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Strategy towards the enantioselective synthesis of schiglautone A†‡

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Herein is described a convergent enantioselective route to an advanced intermediate in the synthesis of schiglautone A, a *Schisandra* triterpenoid with an unusual architecture. The synthetic route to this intermediate displaying 6 of the 7 stereocenters builds upon two fragments, an aldehyde elaborated from the Wieland–Miescher ketone, and a ketone. The preparation of the latter features a lithiation–borylation enzymatic resolution sequence, which led to the formation of the desired product with high enantio- and diastereoselectivities. After aldol coupling of the two fragments, the final quaternary stereocenter was installed by cyclopropane opening. The functionalized intermediate was isolated as a single diastereoisomer and thus offers a valuable starting point for further synthetic exploration.

Introduction

The plants of the Schisandraceae family have been used as part of traditional Chinese medicine since antiquity.[1] Numerous triterpenoids have been extracted from these climbing plants, which have received increasing attention over the past few years. The diversity of their complex scaffolds as well as their biological activities render them attractive synthetic targets.[2–7] However, due to their challenging architectures, only five *Schisandra* triterpenoids have been synthesized to date, all being nortriterpenoids.[8–13] Extracted in 2011 from the stems of *Schisandra glaucescens*, schiglautone A (**1**) exhibits an intriguing 6/7/9 fused tricyclic skeleton which is unprecedented among natural products (Fig. 1), and can be considered as a rearranged lanostane.[13] Schiglautone A displays weak cytotoxic activity against HeLa, HepG2 and SGC-7901 cancer cell lines.[14] As anwuweizic acid (**2**) is the main triterpenoid extracted from *Schisandra glaucescens* and presents structural analogies with **1**, it was proposed to be the biosynthetic precursor of schiglautone A.[14] Nevertheless, the biosynthetic pathway has not yet been elucidated. The structure of schiglautone A was determined by NMR studies, and the relative stereochemistry at C(20) as well as the connectivity throughout the molecule were confirmed by single-crystal X-ray analysis (Fig. 1). Its absolute stereochemistry was deduced by comparison with similar natural products.[14] Noteworthy structural features of schiglautone A are a bridged [6.4.1] ring system, a bridgehead alkene, and seven stereocenters, which contain three angular methyl groups. Interestingly, the hydroxyl group at the C(3) position is axial and the carbonyl at the C(8) position is not conjugated to the bridgehead alkene. These distinct characteristics were expected to render the synthesis of schiglautone A particularly challenging.

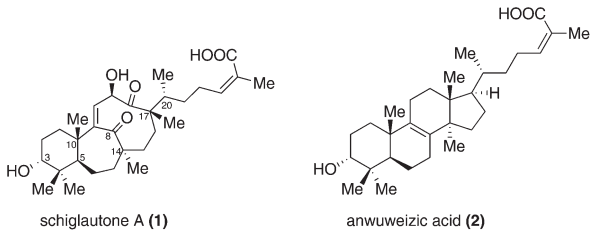

Fig. 1 Structures of schiglautone A (**1**), its putative biosynthetic precursor anwuweizic acid (**2**).

A synthesis of the tricyclic core of schiglautone A has been recently reported.[15] However, inversion of the stereocenter at C(3) was required. Furthermore, no solution is known to introduce the contiguous tertiary and quaternary centers at C(17) and C(20), respectively. Oxidation at C(8) may also prove challenging at a late stage. A different approach is described herein, which focuses on the installation of 6 of the 7 stereocenters.

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‡ Electronic supplementary information (ESI) available: Full experimental, copies of NMR spectra for all new compounds, SFC chromatograms. See DOI: 10.1039/c7ob00766c

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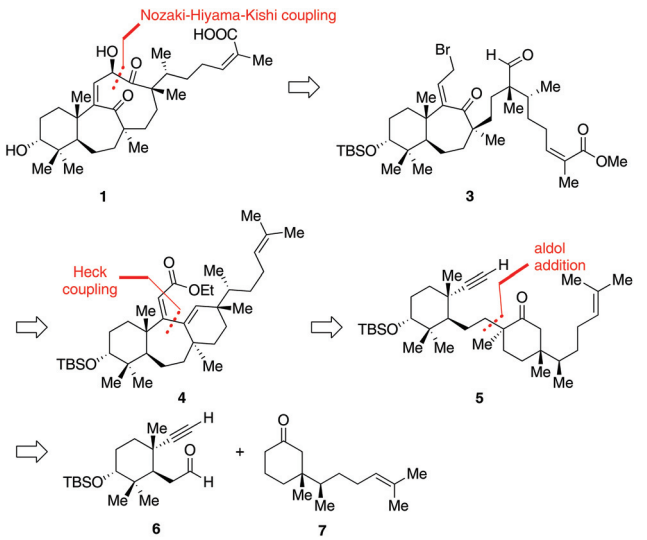
Results and discussion

Retrosynthetic analysis

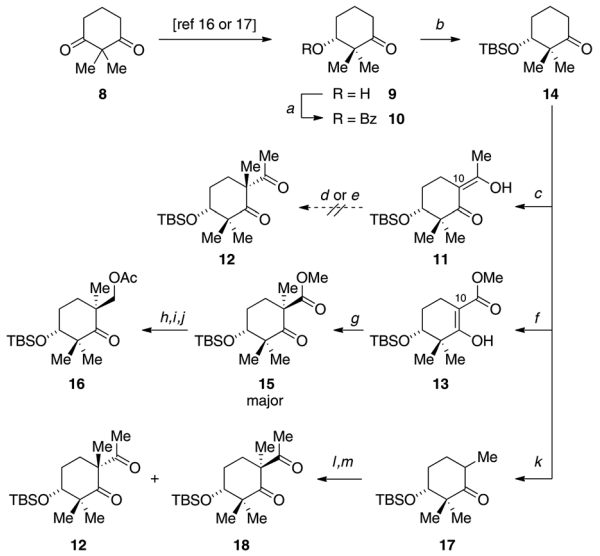
A convergent strategy was designed to access triterpenoid **1** (Scheme 1). The stereoselective installation of the methyl groups at a late stage of the synthesis was expected to be challenging, leading to the design of an intermediate, which would display all the requisite tertiary and quaternary stereocenters, and be versatile to enable exploration of the cyclization step delivering the central core. It was expected that the nine-membered ring of **1** could arise from a Nozaki–Hiyama–Kishi coupling of aldehyde **3**. The seven-membered ring ketone could be accessed by an ozonolysis of alkene **4**, which could in turn originate from a Heck reaction on a derivative of ketone **5**. Ketone **5** was chosen as a pivotal intermediate, which could be disconnected further into two fragments of similar sizes and complexities, aldehyde **6** and ketone **7**. Herein the enantioselective syntheses of these two fragments is reported as well as their coupling and the elaboration to ketone **5** bearing 6 stereocenters.

Synthesis of aldehyde 6

In a first approach, diketone **8** was desymmetrized to keto-alcohol **9**. This could be accomplished by (*S*)-(−)-2-butyl-CBS-oxazaborolidine mediated reduction,[16] or by enzymatic resolution of the *cis*-diol derived from diketone **8** (Scheme 2).[17] The ee was determined on benzoate **10**, and evaluated to be 94% for the enzymatic sequence, readily applicable on a large scale. Diketone **11** was obtained in two steps from keto-alcohol **9**.[18] Unfortunately, methylation of diketone **11** gave a complex mixture of *O*- and *C*-methylated compounds, and the desired diketone **12** could not be isolated. Keto-ester **13** was also generated from ketone **14** and could be easily methylated to keto-ester **15**. Disappointingly, after further synthetic elaboration to keto-acetate **16**, the major product was found to be the undesired diastereoisomer, with a dr of 3.4 : 1. The stereochemistry was established by comparison with the epimer obtained *via* another synthetic route (*cf.* the ESI‡ for details). Introduction of the substituents in a reverse order was then attempted. Hence, different conditions were screened to obtain diketone **12** from α-methylated ketone **17** (Table S1‡). Ketone **18** could be obtained as a single diastereoisomer (Table S1,‡ entries 1–3), enabling determination of its relative stereochemistry by NOESY analysis. Disappointingly, a 1 : 1 mixture of diastereoisomers **12** and **18** was obtained at best. The synthesis was nevertheless pursued from this mixture.

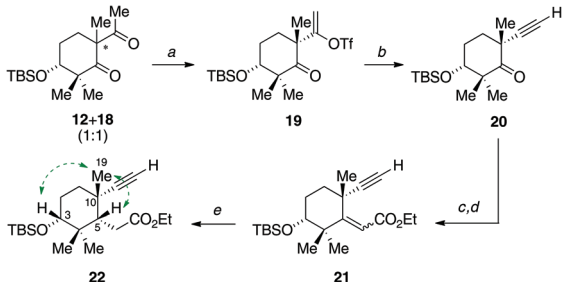


Scheme 1 Retrosynthetic strategy to schiglautone A.



Scheme 2 Methylation attempts at C(10). Reagents and conditions: (a) Et_3N, BzCl, DMAP, DCM, rt, 36 h, 89%, 93.8% ee with ref. 17; (b) 2,6-lutidine, TBSOTf, DCM, 0 °C, 4 h, 86%; (c) LDA, MeC(O)CN, THF, −78 °C, 1.25 h, 76%; (d) KH, 18-c-6, DME, MeI, 0 °C to rt, 12 h; (e) NaH, MeI, THF, 0 °C to rt, 12 h; (f) NaH, dimethyl carbonate, THF, 70 °C, 12 h, 96%; (g) NaH, HMPA, MeI, THF, rt, 1.25 h; (h) $LiAlH_4$, THF, 0 °C, 3 h; (i) Ac_2O, pyridine, rt, 30 min; (j) PCC, DCM, rt, 12 h, 57% over 4 steps, dr = 3.4 : 1; (k) LDA, HMPA, MeI, THF, −78 °C to rt, 12 h, 96%; (l) LDA, TMEDA, MeCHO, THF, −78 °C to −20 °C, 4 h; and (m) PCC, DCM, rt, 12 h, 71%, dr = 1 : 1.

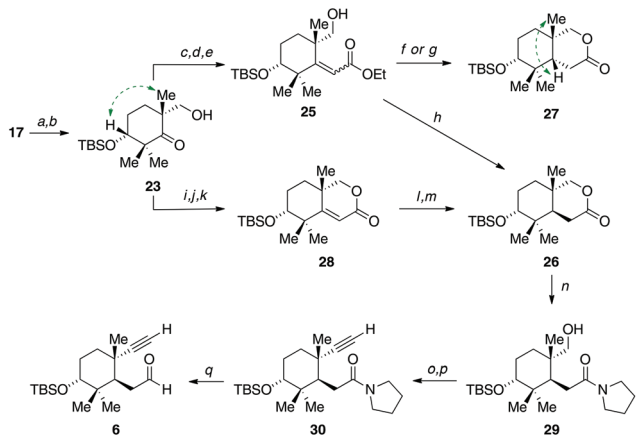
Treatment of the diketones with KHMDS and phenyltriflimide delivered enol triflate **19**, which could be separated easily from its diastereoisomer by column chromatography (Scheme 3).[19] It was further converted to alkyne **20** by heating in pyridine.[20] The undesired enol triflate could be recycled to ketone **17** under basic conditions.[21] The next task was the functionalization of the sterically hindered ketone moiety. To this end, deprotonated ethoxyethyne was added onto the ketone. The resulting alkynols underwent a Meyer–Schuster rearrangement when treated with a catalytic amount of $Sc(OTf)_3$, leading to the formation of enoate **21** as a mixture of (*E*) and (*Z*) isomers.[22] Next, conjugate reduction was attempted to introduce the last stereocenter. No conversion was observed when exposing enoate **21** to an excess of Stryker's reagent.[23] Furthermore, treatment with Mg/MeOH afforded exclusively the undesired diastereoisomer **22**, as was established by NOESY analysis.[24] Since the presence of the alkyne moiety



Scheme 3 Attempted conjugate reduction. Reagents and conditions: (a) KHMDS, $PhNTf_2$, THF, −78 °C, 2 h, 47% (46% of undesired diastereoisomer); (b) pyridine, 60 °C, 36 h, 91%; (c) ethoxyethyne, *n*-BuLi, Et_2O, −78 °C to rt, 12 h, 80%, dr = 4 : 1; (d) $Sc(OTf)_3$ (1 mol%), DCM/EtOH (4 : 1), rt, 6 h, 69%, 5 : 4 mixture of (*E*) and (*Z*) isomers; and (e) Mg, MeOH, rt, 4 h, 80%. Green dashed arrows represent relevant NOESY correlations.

limited the choice of the reducing reagent and the steric bulk of the TBS-protected alcohol was speculated to block the approach of any reagent from the α-face, this route was abandoned in favor of an alternative approach.

