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Silver-catalyzed benzannulation, part 1: Total synthesis of (7*S*,10*R*)-2,15-dihydroxycalamene, (7*S*,10*R*)-2-Hydroxy-15-calamenenal and (7*S*,10*R*)-2-hydroxy-15-calamenenoic acid

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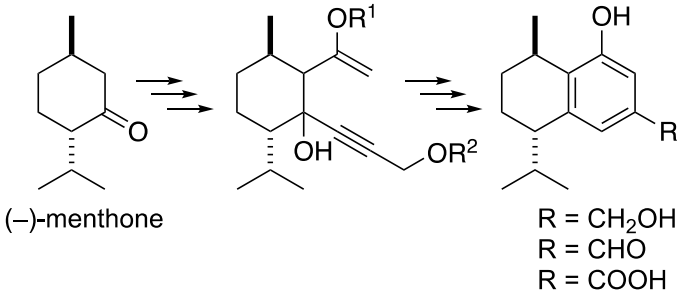
Abstract

This paper reports the development of a silver-catalyzed 6-*endo-dig* cyclisation of 5-alkoxy-1,5-enynes enabling benzannulation of (–)-menthone with construction of the calamenene skeleton as a single isomer. The total syntheses of (7*S*,10*R*)-2,15-dihydroxycalamenene (6 steps, 39.6%), (7*S*,10*R*)-2-hydroxy-15-calamenenal (7 steps, 10.7%) and (7*S*,10*R*)-2-Hydroxy-15-calamenenoic acid (9 steps, 33.6%) were achieved from (–)-menthone via a common intermediate. Analysis of the spectroscopic data as well as the specific rotations allowed for confirmation of the stereochemistry at C1 and C4 of the natural compounds isolated from *Tarenna madagascariensis* as (7*R*,10*S*)-2,15-dihydroxycalamenene and (7*R*,10*S*)-2-hydroxy-15-calamenenal, and the carboxylic acid isolated from *Alpinia oxymitra* was confirmed as (7*S*,10*R*)-2-hydroxy-15-calamenenoic acid.



Keywords: *Benzannulation, calamenene, 5-alkoxy-1,5-enynes, 6-endo-dig cyclisation, tetrahydronaphthalene*

Introduction

Compounds containing the generic sesquiterpene calamenene skeleton have been isolated from a variety of natural sources, commonly with oxygenation at C2 and C15 (cadinene numbering) and containing both *cis* and *trans* isomers.[1]

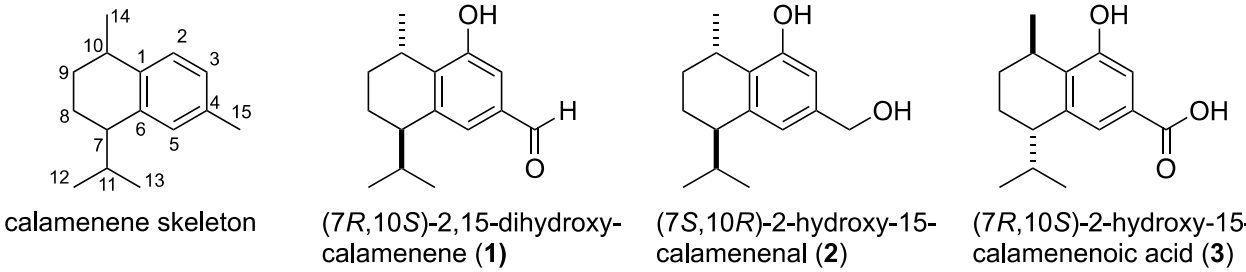
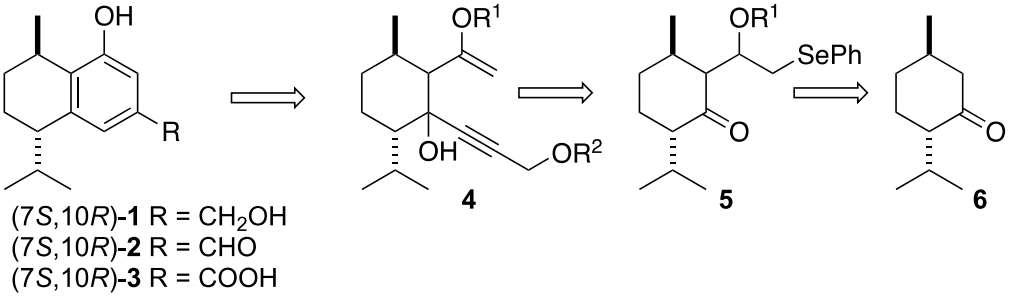


Figure 1. Calamenene Natural Products.

The compounds (7*R*,10*S*)-2,15-dihydroxycalamenene (**1**) and (7*R*,10*S*)-2-hydroxy-15-calamenenal (**2**) were previously reported[2] to be isolated from the shrub *Tarenna madagascariensis,* with their relative and absolute configurations based on NMR analysis and the sign of their optical rotations in comparison to analogous compounds. The related carboxylic acid (7*S*,10*R*)-2-hydroxy-15-calamenenoic acid (**3**) was isolated from the rhizomes of *Alpinia oxymitra* (Zingiberaceae),[3] and again the absolute configuration was based on NMR analysis and the sign of the optical rotation. As part of our efforts towards the synthesis of serrulatane natural products[4] we targeted these compounds as a model system for the development of a new benzannulation approach to the tetrahydronaphthalene ring.

We investigated the aromatic ring construction of the 8 hydroxy-calamenenes (7*S*,10*R*)-**1**, (7*S*,10*R*)-**2** and (7*S*,10*R*)-**3** using a 6-*endo*-*dig* cyclisation of ene-yne-ol **4**. This intermediate was to be formed by selenoxide elimination and alkyne addition to ketone **5** with the stereochemistry originating from (–)-menthone **6**.

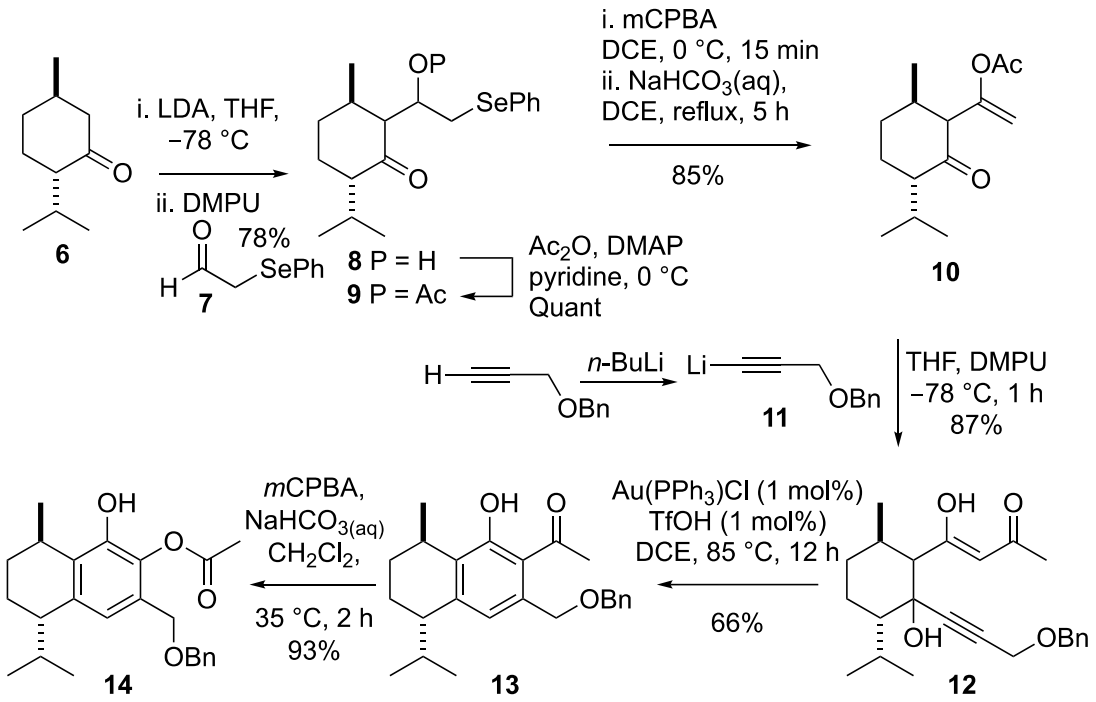


Scheme 1. Retrosynthetic analysis.

Results and Discussion

The synthetic sequence began with an LDA aldol between the commercially available (−)-menthone (**6**) and phenylselenoacetaldehyde[5] (**7**) (Scheme 2). The hydroxyselenide **8** was protected as the acetate derivative **9** and was then treated with *m*-chloroperbenzoic acid in anhydrous benzene for 15 min at 0 °C.[6] A saturated

aqueous solution of $NaHCO_3$ was then added and the intermediate selenoxide heated at reflux in the biphasic mixture. The forcing conditions promoted the unfavorable elimination towards oxygen, producing the enol ester **10**. Treatment of enol ester **10** with two equivalents of lithium acetylide **11** achieved addition to the carbonyl but also unexpectedly caused the enol acetate to rearrange giving the enol tautomer **12**. The structure of this product was indicated by the presence of the enol =CH– singlet at 5.56 ppm and presence of two unsubstituted carbons at 201.0 and 187.5 ppm as well as the newly formed tertiary alcohol at 89.7 ppm. The assignment of this structure was confirmed by the subsequent cyclisation. This substrate **12** would not be expected to give the desired 8-hydroxy-calamenenes but it was expected to still be a substrate for the 6-*endo-dig* cyclisation.

