic analysis and nOe experiments.[21]

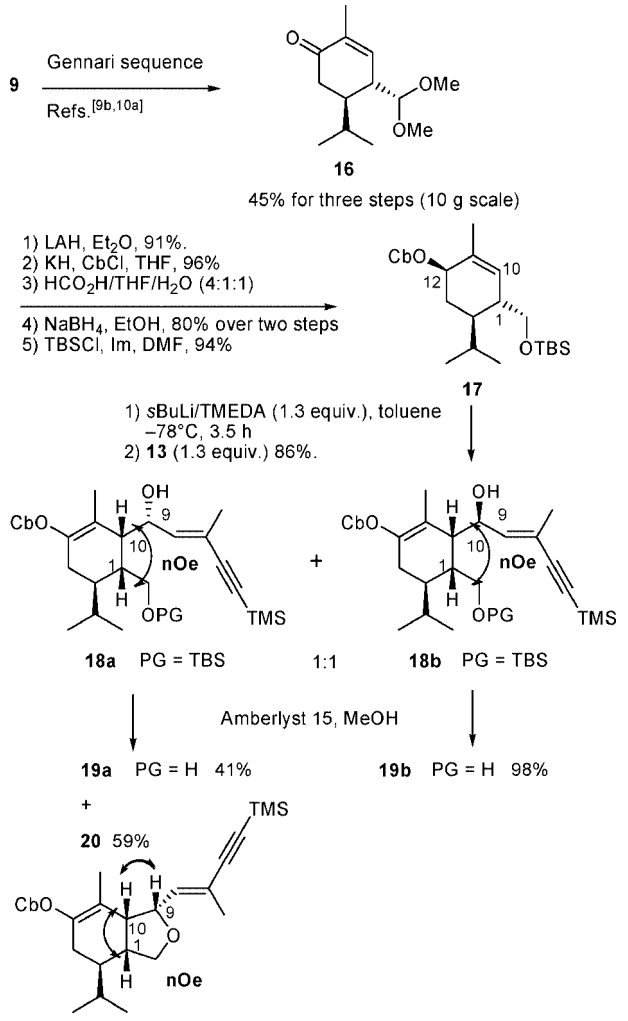


Scheme 4. Reaction between titanium carveyl (*R*)-diisopropylcarbamate (*R*)-"Ti"-**12** and enynal **13**.

In order to apply this method to our strategic goal, allyl carbamate **17**, substituted at the C1 centre, was prepared from Gennari product **16**[9a,10a] in eight steps and 29.6% overall yield from carvone (Scheme 5).

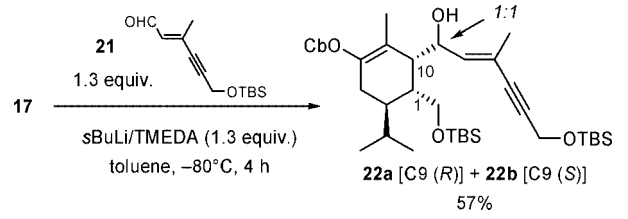
Allyl carbamate **17**, when deprotonated with *s*BuLi/TMEDA (3.5 h deprotonation time instead of 30 min) furnished the expected C1–C10 *cis*-disubstituted compounds **18a** and **18b** as a 1:1 mixture in 86% yield.[13]

Structural assignment of the two separated diastereomers **18a** and **18b** was realized by NMR spectroscopic analysis and nOe experiments of diol derivatives **19a** and **19b** and of ether **20**, which resulted from acidic treatment (Amberlyst 15/MeOH). Absolute configurations were deduced from NMR spectroscopic analysis of the corresponding (*R*) and (*S*) mandelate esters of **18a** and **18b**.



Scheme 5. Formation of the homoaldols **18a** and **18b**.

Finally, in a more convergent synthetic approach of sarcodictyins and eleutherobin, enynal **21**[20] was treated with **17** under the same conditions used before to deliver the two separable alcohols **22a** and **22b** in 57% unoptimized yield (Scheme 6).



Scheme 6. Formation of the homoaldols **22a** and **22b**.

Further work is in progress to access the ten-membered ring B of sarcodictyins and eleutherobin from adducts **18a**,**b** and **22a**,**b**.

Conclusions

We performed an efficient *syn* S_E' reaction involving a cyclic (*Z*) secondary allyl α-lithiodiisopropylcarbamate. The C1,C10 *cis*-disubstituted precursors **18a**,**b** and **22a**,**b** were prepared starting from (*R*)-(–)-carvone by introduction of a side chain at C10 with the desired configuration. These compounds can be considered as promising intermediates in a new synthetic approach to sarcodictyins A and B and eleutherobin.

Experimental Section

General Remarks: All reactions were carried out in oven-dried or flame-dried glassware under an argon atmosphere by employing standard techniques in handling air-sensitive materials. All solvents were of reagent grade. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were freshly distilled from sodium/benzophenone under a nitrogen atmosphere immediately prior to use. Dichloromethane (DCM) was freshly distilled from calcium hydride. All other reagents were used as supplied. Reactions were magnetically stirred and monitored by thin layer chromatography with 0.20 mm SDS 60F254 precoated silica gel plates. Flash chromatography was performed with silica gel 60 (particle size 0.040–0.063 mm) supplied by SDS. Yield refers to chromatographically and spectroscopically pure compounds, unless otherwise noted. Proton NMR spectra were recorded by using an internal deuterium lock at ambient temperature with a Jeol 270 or 400 MHz spectrometer. An internal reference of δ_H = 7.26 ppm was used for $CDCl_3$. Data are represented as follows: chemical shift, multiplicity (s = single, d = doublet, t = triplet, q = quartet), integration and coupling constant. Carbon-13 NMR spectra were recorded with a Jeol 67.8 or 100.5 MHz spectrometer. An internal reference of δ_C = 77.14 ppm was used for $CDCl_3$. Infrared spectra were recorded with a Nicolet Impact-400.

(*1R*,5*R*)-5-Isopropenyl-2-methylcyclohex-2-enol (10): To a solution of lithium aluminium hydride (LAH; 1 M, 6.7 mL, 6.7 mmol, 0.5 equiv.) at –78 °C was slowly added (*R*)-(–)-carvone (**9**; 2 g, 13.3 mmol) in Et_2O (10 mL). After 30 min, H_2O (450 μL, 25 mmol), NaOH (450 μL, 25 mmol) and more H_2O (450 μL, 25 mmol) was successively added. The solution was stirred until a white precipitate appeared, then dried with $MgSO_4$ and filtered off. The solvent was remove under reduce pressure, and the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 80:20) to deliver compound **10** (1.9 g, 94%, 95% *de*). $[\alpha]_D^{20}$ = –35.5 (*c* = 2.28, $CHCl_3$) {ref.[14b,19] $[\alpha]_D^{20}$ = –35.0 (*c* = 4.00, $CHCl_3$)}.^{1}H NMR (270 MHz, $CDCl_3$): δ = 5.49 (dd, *J* = 2.6, 1.3 Hz, 1 H), 4.72 (s, 2 H), 4.18 (m, 1 H), 2.30–1.86 (m, 4 H), 1.75 (s, 3 H, CH_3), 1.74 (s, 3 H, CH_3), 1.65 (s, 1 H, OH), 1.56–1.41 (td, *J* = 12.2, 9.9 Hz, 1 H) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 148.9 (C), 136.2 (C), 123.7 (CH), 109.0 (CH_2), 70.7 (CH), 40.4 (CH), 37.9 (CH_2), 30.9 (CH_2), 20.5 (CH_3), 18.9 (CH_3) ppm. MS (GC, EI): *m*/*z* = 152. $C_{10}H_{16}O$ (152.24): calcd. C 78.90, H 10.59; found C 79.15, H 10.68.

