Synthesis of the First "Inside-Outside" Eight-Membered Ring via Ring-Closing Metathesis: A Total Synthesis of (+/−)-Asteriscanolide

Marie E. Krafft,* Yiu-Yin Cheung, Carmelinda A. Juliano-Capucao

Department of Chemistry, Florida State University, Tallahassee, FL 32306, USA

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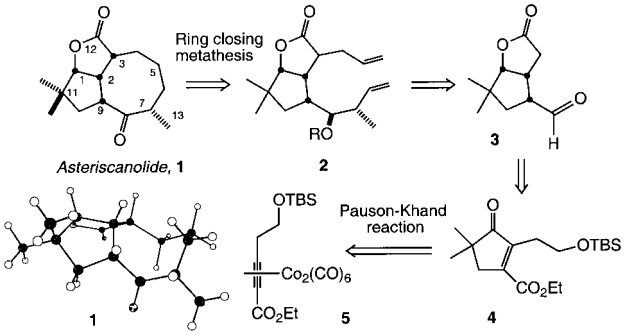
Abstract: A total synthesis of (+/-)-asteriscanolide which features two transition metal-mediated carbocyclic ring forming reactions as key elements of our strategy (Scheme 1) is described. The highly functionalized cyclopentenone **4**, the product of a cobalt-mediated Pauson-Khand [2+2+1]cycloaddition, is the key starting point for the synthesis. Excellent regiocontrol was obtained in the intermolecular Pauson-Khand reaction. Further synthetic manipulations of **4** led to diene **16** which underwent ring-closing metathesis using $(PPh_3)_2Cl_2Ru(CHPh)$] to provide the desired 'inside-outside' tricycle **17**. Conversion of **17** to **1** was achieved in a minimal number of steps. The synthesis of asteriscanolide has been achieved in **19** steps and 12 % overall yield.

Key words: ring-closing, metathesis, total synthesis, Pauson−Khand cycloaddition, transition metal mediated reactions



Scheme 1

Asteriscanolide, **1**, is a cyclooctane sesquiterpene lactone which was isolated from the hexane extract of *Asteriscus aquaticus* in 1985.[1] The structure was determined by spectroscopic means and confirmed by X-ray analysis. One total synthesis of asteriscanolide[2] and three synthetic approaches have been reported.[3-5] The structure exhibits a number of challenging features which include the [6.3.0] carbocyclic system and a bridging butyrolactone and any synthetic strategy would need to accomodate three contiguous stereocenters in a *cis* orientation on a cyclopentane ring. More importantly, it has been reported that introduction of the C-7 methyl was not possible via alkylation of the corresponding des-methyl cyclooctane. Thus, the stereocenter must be established prior to eight-membered ring formation.[4]

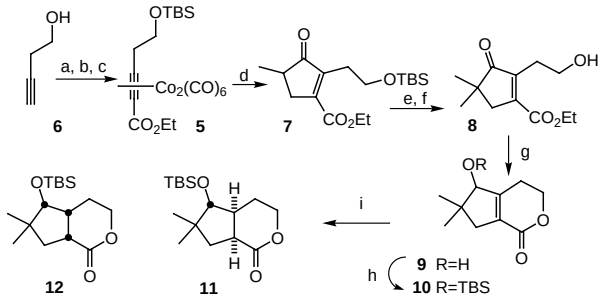
We now report a total synthesis of (+/−)-asteriscanolide which features two transition metal-mediated carbocyclic ring forming reactions, the Pauson−Khand cycloaddition and a ring-closing metathesis, as key elements of our strategy (Scheme 1). The latter of these resulted in the first stereoselective synthesis of an 'inside-outside'[6] eight-membered ring by RCM.[7] The significance of this result lies in its potential application for the synthesis of natural products with skeletons that exhibit the 'in-out' intrabridgehead stereochemistry as exemplified by the ingenane diterpenes.[8] The research efforts of Rigby,[9] Winkler,[10] Funk,[11] and Kuwajima[12] provide four fundamentally different approaches to the 'in-out' ingenane tricyclic system. However, these strategies require multistep transformations or isomerization of the corresponding 'out-out' epimer. This work provides an example of a direct carbocyclization to give exclusively an 'in-out' bridging ring system.