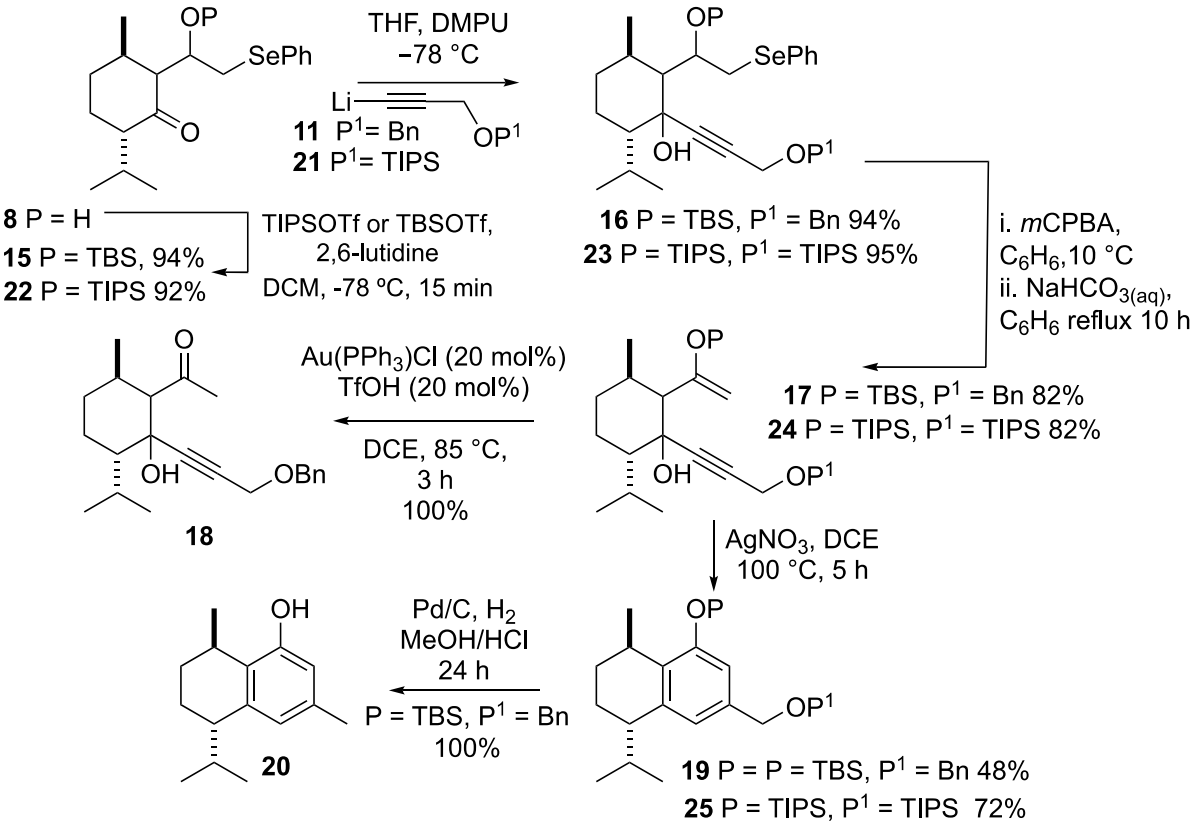


Scheme 2. Synthesis of *ortho*-diphenol **14**.

The 6-*endo-dig* cyclisation of compound **12** was thus attempted using the gold-catalyzed literature conditions published by Barriault and co-workers.[7] Treatment of compound **12** with $Au(Ph_3P)Cl$ (1 mol %) and TfOH (1 mol %) in DCE heated at reflux pleasingly formed the aromatic ketone **13**. This compound showed the expected signals in the ^{13}C NMR spectrum for the newly formed aromatic ring, most notably the phenol carbon at 161.6 ppm, the acetate carbonyl at 206.1 ppm and the corresponding methyl ^{1}H NMR signal at 2.77 ppm. The potential to convert this ketone to an *ortho*-diphenol was noted and it was thus found that Baeyer-Villiger oxidation with *m*CPBA afforded the aromatic ester **14**. Although unfortunate that the enol ester **10** underwent this rearrangement, this route could potentially be applied to the synthesis of a variety of *ortho*-diphenol natural products such as the pseudopterosins,[8,9] and various 7,8-dihydroxyserrulatanes.[10-13]

To circumvent the enol-acetate rearrangement and target the calamenene-type natural products, the synthetic sequence was revised to feature both an alternative protecting group strategy and addition of the acetylide before elimination of the selenoxide. The TBS-protected phenylselenide **15** was prepared by treatment of alcohol **8** with TBSOTf using standard conditions. Lithium acetylide **11** was successfully added to the TBS-protected phenylselenide **15** to give the 3-hydroxy alkyne **16**, which was then eliminated to afford the enol ether **17** (Scheme 3). However, subsequent treatment of this substrate with $Au(Ph_3P)Cl$ only resulted in hydrolysis of

the TBS-protecting group to give ketone **18**. The hydrolysis of the enol ether was attributed to either protecting group instability or the reaction conditions, and in particular the use of $Au(Ph_3P)Cl$ as catalyst. To circumvent this problem, a series of other transition metals and conditions were screened. Silver nitrate was thus identified as a novel and efficient catalyst for the 6-*endo-dig* cyclisation of these 3-hydroxy-1,5-enynes. The only other analogous report of the use of a Ag(I) catalyst was the use of Ag(I)OTf in the ene-yne benzannulation of quinolines to give acridines.[14] Under the optimized conditions, enyne **17** was heated at reflux in DCE for 5 h under darkness, affording compound **19** in 48% yield.

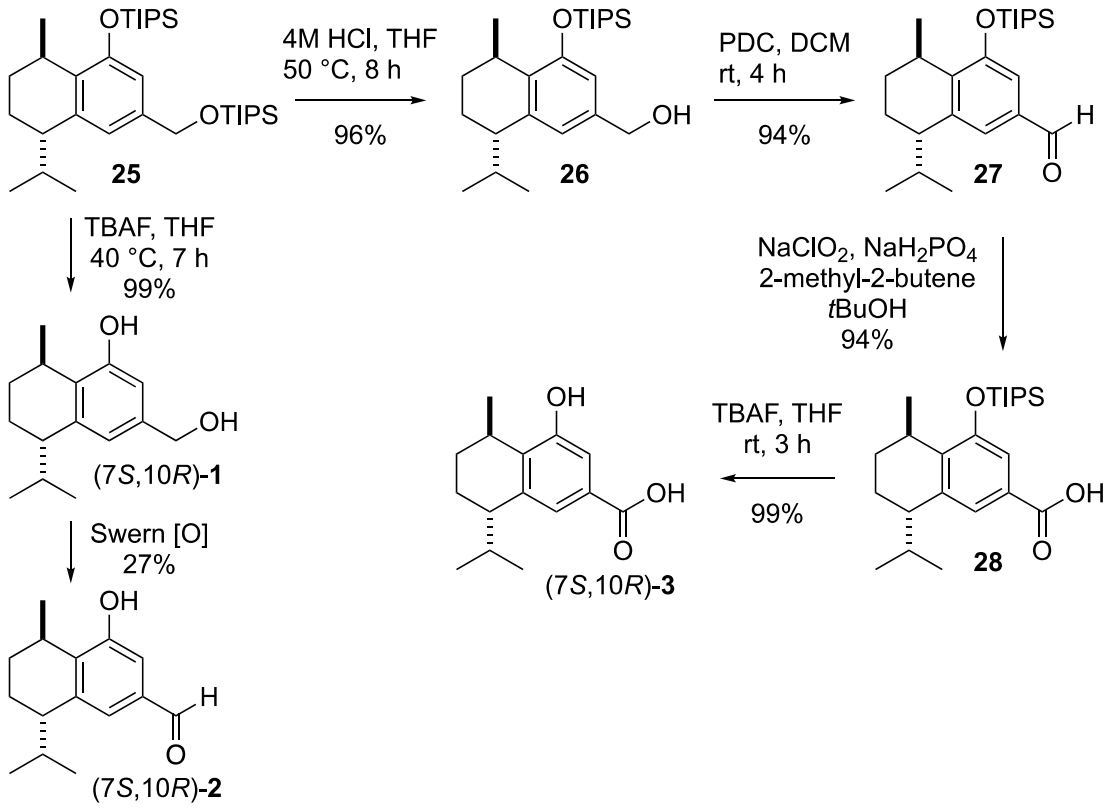


Scheme 3. Synthesis of deoxy-calamenene **20**.

Attempted benzyl deprotection via hydrogenation under acidic conditions achieved removal of the TBS protecting group but resulted in hydrogenolysis of the wrong benzyl ether, giving deoxy-calamenene **20**. To overcome this problem the protecting group strategy was modified to enable orthogonal deprotection of the benzyloxy position. Following the same synthetic methodology, addition of lithium acetylide **21** to **22** afforded **23** in 95% yield, followed by selenoxide oxidation and elimination to give **24** in 82%. Notably, use of the di-TIPS-protected system **24** gave an improved yield for the silver nitrate-catalyzed 6-*endo-dig* cyclisation, giving the bis-TIPS-compound **25** in 82 vs 48% for the TBS/Bn system (Scheme 3). Compound **25** was thus produced in five steps from (–)-menthone with an overall yield of 40%. It is also noted that addition of lithium acetylides **11** and **21** to the ketones **15** and **22**, respectively, were remarkably stereoselective giving one major isomer in each case, but the stereochemistry of the major isomers was not determined (See ^1H and ^{13}C NMR spectra in the supplementary information).

Compound **25** was then used as a common precursor for construction of the three natural products (Scheme 4). Treatment of **25** with TBAF for 7 h at 40 °C allowed for universal deprotection and synthesis of (7*S*,10*R*)-**1** in

almost quantitative yield. This compound could be oxidized under Swern conditions[15] to give the aldehylde (7*S*,10*R*)-**2** in moderate yield. To synthesize the corresponding carboxylic acid, the benzylic silyl ether was selectively deprotected with 4 M HCl to give alcohol **26**. Subsequent oxidation with PDC[16] afforded the aldehyde **27**, with Pinnick oxidation[17] giving carboxylic acid **28**. The final step in the synthesis was the deprotection of the remaining silyl ether by treatment with TBAF. The carboxylic acid (7*S*,10*R*)-**3** was thus obtained in 84% overall yield from the bis-silyl precursor **25**.



Scheme 4. Total synthesis of calamenenes (7*S*,10*R*)-**1**, (7*S*,10*R*)-**2** and (7*S*,10*R*)-**3**.

The ^{1}H and ^{13}C NMR spectroscopic data for the synthetic (7*S*,10*R*)-**1** (Table 1) and (7*S*,10*R*)-**2** (Table 2) were essentially identical to those reported[2] for the natural products (7*R*,10*S*)-2,15-dihydroxycalamenene (**1**) and (7*R*,10*S*)-2,15-dihydroxycalamenene (**2**) with less than a 0.1 ppm difference (0.2 ppm for one carbon) in the reported carbon shifts for our synthetic samples and those reported for the natural product. There is also a good correlation for all the ^{1}H chemical shifts and coupling patterns. The negative signs of the optical rotations for the synthetic isomers (7*S*,10*R*)-**1** $[\alpha]_D^{20}$ –34 (*c* 0.79, $CHCl_3$) and (7*S*,10*R*)-**2** $[\alpha]_D^{20}$ –49 (*c* 0.6, $CHCl_3$) confirms the assignment of the corresponding natural products, with reported[2] rotations of $[\alpha]_D^{20}$ +22 (*c* 0.79, $CHCl_3$) (diol) and $[\alpha]_D^{20}$ +66 (*c* 1.8, $CHCl_3$) (aldehyde), as the *enantiomeric* (7*R*,10*S*)-2,15-dihydroxycalamenene (**1**) and (7*R*,10*S*)-2-hydroxy-15-calamenenal (**2**). The significant difference in the magnitudes of our observed rotations compared to those reported for the natural products may lie in a deviation in those reported for the natural products. This is supported by the good agreement of our reported optical rotation for (7*S*,10*R*)-**1** with that reported by Serra[18] $[\alpha]_D^{20}$ –46.9 (c 1, $CHCl_3$) for the previous synthesis of (7*S*,10*R*)-**1**.