(1*R*,4*R*,5*R*)-5-Isopropenyl-2-methylcyclohex-2-enyl Diisopropylcarbamate (11): To a solution of **10** (1.47 g, 9.6 mmol) in pyridine (10 mL) at 0 °C was slowly added diisopropylcarbamoyl chloride (4.8 g, 29 mmol, 3 equiv.). The mixture was stirred for 12 h at 80 °C, and the mixture was then diluted at 0 °C with Et_2O (20 mL), H_2O (10 mL) and an aqueous saturated NH_4Cl solution (15 mL). After extraction with Et_2O, the combined organic layers were

washed with brine, dried with $MgSO_4$ and filtered off. After the solvent was removed under reduced pressure, the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 80:20) to deliver product **11** (2.25 g, 84%). $[\alpha]_D^{20}$ = +0.7 (*c* = 3.0, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.52–5.51 (m, 1 H), 5.47–5.37 (m, 1 H), 4.68 (s, 2 H), 4.17–3.93 (m, 1 H), 3.93–3.65 (m, 1 H), 2.27 (tdd, *J* = 12.3, 5.2, 1.6 Hz, 1 H), 2.17 (ddt, *J* = 12.3, 6.0, 1.4 Hz, 1 H), 2.05 (m, 1 H), 1.95 (m, 1 H), 1.69 (s, 3 H, CH_3), 1.64 (s, 3 H, CH_3), 1.47 (td, *J* = 12.4, 10.1 Hz, 1 H), 1.19 (s, 6 H, 2 CH_3), 1.17 (s, 6 H, 2 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6 (C), 148.6 (C), 134.2 (C), 125.0 (CH), 109.1 (CH_2), 73.1 (CH), 46.2 (CH), 45.3 (CH), 40.5 (CH), 34.5 (CH_2), 30.8 (CH_2), 21.8 (2 CH_3), 20.6 (CH_3), 20.4 (2 CH_3), 19.2 (CH_3) ppm. IR (film): $\tilde{\nu}$ = 1698, 1451, 1290, 1160 cm^{-1}. MS (GC, EI): *m*/*z* = 279 $[M]^+$, 220, 146. $C_{17}H_{29}NO_2$ (279.42): calcd. C 73.07, H 10.46, N 5.01; found C 73.14, H 10.52, N 5.05.

(2*E*)-3-Methyl-5-trimethylsilylpent-2-en-4-ynal (13): To a suspension of $Pd(OAc)_2$ (180 mg, 0.75 mmol, 0.05 equiv.) in THF (34 mL) at 20 °C was added tris(2,6-dimethoxyphenyl)phosphane (340 mg, 1.5 mmol, 0.05 equiv.). After stirring for 15 min, ethyl butynoate (1.75 mL, 15.0 mmol, 1 equiv.) was introduced. To the resulting clear brown mixture obtained after 5 min, was added trimethylsilylacetylene (2.12 mL, 15.0 mmol, 1 equiv.). The reaction mixture became dark brown. After 2 h, the mixture was concentrated under reduced pressure, and the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 95:5) to deliver ethyl (2*E*)-3-methyl-5-trimethylsilylpent-2-en-4-ynoate (3.0 g, 95%).^{1}H NMR (270 MHz, $CDCl_3$): δ = 6.04 (s, 1 H), 4.11 (q, *J* = 7.1 Hz, 2 H), 2.22 (s, 3 H, CH_3), 1.22 (t, *J* = 7.1 Hz, 3 H, CH_3), 0.15 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 166.3 (C), 137.8 (C), 125.3 (CH), 106.8 (C), 99.4 (C), 60.3 (CH_2), 19.9 (CH_3), 14.5 (CH_3), 0.0 (3 CH_3) ppm. MS (GC, CI, CH_4): *m*/*z* = 211 $[M + H]^+$.

To a solution of ethyl (2*E*)-3-methyl-5-trimethylsilyl pent-2-ene-4-ynoate (2.4 g, 11.5 mmol) in CH_2Cl_2 (24.6 mL) at –78 °C was added dropwise a solution of DIBAL-H (1 M in CH_2Cl_2, 31 mL, 31 mmol, 2.7 equiv.). After 2 h at –78 °C, to the reaction mixture was added ethyl acetate then potassium tartrate (46 mmol, 4 equiv.), and the mixture was stirred for 1 h. The aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After the solvent was removed under reduced pressure, the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 80:20) to deliver the (2*E*)-3-methyl-5-trimethylsilyl pent-2-en-4-ynol (1.65 g, 86%). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 6.05 (t, *J* = 6.6 Hz, 1 H), 4.19 (d, *J* = 6.6 Hz, 2 H), 1.81 (s, 3 H, CH_3), 1.67 (s, 1 H, OH), 0.17 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 136.6 (CH), 120.7 (C), 107.4 (C), 92.2 (C), 59.1 (CH_2), 17.4 (CH_3), 0.0 (3 CH_3) ppm. IR (film): $\tilde{\nu}$ = 3339, 2960, 2146, 1634, 1445, 1245, 1009 cm^{-1}. MS (GC, EI): *m*/*z* = 168.

IBX[24] (734 mg, 2.62 mmol, 2.2 equiv.) was dissolved in DMSO (5 mL) at 20 °C. When the mixture became transparent, a DMSO solution (3 mL) of (2*E*)-3-methyl-5-trimethylsilyl pent-2-en-4-ynol (200 mg, 1.19 mmol) was added. After stirring for 2 h at 20 °C, H_2O was added at 0 °C, and the reaction mixture was filtered through a short pad of celite. After extraction with Et_2O, the combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off, and the solvents were removed under reduced pressure. Crude aldehyde **13** (195 mg) was used without further purification in the next step. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.95 (d, *J* = 8.2 Hz, 1 H), 6.13 (dq, *J* = 8.2, 1.4 Hz, 1 H), 2.21 (d, *J* = 1.4 Hz, 3 H, CH_3), –0.15 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.2 (CH), 140.0 (C), 134.0 (CH), 105.5 (C), 105.0 (C), 18.3 (CH_3), –0.5 (3 CH_3) ppm. MS (GC, EI): *m*/*z* = 166 $[M]^+$.

Reaction of Carbamate 11 with Enynal 13 Under *s*BuLi/TMEDA/toluene Conditions

[3*R*(1*R*,2*E*),5*R*]-3-[1-Hydroxy-3-methyl-5-(trimethylsilyl)pent-2-en-4-ynyl]-2-methyl-5-(prop-1-en-2-yl)cyclohex-1-enyl Diisopropylcarbamate (14a) and [3*R*(1*S*,2*E*),5*R*]-3-[1-Hydroxy-3-methyl-5-(trimethylsilyl)pent-2-en-4-ynyl]-2-methyl-5-(prop-1-en-2-yl)cyclohex-1-enyl Diisopropylcarbamate (14b): To a solution of carbamate **11** (500 mg, 1.8 mmol) and TMEDA (300 μL, 2 mmol, 1.1 equiv.) in toluene (10 mL) at –78 °C was slowly added *s*BuLi (1.28 M in hexanes, 1.5 mL, 2 mmol, 1.1 equiv.). The clear reaction mixture became deep yellow. After 30 min deprotonation time at –78 °C, a solution of aldehyde 13 (330 mg, 2 mmol, 1.1 equiv.) in toluene (5 mL) was added. After stirring for 1 h at –78 °C the reaction was quenched by the addition of a MeOH/H_2O/HCl (1 N) (10 mL/4 mL/1 mL) mixture. The temperature was warmed to 20 °C, and the mixture was extracted with Et_2O. The combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After the solvent was removed under reduced pressure, the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 90:10) to deliver title products **14a** (285 mg) and **14b** (280 mg) in an overall yield of 70% (565 mg); **14a**/**14b**, 1:1. Data for **14a**: $[\alpha]_D^{20}$ = +3.1 (*c* = 1.08, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.04 (dq, *J* = 7.8, 1.0 Hz, 1 H), 4.74 (d, *J* = 0.5 Hz, 1 H), 4.72 (d, *J* = 0.5 Hz, 1 H), 4.67 (dd, *J* = 7.8, 3.7 Hz, 1 H), 4.08 (m, 1 H), 3.81 (m, 1 H), 2.94 (m, 1 H), 2.26 (m sharp, 1 H), 2.18 (m, 1 H), 2.08 (m, 1 H), 1.98 (m, 1 H), 1.85 (d, *J* = 1.4 Hz, 3 H, CH_3), 1.75 (s, 3 H, CH_3), 1.63 (s, 3 H, CH_3), 1.52 (td, *J* = 13.3, 6.0 Hz, 1 H), 1.26 (s, 6 H, 2 CH_3), 1.20 (s, 6 H, 2 CH_3), 0.18 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 149.3 (C), 145.7 (C), 139.6 (CH), 119.5 (C), 119.5 (C), 109.3 (CH_2), 108.1 (C), 91.6 (C), 69.3 (CH), 47.2 (CH), 46.0 (CH), 45.4 (CH), 38.2 (CH), 32.7 (CH_2), 28.2 (CH_2), 21.7 (2 CH_3), 20.7 (CH_3), 20.6 (2 CH_3), 18.2 (CH_3), 14.8 (CH_3), 0.4 (3 CH_3) ppm. IR (film): $\tilde{\nu}$ = 3421, 2966, 2141, 1680, 1445, 1296, 1148 cm^{-1}. MS (GC, CI, CH_4): *m*/*z* = 446 $[M + H]^+$, 279, 128, 109, 86, 73. $C_{26}H_{43}NO_3Si$ (445.72): calcd. C 70.06, H 9.72, N 3.14; found C 70.14, H 9.77, N 3.18. Data for **14b**: $[\alpha]_D^{20}$ = –4.9 (*c* = 0.95, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.94 (dq, *J* = 9.2, 1.4 Hz, 1 H), 4.78–4.70 (m, 2 H), 4.49 (dd, *J* = 9.2, 5.5 Hz, 1 H), 4.15–4.00 (m, 1 H), 3.92–3.72 (m, 1 H), 2.72–2.60 (m, 1 H), 2.37–2.31 (m, 1 H), 2.20–2.04 (m, 2 H), 1.82 (s, 3 H, CH_3), 1.72–1.58 (m, 2 H), 1.71 (s, 3 H, CH_3), 1.69 (s, 3 H, CH_3), 1.32–1.19 (m, 12 H, 4 CH_3), 0.12 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8 (C), 149.0 (C), 144.9 (C), 141.5 (CH), 120.4 (C), 119.7 (C), 109.7 (CH_2), 108.0 (C), 92.1 (C), 72.7 (CH), 47.1 (CH), 46.0 (CH), 45.9 (CH), 38.2 (CH), 33.0 (CH_2), 31.5 (CH_2), 21.8 (2 CH_3), 20.8 (2 CH_3), 20.7 (CH_3), 18.1 (CH_3), 17.3 (CH_3), 0.3 (3 CH_3) ppm. MS (GC, CI, CH_4): *m*/*z* = 446 $[M + H]^+$, 279, 128, 109, 86, 73. $C_{26}H_{43}NO_3Si$ (445.72): calcd. C 70.06, H 9.72, N 3.14; found C 70.14, H 9.77, N 3.18.