The introduction of a hydroxymethyl group at C(10) was surmised to direct the formation of the stereocenter at C(5). Therefore keto-alcohol **23** was required as a precursor of aldehyde **6**, and introduction of a hydroxymethyl moiety at C(10) was investigated (Scheme 4, Table S2‡). Only very modest

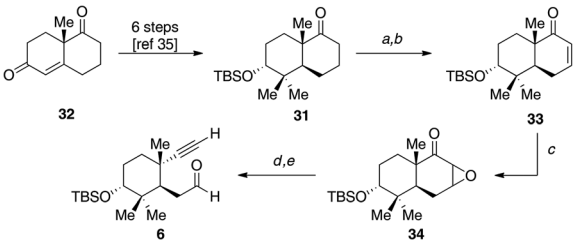


Scheme 4 First generation synthesis of aldehyde **6**. Reagents and conditions: (a) LDA, TMSCl, THF, −20 °C to rt, 4.5 h; (b) $Sc(OTf)_3$, formalin, THF, rt, 1 h, 64% over 2 steps, dr = 1.3 : 1; (c) Et_3N, TMSCl, DCM, 0 °C, 2 h, 94%; (d) ethoxyethyne, *n*-BuLi, Et_2O, −78 °C to rt, 12 h, 71%, dr > 99 : 1; (e) $Sc(OTf)_3$ (1 mol%), DCM/EtOH (4 : 1), rt, 20 min, 93%; (f) KOH, Pd/C (2 mol%), dioxane/H_2O (1 : 1), H_2, rt, 12 h, 68%, dr > 99 : 1; (g) Li, NH_3, *t*BuOH, Et_2O, −78 °C, 5 min, 65%, dr > 99 : 1; (h) [Ir(cod)(PCy_3)(pyr)]PF_6 (20 mol%), $B(OiPr)_3$, 4 Å m.s., DCE, H_2 (1 atm), 80 °C, 24 h, 35%, dr > 99 : 1; (i) Et_3N, DMAP (cat.), Ac_2O, DCM, rt, 2 h, 96%; (j) LDA, THF, −78 °C, 2 h, 94%; (k) pyridine, $SOCl_2$, DCM, 0 °C, 45 min, 77%; (l) Li, liq. NH_3, THF/*t*BuOH (2.5 : 1), −78 °C to −33 °C, 3 h; (m) Ag_2CO_3 (50% on Celite), toluene, 115 °C, 4 h, 54% **26** and 22% **27** over 2 steps (dr = 2.5 : 1); (n) Et_3N, pyrrolidine, 80 °C, 12 h, 70%; (o) DMP, DCM, 0 °C, 1 h, 97%; (p) dimethyl(diazomethyl)phosphonate, KO*t*Bu, THF, −78 °C to rt, 12 h, 91%; and (q) $Ti(OiPr)_4$, Ph_2SiH_2, rt, 12 h, 61%. Green dashed arrows represent relevant NOESY correlations.

diastereoselectivity in favor of **23** was observed. However, both isomers could be separated by column chromatography, the stereochemistry determined by NOESY analysis, and the undesired isomer **24** could be recycled by retro-aldol to give back ketone **17**. With the C(10) stereocenter introduced, the next goal was the installation of the stereocenter at C(5). Hence, keto-alcohol **23** was derivatized to enoate **25** following a similar sequence of reactions as previously described (Scheme 4).

To accomplish the directed hydrogenation of the enoate moiety of **25**, Crabtree's iridium catalyst was selected as the reagent of choice.[25] Therefore, enoate **25** was subjected to 5 mol% of Crabtree's catalyst under 1 atm of H_2. To our dismay, only 15% conversion was observed after 24 h, and the isolated product was lactone **26**. Increasing the H_2 pressure, the catalyst loading or exchanging the counteranion to the less coordinating BArF (tetrakis[3,5-bis(trifluoromethyl)phenyl] borate) did not generate any improvement.[26] Thereby the use of additives was then explored. As the ester moiety could compete with the hydroxyl group for coordination to the iridium complex, it was surmised that the presence of a Lewis acid such as $B(OiPr)_3$ could help circumvent this issue and increase the catalytic turnover, as previously reported.[27] Employing an equivalent of $B(OiPr)_3$ in combination with 20 mol% Crabtree's catalyst and molecular sieves at 80 °C increased the yield to 35%. Once again, no change in the reaction parameters enabled a higher conversion, as it seemed that the cyclization to the lactone, which occurred during the course of the reaction, precluded hydrogenation from proceeding further. However, the selectivity was the desired one, and the formation of diastereoisomer **27** was not observed. In contrast, other methods such as Pd/C catalyzed hydrogenation or Birch reduction gave **27** as the major product (Scheme 4).[28]

As the implementation of this directed hydrogenation strategy proved more complicated than planned, a new approach was investigated. Given the observed facile formation of the lactone and the documented favored formation of the *trans*-decalone system under thermodynamic conditions, it was speculated this result may also apply to an unsaturated lactone.[29] Henceforth, unsaturated lactone **28** was prepared in 3 steps from keto-alcohol **23** (Scheme 4). Exposure of the substrate to Birch-type conditions enabled complete conversion to a mixture of over-reduced lactols, which were re-oxidized immediately with Fetizon's reagent to give a 2.5 : 1 mixture of lactones **26** and **27**.[30] When the reaction was conducted at −78 °C, only partial conversion of the starting material was observed, even after 3 hours. Although only the desired epimer **26** was formed in that case, it could not be separated from the unsaturated lactone **28**, whereas the two epimers **26** and **27** could be easily isolated. In contrast, treating the unsaturated lactone **28** with catalytic Pd/C under a H_2 atmosphere only led to the formation of **27**. Further elaboration to aldehyde **6** entailed opening of the lactone, which was accomplished by using pyrrolidine and Et_3N, as formation of a Weinreb amide under standard conditions did not occur.[31] After oxidation of the alcohol moiety of **29** to an aldehyde, this latter could be



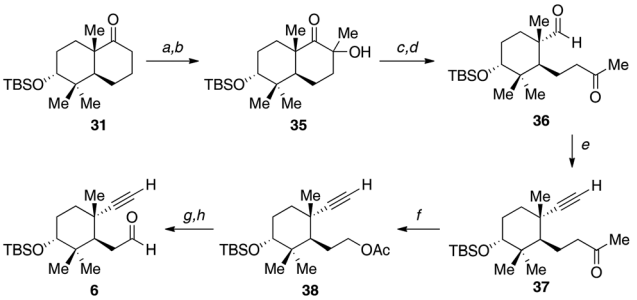
Scheme 5 Eschenmoser–Tanabe fragmentation. Reagents and conditions: (a) LDA, TMSCl, Et_3N, 0 °C, 2 h; (b) $Pd(OAc)_2$, MeCN, rt, 12 h, 56% over 2 steps, 85% brsm; (c) 5 M aq. NaOH, 30% H_2O_2, MeOH, 0 °C, 5 h, 92%, dr = 3 : 1; (d) $H_2NC(O)NHNH_2{\cdot}HCl$, $NaOAc{\cdot}3H_2O$, EtOH/H_2O (2 : 1), rt, 12 h; and (e) $Pb(OAc)_4$, DCM, −10 °C, 4 h, 29% over 2 steps.

converted to the terminal alkyne **30** in good yield with the Seyferth–Gilbert reagent.[32] The amide moiety was then selectively reduced to aldehyde **6** by treatment with neat $Ti(OiPr)_4$ and diphenylsilane.[33]

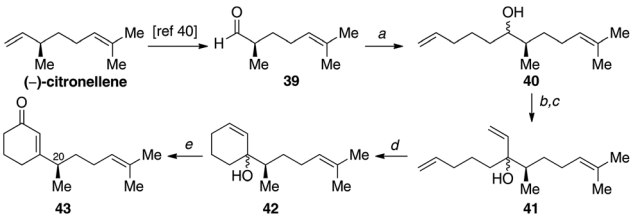
Altogether, while this strategy resulted in the formation of aldehyde **6**, it suffered a lack of selectivity, both in the hydroxymethylation step and in the saturated lactone reduction, rendering scale-up tedious. As a result, an alternative approach was explored, starting from a different building block.

Ketone **31** was thus chosen as it bears the three requisite stereocenters of aldehyde **6** and can be easily derived from the Wieland–Miescher ketone **32** (Scheme 5).[34] At first, an Eschenmoser–Tanabe fragmentation was considered. Enone **33** was accessed by a Saegusa oxidation of ketone **31**.[35] Nucleophilic epoxidation delivered keto-epoxide **34** as a mixture of diastereoisomers.[36] While several attempts at forming the corresponding hydrazone were hampered, presumable by the presence of the neighboring quaternary stereocenter,[37] oxidative fragmentation was achieved by employing a semi-carbazone.[38] Application of this protocol resulted in the formation of a complex mixture of products. Nevertheless, the desired aldehyde **6** was isolated, albeit in a modest yield of 29% over 2 steps. The low yield and poor scalability of this sequence prompted the examination of an alternative route.

α-Methylation of ketone **31** was followed by α-oxygenation using molecular oxygen in the presence of triethylphosphite to afford keto-alcohol **35** in excellent yield and as an inconsequential mixture of diastereoisomers (Scheme 6).[39] This latter was reduced to the corresponding diols, which underwent oxidative cleavage upon treatment with $Pb(OAc)_4$ to give keto-aldehyde **36**. This was converted to the corresponding alkyne **37** by Seyferth–Gilbert homologation.[32] Baeyer–Villiger oxidation with *m*-CPBA furnished the dehomologated acetate **38**, which was elaborated to aldehyde **6** by acetate deprotection and re-oxidation. This final route allowed convenient and stereoselective access to aldehyde **6**. Next, attention was dedicated to the preparation of the second envisioned building block, ketone **7**.



Scheme 6 Final route to aldehyde **6**. Reagents and conditions: (a) LDA, MeI, THF, −78 °C to rt, 5 h, 96%, dr > 99 : 1; (b) LiHMDS, $P(OEt)_3$, O_2 (1 atm), THF, −78 °C to −30 °C, 6 h, 97%, dr = 1.4 : 1; (c) $NaBH_4$, MeOH, 0 °C, 30 min, 97%, dr = 4.8 : 2 : 1.4 : 1; (d) $Pb(OAc)_4$, DCM, rt, 40 min, 77%; (e) KO*t*Bu, dimethyl(diazomethyl)phosphonate, THF, −78 °C to rt, 13 h, 74%; (f) *m*-CPBA, DCM, rt, 48 h, 55%; (g) K_2CO_3, MeOH, rt, 2 h, 71%; and (h) $EtN(iPr)_2$, DMSO, SO_3·pyridine, DCM, 0 °C, 20 min, 81%.

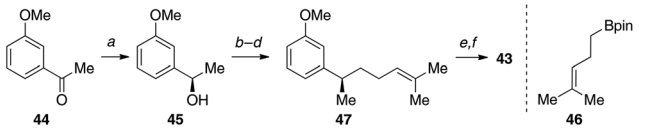


Scheme 7 First route to enone **43**. Reagents and conditions: (a) Mg, 5-bromo-1-pentene, THF, rt, then −78 °C to 0 °C, 1 h, 37% from (−)-citronellene; (b) DMP, pyridine, DCM, 0 °C to rt, 2 h; (c) vinyl magnesium bromide, THF, −78 °C to rt, 5 h, 71% over 2 steps; (d) Grubbs I (2 mol%), DCM, rt, 12 h; and (e) PCC, SiO_2, DCM, rt, 8 h, 49% over 2 steps, 69% ee.

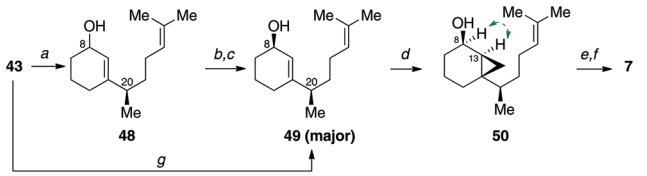
Synthesis of ketone 7

Controlling the stereochemistry of two contiguous tertiary and quaternary stereocenters represents a significant synthetic challenge. Hence it was first envisioned to start the synthesis of ketone **7** from (−)-citronellene, which would furnish the first tertiary stereocenter. (−)-Citronellene was first converted to aldehyde **39** in two steps (Scheme 7).[40] The Grignard addition of 5-bromo-1-pentene followed immediately, to give alcohol **40**. After oxidation to the ketone, a second Grignard addition was performed to deliver diene **41**. Ring-closing metathesis proceeded smoothly with either Grubbs I or Grubbs II catalysts to give allylic alcohol **42**.[41] Oxidative transposition afforded enone **43**. Before installing the quaternary center, assessment of the enantiopurity of the product was conducted. Disappointingly, enone **43** displayed an ee of 69%, indicating that partial racemization had occurred.