Comparison of the ^{1}H and ^{13}C NMR spectroscopic data for the synthetic (7*S*,10*R*)-**3** with the natural product (7*S*,10*R*)-2-hydroxy-15-calamenenoic acid (**3**) isolated from *Alpinia oxymitra* by Jitsaeng *et al.*[3] is shown in Table

3. In this case the optical rotations for the synthetic isomer (7*S*,10*R*)-**3** $[\alpha]_D^{20}$ –29 (*c* 0.5, $CHCl_3$) is the same sign as the reported[3] $[\alpha]_D^{20}$ –10.95 (*c* 0.00065, $CHCl_3$), and is thus consistent with the assigned absolute configuration of the natural product as (7*S*,10*R*)-2-hydroxy-15-calamenenoic acid (**3**).

Table 1. ^1H and ^{13}C NMR data for natural (7*R*,10*S*)-2,15-dihydroxycalamenene (**1**) as reported in Salmoun *et al.*[2] compared to the synthetic (7S,10R)-**1**

Carbon Number	Natural (7*R*,10*S*)-**1**[a]		Synthetic (7*S*,10*R*)-**1**[b]		
	δ_H[c] (*J* in Hz)[c]	δ_C[c]	δ_H[c] (*J* in Hz)	δ_C[c]	$\Delta\delta_C$[d]
2		153.6		153.5	0.1
6		141.6		141.7	–0.1
4		137.9		137.9	0.0
1		128.9		128.8	0.1
5	6.72 (s, 1H),	120.6	6.72 (s, 1H)	120.7	–0.1
3	6.65 (s, 1H)	111.2	6.66 (d, *J*=1.2, 1H)	111.1	0.1
15	4.58 (s, 2H)	65.4	5.40 (bs, 1H) *OH* 4.58(s, 2H)	65.4	0.0
7	2.49 (m, 1H)	43.1	2.50-2.48 (m, 1H)	43.1	0.0
11	1.97 (m, 1H) 1.93 (m, 1H)	33.2	2.02-1.95 (m, 1H) 1.95-1.87 (m, 1H)	33.2	0.0
9	1.49 (m, 1H)	27.0	1.53-1.51 (m, 1H)	26.9	0.1
10	3.11 (m, 1H)	26.8	3.14-3.09 (m,1H)	26.7	0.1
13	0.97 (d, *J*=7, 3H)	22.1	0.98 (d,*J*=6.6Hz,3H)	22.1	0.0
14	1.19 (d, *J*=7, 3H)	21.1	1.20 (d, *J*=7.2,3H)	21	0.1
12	0.81 (d, *J*=7, 3H) 1.82 (m, 1H)	19.6	0.82 (d, *J*=7.2,3H) 1.87-1.81 (m, 1H)	19.6	0.0
8	1.75 (m, 1H)	19.0	1.80-1.76 (m, 1H)	18.9	0.1

[a] Chemical shifts and coupling constants as reported in Salmoun *et al.*[2]

[b] Chemical shifts and coupling constants for prepared compounds, Bruker 600 MHz NMR Spectrometer.

[c] Chemical shifts in ppm referenced to $CHCl_3$ at 7.26 ppm and to $CDCl_3$ at 77.00 ppm.

[d] This is the difference in the ^{13}C chemical shift (ppm) of the synthetic isomer and that reported for the natural product.

Table 2. ^{1}H and ^{13}C NMR data for natural (7*R*,10*S*)-2-hydroxy-15-calamenenal (**2**) as reported in Salmoun *et al.*[2] compared to the synthetic (7*S*,10*R*)-**2**

Carbon Number	Natural (7*R*,10*S*)-**2**[a]		Synthetic (7*S*,10*R*)-**2**[b]		
	δ_H (*J* in Hz)[c]	δ_C[c]	δ_H (*J* in Hz)[c]	δ_C[c]	$\Delta\delta_C$[d]
15	9.86 (s, 1H)	192.9	9.86 (s, 1H)	192.9	0.0
2		154.3	5.79 (bs, 1H) *OH*	154.1	0.2
6		142.3		142.3	0
1		138.0		137.9	0.1
4		134.0		134	0.0
5	7.28 (s, 1H)	125.9	7.28 (s, 1H)	126	–0.1
3	7.23 (s, 1H)	110.9	7.18 (d, *J*=1.2,1H)	110.8	0.1
7	2.59 (m, 1H)	43.1	2.60-2.58 (m, 1H)	43.1	0.0
11	2.05 (m, 1H)	33.3	2.04 (qn, *J*=6.6, 1H)	33.3	0.0
10	3.25 (m, 1H)	27.5	3.25-3.21 (m, 1H)	27.5	0.0
9	1.99 (m, 1H) 1.57 (m, 1H)	26.6	2.00-1.95 (m, 1H) 1.58-1.54 (m, 1H)	26.6	0.0
13	1.01 (d, *J*=7,3H)	22.0	1.00 (d, *J*=6.6, 3H)	22.0	0.0
14	1.23 (d, *J*=7,3H)	20.8	1.23 (d, *J*=7.2, 3H)	20.8	0.0
12	0.85 (d, *J*=7,3H)	19.5	0.84 (d, *J*=7.2, 3H)	19.5	0.0
8	1.88 (m, 1H) 1.84 (m, 1H)	18.9	1.90-1.80 (m, 2H)	18.8	0.1

[a] Chemical shifts and coupling constants as reported in Salmoun *et al.*[2]

[b] Chemical shifts and coupling constants for prepared compounds, Bruker 600 MHz NMR Spectrometer.

[c] Chemical shifts in ppm referenced to $CHCl_3$ at 7.26 ppm and to $CDCl_3$ at 77.00 ppm.

[d] This is the difference in the ^{13}C chemical shift (ppm) of the synthetic isomer and that reported for the natural product.

Table 3. ^{1}H and ^{13}C NMR data for natural (7*S*,10*R*)-2-hydroxy-15-calamenenoic acid (**3**) as reported in Jitsaeng *et al.*[3] compared to the synthetic (7*S*,10*R*)-2-hydroxy-15-calamenenoic acid (**3**)

Carbon Number	Natural (7*S*,10*R*)-(**3**)[a]		Synthetic (7*S*,10*R*)-(**3**)[b]		
	δ_H (*J* in Hz)[c]	δ_C[c]	δ_H (*J* in Hz)[c]	δ_C[c]	$\Delta\delta_C$[d]
15		170.8		170.0	0.8
2		153.1	8.04 (bs, 1H) *OH*	154.3	–1.2
6		141.6		141.0	0.6
1		136.1		135.7	0.4
4		126.3		127	–0.7
5	7.53 (br s, 1H)	124.4	7.40 (s, 1H)	122.8	1.6
3	7.28 (br s, 1H)	113.2	7.33 (s, 1H)	113.0	0.2
7	2.57 (br s, 1H)	43.1	2.51-2.50 (m, 1H)	42.9	0.2
11	2.02 (m, 1H)	33.2	2.03-1.97 (m, 1H)	33.2	0.0
10	3.19 (m, 1H)	27.1	3.20-3.18 (m, 1H)	27.1	0.0
9	1.97 (m, 1H) 1.55 (br d, *J*=12.6, 1H)	26.5	1.94-1.88 (m, 1H) 1.49-1.47 (m, 1H)	26.7	0.0
12	0.98 (d, *J*=6.6, 3H)	21.9	0.94 (d, *J*=6.6, 3H)	21.9	0.0
14	1.21 (d, *J*=6.9, 3H)	20.7	1.16 (d, *J*=7.2, 3H)	20.7	0.0
13	0.82 (d, *J*=6.9, 3H)	19.6	0.77 (d, *J*=6.6, 3H)	19.4	0.2
8	1.82 (m, 2H)	18.8	1.84-1.78 (m, 1H) 1.75-1.73 (m, 1H)	18.8	0.0

[a] Chemical shifts and coupling constants as reported in Jitsaeng *et al.*[3]

[b] Chemical shifts and coupling constants for prepared compounds, Bruker 600 MHz NMR Spectrometer.

[c] Chemical shifts in ppm referenced to $CHCl_3$ at 7.26 ppm and to $CDCl_3$ at 77.00 ppm.

[d] This is the difference in the ^{13}C chemical shift (ppm) of the synthetic isomer and that reported for the natural product. Note that the carbon shifts reported in Jitsaeng *et al.*[3] are extracted from HSQC and HMBC.

Conclusions

This paper has demonstrated the development of a novel method for the benzannulation of menthone, proceeding via an efficient 6-*endo*-*dig* cyclisation of a 3-hydroxy-1,5-enyne to give the aromatic ring, for which silver nitrate was identified as the optimum catalyst. This reaction sequence enabled the total syntheses of (7*S*,10*R*)-2,15-dihydroxycalamenene (**1**) (6 steps, 39.6%), (7*S*,10*R*)-2-hydroxy-15-calamenenal (**2**) (7 steps, 10.7%) and (7*S*,10*R*)-2-hydroxy-15-calamenenoic acid (**3**) (9 steps, 33.6%) from (–)-menthone via a common intermediate. This benzannulation method was subsequently also applied to the synthesis of two related serrulatane natural products.[19]

Experimental Section

General. All reactions were carried out under an inert atmosphere of nitrogen unless otherwise specified. All glassware was either oven or flame-dried prior to use. Benzene, dichloromethane and triethylamine were distilled over CaH_2. DMPU was distilled under reduced pressure from CaH_2. Tetrahydrofuran and diethyl ether were distilled over sodium and benzophenone. All other reagents were used as received. Thin layer chromatography was performed with Merck silica gel 60 F_{254} aluminium backed sheets and developed with $KMnO_4$ or anisaldehyde, or monitored by ultraviolet lamp. Column chromatography was performed with Merck Silica gel (particle size: 0.04-0.063 mm) 230-400 mesh silica. When purifying compounds with acid sensitivity, column chromatography was performed on buffered silica as indicated. Buffered silica was prepared by spinning 100 g of silica gel 60 (mesh size 0.040-0.063 mm) with 10 mL of pH 7 phosphate buffer on a rotary evaporator overnight at atmospheric pressure.[20] ^{1}H NMR spectra were recorded using either a Bruker 400 MHz or Bruker 600 MHz Spectrometer. Where $CDCl_3$ was used as the solvent and internal lock, it was referenced to $CHCl_3$ (δ_H 7.26) for ^{1}H NMR and $CDCl_3$ (δ_C 77.00) for ^{13}C NMR. Chemical shift values are reported in parts per million (ppm) and coupling constants are reported in hertz (Hz). Abbreviations used for assigning ^{1}H NMR spectra: Ar = aromatic, s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet, br = broad, app. = apparent. Optical rotations were recorded on a PolA AR21 polarimeter referenced to the sodium D line (589 nm) at 20 °C. Concentrations are reported in g/100 mL using analytical grade solvents.