(*R*)-Mandelate Ester of 14a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.28 (m, 5 H), 5.89 (dq, *J* = 9.2, 1.4 Hz, 1 H), 5.85 (dd, *J* = 9.2, 4.6 Hz, 1 H), 4.67 (s, 1 H), 4.64 (s, 1 H), 4.59 (s, 1 H), 4.05–3.90 (m, 1 H), 3.90–3.75 (m, 1 H), 3.36 (s, 3 H, CH_3), 2.34–2.25 (m, 1 H), 2.28–2.23 (m, 1 H), 2.05–1.98 (m, 1 H), 1.89 (d, *J* = 1.4 Hz, 3 H, CH_3), 1.85–1.60 (m, 2 H), 1.57 (s, 3 H, CH_3), 1.51 (s, 3 H, CH_3), 1.42 (td, *J* = 13.3; 6.4 Hz, 1 H), 1.3–1.15 (m, 12 H, 4 CH_3), 0.16 (s, 9 H, 3 CH_3) ppm.

(*S*)-Mandelate Ester of 14a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.28 (m, 5 H), 5.82 (dd, *J* = 9.2, 4.6 Hz, 1 H), 5.72 (dq, *J* = 9.2, 1.4 Hz, 1 H), 4.80 (s, 1 H), 4.71 (s, 1 H), 4.70 (s, 1 H), 4.1–

3.92 (m, 1 H), 3.92–3.74 (m, 1 H), 3.40 (s, 3 H), 2.70–2.59 (m, 1 H), 2.38–2.32 (m, 1 H), 2.16–2.10 (m, 1 H), 1.9–1.76 (m, 1 H), 1.81 (d, J = 1.4 Hz, 3 H, CH_3), 1.68 (s, 3 H, CH_3), 1.58 (s, 3 H, CH_3), 1.55 (td, J = 13.3, 6.4 Hz, 1 H), 1.3–1.16 (m, 12 H, 4 CH_3), 0.16 (s, 9 H, 3 CH_3) ppm.

Reaction of Carbamate 11 with Enynal 13 under *s*BuLi/TMEDA/Toluene/Ti(O*i*Pr)$_4$ Conditions

[3*R*(1*R*,2*E*),5*R*]-3-[1-Hydroxy-3-methyl-5-(trimethylsilyl)pent-2-en-4-ynyl]-2-methyl-5-(prop-1-en-2-yl)cyclohex-1-enyl Diisopropylcarbamate (14a), [3*R*(1*S*,2*E*),5*R*]-3-[1-Hydroxy-3-methyl-5-(trimethylsilyl)pent-2-en-4-ynyl]-2-methyl-5-(prop-1-en-2-yl)cyclohex-1-enyl Diisopropylcarbamate (14b) and [3*S*(1*R*,2*E*),5*R*]-3-[1-Hydroxy-3-methyl-5-(trimethylsilyl)pent-2-en-4-ynyl]-2-methyl-5-(prop-1-en-2-yl)cyclohex-1-enyl Diisopropylcarbamate (15): To a solution of carbamate **11** (137 mg, 0.49 mmol) and TMEDA (170 μL, 0.54 mmol, 1.1 equiv.) in toluene (4 mL) at –78 °C was slowly added *s*BuLi (1.2 M in hexanes, 82 μL, 0.54 mmol, 1.1 equiv.). The clear reaction mixture became deep yellow. After 30 min deprotonation time at –78 °C, a solution of Ti(O*i*Pr)$_4$ (432 μL, 1.5 mmol, 3 equiv.) in toluene (1 mL) was added at –78 °C, and the reaction mixture became brown green. Stirring was maintained for 30 min at –78 °C before the addition of a solution of aldehyde **13** (90 mg, 0.54 mmol, 1.1 equiv.) in toluene (1.5 mL). The orange-coloured reaction mixture was stirred at –78 °C for 1 h and diluted at 0 °C with Et_2O and an aqueous saturated NH_4Cl solution. The aqueous phase was extracted with Et_2O, and the combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After removal of the solvents under reduced pressure, the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 80:20) to deliver starting material **11** (41 mg, 30%), title compounds **14a** and **14b** (35 mg, 16%; **14a**/**14b**, 1:1) and **15** (33 mg, 15%, see below for description).

Reaction of Carbamate 11 with Enynal 13 under *s*BuLi/TMEDA/Toluene/TiCl(O*i*Pr)$_3$ Conditions

[3*S*(1*R*,2*E*),5*R*]-3-[1-Hydroxy-3-methyl-5-(trimethylsilyl)pent-2-en-4-ynyl]-2-methyl-5-(prop-1-en-2-yl)cyclohex-1-enyl Diisopropylcarbamate (15): To a solution of carbamate **11** (305 mg, 1.09 mmol) and TMEDA (182 μL, 1.2 mmol, 1.1 equiv.) in toluene (4.5 mL) at –78 °C was slowly added *s*BuLi (1.3 M in hexanes, 923 μL, 1.2 mmol, 1.1 equiv.). The clear reaction mixture became deep yellow. After 30 min deprotonation time at –78 °C, a solution of TiCl(O*i*Pr)$_3$ (781 μL, 3.27 mmol, 3 equiv.) in toluene (1.5 mL) was added at – 78 °C, and the reaction mixture became brown green. Stirring was maintained for 20 min at –78 °C before the addition of a solution of aldehyde **13** (200 mg, 1.2 mmol, 1.1 equiv.) in toluene (2.5 mL). The orange-coloured reaction mixture was stirred at –78 °C for 1 h and diluted at 0 °C with Et_2O and an aqueous saturated NH_4Cl solution. The aqueous phase was extracted with Et_2O, and the combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After the solvents were removed under reduced pressure, the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 80:20) to deliver compound **15** (367 mg, 47%) together with starting material **11** (241 mg, 31%) and **14a** and **14b** (25 mg, 3%; **14a**/**14b**, 1:1). Data for **15**: $[\alpha]_D^{20}$ = +21.7 (c = 2.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.02 (dq, J = 8.2, 1.4 Hz, 1 H), 4.75 (s, 2 H), 4.59 (dd, J = 8.2, 4.2 Hz, 1 H), 3.99 (m, 1 H), 3.87 (m, 1 H), 2.68 (m, 1 H), 2.35 (m, 1 H), 2.18 (tq, J = 14.0, 2.5 Hz, 1 H), 2.14 (m, 1 H), 1.97 (ddt, J = 13.3, 6.3, 2.5 Hz, 1 H), 1.90 (d, J = 1.4 Hz, 3 H, CH_3), 1.75 (s, 3 H, CH_3), 1.55 (s, 3 H, CH_3), 1.42 (s, 1 H, OH), 1.37 (q, J = 13.3 Hz, 1 H), 1.26 (m, 6 H, 2 CH_3), 1.24 (m, 6 H, 2 CH_3), 0.19 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.1 (C), 148.7 (C), 144.7 (C), 137.8 (CH), 121.7 (C), 119.1 (C), 109.3 (CH_2), 107.7 (C), 92.3 (C), 70.0 (CH), 46.5 (CH), 45.8 (CH), 45.2 (CH), 40.9 (CH), 33.3 (CH_2), 30.0 (CH_2), 21.8 (2 CH_3), 20.7 (CH_3), 20.6 (CH_3), 20.4 (CH_3), 17.9 (CH_3), 13.9 (CH_3), –0.02 (3 CH_3) ppm. IR (film): $\tilde{\nu}$ = 3402, 2929, 1653, 1409, 1249, 1211, 1044, 1010, 841, 800, 744 cm^{-1}. MS (GC, CI, CH_4): m/z = 446 [M + H]$^+$. $C_{26}H_{43}NO_3Si$ (445.72): calcd. C 70.06, H 9.72, N 3.14; found C 70.12, H 9.75, N 3.18.