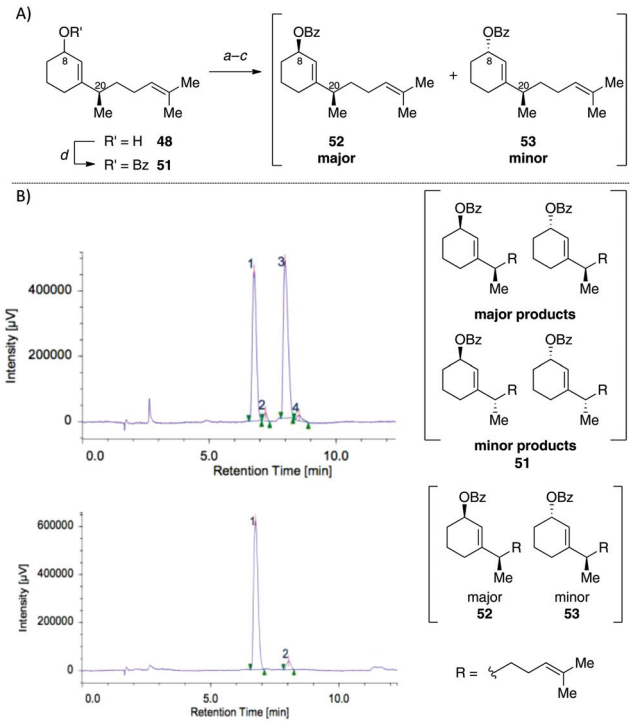
In a revised strategy, the lithiation–borylation protocol developed by Aggarwal *et al.* was implemented to introduce the tertiary stereogenic center, relying on a chirality transfer from a secondary alcohol to the methyl group.[42] Thereby, 3-methoxyacetophenone **44** was reduced using Noyori's catalyst to deliver secondary alcohol **45** with 98% ee (Scheme 8).[43] The carbamate derived from alcohol **45** was treated successively with *s*-BuLi and boronate ester **46**, and addition of $MgBr_2$ in methanol enabled 1,2-alkyl migration. The intermediate boronic ester thus obtained was immediately protodeboronated by



Scheme 8 Second route to enone **43**. Reagents and conditions: (a) {RuCl[(*R*,*R*)-TsDPEN](mesitylene)} (0.5 mol%), HCOOH/Et_3N (5 : 2), 0 °C to rt, 50 h, 99%, 98% ee; (b) $(iPr)_2NC(O)Cl$, Et_3N, toluene, 150 °C (sealed tube), 2 h, 98%; (c) *s*-BuLi, **46**, Et_2O, −78 °C, 2 h, then $MgBr_2$, MeOH, −78 °C to rt, 4 h; (d) TBAF·$3H_2O$, toluene, 50 °C, 12 h, 82% over 2 steps; (e) Li, NH_3, THF/EtOH (10 : 1), −78 °C, 1 h; and (f) 1 M aq. HCl, THF, rt, 12 h, 67% over 2 steps, 90% ee. DPEN = 1,2-diphenyl-1,2-ethylenediamine.



Scheme 9 Synthesis of ketone **7**. Reagents and conditions: (a) $CeCl_3·7H_2O$, $NaBH_4$, MeOH, 0 °C, 25 min, quant.; (b) vinyl acetate, lipase Amano AK, 4 Å m.s., *n*-hexane, rt, 7.5 h, 46%, dr = 17 : 1; (c) K_2CO_3, MeOH, rt, 2 h, 93%; (d) Et_2Zn, CH_2I_2, *n*-BuLi, Et_2O/benzene (1 : 1), −20 °C to rt, 24 h, 66%, dr > 99 : 1; (e) PCC, DCM, rt, 2.5 h, 79%; (f) Li, NH_3, THF, −78 °C to −20 °C, 30 min, 71%; and (g) CBS, BH_3·DMS, THF, 0 °C, 15 min, 74%. Green dashed arrows represent relevant NOESY correlations.



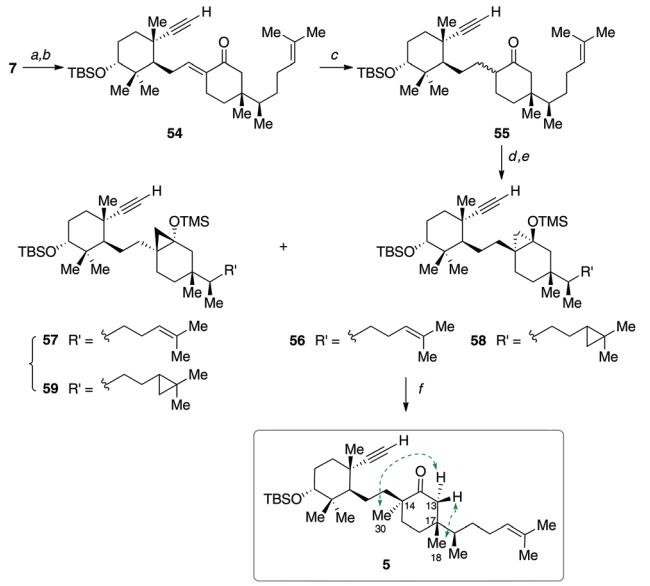
Scheme 10 Determination of the stereochemical outcome of the enzymatic resolution. (A) Reagents and conditions: (a) vinyl acetate, lipase Amano AK, 4 Å m.s., *n*-hexane, rt, 7.5 h, 46%, dr = 17 : 1; (b) K_2CO_3, MeOH, rt, 2 h, 93%; (c) BzCl, Et_3N, DCM, rt, 12 h, 96%; and (d) BzCl, Et_3N, DCM, rt, 12 h, 85%. (B) SFC chromatograms of **51** and the inseparable mixture of **52** and **53**. Full experimental details are provided in the ESI.‡

treatment with TBAF·$3H_2O$ in toluene at 50 °C to give substituted anisole **47** in good yield and with a satisfying ee of 90%.[44] Reduction of the arene under Birch conditions and subsequent acidic treatment delivered enone **43**. The enantiomeric excess of **43** was verified by chiral SFC, in comparison with the racemate prepared by a literature procedure.[45]

Initial attempts to introduce the remaining methyl group by copper-catalyzed conjugate addition of $AlMe_3$ in the presence of a chiral phosphoramidite ligand led to only modest diastereoselectivity.[46] Therefore the installation of the methyl group by cyclopropane opening was chosen. Enone **43** was reduced to allylic alcohol **48** under Luche conditions (Scheme 9). The mixture of inseparable diastereoisomers was subjected to enzymatic resolution with lipase AK Amano in the presence of vinyl acetate.[47] The acetylated compound was deprotected to give allylic alcohol **49**, which was subjected to directed cyclopropanation to provide alcohol **50** in satisfying yield.[48] Oxidation to the ketone and subsequent reductive opening of the cyclopropane under Birch conditions gave ketone **7**, bearing the two desired stereocenters.[49] Analysis of the enzymatic resolution was made by chiral SFC analysis (Scheme 10, *cf.* the ESI‡ for SFC chromatograms). First, allylic alcohol **48** was benzoylated to give **51** as a mixture of four diastereoisomers, the two major products being the epimers at C(8) (Scheme 10A). Similarly, the acetate resulting from the enzymatic resolution was deprotected and the resulting alcohol benzoylated. By comparison with the SFC chromatogram of **51**, which displays 4 diastereoisomers, the two products of the enzymatic resolution were found to be **52** and **53**, and the dr evaluated to 17 : 1 (Scheme 10B). In order to confirm the absolute configuration of **52** and **53**, enone **43** was also reduced with (*S*)-Me-CBS.[50] The major isomer resulting from this reduction was found to be **49**. As the outcome of this reduction is independent of the side chain, this result corroborated the determination of the diastereoisomers obtained by enzyme-catalyzed reduction. It is noteworthy that the enzymatic resolution not only discriminated based on the stereochemistry at C(8) but also led to selective acetylation of the desired epimer at C(20).

Coupling of the two fragments and elaboration to ketone 5

With the synthesis of the second fragment completed and the stereochemistry fully determined, coupling of the two fragments was pursued. Aldol addition between aldehyde **6** and an excess of ketone **7** proceeded smoothly (Scheme 11). The inseparable mixture of unreacted ketone **7** and aldol product was subjected to dehydratation with TFAA and DBU.[51] This two step sequence yielded enone **54** in 64% yield. Conjugate reduction was accomplished with LAH/CuI and delivered ketone **55**.[52] The corresponding thermodynamic silyl enol ether was generated, and subjected to cyclopropanation with Furukawa's reagent.[53] A preference for cyclopropanation from



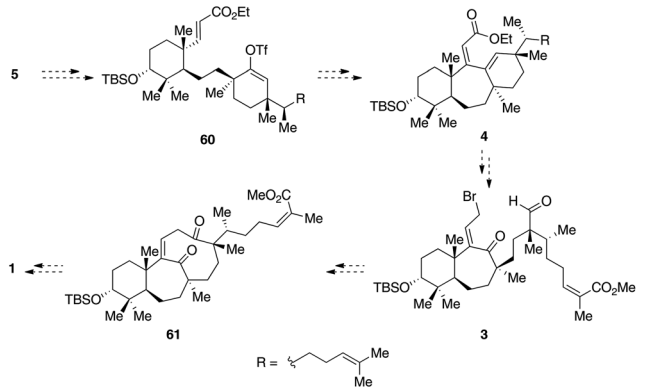
Scheme 11 Synthesis of ketone **5**. Reagents and conditions: (a) LDA, THF, −78 °C, 1 h, then **3**, −78 °C, 15 h; (b) pyridine, TFAA, benzene, 5 °C, 30 min, then DBU, 1 h, 64% over 2 steps, single isomer; (c) CuI, LAH, THF, 0 °C, 10 min, 69%, dr = 2 : 1; (d) Et_3N, TMSCl, NaI, MeCN, rt, 4 h, 88%; (e) Et_2Zn, CH_2I_2, toluene, 0 °C to rt, 1.5 h, 21% **56**, 31% **58**, *ca.* 13% **57** + **59**, 10% **55**; and (f) aq. NaOH, EtOH, 100 °C, 12 h, 69%. Green dashed arrows represent relevant NOE correlations.

the face opposite to the methyl group at C(17) was observed, affording the desired enol silane cyclopropanated product **56** along with diastereoisomer **57** (the relative stereochemistry was determined in the next step). Cyclopropanation of the prenyl group on the side chain also occurred as a side reaction, yielding derivatives **58** and **59**. The desired silyl ether **56** could be isolated and the cyclopropane was opened to reveal the ketone moiety. The determination of the newly formed quaternary center was accomplished by NOE analysis. The installation of this last stereocenter completed the synthesis of the key intermediate **5**. Pleasingly, **5** was obtained as a single diastereoisomer, which should facilitate the exploration of the cyclization step toward the formation of the 7-membered ring.

Conclusion

This pivotal intermediate was designed to be a versatile platform to study the construction of the central core of schiglautone A. The alkyne moiety offers a convenient handle to further functionalize ketone **5**. Several approaches can be envisioned, such as converting terminal alkyne **5** into enoate **60**, which should allow for an intramolecular 7-*exo* Heck cyclization (Scheme 12). Ozonolysis and conversion of the ester to a bromide could afford aldehyde **3**. A Nozaki–Hiyama–Kishi coupling could complete the formation of the tricyclic core **61**, leading ultimately to target **1**.

In summary, after exploration of several routes, the two building blocks, aldehyde **6** and ketone **7**, were successfully



Scheme 12 Possible strategy to schiglautone A from final intermediate **5**.

synthesized in a stereoselective fashion. After their coupling, the last quaternary stereocenter was introduced to give the envisioned ketone **5**, which serves as a pivotal intermediate in the synthesis of schiglautone A. This highly functionalized compound possesses all the tertiary and quaternary stereocenters of the natural product and can be used to explore various strategies to complete the synthetic target; thereby its synthesis represents a significant milestone towards the total synthesis of schiglautone A.