2-(Phenylselanyl)acetaldehyde (7). The reaction was conducted according to a procedure by Baudat and Petrzilka.[5] To a stirred solution of phenylselenenyl chloride (1.1 g; 5.7 mmol) in THF (50 mL) at 0 °C was added ethyl vinyl ether (1.2 mL; 12.5 mmol) and the resulting solution stirred for 10 min at 0 °C. The reaction mixture was poured into 1 M HCl (130 mL) and the resulting biphasic mixture stirred for 1 h at RT. The layers were separated, the aqueous layer extracted with Et_2O (3 × 40 mL), and the combined organic extracts washed with $NaHCO_3$ (2 × 50 mL) and brine (2 × 50 mL). The organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to give the crude *title compound* **7** (1.13 g, 99%) as a yellow/orange liquid.^{1}H NMR ($CDCl_3$, 600 MHz) δ 9.46 (1H, t, *J*=4.0 Hz, C*H*O), 7.50−7.45 (2H, m, Ar-*H*), 7.30−7.20 (3H, m, Ar-*H*), 3.49 (2H, d, *J*=4.0 Hz, CH_2CHO); ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.9, 133.8, 129.5, 128.4, 127.5, 36.9.

(3*R*,6*S*)-2-[1-Hydroxy-2-(phenylselanyl)ethyl]-6-isopropyl-3-methylcyclohexan-1-one (8). A solution of diisopropylamine (3.54 mL, 25.1 mmol) in THF (80 mL) was cooled to -78 °C and *n*BuLi (1.49M in hexanes; 16.0 mL, 23.9 mmol) added dropwise. After 30 min a solution of (–)-menthone (3.92 mL, 22.8 mmol) in THF (8 mL) was added and the solution stirred at -78 °C for 1 h before the addition of DMPU (5.49 mL, 45.6 mmol), which was followed by the dropwise addition of the crude selenoaldehyde **7** (4.76 g, 23.9 mmol) in THF (10 mL). The

resulting yellow solution was stirred at -78 °C for 2.5 h then poured into a rapidly stirred sat. NH_4Cl solution (100 mL), with the mixture allowed to warm to RT before the addition of ether (150 mL) and H_2O (50 mL). The layers were separated and the aqueous layer extracted with ether (50 mL). The combined organic layers were washed with H_2O (100 mL), sat. $NaHCO_3$ (100 mL) and brine (100 mL), then dried and concentrated *in vacuo*. ^{1}H NMR analysis of the crude reaction mixture revealed a dr of ≥99:1. Column chromatography (20% ether/hexane) afforded the *title compound* **8** (6.30 g, 78%) as a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.48 (m, 2H), 7.25-7.22 (m, 3H), 3.82-3.78 (m, 1H), 3.61 (d, *J*=11.4 Hz, 1H), 3.31 (dd, *J*=12.0, 5.4 Hz, 1H), 3.12 (dd, *J*=12.6, 3.1 Hz, 1H), 2.44 (d, *J*=12.0 Hz, 1H), 2.06-2.01 (m, 2H), 1.93 (heptet, *J*=6.6 Hz, 1H), 1.82-1.92 (m, 2H), 1.41 (dq, *J*=13.2, 4.2 Hz, 1H), 1.31 (dq, *J*=13.2, 3.0 Hz, 1H), 1.00 (d, *J*=6.6 Hz, 3H), 0.814 (d, *J*=6.6 Hz, 3H), 0.808 (d, *J*=6.6 Hz, 3H);^{13}C NMR (150 MHz, $CDCl_3$) δ 217.6, 132.9, 129.6, 129.2, 127.1, 70.2, 58.8, 57.7, 38.5, 34.5, 32.7, 29.9, 25.8, 21.4, 20.1, 18.6; IR (thin film) 3516, 2955, 2870, 1691, 1477, 1074, 1022, 737, 691 cm^{-1}; $[\alpha]_D^{20}$ +7 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{18}H_{26}O_2SeNa$ 377.0990, found 377.0979 $[M+Na]^+$.

1-[(3*S*,6*R*)-3-Isopropyl-6-methyl-2-oxocyclohexyl]-2-(phenylselanyl)ethyl acetate (9). The selenide **8** (467 mg, 1.32 mmol) was dissolved in anhydrous pyridine (2.5 mL) and cooled to 0 °C, followed by the addition of acetic anhydride (1.0 mL, 10.6 mmol) and DMAP (16 mg). After stirring at RT for 2.5 h a solution of 2 M HCl (20 mL) was added and the mixture left to stir for 15 min before dilution with ether (40 mL). The layers were separated and the ether layer washed with H_2O (50 mL), sat. $NaHCO_3$ (50 mL) and brine (50 mL). After concentration *in vacuo*, the residue was passed through a plug of silica gel (25% ether/hexane) to give the *title compound* **9** as a colorless oil (522 mg, quant.); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55-7.53 (m, 2H), 7.27-7.21 (m, 3H), 5.28 (dt, *J*=7.2, 1.8 Hz, 1H), 3.39 (dd, *J*=12.6, 7.2 Hz, 1H), 3.27 (dd, *J*=12.6, 7.8 Hz, 1H), 2.53 (dd, *J*=11.7, 0.9 Hz, 1H), 2.06-1.99 (m, 2H), 1.98 (s, 3H), 1.91-1.85 (m, 2H), 1.82-1.75 (m, 1H), 1.46-1.37 (m, 1H), 1.35-1.28 (m, 1H), 1.00 (d, *J*=6.0 Hz, 3H), 0.85 (d, *J*=6.6 Hz, 3H), 0.82 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 210.6, 170.7, 132.6, 129.8, 129.2, 127.0, 72.0, 58.1, 56.8, 37.0, 34.8, 28.1, 27.9, 26.0, 21.4, 21.2, 20.8, 18.7; IR (thin film) 2956, 2872, 1739, 1708, 1371, 1239, 1022, 737, 691 cm^{-1}; $[\alpha]_D^{20}$ –4 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{20}H_{28}O_3SeNa$ 419.1096, found 419.1095 $[M+Na]^+$.

1-[(3*S*,6*R*)-3-Isopropyl-6-methyl-2-oxocyclohexyl]vinyl acetate (10). *m*CBPA (77%, 442 mg, 1.97 mmol) was added portionwise to a solution of the selenide **9** (780 mg, 1.97 mmol) in DCE (15 mL) at 0 °C and the solution stirred for 20 min at RT. The solution was then diluted with DCE (35 mL) and sat. $NaHCO_3$ (50 mL) was added. The colorless biphasic mixture was stirred at 90 °C for 5 h, during which the formation of the yellow diphenyldiselenide by-product is observed. After cooling, the layers were separated and the organic layer washed with sat. $NaHCO_3$ (50 mL) and brine (50 mL), then dried (Na_2SO_4) and concentrated *in vacuo*. Column chromatography [buffered silica gel[22] (0.5% Et_3N), 20-30% ether/hexane] afforded 401 mg (85%) of the *title compound* **10** as a colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.11 (d, *J*=1.8 Hz, 1H), 4.78 (d, *J*=1.8 Hz, 1H), 2.72 (d, *J*=12.0 Hz, 1H), 2.14-2.09 (m, 1H), 2.11 (s, 3H), 2.09-2.04 (m, 2H), 1.99-1.94 (m, 1H), 1.93-1.87 (m, 1H), 1.45-1.39 (m, 1H), 1.34-1.38 (m, 1H), 1.07 (d, *J*=6.6 Hz, 3H), 0.90 (d, *J*=6.6 Hz, 3H), 0.84 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.3, 168.6, 150.5, 104.9, 63.8, 56.3, 37.8, 33.9, 28.0, 26.1, 21.4, 21.2, 20.8, 18.7; IR (thin film) 2957, 2873, 1762, 1713, 1657, 1369, 1197, 1021, 873 cm^{-1}; $[\alpha]_D^{20}$ –5 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{14}H_{22}O_3Na$ 261.1461, found 261.1460 $[M+Na]^+$.

(*Z*)-4-{(3*S*,6*R*)-2-[3-(Benzyloxy)prop-1-yn-1-yl]-2-hydroxy-3-isopropyl-6-methylcyclohexyl}-4-hydroxybut-3-en-2-one (12). To a solution of propargyl benzyl ether (2.75 g, 18.80 mmol) in THF (60 mL) at -78 °C was added *n*BuLi (1.56 M in hexanes; 10.12 mL, 15.79 mmol). The excess dry ice was removed from the bath and the mixture allowed to warm to -30 °C over 1.5 h before recooling to -78 °C. A solution of the vinyl acetate **10** (1.79 g, 7.52 mmol) in THF (10 mL) was added dropwise and the solution stirred at -78 °C for 2 h before pouring into sat.

NH_4Cl (100 mL) and allowing to warm to RT. Ether (100 mL) was added and the layers separated. The organic layer was washed with H_2O (50 mL), sat. $NaHCO_3$ (100 mL) and brine (100 mL). After drying (Na_2SO_4) and concentrating *in vacuo*, ^1H NMR analysis of the crude reaction mixture revealed 100% conversion with the product present as a single isomer. Column chromatography (10-20% ether/hexane) on buffered silica gel[22] (1% NEt_3) afforded the *title compound* **12** (2.45 g, 87%) as a very pale orange oil; ^1H NMR (600 MHz, $CDCl_3$) δ 7.36-7.28 (m, 5H), 5.56 (s, 1H), 4.54-4.4.50 (m, 2H), 4.38 (s, 1H), 4.22-4.15 (m, 2H), 2.51-2.47 (m, 1H), 2.12-2.05 (m, 2H), 1.93 (s, 3H), 1.82 (dq, *J*=13.2, 3.6 Hz, 1H), 1.67 (dq, *J*=13.2, 3.6 Hz, 1H), 1.49 (dq, *J*=13.2, 3.6 Hz, 1H), 1.27-1.24 (m, 1H), 1.05-0.97 (m, 1H), 0.98-0.96 (m, 6H), 0.86 (d, *J*=6.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 201.0, 187.5, 137.5, 128.4, 127.9, 127.7, 103.3, 89.7, 80.2, 72.6, 70.9, 63.4, 57.2, 51.1, 34.5, 30.4, 28.4, 23.7, 23.4, 20.3, 19.5, 18.3; IR (thin film) 3460, 2954, 2871, 1608, 1455, 1386, 1354, 1073, 739, 698 cm^{-1}; $[\alpha]_D^{20}$ +31 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{24}H_{32}O_4Na$ 407.2193, found 407.2187 $[M+Na]^+$.