(*R*)-Mandelate Ester of 15: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.25 (m, 5 H), 5.86 (dq, J = 8.2, 1.4 Hz, 1 H), 5.81 (dd, J = 8.2, 4.2 Hz, 1 H), 4.71 (s, 1 H), 4.67 (s, 1 H), 4.59 (s, 1 H), 3.97 (m, 1 H), 3.84 (m, 1 H), 3.41 (s, 3 H), 2.50 (m, 1 H), 2.08 (m, 1 H), 1.92 (m, 1 H), 1.86 (d, J = 1.4 Hz, 3 H, CH_3), 1.70 (m, 1 H), 1.59 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 1.30–1.27 (m, 1 H), 1.24 (m, 6 H, 2 CH_3), 1.22 (m, 6 H, 2 CH_3), 1.10–1.00 (m, 1 H), 0.19 (s, 9 H, 3 CH_3) ppm.

(*S*)-Mandelate Ester of 15: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43–7.28 (m, 5 H), 5.76 (dd, J = 8.7, 5.0 Hz, 1 H), 5.72 (dq, J = 8.7, 1.4 Hz, 1 H), 5.01 (s, 1 H), 4.74 (s, 1 H), 4.72 (s, 1 H), 3.97 (m, 1 H), 3.85 (m, 1 H), 3.39 (s, 3 H), 2.77 (m, 1 H), 2.29 (m, 1 H), 2.13 (m, 1 H), 1.88 (m, 1 H), 1.72 (s, 3 H, CH_3), 1.56 (d, J = 1.4 Hz, 3 H, CH_3), 1.47 (s, 3 H, CH_3), 1.33–1.28 (m, 1 H), 1.24 (m, 6 H, 2 CH_3), 1.22 (m, 6 H, 2 CH_3), 1.15–1.02 (m, 1 H), 0.17 (s, 9 H, 3 CH_3) ppm.

(4*R*,5*S*)-4-Dimethoxymethyl-5-isopropyl-2-methyl Cyclohex-2-enone (16): This compound was prepared according to the procedure described by Gennari in 45% yield over three steps (4.5 g). $[\alpha]_D^{20}$ = +158.0 (c = 1.07, AcOEt) {ref.[9b] $[\alpha]_D^{20}$ = +146.4 (c = 0.98, AcOEt)}. ^{1}H NMR (270 MHz, $CDCl_3$): δ = 6.80 (d, J = 2.0 Hz, 1 H), 4.49 (d, J = 4.6 Hz, 1 H), 3.48 (s, 6 H, 2 CH_3), 2.72–2.62 (m, 1 H), 2.58 (dd, J = 16.5, 4.6 Hz, 1 H), 2.32 (dd, J = 16.5, 8.9 Hz, 1 H), 2.10–2.04 (m, 1 H), 1.90–1.74 (m, 1 H), 1.74 (s, 3 H, CH_3), 0.95 (d, J = 6.6 Hz, 3 H, CH_3), 0.91 (d, J = 6.6 Hz, 3 H, CH_3). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 199.9 (C), 143.8 (C), 136.0 (CH), 105.4 (CH), 55.9 (CH_3), 54.6 (CH_3), 42.3 (CH), 41.3 (CH), 37.2 (CH_2), 28.2 (CH), 20.9 (CH_3), 17.7 (CH_3), 15.8 (CH_3) ppm. IR (film): $\tilde{\nu}$ = 2960, 2832, 1690, 1465, 1373, 1076 cm^{-1}. MS (GC, CI, CH_4): m/z = 227 [M + H]$^+$. $C_{13}H_{22}O_3$ (226.32): calcd. C 68.99, H 9.80; found C 69.11, H 9.84.

(1*R*,4*R*,5*R*)-5-Isopropyl-4-{[(*tert*-butyldimethylsilyl)oxy]methyl}-2-methylcyclohex-2-enyl Diisopropylcarbamate (17): To a solution of LAH (1 M in Et_2O, 11 mL, 11 mmol, 0.5 equiv.) at –78 °C was slowly added a solution of enone **16** (5 g, 22 mmol) in Et_2O (16 mL). After 30 min H_2O (900 μL, 50 mmol), NaOH (15% sol, 900 μL, 3.38 mmol) and more H_2O (2.6 mL, 142.3 mmol) were successively added to the mixture. The mixture was stirred until a white precipitate appeared; the solution was dried with $MgSO_4$ and filtered off, and the solvent was removed under reduced pressure. The crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 80:20) to deliver (1*R*,4*R*,5*R*)-4-dimethoxymethyl-5-isopropyl-2-methyl cyclohex-2-enol (4.6 g, 91%, 84% *de*). $[\alpha]_D^{20}$ = +112.0 (c = 1.8, $CHCl_3$). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 5.54 (s, 1 H), 4.26 (d, J = 4.0 Hz, 1 H), 4.13–4.09 (m, 1 H), 3.40 (s, 3 H, CH_3), 3.39 (s, 3 H, CH_3), 2.34–2.40 (m, 1 H), 2.03–1.91 (m, 2 H), 1.77 (s, 3 H, CH_3), 1.64–1.54 (m, 1 H), 1.61–1.45 (m, 1 H, OH), 1.35–1.23 (td, J = 11.8, 9.2 Hz, 1 H), 0.95 (d, J = 6.9 Hz, 3 H, CH_3), 0.84 (d, J = 6.9 Hz, 3 H, CH_3) ppm. ^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 137.7 (C), 123.2 (CH), 106.7 (CH), 70.6 (CH), 56.3 (CH_3), 55.4 (CH_3), 42.1 (CH), 39.4 (CH), 31.8 (CH_2), 27.1 (CH_3), 21.5 (CH), 19.1 (CH_3), 16.4 (CH_3) ppm. IR (film): $\tilde{\nu}$ = 3442, 2940, 1670, 1450, 1122, 1061 cm^{-1}. MS (GC, EI): m/z =

228. $C_{13}H_{24}O_3$ (228.33): calcd. C 68.38, H 10.59; found C 68.47, H 10.65.

To a suspension of KH (30% in oil, 1.76 g, 44 mmol, 1.5 equiv.) in THF (20 mL) at 0 °C was slowly added a solution of (1*R*,4*R*,5*R*)-4-dimethoxymethyl-5-isopropyl-2-methyl cyclohex-2-enol (2.0 g, 8.8 mmol) in THF (10 mL). The mixture was stirred for 30 min at 20 °C and then diisopropylcarbamoyl chloride (1.72 g, 10.5 mmol, 1.2 equiv.) was added. After stirring for 30 min at 20 °C, the mixture was diluted at 0 °C with H_2O (5 mL) and an aqueous saturated NH_4Cl solution (25 mL). After extraction with Et_2O, the combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After the solvent was removed under reduced pressure, the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 80:20) to deliver (1*R*,4*R*,5*R*)-5-isopropyl-4-(dimethoxymethyl)-2-methylcyclohex-2-enyl diisopropylcarbamate (3 g, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.57 (m sharp, 1 H), 5.26 (m, 1 H), 4.23 (d, J = 4.1 Hz, 1 H), 4.02–3.75 (m, 2 H), 3.38 (s, 3 H, CH_3), 3.36 (s, 3 H, CH_3), 2.39 (m, 1 H), 1.96 (ddd, J = 12.4, 5.5, 2.3 Hz, 1 H), 1.92 (septd, J = 6.9, 2.2 Hz, 1 H), 1.67 (s, 3 H, CH_3), 1.61–1.54 (m, 1 H), 1.48 (ddd, J = 12.4, 10.5, 7.8 Hz, 1 H), 1.24–1.12 (m, 12 H, 4 CH_3), 0.91 (d, J = 6.9 Hz, 3 H, CH_3), 0.81 (d, J = 6.9 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.7 (C), 135.8 (C), 124.7 (CH), 106.8 (CH), 72.5 (CH), 56.3 (CH_3), 55.2 (CH_3), 46.2 (CH), 45.8 (CH), 41.9 (CH), 39.3 (CH), 28.4 (CH_2), 27.5 (CH), 21.8 (CH_3), 21.4 (2 CH_3), 21.0 (2 CH_3), 20.0 (CH_3), 17.5 (CH_3) ppm.