Experimental section

For structures of compounds **62** to **75**, general methods and full experimental data, see the ESI.‡

(4a*S*,6*R*,8a*S*)-6-((*tert*-Butyldimethylsilyl)oxy)-5,5,8a-trimethyl-4a,5,6,7,8,8a-hexahydronaphthalen-1(4*H*)-one (33)

n-BuLi (1.6 M in hexanes, 6.24 mL, 9.98 mmol) was added dropwise to a solution of $(iPr)_2NH$ (1.54 mL, 10.8 mmol) in THF (10 mL) at 0 °C. The resulting yellow solution was stirred at 0 °C for 30 min. A solution of **31** (2.70 g, 8.32 mmol) in THF (11 mL) was then added dropwise. The solution was stirred at 0 °C for 30 min, before dropwise addition of a mixture of TMSCl (2.13 mL, 16.6 mmol) and Et_3N (2.32 mL, 16.6 mmol) in THF (5 mL). The solution was stirred at 0 °C for 1 h, and then poured into a mixture of sat. aq. $NaHCO_3$ and hexanes (1 : 1). The aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford a yellow oil that was used directly in the next step.

The crude product from the previous step was dissolved in MeCN (78 mL) and treated with $Pd(OAc)_2$ (2.80 g, 12.5 mmol). The mixture was then stirred at rt for 12 h, filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexane/EtOAc, 15 : 1) to give **33** (1.50 g, 56%) as a white solid. R_f = 0.33 (hexane/EtOAc, 10 : 1); melting point: 77–79 °C; ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 6.92 (ddd, J = 10.0, 4.7, 3.2 Hz, 1H), 5.89 (dt, J = 10.0, 2.0 Hz, 1H), 3.41–3.39 (m, 1H), 2.29–2.26 (m, 2H),

2.14–2.10 (m, 1H), 1.93–1.83 (m, 2H), 1.59–1.54 (m, 1H), 1.07 (s, 3H), 0.98 (s, 3H), 0.90 (s, 3H), 0.88–0.84 (m, 1H), 0.87 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 206.0, 149.1, 127.8, 76.1, 45.2, 42.6, 38.7, 28.5, 26.1 (3C), 25.8, 25.3, 24.4, 22.6, 18.3, 17.5, −4.2, −4.8 ppm; IR (thin film): ν 3034, 2931, 2857, 1671, 1461, 1387, 1251, 1062, 1016, 833, 771 cm^{-1}; HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{19}H_{35}O_2Si$ 323.2401, found 323.2399; $[\alpha]_D^{23}$ −47.1 (*c* 1.00, $CHCl_3$).

(2a*S*,5*R*,6a*S*)-5-((*tert*-Butyldimethylsilyl)oxy)-2a,6,6-trimethyl octahydronaphtha[2,3-*b*]oxiren-2(1a*H*)-one (34)

H_2O_2 (30% in water, 0.600 mL, 5.90 mmol) was added dropwise to a solution of **33** (634 mg, 1.97 mmol) in MeOH (20 mL) at 0 °C. The mixture was stirred for 5 min, before NaOH (5 M in water, 0.790 mL, 3.93 mmol) was added dropwise. The mixture was stirred at 0 °C for 5 h, and then poured into a mixture of ice and brine. The aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford **34** (612 mg, 92%) as a 3 : 1 mixture of diastereoisomers. R_f = 0.18 and 0.37 (hexane/EtOAc, 16 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 3.63–3.61 (m, 0.25H), 3.54–3.52 (m, 0.75H), 3.39–3.37 (m, 0.75H), 3.33–3.32 (m, 0.25H), 3.17–3.15 (m, 1H), 2.21 (dt, *J* = 14.7, 2.9 Hz, 1H), 2.11–1.91 (m, 2H), 1.88–1.74 (m, 2H), 1.58–1.51 (m, 2H), 1.18 (s, 0.75H), 1.04 (s, 2.25H), 0.92–0.86 (m, 6H), 0.89–0.87 (m, 10H), 0.03–0.01 (m, 6H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz, the asterisk denotes minor diastereoisomer signals): δ 210.9*, 207.9, 76.1*, 75.9, 58.2*, 53.8*, 52.9, 51.9, 46.2, 46.0*, 45.4, 39.3*, 38.2, 32.2, 29.0, 28.9*, 26.9*, 26.1 (6C), 25.7, 25.1, 24.9*, 23.0, 22.0*, 21.2, 20.9*, 18.3*, 17.8, 17.7*, −4.2*, −4.2, −4.8, −4.8* ppm; IR (thin film): ν 2951, 2856, 1706, 1461, 1363, 1252, 1076, 1007, 832, 772, 674 cm^{-1}; HRMS (ESI) *m*/*z*: $[M + H]^+$ calcd for $C_{19}H_{35}O_3Si$ 339.2350, found 339.2353.

2-((1*R*,3*R*,6*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclohexyl) acetaldehyde (6)

Semicarbazide hydrochloride (717 mg, 6.43 mmol) and NaOAc·3H_2O (230 mg, 1.69 mmol) were added to a solution of **33** (272 mg, 0.803 mmol) in water/EtOH (1 : 2, 2.7/5.4 mL). The mixture was stirred at rt for 12 h. EtOH was removed under reduced pressure and DCM was added. The aqueous layer was extracted three times with DCM. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford a semi-carbazone that was used directly in the next step without purification.

The residue was dissolved in DCM (5.1 mL) at −10 °C. $Pb(OAc)_4$ (277 mg, 0.607 mmol) was added in one portion, and the mixture was stirred at −10 °C for 4 h. Ice-cold water was added, followed by 2 M HCl (1.5 mL). The mixture was stirred at 0 °C for 30 min, and then filtered through a pad of Celite, washing DCM. The aqueous layer was extracted three times with DCM. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexane/DCM, 2 : 1) to afford **6** (52 mg, 29% over 2 steps) as a yellow oil. R_f = 0.30 (hexane/EtOAc, 10 : 1); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 9.74 (dd, *J* = 3.3, 1.8 Hz, 1H), 3.42–3.41 (m, 1H), 2.66–2.57 (m, 2H), 2.39 (ddd, *J* = 17.9, 8.0, 3.3 Hz, 1H), 2.33–2.22 (m, 1H), 2.14 (s, 1H), 1.87–1.75 (m, 1H), 1.58–1.45 (m, 2H), 1.20 (s, 3H), 0.93 (s, 9H), 0.85 (s, 3H), 0.82 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 203.8, 93.6, 75.7, 68.9, 42.8, 41.8, 39.2, 35.6, 33.1, 29.3, 26.1 (3C), 25.4, 22.5, 21.8, 18.4, −4.2, −4.7 ppm; IR (thin film): ν 3312, 2954, 2858, 1726, 1472, 1254, 1080, 835 cm^{-1}; HRMS (ESI) *m*/*z*: $[M + Na]^+$ calcd for $C_{19}H_{34}NaO_2Si$ 345.2220, found 345.2222; $[\alpha]_D^{21}$ −65.3 (*c* 1.05, $CHCl_3$).

(4a*S*,6*R*,8a*S*)-6-((*tert*-Butyldimethylsilyl)oxy)-2,5,5,8a-tetramethyloctahydro-naphthalen-1(2*H*)-one (69)

n-BuLi (1.6 M in hexane, 6.00 mL, 9.60 mmol) was added dropwise to a solution of $(iPr)_2NH$ (1.67 mL, 11.9 mmol) in THF (30 mL) at 0 °C. The light yellow solution was stirred at 0 °C for 10 min, then cooled to −78 °C. Ketone **31** (1.80 g, 5.53 mmol) in THF (9.7 mL) was added dropwise, and the resulting solution was stirred at −78 °C for 1 h. Then MeI (2.49 mL, 40.0 mmol) was added dropwise and the mixture let to warm up to rt over 4 h. Sat. aq. NH_4Cl was added, followed by Et_2O. The aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexane/EtOAc, 25 : 1) to give **69** (2.59 g, 96%) as a single diastereoisomer. R_f = 0.56 (hexane/EtOAc, 12 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 3.35 (br s, 1H), 2.70–2.60 (m, 1H), 2.11–2.03 (m, 2H), 1.87–1.79 (m, 1H), 1.72–1.60 (m, 3H), 1.58–1.51 (m, 1H), 1.29–1.18 (m, 2H), 1.11 (d, *J* = 0.5 Hz, 3H), 0.98 (d, *J* = 6.4 Hz, 3H), 0.91 (s, 3H), 0.88 (s, 9H), 0.87 (s, 3H), 0.04 (s, 3H), 0.01 (s, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 216.5, 76.3, 48.6, 47.4, 40.1, 39.4, 35.8, 29.3, 26.4, 26.1 (3C), 25.5, 22.5, 21.0, 19.1, 18.4, 15.2, −4.2, −4.8 ppm; IR (thin film): ν 2930, 2854, 1704, 1460, 1361, 1253, 1076, 831, 771, 673 cm^{-1}; HRMS (ESI) *m*/*z*: $[M + Na]^+$ calcd for $C_{20}H_{38}NaO_2Si$ 361.2533, found 361.2528.

(4a*S*,6*R*,8a*S*)-6-((*tert*-Butyldimethylsilyl)oxy)-2-hydroxy-2,5,5,8a-tetramethyloctahydronaphthalen-1(2*H*)-one (35)

LiHMDS (1 M in THF, 23.0 mL, 23.0 mmol) was added dropwise to a solution of ketone **69** (2.59 g, 7.65 mmol) in THF (76 mL) at −78 °C. The solution was stirred at −78 °C for 1 h. Then $P(OEt)_3$ (5.35 mL, 30.6 mmol) was added dropwise, and Ar was replaced by O_2. The solution was let to warm up to −30 °C and stirred at −30 °C for 5 h. 2 M HCl was added slowly, followed by EtOAc. The aqueous layer was extracted three times with EtOAc. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexane/EtOAc, 12 : 1) to give **35** (2.63 g, 97%) as a mixture of epimers, which were not separated (dr = 1.4 : 1). R_f = 0.25 and 0.37 (hexane/EtOAc, 8 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 3.37 (ddd, *J* = 10.0, 3.3, 1.9 Hz, 1H), 2.21–2.18 (m, 0.4H), 2.05–1.94 (m, 1.6H), 1.93–2.05 (m, 9H),

1.40 (s, 1.4H), 1.34 (s, 1.6H), 1.21 (1.6H), 1.15 (1.4H), 0.93 (s, 1.6H), 0.91 (s, 1.4H), 0.90 (s, 1.4H), 0.88 (s, 1.6H), 0.87 (m, 9H), 0.02–0.04 (m, 6H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 218.8, 218.1, 76.0, 76.0, 75.9, 74.4, 48.0, 47.4, 47.0, 41.7, 40.5, 39.5, 39.4, 34.5, 29.2, 28.8, 28.3, 27.8, 27.6, 27.3, 26.1 (3C), 26.1 (3C), 25.4, 25.3, 22.4, 22.0, 19.9, 19.0, 18.6, 18.3, 18.3, 16.7, −4.2 (2C), −4.8, −4.8 ppm; IR (thin film): ν 3427, 2927, 2856, 1692, 1460, 1253, 1083 cm^{-1}; HRMS (ESI) *m*/*z*: [M + Na]$^+$ calcd for $C_{20}H_{38}NaO_3Si$ 377.2482, found 377.2488.