1-{(5*S*,8*R*)-3-[(Benzyloxy)methyl]-1-hydroxy-5-isopropyl-8-methyl-5,6,7,8-tetrahydronaphthalen-2-yl}ethan-1-one (13). To a mixture of $AuCl(Ph_3P)$ (6.2 mg, 0.013 mmol, 1 mol %) and TfOH (0.1M in Et_2O, 1.26 mL, 0.013 mmol, 1 mol %) in DCE (20 mL) was added a solution of enyne **12** (484 mg, 1.26 mmol) in DCE (5 mL). The solution was left to stir at 100 ˚C overnight, then allowed to cool before quenching with sat. $NaHCO_3$ (5 mL). H_2O (20 mL) was added and the layers separated. The organic layer was washed with brine (20 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Column chromatography (5% ether/hexane) afforded the *title compound* **13** (303 mg, 66%) as a pale yellow oil; ^1H NMR (600 MHz, $CDCl_3$) δ 13.14 (s, 1H) 7.37-7.29 (m, 5H), 6.70 (s, 1H), 4.77 (d, *J*=12.0 Hz, 1H), 4.69 (d, *J*=12.0 Hz, 1H), 4.50-4.52 (m, 2H), 3.27-3.23 (m, 1H), 2.77 (s, 3H), 2.49-2.51 (m, 1H), 2.08-2.03 (m, 1H), 1.95-1.89 (m, 1H), 1.88-1.78 (m, 2H), 1.56-1.54 (m, 1H), 1.20 (d, *J*=6.6 Hz, 3H), 1.03 (d, *J*=6.6 Hz, 3H), 0.84 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.1, 161.6, 147.1, 137.6, 133.9, 132.8, 128.4, 127.83, 127.78, 124.0, 117.3, 72.7, 72.1, 43.2, 33.1, 31.0, 26.8, 26.6, 22.1, 20.5, 19.5, 18.4; IR (thin film) 2956, 2870, 1607, 1396, 1363, 1308, 1254, 1073 cm^{-1}; $[\alpha]_D^{20}$ −44 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{24}H_{30}O_3Na$ 389.2087, found 389.2085 $[M+Na]^+$.

(5*S*,8*R*)-3-[(Benzyloxy)methyl]-1-hydroxy-5-isopropyl-8-methyl-5,6,7,8-tetrahydronaphthalen-2-yl acetate (14) To a solution of phenol **13** (205 mg, 0.56 mmol) in DCM (8 mL) was added *m*CPBA (77%, 314 mg, 1.40 mmol) and $NaHCO_3$ (117 mg, 1.40 mmol). After stirring at ~35 °C for 2 h, sat. Na_2SO_3 (8 mL) was added and the mixture left to stir for 15 min. DCM (20 mL) was added and the organic layer was washed with H_2O (2 × 20 mL) and brine (20 mL). The solution was concentrated *in vacuo* and purified via column chromatography (30% ether/hexane) to give 199 mg (93%) of a pale yellow oil consisting of a rotameric mixture of the *title compound* **14**; ^1H NMR (600 MHz, $CDCl_3$, two rotamers) δ 7.41-7.36 (m, 5H), 6.84 and 6.77 (s, 1H), 4.77-4.75 and 4.52-4.50 (m, 2H), 4.63-4.61 and 4.49-4.44 (m, 2H), 3.24-3.20 and 3.05-3.00 (m, 1H), 2.54-2.51 and 2.50-2.47 (m, 1H), 2.39 and 2.26 (s, 3H), 2.08-1.91 (m, 2H), 1.89-1.83 (m, 1H), 1.81-1.78 (m, 1H), 1.57-1.50 (m, 1H), 1.25 and 1.20 (d, *J*=6.6 and 7.2 Hz, 3H), 1.04 and 1.02 (d, *J*=6.6 and 7.2 Hz, 3H), 0.89 and 0.86 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) Major rotamer: δ 168.9, 145.2, 138.1, 136.7, 135.7, 131.5, 128.5, 128.2, 128.1, 126.1, 120.2, 72.4, 71.2, 42.1, 33.3, 27.5, 26.7, 22.0, 21.5, 20.6, 19.3, 18.7; Minor rotamer: δ 169.4, 144.9, 138.2, 137.0, 135.0, 131.5, 128.3, 127.8, 127.5, 126.5, 122.4, 71.8, 68.0, 42.8, 33.0, 27.2, 26.6, 22.1, 21.0, 20.1, 19.6, 19.0; IR (thin film) 3383, 2955, 2868, 1768, 1748, 1489, 1367, 1198 cm^{-1}; $[\alpha]_D^{20}$ –21 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{20}H_{30}O_4Na$ 405.2036, found 405.2033 $[M+Na]^+$.

(3*R*,6*S*)-2-{1-[(*Tert*-butyldimethylsilyl)oxy]-2-(phenylselanyl)ethyl}-6-isopropyl-3-methylcyclohexan-1-one (15). To a solution of the hydroxyselenide **8** (460 mg, 1.30 mmol) in DCM (10 mL) at -78 °C was added 2,6-lutidine (0.30 mL, 2.60 mmol) followed by TBSOTf (0.45 mL, 1.95 mmol). After stirring for 15 min sat. $NaHCO_3$ (10 mL) was added and the mixture allowed to warm to RT. DCM (10 mL) was added and the layers separated, with the

organic layer washed with H_2O (10 mL) and brine (10 mL). Chromatography over a plug of silica gel (10% ether/hexane) afforded the *title compound* **15** (519 mg, 94%) as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (d, *J*=7.2 Hz, 2H), 7.26-7.23 (m, 2H), 7.20 (d, *J*=7.2 Hz, 1H), 4.38-4.33 (bm, 1H), 3.37 (dd, *J*=12.0, 5.7 Hz, 1H), 3.12 (dd, *J*=12.0, 7.8 Hz, 1H), 2.34 (d, *J*=12.0 Hz, 1H), 2.11 (quintet, *J*=6.6 Hz, 1H), 2.00-1.88 (m, 4H), 1.44 (dq, *J*=12.6, 3.0 Hz, 1H), 1.33 (dq, *J*=12.6, 3.0 Hz, 1H), 1.12 (d, *J*=6.6 Hz, 3H), 0.88-0.87 (m, 12H), 0.82 (d, *J*=6.6 Hz, 3H), 0.07 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 211.4, 132.1, 131.0, 128.9, 126.4, 70.8, 61.2, 56.7, 36.4, 34.9, 32.1, 27.3, 25.9, 25.8, 21.5, 21.3, 18.5, 18.0, -4.3, -4.4; IR (thin film) 2954, 2928, 2855, 1704, 1472, 1252, 1108, 1052, 912, 836, 774, 734, 690 cm^{-1}; $[\alpha]_D^{20}$ –3 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{24}H_{40}O_2SeSiNa$ 491.1855, found 491.1867 $[M+Na]^+$.

(3*R*,6*S*)-1-[3-(Benzyloxy)prop-1-yn-1-yl]-2-{1-[(*tert*-butyldimethylsilyl)oxy]-2-(phenylselanyl)ethyl}-6-isopropyl-3-methylcyclohexan-1-ol (16) To a solution of [(prop-2-yn-1-yloxy)methyl]benzene (827 mg, 5.65 mmol) in THF (35 mL) at -78 °C was added *n*BuLi (2.42 M in hexanes; 2.12 mL, 5.13 mmol). The excess dry ice was removed from the bath and the mixture warmed to -20 °C over 1 h before recooling to -78 °C. DMPU (0.62 mL, 5.13 mmol) was added and the mixture left for 10 min before a solution of the selenide **15** (1.20 g, 2.57 mmol) in THF (5 mL) was added dropwise. After stirring for 1 h the reaction mixture was poured into a vigorously stirred sat. NH_4Cl solution (100 mL) and the mixture allowed to warm to RT. Ether (100 mL) was added and the layers separated. The organic layer was washed with H_2O (50 mL), sat. $NaHCO_3$ (50 mL) and brine (50 mL), then dried (Na_2SO_4) and concentrated *in vacuo*. Column chromatography (5% ether/hexane) afforded the *title compound* **16** (1.48 g, 94%) as a colorless oil existing as an inseparable mixture of rotamers; ^{1}H NMR (600 MHz, $CDCl_3$) major rotamer: δ 7.59-7.58 (m, 2H), 7.42-7.38 (m, 4H), 7.36-7.28 (m, 4H), 5.11 (s, 1H), 4.68 (s, 2H), 4.36-4.33 (m, 4H), 3.12-3.08 (m, 1H), 2.72-2.70 (m, 1H), 2.00-1.99 (m, 1H), 1.96-1.90 (m, 1H), 1.87-1.85 (m, 1H), 1.64-1.62 (m, 1H), 1.49-1.48 (m, 2H), 1.34-1.32 (m, 1H), 1.19-1.15 (m, 2H), 1.01-0.93 (m, 18H), 0.03-0.00 (m, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.7, 133.7, 130.0, 129.0, 128.3, 128.0, 127.7, 127.3, 92.6, 81.7, 74.7, 73.8, 71.4, 57.7, 53.7, 50.7, 35.7, 34.9, 29.1, 27.7, 25.7, 24.0, 20.5, 19.6, 18.5, 17.8, -4.4, -5.0; IR (thin film) 3452, 2953, 2928, 2856, 1452, 1254, 1072, 1024, 836, 776, 735, 694 cm^{-1}; $[\alpha]_D^{20}$ –35 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{34}H_{50}O_3SeSiNa$ 637.2587, found 637.2605 $[M+Na]^+$.