To a solution of (1*R*,4*R*,5*R*)-5-isopropyl-4-(dimethoxymethyl)-2-methylcyclohex-2-enyl diisopropylcarbamate (3.7 g, 10.4 mmol) in THF (10 mL) and H_2O (10 mL) at 0 °C was slowly added formic acid (40 mL, 1 mol, 10 equiv.). After stirring for 2 h at 20 °C, the mixture was diluted at 0 °C with Et_2O (40 mL) and NaOH (10 M, 100 mL). The aqueous phase was treated with NaOH until pH 8 and extracted with Et_2O. The combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After the solvent was removed under reduced pressure, the crude (1*R*,4*R*,5*R*)-4-formyl-5-isopropyl-2-methylcyclohex-2-enyl diisopropylcarbamate (3.4 g) was used without purification for the next step. MS (GC, EI): m/z = 309 $[M]^+$.

To a solution of (1*R*,4*R*,5*R*)-4-formyl-5-isopropyl-2-methylcyclohex-2-enyl diisopropylcarbamate (3.2 g, 10.4 mmol) in EtOH at 0 °C was added $NaBH_4$ (100 mg, 2.6 mmol, 0.25 equiv.). After 20 min, the mixture was diluted with Et_2O (45 mL) and HCl (45 mL). The aqueous phase was saturated by the addition of NaCl and extracted with Et_2O. The combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After the solvent was removed under reduced pressure, the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 80:20) to deliver (1*R*,4*R*,5*R*)-4-(hydroxymethyl)-5-isopropyl-2-methylcyclohex-2-enyl diisopropylcarbamate (2.6 g, 80% over two steps). $[\alpha]_D^{20}$ = +86.0 (c = 1.29, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.58 (s sharp, 1 H), 5.37–5.30 (m, 1 H), 4.08–3.72 (m, 2 H), 3.66 (dd, J = 10.6, 3.4 Hz, 1 H), 3.52 (dd, J = 10.6, 5.5 Hz, 1 H), 2.24–2.17 (m, 1 H), 1.99 (ddd, J = 12.2, 5.5, 2.3 Hz, 1 H), 1.91 (septd, J = 6.9, 3.2 Hz, 1 H), 1.69 (s, 3 H, CH_3), 1.62 (s large, 1 H, OH), 1.55 (dddd, J = 12.4, 9.6, 3.2, 2.3 Hz, 1 H), 1.45–1.33 (m, 1 H), 1.21 (s, 6 H, 2 CH_3), 1.19 (s, 6 H, 2 CH_3), 0.94 (d, J = 6.9 Hz, 3 H, CH_3), 0.80 (d, J = 6.9 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9 (C), 137.5 (C), 127.3 (CH), 73.2 (CH), 64.7 (CH_2), 46.4 (CH), 45.7 (CH), 41.6 (CH), 39.4 (CH), 28.7 (CH_2), 27.7 (CH), 21.9 (CH_3), 21.1 (2 CH_3), 20.7 (2 CH_3), 19.6 (CH_3), 16.8 (CH_3) ppm. IR (film): $\tilde{\nu}$ = 3437, 2965, 1696, 1445, 1286, 1158 cm^{-1}. MS (GC, EI): m/z = 311 $[M]^+$. $C_{18}H_{33}NO_3$ (311.46): calcd. C 69.41, H 10.68, N 4.50; found C 69.47, H 10.72, N 4.54.

To a solution of (1*R*,4*R*,5*R*)-4-(hydroxymethyl)-5-isopropyl-2-methylcyclohex-2-enyl diisopropylcarbamate (1.03 g, 3.3 mmol) in DMF (10 mL) at 20 °C was added imidazole (610 mg, 9.9 mmol, 3 equiv.) and *tert*-butyldimethylsilyl chloride (750 mg, 4.9 mmol, 1.5 equiv.). After stirring for 3 h at 20 °C, the mixture was diluted with Et_2O (10 mL) and H_2O (10 mL). After extraction with Et_2O, the combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After the solvent was removed under reduced pressure, the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 100:0) to deliver title product **17** (1.32 g, 94%). $[\alpha]_D^{20}$ = +89.0 (c = 1.04, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.55–5.51 (m, 1 H), 5.34–5.28 (m, 1 H), 4.11–3.73 (m, 2 H), 3.65 (dd, J = 9.8, 4.3 Hz, 1 H), 3.37 (dd, J = 9.8, 7.1 Hz, 1 H), 2.21–2.13 (m, 1 H), 1.97 (dd, J = 9.6, 5.5 Hz, 1 H), 1.92 (septd, J = 6.9, 2.7 Hz, 1 H), 1.68 (s, 3 H, CH_3), 1.46–1.34 (m, 2 H), 1.23 (s, 6 H, 2 CH_3), 1.21 (s, 6 H, 2 CH_3), 0.92 (d, J = 6.9 Hz, 3 H, CH_3), 0.88 (s, 9 H, 3 CH_3), 0.80 (d, J = 6.9 Hz, 3 H, CH_3), 0.03 (s, 6 H, 2 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9 (C), 135.2 (C), 128.4 (CH), 73.4 (CH), 65.8 (CH_2), 46.2 (2 CH), 41.6 (CH), 40.2 (CH), 28.6 (CH_2), 27.7 (CH), 26.2 (3 CH_3), 21.9 (CH_3), 21.8 (2 CH_3), 21.0 (2 CH_3), 19.6 (CH_3), 18.6 (C), 17.0 (CH_3), –5.0 (2 CH_3) ppm. IR (film): $\tilde{\nu}$ = 2955, 1696, 1434, 1296, 1050 cm^{-1}. MS (GC, CI, CH_4): m/z = 426 $[M + H]^+$. $C_{24}H_{47}NO_3Si$ (425.73): calcd. C 67.71, H 11.13, N 3.29; found C 67.78, H 11.21, N 3.32.

[3*R*(1*R*,2*E*),4*R*,5*R*]-3-[1-Hydroxy-3-methyl-5-(trimethylsilyl)pent-2-en-4-ynyl]-2-methyl-5-isopropylcyclohex-1-enyl Diisopropylcarbamate (18a) and [3*R*(1*S*,2*E*),4*R*,5*R*]-3-[1-Hydroxy-3-methyl-5-(trimethylsilyl)pent-2-en-4-ynyl]-2-methyl-5-isopropylcyclohex-1-enyl Diisopropylcarbamate (18b): To a solution of carbamate **17** (2.5 g, 5.9 mmol) and TMEDA (1.2 mL, 7.6 mmol, 1.3 equiv.) in toluene (25 mL) at –85 °C was slowly added *s*BuLi (1.27 M in Et_2O, 6 mL, 7.6 mmol, 1.3 equiv.). During the addition, the temperature was kept between –85 °C and –80 °C. The clear reaction mixture became deep yellow. After 4 h deprotonation time at –80 °C a solution of aldehyde **13** (1.4 g, 8.2 mmol, 1.4 equiv.) in toluene (3 mL) was introduced. After stirring for 1.5 h at –78 °C the reaction was quenched by the addition of a MeOH/H_2O/HCl (1 N) (15 mL/3 mL/2 mL) mixture. The temperature was warmed to 20 °C, and the mixture was extracted with Et_2O. The combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After the solvent was removed under reduced pressure, the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 90:10) to deliver title products **18a** and **18b** (3 g, 86%; **18a**/**18b**, 1:1). An aliquot was purified by chromatography on silica gel (cyclohexane/AcOEt, 100:0 to 90:10) to deliver the two pure **18a** and **18b** isomers. Data for **18a**: $[\alpha]_D^{20}$ = +88.5 (c = 1.17, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.10 (dq, J = 8.7, 1.4 Hz, 1 H), 4.65 (m, 1 H), 4.10 (m, 1 H), 3.91 (dd, J = 10.5, 8.7 Hz, 1 H), 3.83 (m, 1 H), 3.66 (dd, J = 10.5, 2.5 Hz, 1 H), 2.42–2.37 (m sharp, 1 H), 2.13–1.94 (m, 3 H), 1.79 (d, J = 1.4 Hz, 3 H, CH_3), 1.78–1.67 (m, 2 H), 1.65 (s, 3 H, CH_3), 1.34–1.16 (m, 12 H, 4 CH_3), 0.92 (s, 9 H, 3 CH_3), 0.91–0.85 (m, 6 H), 0.15 (s, 9 H, 3 CH_3), 0.04 (s, 6 H, 2 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.5 (C), 143.3 (C), 141.2 (CH), 120.1 (C), 118.6 (C), 108.3 (C), 90.8 (C), 68.3 (CH), 65.0 (CH_2), 46.6 (CH), 46.5 (CH), 45.7 (CH), 39.9 (CH), 39.6 (CH), 27.6 (CH), 26.7 (CH_2), 26.0 (3 CH_3), 21.7 (2 CH_3), 20.7 (2 CH_3), 20.6 (CH_3), 18.3 (C), 17.8 (CH_3), 17.6 (CH_3), 15.2 (CH_3), 0.2 (3 CH_3), –5.2 (CH_3), –5.4 (CH_3) ppm. IR (film): $\tilde{\nu}$ = 3442, 2955, 2146, 1685, 1440, 1286, 1086 cm^{-1}. MS (GC, CI, CH_4): m/z = 593 $[M + H]^+$. $C_{33}H_{61}NO_4Si_2$ (592.02): calcd. C 66.95, H 10.39, N 2.37; found C 67.10, H 10.51, N 2.41. Data for **18b**: $[\alpha]_D^{20}$ = +25.5 (c = 0.99, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.94 (dq, J = 8.2,