(4a*S*,6*R*,8a*S*)-6-((*tert*-Butyldimethylsilyl)oxy)-2,5,5,8a-tetramethyldecahydro-naphthalene-1,2-diol (70)

$NaBH_4$ (561 mg, 14.8 mmol) was added portionwise to a solution of **35** (2.63 g, 7.42 mmol) in MeOH (37 mL) at 0 °C. The slurry was stirred at 0 °C for 30 min. MeOH was removed under reduced pressure, and the residue was diluted with sat. aq. $NaHCO_3$ and DCM. The aqueous layer was extracted three times with DCM. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford **70** (2.56 g, 97%) as an inconsequential mixture of 3 diastereoisomers, which were not separated (dr = 4.8 : 2 : 1.4 : 1). R_f = 0.13 and 0.18 (hexane/EtOAc, 8 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 3.36–3.34 (m, 1H), 3.18 (d, *J* = 3.0 Hz, 0.45H), 2.93 (d, *J* = 5.9 Hz, 0.30H), 2.87 (d, *J* = 5.3 Hz, 0.25H), 2.15 (td, *J* = 13.0, 3.7 Hz, 0.25H), 2.01–1.75 (m, 3H), 1.73 (dd, *J* = 12.6, 2.6 Hz, 0.35H), 1.67–1.62 (m, 0.75H), 1.57–1.39 (m, 5H), 1.36–1.31 (m, 1H), 1.29–1.25 (m, 1.35H), 1.23 (s, 0.9H), 1.21 (s, 1.35H), 1.16 (s, 0.75H), 1.01 (s, 0.9H), 0.91–0.90 (m, 9H), 0.87 (br s, 1.35H), 0.86 (br s, 0.75H), 0.86 (br s, 0.9H), 0.84 (br s, 0.9H), 0.83 (br s, 0.75H), 0.81 (br s, 1.35H), 0.05–0.02 (m, 6H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 87.0, 84.3, 83.6, 76.9, 76.5, 76.5, 74.0, 73.9, 72.7, 46.1, 46.0, 40.4, 39.6, 39.2, 39.2, 39.1, 39.0, 38.1, 38.1, 38.0, 36.4, 32.0, 31.8, 30.3, 29.6, 29.5, 29.4, 29.3, 28.5, 26.2 (3C), 26.2 (3C), 26.1 (3C), 25.6, 25.4, 25.4, 22.4, 22.3, 22.2, 22.1, 20.7, 19.6, 18.4, 18.4, 17.9, 17.5, 13.9, 13.8, −4.2, −4.3, −4.3, −4.7, −4.7, −4.7 ppm; IR (thin film): ν 3431, 2931, 2857, 1461, 1386, 1363, 1252, 1079, 1014, 934, 833, 771, 670 cm^{-1}; HRMS (ESI) *m*/*z*: [M + Na]$^+$ calcd for $C_{20}H_{40}NaO_3Si$ 379.2639, found 379.2638.

(1*S*,2*S*,4*R*)-4-((*tert*-Butyldimethylsilyl)oxy)-1,3,3-trimethyl-2-(3-oxobutyl)cyclo-hexanecarbaldehyde (36)

$Pb(OAc)_4$ (2.72 g, 5.83 mmol) was added in one portion to a solution of **70** (1.60 g, 4.49 mmol) in DCM (56 mL). The slurry was stirred at rt for 40 min, before being filtered through a pad of silica gel, washing Et_2O. The filtrate was washed with 5% $NaHSO_3$, sat. aq. $NaHCO_3$ and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexane/EtOAc, 10 : 1) to give **36** (1.23 g, 77%) as a single diastereoisomer. R_f = 0.15 (hexane/EtOAc, 15 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 9.28 (s, 1H), 3.42 (dd, *J* = 4.1, 1.9 Hz, 1H), 2.37 (app ddd, *J* = 17.1, 11.3, 5.7 Hz, 1H), 2.31–2.22 (m, 1H), 2.09 (s, 3H), 1.97 (td, *J* = 12.9, 3.8 Hz, 1H), 1.90–1.81 (m, 2H), 1.68 (ddt, *J* = 15.7, 11.2, 4.7 Hz, 1H), 1.52 (dq, *J* = 13.8, 3.8 Hz, 1H), 1.37–1.27 (m, 2H), 1.09 (s, 3H), 0.93 (s, 3H), 0.91 (s, 12H), 0.91–0.88 (m, 1H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 208.4, 206.2, 76.0, 50.3, 44.7, 41.0, 38.8, 30.1, 28.9, 26.1 (3C), 25.8, 24.7, 22.6, 20.9, 18.4, 15.0, −4.2, −4.7 ppm; HRMS (ESI) *m*/*z*: [M + H]$^+$ calcd for $C_{21}H_{39}O_2Si$ 351.2714, found 351.2712; $[\alpha]_D^{24}$ −84.7 (*c* 0.251, $CHCl_3$).

4-((1*R*,3*R*,6*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclohexyl)butan-2-one (37)

To a suspension of KO*t*Bu (467 mg, 4.17 mmol) in THF (10 mL) at −78 °C was added a solution of dimethyl(diazomethyl)phosphonate (781 mg, 5.20 mmol) in THF (10 mL). The mixture was stirred for 10 min; then a solution of **36** (1.23 g, 3.47 mmol) in THF (23 mL) was added dropwise. The mixture was stirred at −78 °C for 12 h, then warmed up to rt. Water and Et_2O were added. The aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexane/EtOAc, 20 : 1) to give alkyne **37** (906 mg, 74%). R_f = 0.32 (hexane/EtOAc, 12 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 3.37–3.35 (m, 1H), 2.88–2.79 (m, 1H), 2.55–2.47 (m, 1H), 2.21–2.14 (m, 1H), 2.14 (s, 3H), 2.08 (s, 1H), 1.83–1.74 (m, 1H), 1.73–1.40 (m, 6H), 1.22 (s, 3H), 0.92 (s, 9H), 0.87 (s, 3H), 0.85 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 209.6, 94.9, 75.9, 67.2, 47.5, 46.4, 39.8, 35.4, 33.8, 30.1, 29.1, 26.1 (3C), 25.4, 22.3, 21.7 (2C), 18.4, −4.2, −4.7 ppm; IR (thin film): ν 3257, 2954, 2885, 2857, 1709, 1471, 1357, 1256, 1075, 1029, 1007, 833, 778 cm^{-1}; HRMS (ESI) *m*/*z*: [M + H]$^+$ calcd for $C_{21}H_{39}O_2Si$ 351.2714, found 351.2712; $[\alpha]_D^{23}$ −29.5 (*c* 0.520, $CHCl_3$).

2-((1*R*,3*R*,6*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclohexyl)ethyl acetate (38)

m-CPBA (108 mg, 0.626 mmol) was added to a solution of **37** (209 mg, 0.596 mmol) in DCM (6.0 mL) at 0 °C. The white slurry was allowed to warm up to rt and stirred for 48 h. The mixture was cooled to 0 °C, diluted with DCM, and sat. aq. $NaHCO_3$ and sat. aq. $Na_2S_2O_3$ were added. The aqueous layer was extracted three times with DCM. The organic phase was washed with sat. aq. $NaHCO_3$ and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexane/EtOAc, 20 : 1) to give **38** (120 mg, 55%). R_f = 0.44 (hexane/EtOAc, 10 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 4.25–4.13 (m, 2H), 3.38 (br s, 1H), 2.22–2.15 (m, 1H), 2.10 (s, 1H), 2.04 (s, 3H), 1.84–1.75 (m, 1H), 1.74–1.63 (m, 1H), 1.52–1.42 (m, 2H), 1.22 (s, 3H), 0.92 (s, 9H), 0.90 (s, 3H), 0.84 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 171.2, 94.3, 75.7, 67.4, 66.6, 43.0, 39.4, 35.4, 33.6, 29.1, 26.8, 26.1 (3C), 25.4, 22.4, 21.7, 21.2, 18.4, −4.2, −4.7 ppm; IR (thin film): ν 3308, 2930, 2858, 1773, 1739, 1462, 1243, 1079, 1028, 834, 772 cm^{-1}; HRMS (ESI) *m*/*z*: [M + H]$^+$ calcd for $C_{21}H_{39}O_3Si$ 367.2663, found 367.2661; $[\alpha]_D^{23}$ −25.1 (*c* 0.675, $CHCl_3$).

2-((1*R*,3*R*,6*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclohexyl)ethanol (71)

To a solution of **38** (125 mg, 0.341 mmol) in MeOH (3.41 mL) was added K_2CO_3 (94.0 mg, 0.682 mmol) in one portion. The mixture was stirred at rt for 2 h. MeOH was then removed under reduced pressure. Water and Et_2O were added. The aqueous layer was extracted three times with Et_2O. The organic phase was washed with 1 M HCl, brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexane/EtOAc, 10 : 1) to give alcohol **71** (78 mg, 71%). R_f = 0.16 (hexane/EtOAc, 10 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 3.72 (ddd, J = 7.8, 7.0, 1.1 Hz, 2H), 3.38–3.36 (m, 1H), 2.24–2.14 (m, 1H), 2.12 (s, 1H), 1.85–1.65 (m, 5H), 1.53–1.40 (m, 2H), 1.21 (s, 3H), 0.90 (s, 9H), 0.88 (s, 3H), 0.84 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 95.2, 75.8, 67.3, 64.6, 42.9, 39.4, 35.4, 33.6, 31.0, 29.1, 26.1 (3C), 25.4, 22.4, 21.7, 18.3, −4.2, −4.7 ppm; IR (thin film): ν 3254, 2952, 2858, 1471, 1461, 1360, 1253, 1084, 1025, 833, 772, 626 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{19}H_{36}NaO_2Si$ 347.2377, found 347.2376; $[\alpha]_D^{23}$ −35.1 (c 0.105, $CHCl_3$).

2-((1*R*,3*R*,6*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclohexyl) acetaldehyde (6)

To a solution of alcohol **71**, $NH(iPr)_2$ (0.101 mL, 0.578 mmol) and DMSO (0.164 mL, 2.31 mmol) in DCM (2.31 mL) at 0 °C was added SO_3·pyridine complex (92.0 mg, 0.578 mmol). The mixture was stirred for 20 min, and then diluted with DCM. Sat. aq. $NaHCO_3$ was added and the aqueous layer was extracted three times with DCM. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexane/EtOAc, 20 : 1) to give **6** (62 mg, 83%). For full characterization, see above. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 9.75 (dd, J = 3.3, 1.8 Hz, 1H), 3.42–3.40 (m, 1H), 2.65–2.57 (m, 2H), 2.40 (ddd, J = 17.9, 8.0, 3.3 Hz, 1H), 2.33–2.22 (m, 1H), 2.14 (s, 1H), 1.86–1.76 (m, 1H), 1.59–1.45 (m, 2H), 1.21 (s, 3H), 0.93 (s, 9H), 0.86 (s, 3H), 0.82 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H) ppm.

(*R*)-1-(3-Methoxyphenyl)ethanol (45)

Formic acid (2.48 mL, 64.6 mmol) was added dropwise to Et_3N (3.60 mL, 25.8 mmol) at 0 °C. The solution was allowed to warm up to rt over 20 min. 1-(3-methoxyphenyl) ethanone (2.00 g, 12.9 mmol) was then added dropwise, followed by the addition of (*R*)-RuCl[(1*R*,2*R*)-*p*-TsNCH(C_6H_5)CH(C_6H_5)NH_2] (η^6-mesitylene) (40.0 mg, 65.0 μmol). The resulting solution was stirred at rt for 50 h. The mixture was diluted with water and the aqueous layer was extracted three times with EtOAc. The organic phase was washed with sat. aq. $NaHCO_3$ solution, and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexane/EtOAc, 2 : 1) to afford **45** (1.95 g, 99%) as a pale orange oil. The analytical data were found to be in accordance with the ones reported in the literature.[43] R_f = 0.38 (hexane/EtOAc, 2 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.28 (t, J = 8.1 Hz, 1H), 6.97–6.95 (m, 2H), 6.83 (ddd, J = 8.3, 2.5, 0.9 Hz, 1H), 4.88 (q, J = 6.1 Hz, 1H), 3.83 (s, 3H), 2.14 (br s, 1H), 1.51 (d, J = 6.4 Hz, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 159.9, 147.7, 129.6, 117.8, 113.0, 111.0, 70.4, 55.3, 25.2 ppm; IR (thin film): ν 3369, 2971, 1586, 1487, 1455, 1253, 1156, 1043, 852, 781, 698 cm^{-1}; HRMS (EI) m/z: $[M]^+$ calcd for $C_9H_{12}O_2$ 152.0834, found 152.0832; $[\alpha]_D^{24}$ +37.4 (c 1.00, $CHCl_3$); SFC (column OJ-H; CO_2/iPrOH, 95 : 5; 2.00 mL min^{-1}; 100 bar; 25 °C): minor enantiomer t_R = 5.183, major enantiomer t_R = 6.017, 97.7% ee.