(3*R*,6*S*)-1-[3-(Benzyloxy)prop-1-yn-1-yl]-2-{1-[(*tert*-butyldimethylsilyl)oxy]vinyl}-6-isopropyl-3-methylcyclohexan-1-ol (17). *m*CPBA (328 mg, 1.46 mmol) was added to a solution of the selenide **16** (897 mg, 1.46 mmol) in benzene (20 mL) at 10 °C and the resulting mixture was stirred for 20 min. A further portion of benzene was added (30 mL) and the solution was washed with sat. $NaHCO_3$ (2 × 20 mL). The benzene solution was transferred to a flask and sat. $NaHCO_3$ (50 mL) was added before the biphasic mixture was stirred at 90 °C for 4.5 h. After cooling the layers were separated and the organic layer was washed with sat. $NaHCO_3$ (50 mL) and brine (50 mL), then dried (Na_2SO_4) and concentrated *in vacuo*. Purification via column chromatography (5% ether/hexane) afforded the *title compound* **17** (545 mg, 82%) as a colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35-7.34 (m, 4H), 7.31-7.27 (m, 1H), 4.63 (d, *J*=11.4 Hz, 1H), 4.59 (d, *J*=11.4 Hz, 1H), 4.27-4.22 (m, 2H), 4.16 (s, 1H), 4.12 (d, *J*=1.2 Hz, 1H), 3.79 (bs, 1H), 2.57-2.50 (m, 1H), 1.96-1.89 (m, 1H), 1.84-1.80 (m, 1H), 1.77 (d, *J*=11.4 Hz, 1H), 1.61 (dq, *J*=13.2, 3.6 Hz, 1H), 1.47-1.43 (m, 1H), 1.28-1.26 (m, 1H), 1.02-0.92 (m, 16H), 0.86 (d, *J*=6.6 Hz, 3H), 0.25 (s, 3H), 0.23 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.9, 137.8, 128.3, 128.1, 127.7, 93.0, 90.3, 80.2, 75.0, 70.9, 61.3, 57.5, 51.8, 34.6, 29.0, 28.1, 25.8, 23.9, 20.4, 19.8, 18.5, 18.1, -4.4, -5.2; IR (thin film) 3527, 2952, 2929, 2862, 1627, 1279, 1254, 1012, 839, 696 cm^{-1}; $[\alpha]_D^{20}$ –15 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{28}H_{44}O_3SiNa$ 479.2952, found 479.2950 $[M+Na]^+$.

1-{(3*S*,6*R*)-2-[3-(Benzyloxy)prop-1-yn-1-yl]-2-hydroxy-3-isopropyl-6-methylcyclohexyl}ethan-1-one (18). A solution of TfOH in ether (0.01 M, 2.36 mL, 0.024 mmol, 20 mol %) was added to a solution of $Au(Ph_3P)Cl$ (12 mg, 0.024 mmol, 20 mol %) in DCE (0.5 mL). The mixture was concentrated to half the volume under a stream of N_2, after which a solution of the TBS-protected enyne (54 mg, 0.12 mmol) in DCE (1.5 mL) was added. After stirring at reflux for 3 h the solution was allowed to cool then quenched with sat. $NaHCO_3$ (2 mL). The mixture was diluted with ether (10 mL) and the organic layer washed with H_2O (10 mL), sat. $NaHCO_3$ (10 mL) and brine (10 mL), then dried (Na_2SO_4) and concentrated *in vacuo*. ^{1}H NMR analysis of the resulting colorless oil revealed quantitative conversion to the *title compound* **18**; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37-7.32 (m, 4H), 7.31-7.27 (m, 1H), 4.56 (s, 2H), 4.32 (d, *J*=1.8 Hz, 1H), 4.21-4.17 (m, 2H), 2.54 (d, *J*=10.8 Hz, 1H), 2.48-2.42 (m, 1H), 2.33 (s, 3H), 2.03-1.96 (m, 1H), 1.79-1.75 (m, 1H), 1.67-1.59 (m, 1H), 1.49-1.45 (m, 1H), 1.25-1.21 (m, 1H), 1.06-0.99 (m, 1H), 0.96-0.95 (m, 6H), 0.88 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 217.2, 137.3, 128.4, 128.0, 127.9, 89.6, 80.2, 71.6, 71.4, 65.3, 57.3, 50.9, 35.3, 34.4, 31.1, 28.3, 23.7, 20.2, 19.5, 18.3.

({(5*S*,8*R*)-3-[(Benzyloxy)methyl]-5-isopropyl-8-methyl-5,6,7,8-tetrahydronaphthalen-1-yl}oxy)(*tert*-butyl)dimethylsilane (19). To a solution of the enyne **17** (70 mg, 0.15 mmol) in anhydrous DCE (3.5 mL) in the dark was added finely ground $AgNO_3$ (3 mg, 0.015 mmol). The mixture was stirred at 100 °C in the dark for 3 h, after which another portion of $AgNO_3$ (3 mg, 0.015 mmol) was added, and then stirring was continued at this temperature for a further 2 h. After cooling to RT the mixture was quenched with sat. $NaHCO_3$ (5 mL) and diluted with DCM (10 mL). The layers were separated and the organic phase washed with H_2O (10 mL) and brine (10 mL), then dried (Na_2SO_4) and concentrated *in vacuo*. Column chromatography (5% ether/hexane) afforded the *title compound* **19** (32 mg, 48%) as a colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39-7.29 (m, 4H), 7.32-7.29 (m, 1H), 6.76 (s, 1H), 6.67 (s, 1H), 4.55 (s, 2H), 4.48 (s, 2H), 3.17-3.15 (m, 1H), 2.53-2.50 (m, 1H), 2.01 (sextet, *J*=6.6 Hz, 1H), 1.97-1.92 (m, 1H), 1.89-1.83 (m, 1H), 1.81-1.77 (m, 1H), 1.53-1.49 (m, 1H), 1.16 (d, *J*=7.2 Hz, 3H), 1.04 (s, 9H), 1.00 (d, *J*=7.2 Hz, 3H), 0.85 (d, *J*=6.6 Hz, 3H), 0.29 (s, 3H), 0.23 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.3, 141.2, 138.5, 134.8, 133.1, 128.3, 127.8, 127.5, 122.0, 114.8, 72.2, 71.7, 43.0, 33.4, 27.0, 26.9, 25.9, 22.2, 21.4, 19.7, 19.0, 18.3, -4.0, -4.3; IR (thin film) 2955, 2929, 2860, 1574, 1471, 1427, 1281, 1253, 1078, 852, 833, 779, 696 cm^{-1}; $[\alpha]_D^{20}$ –26 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{28}H_{42}O_2SiNa$ 461.2846, found 461.2849 $[M+Na]^+$.

(5S,8*R*)-5-Isopropyl-3,8-dimethyl-5,6,7,8-tetrahydronaphthalen-1-ol (20). A mixture of the benzyl ether (63 mg, 0.147 mmol) and Pd/C (10 wt %, 12 mg) were stirred vigorously for 24 h under H_2 in a solution of MeOH (1.5 mL) containing 4 drops of 6 M HCl. The mixture was filtered through Celite and concentrated *in vacuo*. The residue was redissolved in ether (10 mL) and washed with sat. $NaHCO_3$ (10 mL) and brine (10 mL), then dried (Na_2SO_4) and concentrated *in vacuo*. Purification through a plug of silica gel (10% ether/hexane) afforded the *title compound* **20** (34 mg, 99%) as a colorless oil; spectroscopic data was in accordance with that published in the literature:[21,22] ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.60 (s, 1H), 6.45 (s, 1H), 4.69 (br s, 1H), 3.08 (qn, *J*=6.5 Hz, 1H), 2.49-2.46 (m, 1H), 2.26 (s, 3H), 2.04-1.95 (m, 2H), 1.88-1.76 (m, 2H), 1.54-1.50 (m, 1H), 1.22 (d, *J*=7.0 Hz, 3H), 1.00 (d, *J*=6.9 Hz, 3H), 0.84 (d, *J*=6.8 Hz, 3H).

(3*R*,6*S*)-6-Isopropyl-3-methyl-2-{2-(phenylselanyl)-1-[(triisopropylsilyl)oxy]ethyl}cyclohexan-1-one (22). To a solution of the hydroxyselenide **8** (732 mg, 2.07 mmol) in DCM (20 mL) at -78 °C was added 2,6-lutidine (0.48 mL, 4.14 mmol), followed by TIPSOTf (0.81 mL, 3.01 mmol). After stirring at -78 °C for 5 h the solution was allowed to warm to 0 °C over 30 min before quenching with sat. $NaHCO_3$ (10 mL). DCM (30 mL) was added and the layers separated. The organic phase was washed with H_2O (2 × 50 mL) and brine (50 mL), then dried (Na_2SO_4) and concentrated *in vacuo*. Column chromatography (5% ether/hexane) afforded the *title compound* **22** (972 mg, 92%) as a colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54-7.52 (m, 2H), 7.26-7.19 (m, 3H), 4.61-4.57 (bm, 1H), 3.45-3.42 (bm, 1H), 3.17 (dd, *J*=12.0, 6.0 Hz, 1H), 2.40 (d, *J*=12.0 Hz, 1H), 2.21-2.16 (m, 1H), 2.04-1.95 (m, 2H), 1.94-1.90 (m, 2H), 1.48-1.41 (m, 1H), 1.40-1.33 (m, 1H), 1.15 (d, *J*=6.6 Hz, 3H), 1.08-1.02 (m, 21H), 0.87 (d, *J*=6.6

Hz, 3H), 0.82 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 210.8, 132.5, 130.8, 128.9, 126.6, 70.7, 60.9, 56.6, 35.9, 34.9, 32.1, 26.6, 25.7, 21.6, 21.2, 18.3, 18.2, 12.8; IR (thin film) 2944, 2866, 1705, 1579, 1462, 1383, 1366, 1107, 1054, 882, 735, 680 cm^{-1}; $[\alpha]_D^{20}$ –20 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{27}H_{46}O_2SiSe^{80}Na$ 533.2330, found 533.2340 $[M+Na]^+$.

(3*R*,6*S*)-6-Isopropyl-3-methyl-2-{2-(phenylselanyl)-1-[(triisopropylsilyl)oxy]ethyl}-1-{3-[(triisopropylsilyl)oxy]prop-1-yn-1-yl}cyclohexan-1-ol (23). *n*BuLi (1.52 M in hexanes; 2.0 mL, 3.04 mmol) was added to a solution of triisopropyl(prop-2-yn-1-yloxy)silane (672 mg, 3.16 mmol) in THF at -78 °C. After being allowed to slowly warm to -40 °C over 1.5 h, the solution was recooled to -78 °C and DMPU (0.37 mL, 3.04 mmol) was added. After 10 min a solution of the selenide **22** (645 mg, 1.26 mmol) in THF (3 mL) was added dropwise, then the mixture was left to stir at -78 °C for 6 h, before being allowed to warm to -20 °C over a further hour. The mixture was poured into a stirred solution of sat. NH_4Cl (30 mL) and allowed to warm to RT, before the addition of H_2O (40 mL) and Et_2O (40 mL). The layers were separated and the organic phase was washed with H_2O (50 mL), $NaHCO_3$ (50 mL) and brine (50 mL), before drying (Na_2SO_4) and concentration *in vacuo*. Column chromatography (20-30% DCM/hexane) afforded the *title compound* **23** (865 mg, 95%) as a colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, major rotamer) δ 7.57-7.53 (m, 2H), 7.25-7.22 (m, 3H), 4.90 (s, 1H), 4.47-4.42 (m, 4H), 3.07-3.06 (m, 1H), 2.64-2.56 (m, 1H), 1.99-1.92 (m, 1H), 1.86 (d, *J*=10.8 Hz, 1H), 1.82-1.79 (m, 1H), 1.61-1.53 (m, 1H), 1.40-1.37 (m, 1H), 1.18-0.99 (m, 43H), 0.92-0.88 (m, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 134.3, 132.3, 130.0, 129.0, 127.4, 90.3, 84.3, 75.3, 73.5, 53.5, 52.3, 51.4, 36.1, 35.3, 29.5, 27.5, 23.9, 20.9, 19.6, 18.5, 18.1, 18.0, 12.9, 12.0; IR (thin film) 3462, 2944, 2866, 1463, 1384, 1367, 1085, 1065, 1037, 882, 736, 689 cm^{-1}; $[\alpha]_D^{20}$ –39 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{39}H_{70}O_3SiSe^{80}Na$ 745.3926, found 745.3934 $[M+Na]^+$.