1.4 Hz, 1 H), 4.66 (ddd, J = 10.5, 8.2, 3.4 Hz, 1 H), 4.15 (m, 1 H), 3.85 (dd, J = 10.5, 4.6 Hz, 1 H), 3.80 (m, 1 H), 3.70 (t, J = 10.5 Hz, 1 H), 3.24 (d, J = 10.5 Hz, 1 H, OH), 2.61 (d, J = 3.4 Hz, 1 H), 2.28 (m, 1 H), 2.04–1.94 (m, 1 H), 1.94–1.76 (m, 3 H), 1.84 (d, J = 1.4 Hz, 3 H, CH_3), 1.63 (s, 3 H, CH_3), 1.33–1.19 (m, 12 H, 4 CH_3), 0.88 (s, 9 H, 3 CH_3), 0.85 (d, J = 6.9 Hz, 3 H, CH_3), 0.78 (d, J = 6.9 Hz, 3 H, CH_3), 0.16 (s, 9 H, 3 CH_3), 0.05 (s, 6 H, 2 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 145.7 (C), 143.4 (CH), 119.2 (C), 117.1 (C), 108.5 (C), 90.5 (C), 67.1 (CH), 63.1 (CH_2), 47.2 (CH), 47.0 (CH), 45.6 (CH), 41.7 (CH), 36.8 (CH), 27.0 (CH), 26.6 (CH_2), 26.1 (3 CH_3), 21.7 (2 CH_3), 20.9 (CH_3), 20.7 (2 CH_3), 18.5 (C), 17.8 (CH_3), 17.2 (CH_3), 14.5 (CH_3), 0.21 (3 CH_3), –5.1 (CH_3), –5.3 (CH_3) ppm. IR (film): $\tilde{\nu}$ = 3442, 2955, 2146, 1685, 1440, 1286, 1086 cm^{-1}. MS (GC, CI, CH_4): m/z = 593 [M + H]$^+$. $C_{33}H_{61}NO_4Si_2$ (592.02): calcd. C 66.95, H 10.39, N 2.37; found C 67.05, H 10.44, N 2 45.

(*R*)-Mandelate Ester of 18a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.28 (m, 5 H), 5.94 (dq, J = 9.6, 1.4 Hz, 1 H), 5.87 (dd, J = 10.1, 2.8 Hz, 1 H), 4.62 (s, 1 H), 4.1–3.75 (m, 2 H), 3.69 (dd, J = 11.0, 6.4 Hz, 1 H), 3.48 (dd, J = 11.0, 9.0 Hz, 1 H), 3.34 (s, 3 H, CH_3), 2.50 (m, 1 H), 2.05–1.80 (m, 3 H), 1.94 (d, J = 1.4 Hz, 3 H, CH_3), 1.75–1.60 (m, 2 H), 1.37 (s, 3 H, CH_3), 1.25 (m, 12 H, 4 CH_3), 0.81 (s, 9 H, 3 CH_3), 0.79 (d, J = 6.4 Hz, 3 H, CH_3), 0.76 (d, J = 6.4 Hz, 3 H, CH_3), 0.17 (s, 9 H, 3 CH_3), 0.02 (s, 3 H, CH_3), 0.01 (s, 3 H, CH_3) ppm.

(*S*)-Mandelate Ester of 18a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.28 (m, 5 H), 5.85 (dd, J = 9.6, 3.2 Hz, 1 H), 5.71 (dq, J = 9.6, 2.8 Hz, 1 H), 4.68 (s, 1 H), 4.1–3.8 (m, 2 H), 3.75 (dd, J = 10.6, 6.4 Hz, 1 H), 3.53 (dd, J = 10.6, 9.2 Hz, 1 H), 3.39 (s, 3 H, CH_3), 2.70 (m, 1 H), 2.05–1.90 (m, 3 H), 1.82 (d, J = 1.8 Hz, 3 H, CH_3), 1.80–1.60 (m, 2 H), 1.54 (s, 3 H, CH_3), 1.25 (m, 12 H, 4 CH_3), 0.84 (s, 9 H, 3 CH_3), 0.81 (d, J = 5.0 Hz, 3 H, CH_3), 0.80 (d, J = 5.0 Hz, 3 H, CH_3), 0.15 (s, 9 H, 3 CH_3), 0.02 (s, 6 H, 2 CH_3) ppm.

(*R*)-Mandelate Ester of 18b: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.28 (m, 5 H), 5.77 (d, J = 3.7 Hz, 1 H), 5.65 (dq, J = 8.7, 1.4 Hz, 1 H), 4.75 (s, 1 H), 4.1–3.80 (m, 2 H), 3.74 (dd, J = 10.6, 5.5 Hz, 1 H), 3.49 (t, J = 10.5 Hz, 1 H), 3.42 (s, 3 H, CH_3), 2.69 (m, 1 H), 2.10–1.80 (m, 3 H), 1.75 (d, J = 1.4 Hz, 3 H, CH_3), 1.70–1.65 (m, 2 H), 1.65 (s, 3 H, CH_3), 1.26 (m, 12 H, 4 CH_3), 0.87 (s, 9 H, 3 CH_3), 0.82 (d, J = 6.4 Hz, 3 H, CH_3), 0.82 (d, J = 6.4 Hz, 3 H, CH_3), 0.14 (s, 9 H, 3 CH_3), 0.03 (s, 3 H, CH_3), 0.02 (s, 3 H, CH_3) ppm.

(*S*)-Mandelate Ester of 18b: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.25 (m, 5 H), 5.88 (dq, J = 9.1, 1.4 Hz, 1 H), 5.79 (d, J = 3.7 Hz, 1 H), 4.69 (s, 1 H), 4.1–3.80 (m, 2 H), 3.65 (dd, J = 10.5, 5.5 Hz, 1 H), 3.42 (t, J = 10.5 Hz, 1 H), 3.33 (s, 3 H, CH_3), 2.61 (m, 1 H), 1.92 (d, J = 1.4 Hz, 3 H, CH_3), 1.90–1.50 (m, 5 H), 1.55 (s, 3 H, CH_3), 1.25 (m, 12 H, 4 CH_3), 0.86 (s, 9 H, 3 CH_3), 0.69 (d, J = 6.9 Hz, 3 H, CH_3), 0.55 (d, J = 6.9 Hz, 3 H, CH_3), 0.17 (s, 9 H, 3 CH_3), 0.01 (s, 3 H, CH_3), 0.00 (s, 3 H, CH_3) ppm.