(*R*)-1-(3-Methoxyphenyl)ethyl diisopropylcarbamate (72)

Alcohol **45** (1.95 g, 12.8 mmol) and diisopropylcarbamyl chloride (2.52 g, 15.4 mmol) were dissolved in toluene (12.81 mL) in a tube under Ar. Et_3N (2.32 mL, 16.7 mmol) was added dropwise and the tube was sealed and heated at 150 °C for 2 h. The mixture was cooled to rt and filtered through a pad of silica, washing Et_2O, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexane/EtOAc, 3 : 1) to afford carbamate **72** (3.51 g, 98%) as a colorless oil. R_f = 0.68 (hexane/EtOAc, 2 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.25 (t, J = 7.9 Hz, 1H), 6.96–6.93 (m, 1H), 6.91–6.90 (m, 1H), 6.81 (ddd, J = 8.2, 2.6, 1.0 Hz, 1H), 5.81 (q, J = 6.6 Hz, 1H), 4.18–3.66 (br m, 2H), 3.80 (s, 3H), 1.54 (d, J = 6.6 Hz, 3H), 1.22 (br s, 12H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 159.7, 155.2, 144.7, 129.6, 118.4, 112.9, 111.7, 72.7, 55.3, 46.4 (br), 23.1, 21.3 (br) ppm; IR (thin film): ν 2973, 1660, 1601, 1439, 1285, 1158, 1089, 1026, 916, 740, 698 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{16}H_{26}NO_3$ 280.1907, found 280.1905; $[\alpha]_D^{24}$ −32.3 (c 0.700, $CHCl_3$).

(*R*)-1-Methoxy-3-(6-methylhept-5-en-2-yl)benzene (47)

s-BuLi (1.3 M in cyclohexane/hexane 92 : 8; 16.3 mL, 21.2 mmol) was added dropwise to a solution of carbamate **72** (4.56 g, 16.3 mmol) in Et_2O (272 mL) at −78 °C under Ar. The resulting solution was vigorously stirred at −78 °C for 1 h. Boronate **46** (5.14 g, 24.5 mmol)[42] was added very slowly over 15 min. The resulting solution was stirred at −78 °C for 1 h. $MgBr_2$ (1 M in MeOH; 26.1 mL, 26.1 mmol) was added dropwise over 20 min while the mixture was stirred vigorously. After 15 min, the reaction was warmed up to rt and stirred for 4 h. The reaction mixture was then cooled to 0 °C and KH_2PO_4 (1 M in water, 360 mL) was added dropwise with vigorous stirring. The mixture was then stirred at rt for 15 min. The aqueous layer was extracted three times with Et_2O. The organic phase was washed with water and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure.

The resulting oil was dissolved in toluene (50 mL), TBAF·3H_2O (6.40 g, 24.5 mmol) was added, and the mixture heated at 50 °C for 12 h. The mixture was cooled to rt and filtered through a pad of silica, washing DCM, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; pentane/DCM, 5 : 1) to afford **47** (2.92 g, 82%) as a colorless oil. R_f = 0.73 (hexane/EtOAc, 15 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.21 (td, J = 7.6,

1.0 Hz, 1H), 6.80–6.77 (m, 1H), 6.75–6.71 (m, 1H), 5.09 (app tp, J = 7.1, 1.4 Hz, 1H), 3.81 (s, 3H), 2.67 (dt, J = 7.9, 6.7 Hz, 1H), 1.94–1.83 (m, 2H), 1.67 (br s, 3H), 1.66–1.56 (m, 2H), 1.53 (br s, 3H), 1.23 (d, J = 6.9 Hz, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 159.7, 149.6, 131.6, 129.3, 124.6, 119.7, 113.2, 110.9, 55.3, 39.7, 38.5, 26.3, 25.9, 22.5, 17.8 ppm; IR (thin film): ν 2919, 1584, 1452, 1259, 1044, 776 cm^{-1}; HRMS (EI) m/z: $[M]^+$ calcd for $C_{15}H_{22}O$ 218.1666, found 218.1669; $[\alpha]_D^{22}$ −26.1 (c 1.01, $CHCl_3$).

(*R*)-3-(6-Methylhept-5-en-2-yl)cyclohex-2-enone (43)

NH_3 (250 mL) was condensed in a three-neck flask containing **47** (2.92 g, 13.4 mmol) in THF/EtOH (90 mL, 10 : 1) at −78 °C. Lithium wire (0.743 g, 107 mmol) was added portionwise over 3 h so that the blue color remained. After the addition was complete, the mixture was stirred at −78 °C for 1 h. Solid NH_4Cl was added portionwise until the blue color disappeared, and then Et_2O was added. Ammonia was evaporated under a flow of N_2. Water was added and the aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure to afford a colorless oil that was used in the next step without any purification.

The residue was dissolved in THF (200 mL) and 1 M aq. HCl was added (120 mL). The mixture was stirred at rt for 12 h. Sat. aq. $NaHCO_3$ solution was added and the aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; pentane/Et_2O, 8 : 1 to 4 : 1) to afford **43** (1.85 g, 67%) as a colorless oil. The analytical data were found to be in accordance with the ones reported in the literature for the racemic compound.[45] The enantiomeric excess was determined by chiral SFC. R_f = 0.40 (pentane/Et_2O, 4 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 5.87 (s, 1H), 5.06 (ddt, J = 8.4, 6.8, 1.4 Hz, 1H), 2.38–2.35 (m, 2H), 2.32–2.25 (m, 3H), 2.00–1.89 (m, 4H), 1.67 (s, 3H), 1.57 (s, 3H), 1.54–1.47 (m, 1H), 1.44–1.35 (m, 1H), 1.08 (d, J = 6.8 Hz, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 200.3, 171.0, 132.2, 125.3, 123.9, 41.3, 37.9, 34.9, 27.1, 26.0, 25.8, 23.1, 19.0, 17.9 ppm; IR (thin film): ν 2929, 1666, 1454, 1376, 1254, 1192, 964, 888, 525 cm^{-1}; HRMS (EI) m/z: $[M]^+$ calcd for $C_{14}H_{22}O$ 206.1671, found 206.1666; $[\alpha]_D^{22}$ −20.2 (c 0.735, $CHCl_3$); SFC (column AS-H; CO_2/iPrOH, 99 : 1; 2.00 mL min^{-1}; 100 bar; 25 °C): minor enantiomer t_R = 8.692, major enantiomer t_R = 9.558, 89.9% ee.

3-((*R*)-6-Methylhept-5-en-2-yl)cyclohex-2-enol (48)

To a solution of enone **43** (1.82 g, 8.82 mmol) in MeOH (17.6 mL) at 0 °C was added $CeCl_3{\cdot}7H_2O$ (3.62 g, 9.70 mmol), followed by $NaBH_4$ (0.367 g, 9.70 mmol). The white slurry was stirred at 0 °C for 25 min. Water and Et_2O were added, and the aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; pentane/Et_2O, 3 : 1) to afford **48** (1.83 g, quant.) as a colorless oil. R_f = 0.30 (pentane/Et_2O, 3 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 5.49 (br s, 1H), 5.11–5.06 (m, 1H), 4.22–4.17 (m, 1H), 2.09–2.04 (m, 1H), 1.99–1.70 (m, 6H), 1.68 (br s, 3H), 1.62–1.53 (m, 3H), 1.46–1.36 (m, 1H), 1.33–1.24 (m, 1H), 0.99 (d, J = 6.9 Hz, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 146.9, 146.7, 131.5, 124.8, 124.8, 123.5, 123.3, 66.2, 66.2, 40.7, 40.6, 35.3, 35.1, 32.5, 32.4, 26.2, 26.2, 25.9, 25.6, 25.2, 19.7, 19.5, 19.5, 19.4, 17.8 ppm; IR (thin film): ν 3323, 2924, 1451, 1376, 968 cm^{-1}; HRMS (EI) m/z: $[M]^+$ calcd for $C_{14}H_{24}O$ 208.1822, found 208.1826.

(*R*)-3-((*R*)-6-Methylhept-5-en-2-yl)cyclohex-2-en-1-yl acetate (73)

A solution of **48** (1.83 g, 8.78 mmol) and vinyl acetate (1.62 mL, 17.6 mmol) in hexane (88 mL) with ground 4 Å molecular sieves (900 mg) was stirred at rt for 2 h. Lipase Amano AK (180 mg) was then added, and the resulting suspension stirred at rt for 5.5 h. The mixture was then filtered and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; pentane/Et_2O, 3 : 1) to afford acetate **73** (1.06 g, 48% as a combined yield for the mixture of diastereoisomers, *vide infra* for dr determination on derivative **52**) as a colorless oil and the diastereoisomeric allylic alcohol (842 mg, 46%, dr not determined). R_f = 0.67 (hexane/EtOAc, 4 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 5.44–5.43 (m, 1H), 5.28–5.24 (m, 1H), 5.10–5.05 (m, 1H), 2.13–2.06 (m, 1H), 2.04 (s, 0.40 H), 2.03 (s, 2.50 H), 1.97–1.84 (m, 4H), 1.68 (br s, 3H), 1.81–1.61 (m, 4H), 1.58 (br s, 3H), 1.47–1.37 (m, 1H), 1.33–1.24 (m, 1H), 1.00–0.98 (m, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz, the asterisk denotes the minor diastereoisomer peaks): δ 171.1, 148.8, 131.5, 124.7, 124.7*, 119.4*, 119.3, 69.3*, 69.2, 40.8*, 40.7, 35.2, 35.1*, 28.8, 26.2*, 26.1, 25.9, 25.3, 25.1*, 21.7, 19.6*, 19.5, 19.4, 17.8 ppm; IR (thin film): ν 2928, 1733, 1370, 1239, 1015, 910 cm^{-1}; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{16}H_{26}NaO_2$ 273.1825, found 273.1828.

(*R*)-3-((*R*)-6-Methylhept-5-en-2-yl)cyclohex-2-enol (49)

Method A: K_2CO_3 (1.25 g, 9.05 mmol) was added to a solution of **73** (1.51 g, 6.03 mmol) in MeOH (12.1 mL) at rt. The solution was stirred for 2 h. Water and Et_2O were added, and the aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; pentane/Et_2O, 2 : 1) to afford **49** (1.17 g, 93% as a combined yield for **49** and its epimer at C(8), *vide infra* for dr determination on **52**) as a colorless oil. R_f = 0.30 (pentane/Et_2O, 3 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 5.49 (m, 1H), 5.11–5.06 (m, 1H), 4.19 (br s, 1H), 2.06 (app h, J = 6.9 Hz, 1H), 1.99–1.69 (m, 6H), 1.68 (br s, 3H), 1.64–1.52 (m, 3H), 1.59 (br s, 3H), 1.46–1.37 (m, 1H), 1.31–1.24 (m, 1H), 0.99 (d, J = 6.9 Hz, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz, the asterisk denotes the minor diastereoisomer peaks): δ 146.9, 146.7*, 131.4, 124.8, 124.8*, 123.5*, 123.4, 66.2*, 66.2, 40.7*, 40.6, 35.3, 35.1*, 32.5*, 32.4, 26.2*, 26.2, 25.9, 25.6, 25.2*, 19.7*, 19.5, 19.5*, 19.4, 17.8 ppm; HRMS (EI) m/z: $[M]^+$ calcd for $C_{14}H_{24}O$ 208.1822, found 208.1821.

Method B: CBS-reduction. (*S*)-1-Methyl-3,3-diphenyl hexahydropyrrolo[1,2-*c*][1,3,2]oxaza borole (1 M in toluene, 50 μL, 50 μmol) in THF (0.2 mL) was added dropwise to a solution of BH_3·DMS (2 M in THF, 25 μL, 50 μmol) at 0 °C. The mixture was stirred at 0 °C for 30 min, and then **43** (10 mg, 48 μmol) in THF (0.3 mL) was added very slowly. The resulting mixture was stirred at 0 °C for 15 min. MeOH was added, and the mixture passed through a pad of silica gel, washing pentane/Et_2O (2 : 1). The filtrate was concentrated under reduced pressure to give **49** as the major diastereoisomer (7.5 mg, 74%). The chemical shifts were found to be similar to the ones obtained by method A. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 5.50–5.49 (m, 1H), 5.11–5.06 (m, 1H), 4.19 (br s, 1H), 2.10–2.02 (m, 1H), 1.96–1.70 (m, 6H), 1.68 (br s, 3H), 1.63–1.55 (m, 3H), 1.59 (br s, 3H), 1.46–1.37 (m, 1H), 1.29–1.19 (m, 1H), 0.99 (d, J = 6.9 Hz, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz, the asterisk denotes the minor diastereoisomer peaks): δ 146.9, 131.5, 124.8, 124.7*, 123.5*, 123.3, 66.2*, 66.2, 40.7*, 40.7, 35.3, 35.1*, 32.5*, 32.4, 26.2*, 26.2, 25.9, 25.6, 25.2*, 19.7*, 19.5, 19.5*, 19.4, 17.8 ppm.