(3*R*,6*S*)-6-Isopropyl-3-methyl-1-{3-[(triisopropylsilyl)oxy]prop-1-yn-1-yl}-2-{1-[(triisopropylsilyl)oxy]vinyl}cyclohexan-1-ol (24). To a solution of the selenide **23** (135 mg, 0.187 mmol) in benzene (5 mL) at ~10 °C was added *m*CPBA (42 mg, 0.187 mmol) portionwise. After 20 min both benzene (10 mL) and sat. $NaHCO_3$ (15 mL) were added and the biphasic mixture was allowed to stir at 90 °C overnight. After cooling, the layers were separated and the organic phase washed with $NaHCO_3$ (15 mL) and brine (15 mL), before drying (Na_2SO_4) and concentration *in vacuo*. ^{1}H NMR analysis of the crude material revealed quantitative conversion to the enyne. Flash column chromatography [phosphate-buffered silica gel (prepared according to the method of Gregg and Perkins),[20] 10% DCM/hexane] afforded the *title compound* **24** (87 mg, 82%) as a colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.41 (d, *J*=15.6, Hz, 1H), 4.37 (d, *J*=15.6 Hz, 1H), 4.17 (s, 1H), 4.07 (s, 1H), 3.67 (bs, 1H), 2.55 (quintet, *J*=6.6 Hz, 1H), 1.98-1.91 (m, 1H), 1.83-1.80 (m, 1H), 1.71 (d, *J*=11.4 Hz, 1H), 1.63-1.56 (m, 1H), 1.43-1.40 (m, 1H), 1.27 (sextet, *J*=7.2 Hz, 3H), 1.24-1.20 (m, 1H), 1.14-1.06 (m, 43H), 0.94-0.89 (m, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.0, 92.9, 88.1, 83.2, 74.6, 61.6, 52.1, 51.8, 34.9, 28.8, 28.2, 23.8, 20.8, 19.6, 18.5, 18.14, 18.12, 17.9, 12.9, 12.0; IR (thin film) 3529, 2946, 2867, 1622, 1464, 1384, 1367, 1277, 1255, 1089, 1012, 882, 682 cm^{-1}; $[\alpha]_D^{20}$ –3 (*c* 1.0, $CHCl_3$). HRMS calcd for $C_{33}H_{64}O_3Si_2Na$ 587.4292, found 587.4297 $[M+Na]^+$.

Triisopropyl({(5*R*,8*S*)-8-isopropyl-5-methyl-4-[(triisopropylsilyl)oxy]-5,6,7,8-tetrahydronaphthalen-2-yl}methoxy)silane (25). In the dark, a solution of the enyne **24** (60 mg, 0.106 mmol) in anhydrous DCE (5 mL) was heated to reflux before the addition of finely ground $AgNO_3$ (2 mg, 0.012 mmol). The mixture was stirred at 100 °C for 2.5 h before allowing to cool and quenching with sat. $NaHCO_3$ (3 mL). After diluting with DCM (10 mL), the mixture was washed with brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Column chromatography (10% DCM/hexane) afforded the *title compound* **25** (42 mg, 72%) as a colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.73 (s, 1H), 6.66 (s, 1H), 4.75-4.71 (m, 2H), 3.22-3.18 (m, 1H), 2.50-2.48 (m, 1H), 2.02-1.96 (m, 1H), 1.95-1.89 (m, 1H), 1.88-1.82 (m, 1H), 1.77-1.75 (m, 1H), 1.50-1.48 (m, 1H), 1.33 (septet, *J*=7.2 Hz, 3H), 1.18-1.09 (m, 45H), 0.97 (d, *J*=6.8 Hz, 3H), 0.80 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.6, 140.6, 138.3,

131.7, 119.3, 112.9, 65.0, 43.0, 33.6, 27.1, 27.0, 22.1, 21.5, 19.7, 19.0, 18.2, 18.1, 18.0, 13.2, 12.0; IR (thin film) 2944, 2866, 1576, 1463, 1428, 1367, 1283, 1145, 1098, 1066, 994, 882, 797, 681 cm^{-1}; $[\alpha]_D^{20}$ –26 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{33}H_{62}O_2Si_2Na$ 569.4181, found 569.4188 $[M+Na]^+$.

(5*S*,8*R*)-3-(Hydroxymethyl)-5-isopropyl-8-methyl-5,6,7,8-tetrahydronaphthalen-1-ol (1). To a solution of the bis-TIPS-**25** (52 mg, 0.095 mmol) in THF (1 mL) was added TBAF (1M in THF; 0.48 mL, 0.48 mmol). After stirring at 40 °C for 7 h, sat. NH_4Cl (1 mL) and EtOAc (10 mL) were added. The mixture was washed with H_2O (10 mL) and brine (10 mL), then dried (Na_2SO_4) and concentrated *in vacuo*. Chromatography over a plug of silica gel (30-50% EtOAc/hexane) afforded the dihydroxy compound (22 mg, 99%), which crystallized on standing. A sample was recrystallized via slow evaporation from EtOAc to give colorless crystals of the *title compound* **1**; mp 138.5-139 °C (EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.72 (s, 1H), 6.66 (d, *J*=1.2 Hz, 1H), 5.40 (bs, 1H), 4.58 (s, 2H), 3.14-3.09 (m, 1H), 2.50-2.48 (m, 1H), 2.02-1.95 (m, 1H), 1.95-1.87 (m, 1H), 1.87-1.81 (m, 1H), 1.80-1.76 (m, 1H), 1.53-1.51 (m, 1H), 1.20 (d, *J*=7.2 Hz, 3H), 0.98 (d, *J*=6.6 Hz, 3H), 0.82 (d, *J*=7.2 Hz, 3H); ^{1}H NMR (600 MHz, 1% DMSO-d_6/$CDCl_3$) δ 7.00 (s, 1H), 6.68 (s, 1H), 6.67 (s, 1H), 4.54 (d, *J*=3.0 Hz, 2H), 3.15-3.10 (m, 1H), 2.48-2.45 (m, 1H), 2.22 (bs, 1H), 2.01-1.95 (m, 1H), 1.95-1.90 (m, 1H), 1.84-1.78 (m, 1H), 1.76-1.72 (m, 1H), 1.49-1.46 (m, 1H), 1.17 (d, *J*=6.6 Hz, 3H), 0.96 (d, *J*=7.2 Hz, 3H), 0.79 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.5, 141.7, 137.9, 128.8, 120.7, 111.1, 65.4, 43.1, 33.2, 26.9, 26.7, 22.1, 21.0, 19.6, 18.9; IR (thin film) 3362, 3144, 2960, 2926, 2865, 1616, 1583, 1463, 1428, 1285, 1015, 956, 859 cm^{-1}; $[\alpha]_D^{20}$ –34 (*c* 0.79, $CHCl_3$); HRMS calcd for $C_{15}H_{21}O_2$ 233.1542, found 233.1535 $[M+H]^-$.

(5*R*,8*S*)-4-Hydroxy-8-isopropyl-5-methyl-5,6,7,8-tetrahydronaphthalene-2-carbaldehyde (2). To a solution of oxalyl chloride (2.0 M in DCM, 0.11 mL, 0.22 mmol) in anhydrous DCM (1.5 mL) at –78 °C was added anhydrous DMSO (0.032 mL, 0.45 mmol) dropwise. After stirring for 20 min a solution of the benzyl alcohol **1** (45 mg, 0.19 mmol) in DCM (2 mL, plus 3 drops anhydrous DMSO to assist dissolution) was added. Stirring was continued at –78 °C for 30 min before the addition of Et_3N (0.13 mL, 0.95 mmol), after which the mixture was allowed to warm to 0 °C over 1 h. Sat. NH_4Cl (3 mL) was added and the mixture diluted with DCM (10 mL). The organic phase was washed with H_2O (10 mL) and brine (10 mL), then dried (Na_2SO_4) and concentrated *in vacuo*. Column chromatography (20% ether/hexane) afforded the *title compound* **2** (12 mg, 27%) as a colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.86 (s, 1H), 7.28 (s, 1H), 7.18 (d, *J*=1.2 Hz, 1H), 5.79 (bs, 1H), 3.25-3.21 (m, 1H), 2.60-2.58 (m, 1H), 2.04 (qn, *J*=6.6 Hz, 1H), 2.00-1.95 (m, 1H), 1.90-1.80 (m, 2H), 1.58-1.54 (m, 1H), 1.23 (d, *J*=7.2 Hz, 3H), 1.00 (d, *J*=6.6 Hz, 3H), 0.84 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.9, 154.1, 142.3, 137.9, 134.0, 126.0, 110.8, 43.1, 33.3, 27.5, 26.6, 22.0, 20.8, 19.5, 18.8; IR (thin film) 3350, 2957, 2869, 1678, 1578, 1431, 1387, 1283, 1258, 863, 740 cm^{-1}; $[\alpha]_D^{20}$ –49 (*c* 0.6, $CHCl_3$); HRMS calcd for $C_{15}H_{19}O_2$ 231.1385, found 231.1384 $[M+H]^-$.