[3*R*(1*R*,2*E*),4*R*,5*R*]-3-[-1-Hydroxy-3-methyl-5-(trimethylsilyl)pent-2-en-4-ynyl]-5-isopropyl-4-(methoxymethyl)-2-methylcyclohex-1-enyl Diisopropylcarbamate (19a) and (1*R*,3a*R*,4*R*,7a*R*)-1,3,3a,4,5,7a-Hexahydro-4-isopropyl-7-methyl-1-[(*E*)-2-methyl-4-(trimethylsilyl)-but-1-en-3-ynyl]isobenzofuran-6-yl Diisopropylcarbamate (20): To a solution of **18a** (320 mg, 0.55 mmol) in MeOH (7 mL) was added Amberlyst 15. The reaction mixture was stirred for 5.5 h at 20 °C, filtered through a pad of celite and the solvent was removed under reduced pressure. The crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 80:20) to furnish compounds **19a** (78 mg, 30%) and **20** (113 mg, 43%) in an overall 73% yield. Data for **19a**: $[\alpha]_D^{20}$ = +140.2 (c = 1.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.06 (dq, J = 8.7, 1.4 Hz, 1 H), 4.74 (dd, J = 8.7, 6.0 Hz, 1 H), 4.10–4.00 (m, 1 H), 3.90–3.70 (m, 1 H), 3.82 (dd, J = 11.0, 8.2 Hz, 1 H), 3.71 (dd, J = 11.0, 3.4 Hz, 1 H), 2.43 (m, 1 H), 2.15–1.80 (m, 3 H), 1.80–1.70 (m, 2 H), 1.82 (s, 3 H, CH_3), 1.64 (s, 3 H, CH_3), 1.22 (m, 12 H, 4 CH_3), 0.88 (2 d, J = 5.5 Hz, 3 H, CH_3), 0.86 (2 d, J = 5.5 Hz, 3 H, CH_3), 0.18 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.6 (C), 144.0 (C), 140.0 (CH), 120.3 (C), 119.6 (C), 107.9 (C), 91.9 (C), 68.8 (CH), 64.2 (CH_2), 46.6 (CH), 46.5 (CH), 45.3 (CH), 39.9 (CH), 39.6 (CH), 27.7 (CH), 27.0 (CH_2), 21.8 (2 CH_3), 20.8 (CH_3), 20.7 (2 CH_3), 17.9 (CH_3), 17.5 (CH_3), 15.6 (CH_3), 0.2 (3 CH_3) ppm. MS (GC, CI, CH_4): m/z = 478 [M + H]$^+$. $C_{27}H_{47}NO_4Si$ (477.76): calcd. C 67.88, H 9.92, N 2.93; found C 67.95, H 10.12, N 2.95. Data for **20**: $[\alpha]_D^{20}$ = +28.8 (c = 1.7, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.90 (dq, J = 9.6, 1.4 Hz, 1 H), 4.78 (t, J = 9.6 Hz, 1 H), 4.01–3.89 (m, 2 H), 3.88–3.83 (m, 2 H), 3.01 (m, 1 H), 2.32–2.23 (m, 1 H), 2.23–2.12 (m, 1 H), 1.96–1.94 (m, 1 H), 1.90 (d, J = 1.4 Hz, 3 H, CH_3), 1.84 (septd, J = 6.9, 3.7 Hz, 1 H), 1.70 (tdd, J = 11.9, 4.6, 3.7 Hz, 1 H), 1.46 (s, 3 H, CH_3), 1.27 (s, 6 H, 2 CH_3), 1.25 (s, 6 H, 2 CH_3), 0.95 (d, J = 6.9 Hz, 3 H, CH_3), 0.79 (d, J = 6.9 Hz, 3 H, CH_3), 0.18 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.4 (C), 144.6 (C), 136.0 (CH), 122.5 (C), 116.3 (C), 108.3 (C), 92.5 (C), 75.8 (CH), 70.6 (CH_2), 48.2 (CH), 46.5 (2 CH), 40.9 (CH), 40.4 (CH), 28.6 (CH), 26.9 (CH_2), 21.9 (CH_3), 21.8 (2 CH_3), 21.0 (2 CH_3), 18.0 (CH_3), 15.9 (CH_3), 15.4 (CH_3), 0.04 (3 CH_3) ppm. MS (GC, CI, CH_4): m/z = 460 [M + H]$^+$. $C_{27}H_{45}NO_3Si$ (459.74): calcd. C 70.54, H 9.87, N 3.05; found C 70.62, H 9.93, N 3.12.

[3*R*(1*S*,2*E*),4*R*,5*R*]-3-[-1-Hydroxy-3-methyl-5-(trimethylsilyl)pent-2-en-4-ynyl]-5-isopropyl-4-(methoxymethyl)-2-methylcyclohex-1-enyl Diisopropylcarbamate (19b): To a solution of **18b** (320 mg, 0.55 mmol) in MeOH (7 mL) was added Amberlyst 15. The reaction mixture was stirred for 5.5 h at 20 °C, filtered through a pad of celite and the solvent was removed under reduced pressure. The crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 90:10) to furnish compound **19b** (257 mg, 98%). $[\alpha]_D^{20}$ = +13.6 (c = 0.97, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.98 (dq, J = 8.7, 1.4 Hz, 1 H), 4.71 (d, J = 8.7 Hz, 1 H), 4.20–4.08 (m, 1 H), 3.92 (dd, J = 10.9, 4.6 Hz, 1 H), 3.85–3.73 (m, 1 H), 3.74 (t, J = 10.9 Hz, 1 H), 2.64 (d, J = 3.6 Hz, 1 H), 2.33–2.22 (m, 1 H), 2.06–1.98 (m, 1 H), 1.96–1.76 (m, 3 H), 1.85 (d, J = 1.4 Hz, 3 H, CH_3), 1.64 (s, 3 H, CH_3), 1.33–1.19 (m, 12 H, 4 CH_3), 0.87 (d, J = 6.9 Hz, 3 H, CH_3), 0.79 (d, J = 6.9 Hz, 3 H, CH_3), 0.16 (s, 9 H, 3 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 145.7 (C), 142.6 (CH), 119.1 (C), 117.7 (C), 108.3 (C), 90.9 (C), 67.6 (CH), 62.7 (CH_2), 47.2 (CH), 47.0 (CH), 45.7 (CH), 41.3 (CH), 37.2 (CH), 27.1 (CH), 26.6 (CH_2), 21.7 (2 CH_3), 21.0 (CH_3), 20.8 (2 CH_3), 17.7 (CH_3), 16.9 (CH_3), 14.7 (CH_3), 0.2 (3 CH_3) ppm. MS (GC, CI, CH_4): m/z = 478 [M + H]$^+$. $C_{27}H_{47}NO_4Si$ (477.76): calcd. C 67.88, H 9.92, N 2.93; found C 67.92, H 10.04, N 2.97.

(*E*)-6-(*tert*-Butyldimethylsilyl)-3-methylhex-2-en-4-ynal (21): To a suspension of $Pd(OAc)_2$ (140 mg, 0.63 mmol, 0.025 equiv.) in THF (20 mL) at 20 °C was added tris(2,6-dimethoxyphenyl)phosphane (275 mg,1.5 mmol, 0.25 equiv.). After stirring for 15 min ethyl butynoate (3.36 g, 30.0 mmol, 1 equiv.) was introduced. To the resulting clear brown mixture obtained after 5 min was added a solution of propargyl alcohol (1.4 g, 25.0 mmol, 1 equiv.) in THF (5 mL). The mixture turned dark brown. After 12 h at 20 °C the mixture was concentrated under reduced pressure, and the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 80:20) to deliver ethyl (*E*)-6-hydroxy-3-methylhex-2-en-4-ynoate (3.47 g, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.00 (s, 1

H), 4.38 (s, 2 H), 4.11 (q, *J* = 7.7 Hz, 2 H), 2.80 (s, 1 H, OH), 2.21 (s, 3 H, CH_3), 1.24 (t, *J* = 7.7 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.1 (C), 137.2 (C), 124.3 (CH), 91.8 (C), 87.0 (C), 60.1 (CH_2), 51.4 (CH_2), 19.6 (CH_3), 14.1 (CH_3) ppm. MS (GC, CI, CH_4): *m*/*z* = 168, 150, 139, 123, 111, 95. IR (film): $\tilde{\nu}$ = 3400, 2982, 1712, 1616, 1444, 1367, 1339, 1258, 1153, 1038 cm^{-1}.

To a solution of ethyl (*E*)-6-hydroxy-3-methylhex-2-en-4-ynoate (1.24 g, 7.4 mmol) in THF (15 mL) was added imidazole (0.85 g, 12.5 mmol, 1.7 equiv.), DMAP (catalytic amount) and *tert*-butyldimethylsilyl chloride (1.67 g, 11.0 mmol, 1.5 equiv.). After stirring for 6 h at 20 °C, the reaction mixture was diluted with H_2O. The aqueous phase was extracted with Et_2O, and the combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After the solvent was removed under reduced pressure, the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 97:3) to deliver ethyl (*E*)-6-(*tert*-butyldimethylsilyl)-3-methylhex-2-en-4-ynoate (1.88 g, 90%). ^1H NMR (400 MHz, $CDCl_3$): δ = 6.02 (s, 1 H), 4.46 (s, 2 H), 4.15 (q, *J* = 7.3 Hz, 2 H), 2.27 (d, *J* = 1.4 Hz, 3 H, CH_3), 1.27 (t, *J* = 7.3 Hz, 3 H, CH_3), 0.90 (s, 9 H, 3 CH_3), 0.13 (s, 6 H, 2 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.1 (C), 137.6 (C), 124.3 (CH), 92.5 (C), 86.7 (C), 60.2 (CH_2), 52.2 (CH_2), 25.9 (3 CH_3), 19.8 (CH_3), 18.4 (C), 14.4 (CH_3), –4.9 (2 CH_3) ppm. MS (GC, CI, CH_4): *m*/*z* = 283 $[M + H]^+$.