3-(6-Methylhept-5-en-2-yl)cyclohex-2-en-1-yl benzoate (51)

To a solution of **48** (5.0 mg, 24 μmol) in DCM (0.24 mL) at rt were added Et_3N (10 μL, 72 μmol) and BzCl (7.5 μL, 65 μmol). The solution was stirred at rt overnight. Water was added, and the aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; pentane/Et_2O, 15 : 1) to afford **51** as a mixture of inseparable diastereoisomers (5.9 mg, 79%, combined yield). R_f = 0.59 (hexane/EtOAc, 10 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): 8.07–8.03 (m, 2H), 7.56–7.52 (m, 1H), 7.45–7.40 (m, 2H), 5.59–5.57 (m, 1H), 5.54–5.50 (m, 1H), 5.11–5.06 (m, 1H), 2.15–2.08 (m, 1H), 2.07–1.78 (m, 7H), 1.74–1.69 (m, 1H), 1.69–1.67 (m, 3H), 1.58 (br s, 1.5H), 1.56 (br s, 1.3H), 1.48–1.39 (m, 1H), 1.36–1.28 (m, 1H), 1.03–1.00 (m, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 149.0, 133.0, 129.7, 129.7, 128.4, 124.7, 124.7, 119.4, 119.4, 69.8, 69.6, 40.8, 35.2, 35.1, 28.9, 26.2, 26.1, 25.9, 25.9, 25.3, 25.3, 19.7, 19.7, 19.5, 19.4, 17.8 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{21}H_{28}NaO_2$ 335.1982, found 335.1976; SFC (column IB; CO_2/iPrOH, 99 : 1; 2.00 mL min^{-1}; 100 bar; 25 °C): diastereoisomer **1** t_R = 6.767, diastereoisomer **2** t_R = 7.217, diastereoisomer **3** t_R = 7.983, diastereoisomer **4** t_R = 8.550.

(*R*)-3-((*R*)-6-Methylhept-5-en-2-yl)cyclohex-2-en-1-yl benzoate (52)

To a solution of **49** (5.0 mg, 24 μmol) in DCM (0.24 mL) at rt were added Et_3N (10 μL, 72 μmol) and BzCl (7.5 μL, 65 μmol). The solution was stirred at rt overnight. Water was added, and the aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; pentane/Et_2O, 15 : 1) to afford **52** (7.2 mg, 96%, dr = 17.4 as a mixture with **53**) as a colorless oil. The identity of the two diastereoisomers was deduced by comparison with the SFC chromatogram of **51**. R_f = 0.59 (hexane/EtOAc, 10 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): 8.06–8.03 (m, 2H), 7.56–7.50 (m, 1H), 7.45–7.40 (m, 2H), 5.58–5.57 (m, 1H), 5.53–5.50 (m, 1H), 5.11–5.06 (m, 1H), 2.15–2.08 (m, 1H), 2.06–1.78 (m, 7H), 1.74–1.69 (m, 1H), 1.67 (br s, 3H), 1.58–1.56 (m, 3H), 1.49–1.40 (m, 1H), 1.35–1.25 (m, 1H), 1.01 (d, J = 6.7 Hz, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz, the asterisk denotes the minor diastereoisomer peaks): δ 149.0, 149.0*, 132.8, 129.7, 128.4, 124.7, 124.7*, 119.4, 119.4*, 69.8*, 69.6, 40.8, 35.2, 35.1*, 28.9, 26.2*, 26.1, 25.9, 25.3*, 25.3, 19.7*, 19.7*, 19.5, 19.4, 17.8 ppm; HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{21}H_{28}NaO_2$ 335.1982, found 335.1976; SFC (column IB; CO_2/iPrOH, 99 : 1; 2.00 mL min^{-1}; 100 bar; 25 °C): major diastereoisomer t_R = 6.742, minor diastereoisomer t_R = 8.025, (dr = 17.4).

(1*S*,2*R*,6*R*)-6-((*R*)-6-Methylhept-5-en-2-yl)bicyclo[4.1.0]heptan-2-ol (50)

CH_2I_2 (1.13 mL, 14.1 mmol) was added dropwise to a solution of Et_2Zn (1 M in hexanes, 6.74 mL, 6.74 mmol) in benzene (28.1 mL) at rt and the resulting mixture was stirred for 30 min, then cooled to 0 °C. In a separate flask, a solution of **49** (1.17 g, 5.62 mmol) in Et_2O (20 mL) was treated with *n*-BuLi (1.6 M in hexanes, 3.86 mL, 5.62 mmol) at −20 °C and stirred at −20 °C for 10 min. It was then added dropwise to the previously prepared solution of Furukawa's reagent. The resulting solution was let to warm up to rt and stirred for 24 h. Sat. aq. NH_4Cl solution was added, and the aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; pentane/Et_2O, 3 : 1) to afford **50** (831 mg, 66%) as a colorless oil and **49** (175 mg, 15%). The relative stereochemistry was confirmed by NOESY analysis. R_f = 0.23 (pentane/Et_2O, 3 : 1); ^{1}H-NMR ($CDCl_3$, 600 MHz): δ 5.09–5.06 (m, 1H), 4.17–4.14 (m, 1H), 2.02–1.92 (m, 2H), 1.69–1.65 (m, 1H), 1.67 (br s, 3H), 1.63–1.60 (m, 1H), 1.59 (s, 3H), 1.48–1.38 (m, 3H), 1.27–1.20 (m, 2H), 1.08–1.04 (m, 1H), 1.01–0.92 (m, 2H), 0.88 (d, J = 6.7 Hz, 3H), 0.67–0.61 (m, 1H), 0.48 (t, J = 5.2 Hz, 1H), 0.43–0.41 (m, 1H) ppm; ^{13}C-NMR ($CDCl_3$, 150 MHz, the asterisk denotes the minor diastereoisomer peaks): δ 131.3, 125.1, 125.0*, 67.6, 67.6*, 43.5*, 43.4, 34.3*, 34.1, 30.3*, 30.2, 28.3, 28.2*, 26.4, 26.4*, 25.8, 25.4, 23.4, 21.4, 21.2*, 17.8, 17.2, 16.9*, 15.6 ppm; ^{1}H–^{1}H-NOESY ($CDCl_3$, 600 MHz, relevant cross-peak): δ 4.14 and 0.95 [H(8)–H(13)] ppm; IR (thin film): ν 3340, 2923, 1451, 1375, 1029, 771, 700 cm^{-1}; HRMS (EI) m/z: $[M]^+$ calcd for $C_{15}H_{26}O$ 222.1979, found 222.1982.

(1*S*,6*R*)-6-((*R*)-6-Methylhept-5-en-2-yl)bicyclo[4.1.0]heptan-2-one (74)

PCC (1.66 g, 136.46 mmol) was added portionwise to a solution of **50** (831 mg, 3.74 mmol) in DCM (37.4 mL) at rt. The mixture was stirred at rt for 2 h. SiO_2 was added and the mixture was stirred for 30 min, then filtered on a pad of Celite, washing Et_2O, and the filtrate was concentrated under reduced pressure to afford ketone **74** (652 mg, 79%) as a pale yellow oil. R_f = 0.30 (pentane/Et_2O, 3 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz):

δ 5.06 (tt, J = 6.9, 1.5 Hz, 1H), 2.29–2.22 (m, 1H), 2.06–1.93 (m, 3H), 1.91–1.74 (m, 2H), 1.73–1.69 (m, 1H), 1.68 (s, 3H), 1.66–1.61 (m, 1H), 1.59 (s, 3H), 1.53–1.44 (m, 2H), 1.41 (t, J = 4.8 Hz, 1H), 1.38–1.29 (m, 1H), 0.98–0.94 (m, 4H), 0.88–0.80 (m, 1H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz, the asterisk denotes the minor diastereoisomer peaks): δ 209.7, 131.8, 124.5, 124.4*, 77.5, 77.2, 76.8, 41.9, 41.8*, 36.7*, 36.6, 34.8*, 34.4, 34.2*, 33.4, 33.2, 26.3, 25.8, 21.1*, 21.0, 19.6, 18.9, 18.7*, 17.8, 17.7*, 17.2*, 17.2 ppm; IR (thin film): ν 2923, 1689, 1447, 1377, 1245, 1064, 897, 824 cm^{-1}; HRMS (EI) m/z: $[M]^+$ calcd for $C_{15}H_{24}O$ 220.1822, found 220.1824.

(*R*)-3-Methyl-3-((*R*)-6-methylhept-5-en-2-yl)cyclohexanone (7)

Lithium wire (113 mg, 16.3 mmol) was dissolved in NH_3 (*ca.* 40 mL) at −78 °C under N_2. After stirring for 15 min, a solution of ketone **74** (600 mg, 2.72 mmol) in THF (14 mL) was added dropwise and the mixture was stirred at −20 °C for 30 min. The reaction was treated with solid NH_4Cl until the blue color disappeared. NH_3 was removed under a stream of N_2; then water and Et_2O were added. The aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; pentane/Et_2O, 12 : 1) to afford **7** (429 mg, 71%) as a colorless oil. R_f = 0.37 (hexane/EtOAc, 8 : 1); ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 5.10–5.05 (m, 1H), 2.33–2.20 (m, 3H), 2.13–2.01 (m, 2H), 1.95–1.74 (m, 3H), 1.67 (s, 3H), 1.59 (s, 3H), 1.64–1.44 (m, 3H), 1.29–1.17 (m, 1H), 1.00–0.90 (m, 1H), 0.85 (d, J = 6.7 Hz, 3H), 0.80 (s, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 75 MHz, the asterisk denotes the minor diastereoisomer peaks): δ 212.9, 131.8*, 131.7, 124.8*, 124.7, 52.2*, 52.0, 44.8*, 44.1*, 41.5, 41.3, 41.2, 41.1*, 34.2, 34.1*, 33.9*, 31.3*, 31.0, 26.9, 26.8*, 25.8, 22.1*, 22.0*, 22.0, 21.1*, 20.5, 18.0*, 17.8, 17.1*, 13.6, 13.3* ppm; IR (thin film): ν 2963, 2877, 1708, 1455, 1378, 1228, 1070, 829 cm^{-1}; HRMS (EI) m/z: $[M]^+$ calcd for $C_{15}H_{26}O$ 222.1979, found 222.1981.

(*R*)-2-(2-((1*R*,3*R*,6*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclo-hexyl)ethylidene)-5-methyl-5-((*R*)-6-methylhept-5-en-2-yl)cyclohexanone (54)

LDA (freshly prepared 1 M in THF, 0.270 mL, 0.270 mmol) was added dropwise to a stirred solution of **7** (60.0 mg, 0.270 mmol) in THF (0.6 mL) at −78 °C. The yellow solution was stirred at −78 °C for 1 h, before a solution of **6** (70.0 mg, 0.217 mmol) in THF (1.5 mL) was added slowly. The mixture was stirred at −78 °C for 15 h. Sat. aq. NH_4Cl and Et_2O were added, and the mixture was warmed up to rt. The aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; pentane/Et_2O, 15 : 1) to afford an inseparable mixture of the aldol product and ketone **7**, which was used in the next step.

The mixture of compounds was dissolved in benzene (1.6 mL) and cooled to 5 °C with vigorous stirring. Pyridine (33 μL, 0.41 mmol) and TFAA (58 μL, 0.41 mmol) were added dropwise and the mixture was stirred for 30 min. DBU (250 μL, 1.66 mmol) was added dropwise to the solution that turned bright yellow upon addition. It was then stirred at 0 °C for 1 h. Sat. aq. $NaHCO_3$ and hexanes were added; the aqueous layer was extracted three times with hexanes. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexanes/DCM, 1 : 1) to afford **54** (73 mg, 64% over 2 steps) as a yellow oil. R_f = 0.56 (hexane/EtOAc, 8 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 6.83–6.78 (m, 1H), 5.09–5.05 (m, 1H), 3.37–3.34 (m, 1H), 2.58–2.51 (m, 2H), 2.44–2.37 (m, 1H), 2.35–2.31 (m, 1H), 2.29–2.17 (m, 3H), 2.11–2.06 (m, 1H), 2.11 (dd, J = 7.5, 3.9 Hz, 1H), 2.07 (s, 1H), 1.84–1.80 (m, 1H), 1.78–1.73 (m, 1H), 1.69–1.66 (m, 1H), 1.67 (br s, 3H), 1.61–1.58 (m, 1H), 1.59 (br s, 3H), 1.52–1.51 (m, 1H), 1.49–1.43 (m, 2H), 1.27–1.23 (m, 1H), 1.21 (s, 3H), 1.02–0.96 (m, 1H), 0.91 (s, 9H), 0.88–0.87 (m, 6H), 0.84 (s, 3H), 0.83 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz): δ 201.3, 143.1, 132.6, 131.7, 124.7, 94.4, 76.3, 67.8, 50.7, 47.3, 40.5, 39.6, 37.2, 35.8, 33.6, 32.5, 31.0, 29.9, 27.1, 26.9, 26.1 (3C), 25.9, 25.4, 22.8, 22.7, 21.9, 21.0, 18.4, 17.8, 13.7, −4.3, −4.7 ppm; IR (thin film): ν 3310, 2929, 2858, 1685, 1607, 1461, 1362, 1252, 1038, 1008, 958, 834, 773, 671, 626 cm^{-1}; HRMS (ESI) m/z: $[M + H]^+$ $C_{34}H_{59}O_2Si$ calcd for 527.4279, found 527.4279.