(5*R*,8*S*)-8-Isopropyl-5-methyl-4-[(triisopropylsilyl)oxy]-5,6,7,8-tetrahydronaphthalene-2-carbaldehyde (27). To a solution of the alcohol **26** (51 mg, 0.13 mmol) in anhydrous DCM (2 mL) was added finely ground PDC (74 mg, 0.19 mmol) and the solution left to stir at RT for 4 h. The mixture was then filtered through a pad of Celite, washing with DCM, and the filtrate concentrated *in vacuo*. Flash chromatography through a plug of silica gel (10% ether/hexane) afforded the *title compound* **27** (47.5 mg, 94%) as a colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.85 (s, 1H), 7.27 (s, 1H), 7.10 (d, *J*=1.8 Hz, 1H), 3.30-3.26 (m, 1H), 2.61-2.59 (m, 1H), 2.04 (quintet, *J*=6.6 Hz, 1H), 1.96-1.79 (m, 3H), 1.57-1.53 (m, 1H), 1.36 (septet, *J*=7.8 Hz, 3H), 1.18 (d, *J*=6.6 Hz, 3H), 1.14 (d, *J*=7.8 Hz, 9H), 1.10 (d, *J*=7.2 Hz, 9H), 0.99 (d, *J*=7.2 Hz, 3H), 0.82 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.3, 154.2, 142.0, 141.5, 133.9, 125.7, 113.6, 42.9, 33.7, 27.8, 26.5, 22.0, 21.1, 19.5, 18.7, 18.1, 18.0, 13.0; IR (thin film) 2947, 2868, 1697, 1574, 1464, 1428, 1383, 1284, 1141, 1082, 997, 919, 882, 803, 683 cm^{-1}; $[\alpha]_D^{20}$ –49 (*c* 1.0, $CHCl_3$); HRMS calcd for $C_{24}H_{40}O_2SiNa$ 411.2695, found 411.2688 $[M+Na]^+$.

(5*R*,8*S*)-8-Isopropyl-5-methyl-4-[(triisopropylsilyl)oxy]-5,6,7,8-tetrahydronaphthalene-2-carboxylic acid (28). To a solution of the aldehyde **27** (99 mg, 0.255 mmol) in *tert*-BuOH (2.5 mL) and 2-methyl-2-butene (0.27 mL, 2.55 mmol) was added dropwise a solution of NaH_2PO_4 (352 mg, 2.55 mmol) and $NaClO_2$ (80% technical grade, 72 mg, 0.64 mmol) in H_2O (5 mL). After stirring at RT for 24 h, the organic solvent was removed *in vacuo* and EtOAc (15 mL) added. The organic phase was washed with 1 M HCl (25 mL), the layers separated, and the aqueous phase extracted with EtOAc (2 × 10 mL). The organic layers were combined, then washed with brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Passage through a plug of silica gel (10% EtOAc/hexane) afforded the acid (97 mg, 94%) as a colorless oil that crystallized on standing. A sample was recrystallized via slow evaporation from $CHCl_3$ to give colorless crystals of the *title compound* **28**; mp 176-178 °C ($CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.4 (bs, 1H), 7.56 (s, 1H), 7.35 (d, *J*=1.2 Hz, 1H), 3.30-3.25 (m, 1H), 2.60-2.58 (m, 1H), 2.06-2.00 (m, 1H), 1.96-1.83 (m, 2H), 1.82-1.79 (m, 1H), 1.55-1.53 (m, 1H), 1.37 (septet, *J*=7.8 Hz, 3H), 1.18 (d, *J*=7.2 Hz, 3H), 1.15 (d, *J*=7.2 Hz, 9H), 1.11 (d, *J*=7.2 Hz, 9H), 0.99 (d, *J*=6.6 Hz, 3H), 0.82 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.7, 153.5, 141.4, 140.3, 126.0, 124.3, 115.9, 42.9, 33.7, 27.6, 26.6, 22.0, 21.1, 19.5, 18.7, 18.11, 18.07, 13.0; IR (thin film) 2947, 2868, 2632, 1687, 1573, 1464, 1421, 1292, 1254, 1035, 978, 882, 795, 683 cm^{-1}; $[\alpha]_D^{20}$ –43 (*c* 1.0, $CHCl_3$); HRMS calc for $C_{24}H_{39}O_3Si$ 403.2688, found 403.2675 $[M+H]^-$.

(5*R*,8*S*)-4-Hydroxy-8-isopropyl-5-methyl-5,6,7,8-tetrahydronaphthalene-2-carboxylic acid (3). TBAF (1 M in THF, 0.30 mL, 0.30 mmol) was added to a solution of the TIPS-ether **28** (81 mg, 0.20 mmol) in anhydrous THF (2.5 mL) and the mixture was allowed to stir at RT for 3 h. EtOAc (10 mL) and 1M HCl (20 mL) were then added and the layers separated. The aqueous layer was extracted with EtOAc (2 × 5 mL), then the combined organic layers were washed with brine (20 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Column chromatography (30% EtOAc/hexane + 0.5% AcOH) afforded the product (49 mg, 99%) as a colorless oil that crystallized on standing. A sample was recrystallized via slow evaporation from $CHCl_3$ to give colorless crystals of the *title compound* **3**; mp 165-166 °C ($CHCl_3$) (morphology change 151-153 °C); ^{1}H NMR (600 MHz, 1% DMSO-d_6/$CDCl_3$) δ 8.04 (bs, 1H), 7.40 (s, 1H), 7.33 (s, 1H), 3.20-3.18 (m, 1H), 2.51-2.50 (m, 1H), 2.03-1.97 (m, 1H), 1.94-1.88 (m, 1H), 1.84-1.78 (m, 1H), 1.75-1.73 (m, 1H), 1.49-1.47 (m, 1H), 1.16 (d, *J*=7.2 Hz, 3H), 0.94 (d, *J*=6.6 Hz, 3H), 0.77 (d, *J*=6.6 Hz, 3H); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.54 (bs, 1H), 9.56 (bs, 1H), 7.22 (s, 1H), 7.19 (d, *J*=1.8 Hz, 1H), 3.12-3.08 (m, 1H), 2.49-2.47 (m, 1H), 1.92 (septet, *J*=6.6 Hz, 1H), 1.89-1.83 (m, 1H), 1.80-1.71 (m, 2H), 1.47-1.44 (m, 1H), 1.11 (d, *J*=7.2 Hz, 3H), 0.93 (d, *J*=6.6 Hz, 3H), 0.77 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (150 MHz, 1% DMSO-d_6/$CDCl_3$) δ 170.0, 154.3, 141.0, 135.7, 127.0, 122.8, 113.0, 42.9, 33.2, 27.1, 26.7, 21.9, 20.7, 19.4, 18.8; IR (thin film) 3430, 3306, 2958, 2870, 2636, 1679, 1578, 1424, 1293, 1259, 1024, 962, 755 cm^{-1}; $[\alpha]_D^{20}$ –29 (*c* 0.5, $CHCl_3$). HRMS calcd for $C_{15}H_{19}O_3$ 247.1334, found 247.1334 $[M+H]^-$.

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Supplementary Material

Copies of NMR Spectra for compounds **1, 2, 3, 8-10, 1-28**.

References

1. Bordoloi, M., Shukla, V. S.; Nath, S. C.; Sharma, R. P. *Phytochemistry* **1989**, *28*, 2007-2037. https://doi.org/10.1016/S0031-9422(00)97915-9
2. Salmoun, M.; Braekman, J. C.; Ranarivelo, Y.; Rasamoelisendra, R.; Ralambomanana, D.; Dewelle, J.; Darro, F.; Kiss R. *Nat. Prod. Res.* **2007**, *21*, 111-120. https://doi.org/10.1080/14786410600899084
3. Jitsaeng, K.; De-Eknamkul, W.; Schneider, B. *Rec. Nat. Prod*. **2009**, *3*, 110–113.
4. Lu, J. M. H.; Perkins, M. V; Griesser, H. J. *Tetrahedron* **2013**, *69*, 6468–6473. https://doi.org/10.1016/j.tet.2013.05.082
5. Baudat, R.; Petrzilka, M. *Helv. Chim*. *Acta* **1979**, *62*, 1406–1410. https://doi.org/10.1002/hlca.19790620505
6. Engman, L. *J. Org. Chem.* **1989**, *54*, 884–890. https://doi.org/10.1021/jo00265a031
7. Grisé, C. M.; Rodrigue, E. M.; Barriault, L. *Tetrahedron* **2008**, *64*, 797–808. https://doi.org/10.1016/j.tet.2008.04.018
8. Kerr, R. G.; Kohl, A. C.; Ferns, T. A. *J. Ind. Microbiol. Biotechnol.* **2006**, *33*, 532–538. https://doi.org/10.1007/s10295-006-0106-3
9. Ferns, T. A.; Kerr, R. G. *J. Org. Chem.* **2005**, *70*, 6152–6157. https://doi.org/10.1021/jo050282r
10. Smith, J. E.; Tucker, D.; Watson, K.; Jones, G. L. *J. Ethnopharmacol.* **2007**, *112*, 386–393. https://doi.org/10.1016/j.jep.2007.03.031
11. Barnes, E. C.; Kavanagh, A. M.; Ramu, S.; Blaskovich, M. A.; Cooper, M. A.; Davis, R. A. *Phytochemistry* **2013**, *93*, 162–169. https://doi.org/10.1016/j.phytochem.2013.02.021
12. Croft, K.; Ghisalberti, E.; Jefferies, P.; Proudfoot, G. *Aust. J. Chem.* **1981**, *34*, 1951-1957. https://doi.org/10.1071/CH9811951
13. Tippett, L. M.; Massy-Westropp, R. A. *Phytochemistry* **1993**, *33*, 417–421. https://doi.org/10.1016/0031-9422(93)85531-U
14. Godet, T.; Belmont, P. *Synlett* **2008**, 2513–2517. http://dx.doi.org/10.1055/s-2008-1078178
15. Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480–2482. https://doi.org/10.1021/jo00406a041
16. Corey, E. J.; Schmidt, G. *Tetrahedron Lett*. **1979**, *20*, 399-402. https://doi.org/10.1016/S0040-4039(01)93515-4
17. Bal, B. S.; Childers, W. E.; Pinnick, H. W. *Tetrahedron* **1981**, *37*, 2091–2096. https://doi.org/10.1016/S0040-4020(01)97963-3
18. Serra S. *Nat. Prod. Commun.* **2015**, *10*, 1337–1339. https://doi.org/10.1177%2F1934578X1501000803
19. Rudgley, N.; March, T. L.; Perkins, M. V. *ARKIVOC* **2022**, *iv*, next article.
20. Gregg, C. and Perkins, M. V. *Tetrahedron*, 2013, **69**, 6845-6854. https://doi.org/10.1016/j.tet.2013.06.012
21. Nakashima, K.; Imoto, M.; Sono, M.; Tori, M.; Nagashima, F.; Asakawa, Y. *Molecules* **2002**, *7*, 517-527. https://doi.org/10.3390/70700517

22. Serra S.; Fuganti C. *Tetrahedron Lett.* **2005**, *46*, 4769-4772. https://doi.org/10.1016/j.tetlet.2005.05.037