To a solution of (*E*)-6-(*tert*-butyldimethylsilyl)-3-methylhex-2-en-4-ynoate (1.67 g, 6 mmol) in CH_2Cl_2 (15 mL) was added a solution of DIBAL-H at –78 °C (1 M in CH_2Cl_2, 13 mL, 13 mmol, 2.2 equiv.). After 2 h at –78 °C the reaction mixture was quenched with ethyl acetate and then with potassium tartrate (24 mmol, 4 equiv.) and stirred for 1 h. The aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After the solvent was removed under reduced pressure (*E*)-6-(*tert*-butyldimethylsilyl)-3-methylhex-2-en-4-ynol (1.3 g, 91%) was directly used in the next step without purification. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.94 (t, *J* = 6.9 Hz, 1 H), 4.39 (s, 2 H), 4.19 (d, *J* = 6.9 Hz, 2 H), 1.91 (s large, OH), 1.79 (s, 3 H, CH_3), 0.89 (s, 9 H, 3 CH_3), 0.10 (s, 6 H, 2 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.4 (CH), 120.7 (C), 86.9 (C), 86.3 (C), 59.2 (CH_2), 52.3 (CH_2), 26.0 (3 CH_3), 18.4 (CH_3), 17.6 (C), –4.9 (2 CH_3) ppm. MS (GC, CI, CH_4): *m*/*z* = 241 $[M + H]^+$.

IBX[24] (770 g, 2.75 mmol, 2.2 equiv.) was dissolved at 20 °C in DMSO (5 mL). A solution of (*E*)-6-(4-methoxybenzyloxy)-3-methylhex-2-en-4-ynol (300 mg, 1.25 mmol) in DMSO (3 mL) was then added. After stirring for 30 min the aqueous phase was extracted with Et_2O, and the combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After the solvent was removed under reduced pressure, the resulting crude **21** (300 mg, 91%) was used without further purification for the next step. ^1H NMR (400 MHz, $CDCl_3$): δ = 10.03 (d, *J* = 7.8 Hz, 1 H), 6.17 (d, *J* = 7.8 Hz, 1 H), 4.49 (s, 2 H), 2.28 (s, 3 H, CH_3), 0.91 (s, 9 H, 3 CH_3), 0.13 (s, 6 H, 2 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.4 (CH), 140.3 (C), 135.7 (CH), 97.9 (C), 86.1 (C), 52.3 (CH_2), 25.9 (3 CH_3), 18.5 (CH_3), 18.4 (C), –5.0 (2 CH_3) ppm. MS (GC, CI, CH_4): *m*/*z* = 239 $[M + H]^+$.

[3*R*(1*R*,2*E*),4*R*,5*R*]-3-[1-Hydroxy-3-methyl-6-(*tert*-butylimethylsilyloxy)hex-2-en-4-ynyl]-2-methyl-5-isopropylcyclohex-1-enyl Diisopropylcarbamate (22a). [3*R*(1*S*,2*E*),4*R*,5*R*]-3-[1-Hydroxy-3-methyl-6-(*tert*-butylimethylsilyloxy)hex-2-en-4-ynyl]-2-methyl-5-isopropylcyclohex-1-enyl Diisopropylcarbamate (22b): To a solution of carbamate **17** (540 mg, 1.3 mmol) and TMEDA (260 µL, 1.7 mmol, 1.3 equiv.) in toluene (8 mL), at –85 °C was slowly added *s*BuLi (1.3 M in hexane, 1.3 µL, 1.7 mmol, 1.3 equiv.), and the temperature was kept between –85 °C and –80 °C The clear reaction mixture became deep yellow. After 4 h deprotonation time at –80 °C a solution of aldehyde **21** (400 mg, 1.7 mmol, 1.3 equiv.) in toluene (5 mL) was introduced. After stirring for 2 h at –78 °C the reaction was quenched by the addition of a MeOH/H_2O/HCl (1 N; 10 mL/4 mL/2 mL) mixture. The temperature was warmed to 20 °C, and the mixture was extracted with Et_2O. The combined organic layers were washed with brine, dried with $MgSO_4$ and filtered off. After the solvent was removed under reduced pressure, the crude residue was purified by chromatography on silica gel (cyclohexane/AcOEt, 95:5) to deliver title product **22ab** (490 mg, 57%, **22a**/**22b** 1:1). Data for **22a**: $[\alpha]_D^{20}$ = +60.8 (*c* = 0.6, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 5.99 (dq, *J* = 8.7, 1.4 Hz, 1 H), 4.67 (m, 1 H), 4.41 (s, 2 H), 4.15–4.00 (s large, 1 H), 3.90 (dd, *J* = 11.0, 9.1 Hz, 1 H), 3.85–3.72 (m, 1 H), 3.68 (dd, *J* = 11.0, 3.2 Hz 1 H), 2.40 (m, 1 H), 2.13–1.94 (m, 3 H), 1.79 (d, *J* = 1.4 Hz, 3 H, CH_3), 1.77–1.67 (m, 2 H), 1.65 (s, 3 H, CH_3), 1.35–1.15 (m, 12 H, 4 CH_3), 0.92 (s, 9 H, 3 CH_3), 0.90 (s, 9 H, 3 CH_3), 0.88 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.85 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.05 (s, 12 H, 4 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.5 (C), 143.2 (C), 139.9 (CH), 120.1 (C), 118.2 (C), 87.7 (C), 85.2 (C), 68.1 (CH), 64.9 (CH_2), 52.4 (CH_2), 47.0 (CH), 46.7 (CH), 45.6 (CH), 39.8 (CH), 39.6 (CH), 27.6 (CH), 26.7 (CH_2), 26.0 (3 CH_3), 25.8 (3 CH_3), 21.8 (2 CH_3), 20.6 (CH_3), 20.5 (2 CH_3), 18.4 (C), 18.3 (C), 17.8 (CH_3), 17.7 (CH_3), 15.7 (CH_3), –4.9 (2 CH_3), –5.2 (CH_3), –5.4 (CH_3) ppm. IR (film): $\tilde{\nu}$ = 3395, 2953, 2925, 2852, 1705, 1692, 1458, 1435, 1365, 1318, 1285, 1100 cm^{-1}. $C_{37}H_{69}NO_5Si_2$ (664.13): calcd. C 66.92, H 10.47, N 2.11; found C 67.11, H 10.62, N 2.27. Data for **22b**: $[\alpha]_D^{20}$ = +274.4 (*c* = 1.05, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 5.87 (dq, *J* = 8.2, 1.4 Hz, 1 H), 4.67 (dd, *J* = 8.2, 4.1 Hz, 1 H), 4.40 (s, 2 H), 4.18–4.05 (s large, 1 H), 3.90–3.75 (s large, 1 H), 3.85 (dd, *J* = 10.7, 4.6 Hz, 1 H), 3.70 (t, *J* = 10.7 Hz, 1 H), 3.47–3.3 (s large, 1 H, OH), 2.62 (d, *J* = 4.1 Hz, 1 H), 2.35–2.24 (m, 1 H), 2.04–1.94 (m, 1 H), 1.90–1.75 (m, 3 H), 1.83 (d, *J* = 1.4 Hz, 3 H, CH_3), 1.62 (s, 3 H, CH_3), 1.33–1.19 (m, 12 H, 4 CH_3), 0.90 (s, 9 H, 3 CH_3), 0.88 (s, 9 H, 3 CH_3), 0.85 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.78 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.12 (s, 6 H, 2 CH_3), 0.05 (s, 6 H, 2 CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (C), 145.8 (C), 142.2 (CH), 119.1 (C), 116.8 (C), 87.9 (C), 84.9 (C), 67.0 (CH), 63.1 (CH_2), 52.4 (CH_2), 47.2 (CH), 46.9 (CH), 45.7 (CH), 41.6 (CH), 36.8 (CH), 26.9 (CH), 26.6 (CH_2), 26.1 (3 CH_3), 26.0 (3 CH_3), 21.7 (2 CH_3), 20.9 (CH_3), 20.7 (CH_3), 20.6 (CH_3), 18.5 (2 C), 17.8 (CH_3), 17.2 (CH_3), 14.6 (CH_3), –4.9 (2 CH_3), –5.1 (CH_3), –5.3 (CH_3) ppm. IR (film): $\tilde{\nu}$ = 3400, 2956, 2928, 2856, 1707, 1689, 1463, 1437, 1368, 1315, 1290, 1084, 835 cm^{-1}. $C_{37}H_{69}NO_5Si_2$ (664.13): calcd. C 66.92, H 10.47, N 2.11; found C 67.06, H 10.51, N 2.18.

Supporting Information (see footnote on the first page of this article): NMR spectra of all products.

Acknowledgments

Financial support was provided by the Institut de Recherche Pierre Fabre.

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Received: May 28, 2007
Published Online: August 29, 2007