(5*R*)-2-(2-((1*R*,3*R*,6*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclohexyl)ethyl)-5-methyl-5-((*R*)-6-methylhept-5-en-2-yl)cyclohexanone (55)

LAH (2.4 M in THF, 50.0 μL, 0.120 mmol) was added dropwise to a suspension of copper(I) iodide (112 mg, 0.588 mmol) in THF (0.30 mL) at 0 °C. The black mixture was stirred at 0 °C for 10 min, before a solution of **54** (62 mg, 0.12 mmol) in THF (0.8 mL) was added dropwise. The mixture was stirred at 0 °C for 10 min. Sat. aq. NH_4Cl was added. The mixture was filtered on a small pad of Celite, and the aqueous layer was extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexanes/EtOAc, 50 : 1) to afford **55** (43 mg, 69%) as a 2 : 1 mixture of epimers. R_f = 0.54 (minor) and 0.62 (hexane/EtOAc, 12 : 1); ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 5.11–5.06 (m, 1H), 3.35 (br s, 1H), 2.48 (d, J = 13.1 Hz, 0.33H), 2.27–2.06 (m, 5H), 2.04 (s, 0.33H), 2.03 (s, 0.67H), 2.01–1.97 (m, 0.67H), 1.89–1.71 (m, 4H), 1.70–1.67 (m, 4H), 1.62–1.58 (m, 4H), 1.54–1.40 (m, 5H), 1.38–1.28 (m, 4H), 1.23–1.21 (m, 1H), 1.17 (s, 3H), 0.96 (s, 2H), 0.92 (s, 9H), 0.88 (s, 3H), 0.86 (s, 1H), 0.82 (br s, 3H), 0.80 (s, 1H), 0.75 (s, 2H), 0.04 (s, 6H) ppm; ^{13}C-NMR ($CDCl_3$, 101 MHz, the asterisk denotes the minor diastereoisomer peaks): δ 214.8*, 213.9, 131.7, 131.7*, 124.8*, 124.8, 95.2, 95.1*, 76.0, 75.9*, 66.9*, 66.7, 52.2*, 51.1, 50.6, 50.3*, 47.0, 43.4, 42.9*, 42.1, 39.7, 39.7, 39.4, 35.8, 35.6*, 34.2, 33.8*, 33.7, 32.9, 32.6*, 31.2, 31.0*, 30.1, 29.5*, 29.2, 29.1*, 27.9, 29.6, 26.2, 26.2 (3C), 25.9, 25.6, 25.5*, 22.6, 21.9, 21.3*, 19.6, 18.4, 17.8, 14.3, 13.8, 13.4, −4.2, −4.7 ppm; IR (thin film): ν 3306, 2930, 2858, 1707, 1460, 1383, 1252, 1075, 1006, 957, 834, 773,

672, 626 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{34}H_{61}O_2Si$ 529.4435, found 529.4431.

Cyclopropanes 56, 57, 58, 59

A solution of **55** (13 mg, 25 μmol) in MeCN (0.2 mL) was treated with Et_3N (20 μL, 0.14 mmol) and freshly distilled TMSCl (10 μL, 78 μmol). A solution of NaI (18.4 mg, 123 μmol) in MeCN (0.4 mL) was added over 20 min, and the resulting slurry was stirred at rt for 4 h. It was then poured into sat. aq. $NaHCO_3$. The aqueous layer was extracted three times with hexanes. The organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was passed on a small pad of silica gel, washing pentane/DCM (5 : 1), and the filtrate was concentrated under reduced pressure to afford the silyl enol ether compound (13 mg, 88%) as a colorless oil.

CH_2I_2 (freshly prepared solution, 1 M in toluene, 110 μL, 0.110 mmol) was added to a solution of Et_2Zn (1 M in hexanes, 110 μL, 0.110 mmol) in toluene (0.1 mL) at 0 °C. The white slurry was stirred at rt for 30 min, and a solution of the silyl enol ether (13 mg, 22 μmol) in toluene (0.5 mL) was added dropwise. The resulting mixture was stirred at rt for 1.5 h. Et_2O was added, followed by sat. aq. NH_4Cl. The aqueous layer was extracted three times with Et_2O. The organic phase was washed with sat. aq. $Na_2S_2O_3$ and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; pentane/DCM, 8 : 1) to afford **56** (2.8 mg, 21%), doubly cyclopropanated **58** (4.2 mg, 31%), an inseparable mixture of **57** and corresponding double cyclopropanated **59** (1.7 mg) that was used in the next step without further purification, and recovered **55** (1.2 mg, 10%). As the reaction was conducted on a low milligram scale, the purification was found to be complicated; thus the products were isolated along some minor unidentified impurities.

Data for 56. R_f = 0.32 (pentane/DCM, 5 : 1); ^{1}H-NMR ($CDCl_3$, 600 MHz): δ 5.13–5.10 (m, 1H), 3.35–3.34 (m, 1H), 2.16–2.11 (m, 1H), 2.09–2.03 (m, 1H), 2.05 (s, 1H), 1.85–1.75 (m, 3H), 1.74–1.69 (m, 3H), 1.70 (br s, 3H), 1.67–1.63 (m, 2H), 1.61 (br s, 3H), 1.52–1.42 (m, 4H), 1.29–1.24 (m, 3H), 1.22 (s, 3H), 1.01–0.92 (m, 2H), 0.90 (s, 9H), 0.88 (s, 3H), 0.85 (s, 3H), 0.81 (s, 3H), 0.78 (d, *J* = 6.4 Hz, 3H), 0.74 (td, *J* = 12.9, 5.6 Hz, 1H), 0.41 (d, *J* = 5.2 Hz, 1H), 0.23 (d, *J* = 5.1 Hz, 1H), 0.12 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H) ppm; ^{13}C-NMR ($CDCl_3$, 151 MHz): δ 131.4, 125.2, 95.0, 75.9, 66.8, 60.0, 47.2, 46.1, 43.2, 40.1, 37.9, 35.7, 34.5, 33.7, 31.0, 29.2, 29.0, 27.1, 26.1 (3C), 25.9, 25.7, 25.6, 25.2, 24.7, 22.8, 22.2, 21.9, 19.8, 18.4, 17.8, 13.9, 1.7 (3C), −4.2, −4.8 ppm; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{38}H_{71}O_2Si_2$ 615.4987, found 615.4989.

Data for 58. R_f = 0.43 (pentane/DCM, 5 : 1); ^{1}H-NMR ($CDCl_3$, 600 MHz): δ 3.36–3.33 (m, 1H), 2.17–2.11 (m, 1H), 2.05 (s, 1H), 1.81–1.76 (m, 2H), 1.76–1.73 (m, 2H), 1.71–1.68 (m, 2H), 1.53–1.42 (m, 4H), 1.39–1.33 (m, 1H), 1.30–1.25 (m, 2H), 1.22 (s, 3H), 1.19–1.11 (m, 1H), 1.03–1.01 (m, 6H), 1.00–0.94 (m, 6H), 0.90 (s, 9H), 0.88 (s, 3H), 0.85 (s, 3H), 0.82 (app d, *J* = 3.9 Hz, 3H), 0.77 (app dd, *J* = 6.3, 2.5 Hz, 3H), 0.75–0.70 (m, 1H), 0.47–0.43 (m, 1H), 0.41 (dd, *J* = 5.2, 1.4 Hz, 1H), 0.35 (app td, *J* = 8.1, 4.0 Hz, 1H), 0.24 (app dt, *J* = 5.0, 1.5 Hz, 1H), 0.12 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H), −0.14 (app dt, *J* = 13.9, 4.7 Hz, 1H) ppm; ^{13}C-NMR ($CDCl_3$, 151 MHz): δ 95.0, 75.9, 66.8, 60.0, 47.3, 46.3, 46.1, 43.8, 43.4, 40.1, 38.0, 37.9, 35.7, 34.6, 34.5, 33.7, 31.3, 31.3, 29.9, 29.2, 29.1, 29.1, 29.0, 27.9, 27.9, 26.2 (6C), 25.7, 25.6, 25.3, 25.2, 24.9, 24.7, 22.8, 22.1, 21.9, 21.9, 20.2, 20.1, 20.0, 19.8, 19.8, 19.6, 18.4, 15.6, 15.3, 14.1, 14.1, 1.7 (3C), 1.7 (3C), −4.2, −4.8 ppm; HRMS (ESI) *m/z*: $[M + H]^+$ calcd for $C_{39}H_{73}O_2Si_2$ 629.5144, found 629.5143.

(2*R*,5*R*)-2-(2-((1*R*,3*R*,6*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethyl-cyclohexyl)ethyl)-2,5-dimethyl-5-((*R*)-6-methylhept-5-en-2-yl)cyclohexanone (5)

A solution of **56** (2.8 mg, 4.6 μmol) in EtOH (0.18 mL) was treated with aq. NaOH (0.5 M, 0.18 mL, 90 μmol), and the resulting mixture was refluxed at 100 °C for 12 h. The mixture was cooled to rt, EtOH was removed under reduced pressure and the residue was diluted with EtOAc. The aqueous layer was extracted three times with EtOAc. The organic phase was washed with 1 M HCl, water, and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2; hexane/EtOAc, 18 : 1) to afford **5** (1.7 mg, 69%) along some minor impurities. The relative stereochemistry was determined by NOE analysis. R_f = 0.69 (hexane/EtOAc, 12 : 1); ^{1}H-NMR ($CDCl_3$, 600 MHz): δ 5.09 (br t, *J* = 7.0 Hz, 1H), 3.34 (br s, 1H), 2.40 (d, *J* = 13.5 Hz, 1H), 2.17–2.10 (m, 2H), 2.05 (s, 1H), 2.04–2.00 (m, 1H), 1.87–1.81 (m, 1H), 1.79–1.70 (m, 5H), 1.69 (s, 3H), 1.64–1.63 (m, 1H), 1.60 (s, 3H), 1.59–1.55 (m, 2H), 1.52–1.49 (m, 1H), 1.47–1.40 (m, 3H), 1.19 (s, 3H), 1.18–1.16 (m, 1H), 1.13–1.09 (m, 1H), 1.06 (s, 3H), 0.92 (s, 9H), 0.90–0.88 (m, 1H), 0.87 (br s, 3H), 0.82–0.81 (m, 6H), 0.78 (s, 3H), 0.04 (m, 6H) ppm; ^{13}C-NMR ($CDCl_3$, 151 MHz): δ 216.6, 131.7, 124.8, 95.0, 75.9, 66.9, 49.0, 48.0, 47.1, 41.8, 41.4, 39.9, 38.2, 35.8, 34.3, 33.7, 31.4, 30.9, 29.9, 29.2, 27.0, 26.2 (3C), 25.9, 25.6, 22.7, 22.0, 21.9, 21.7, 18.4, 17.8, 13.3, −4.3, −4.7 ppm; ^{1}H–NOE ($CDCl_3$, 600 MHz, irradiation on H_b(13), relevant correlations): δ 2.40 and 1.07 [H_b(13) and H(30)] ppm; ^{1}H-NOE ($CDCl_3$, 600 MHz, irradiation on H_a(13), relevant correlations): δ 2.14 and 0.78 [H_a(13) and H(18)] ppm; ^{1}H–NOE ($CDCl_3$, 600 MHz, irradiation on H(30), relevant correlations): δ 2.40 and 1.07 [H_b(13) and H(30)] ppm; IR (thin film): ν 3311, 2926, 2855, 1705, 1461, 1378, 1257, 1091, 1076, 1007, 834, 800, 773, 625 cm^{-1}; HRMS (ESI) *m/z*: $[M + NH_4]^+$ calcd for $C_{35}H_{66}NO_2Si$ 560.4857, found 560.4859; $[\alpha]_D^{23}$ −31.3 (*c* 0.100, $CHCl_3$).

Conflict of interest

There are no conflicts of interest to declare.

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