In our retrosynthetic analysis we envisaged that the formation of the bridging eight-membered ring could be achieved through ring-closing metathesis of diene **2**.[13] This would enable stereoselective incorporation of the C-7 methyl prior to cyclooctane ring formation. Further disconnection leads to the [3.3.0] oxabicyclooctane **3** as a key intermediate, which could be derived from the highly functionalized cyclopentenone **4**, the product of a cobalt-mediated Pauson-Khand [2+2+1] cycloaddition.[14]

The strategy that we used for the construction of **4** takes advantage of our recent successes with the Pauson−Khand reaction of alkynoates. These results have shown that excellent regiocontrol in the cycloaddition can be achieved in the reaction of unsymmetrically substituted alkenes with alkynoates to give 1,4 dicarbonyl products. The regioselectivity observed in the cycloaddition across the alkyne has been rationalized on electronic grounds.[15] In addition, intermolecular reactions between internal alkynes and terminal alkenes give rise to 2,3,5-trisubstituted cyclopentenones in preference to the 2,3,4-trisubstituted isomer. A steric argument has been invoked to explain this regioselectivity.[16]

Our initial goal was establishment of the three stereogenic centers on the cyclopentane ring. Toward this end, protection of 3-butyn-1-ol (**6**) as the corresponding *tert*-butyldimethylsilyl (TBS) ether, generation of the lithio alkyne with *s*-BuLi in THF at −78 °C followed by its addition to ethyl chloroformate in THF at −78 °C gave the corresponding alkynoate which was then treated with dicobalt octacarbonyl to give the hexacarbonyldicobalt complexed alkyne **5** (Scheme 2). Pauson−Khand cycloaddition of **5** with excess propene in methylene chloride proceeded via incremental addition of *N*-methylmorpholine-*N*-oxide monohydrate (NMO) to give the highly function-

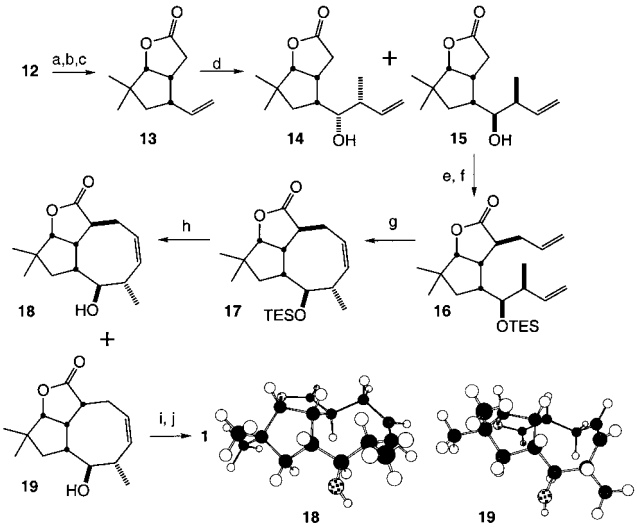
alized cyclopentenone **7** bearing functionality appropriately positioned for further manipulation of the sidechains. No efficient cycloaddition was obtained with isobutene or allylic thioalkyl derivatives[17] of isobutene. Deprotonation of **7** using LiHMDS/HMPA followed by quenching with methyl iodide gave the gem-dimethylated ketone **4**. All attempts to reduce the tetrasubstituted double bond of **4** by catalytic hydrogenation gave recovered starting material. Desilylation of **4** with HF/pyridine yielded hydroxy ketone **8**. Subsequent reduction of ketone **8** with $NaBH_4/CeCl_3.7H_2O$ in ethanol gave the corresponding allylic alcohol which yielded hydroxy lactone **9** after quenching with water and stirring for 12 h in the presence of 2 N HCl. Although hydrogenation of enone **9** (Pd/C, 40 psi of H_2) gave a 1.6:1 ratio of diastereoisomers favoring the all-*cis* diastereoisomer, the corresponding TBS ether **10** underwent hydrogenation (Pd/C, 20 psi of H_2) to give the desired all-*cis* diastereoisomer **12** (90%) in addition to isomer **11** (10%).



a, TBSCl, Et_3N, DMAP (99%); b, *s*-BuLi, THF −78 °C; EtOCOCl (94%); c, $Co_2(CO)_8$, 0 °C, low boiling petroleum ether (99%); d, propene:CH_2Cl_2 (1:1), 6 equiv NMO.H_2O (89%); e, i. LiHMDS, −78 °C THF, ii. MeI (92%); f, HF/pyridine, CH_3CN (93%); g, i. $NaBH_4/CeCl_3.7H_2O$, EtOH, ii. 2N HCl, (89%); h, TBSOTf, pyridine 0 °C (99%); i, 10 mol% Pd/C, EtOH, 20 psi H2 (**12**, 90%; **11**, 10%).

Scheme 2

Having established the requisite *cis* stereochemistry of all three substituents on the cyclopentane ring we proceeded to convert bicyclic lactone **12** to diene **16** for the key metathesis step (Scheme 3). Lactone **12** was reduced with DIBAL-H in toluene[18] at −78 °C to give a mixture of lactols which were treated with 10 equivalents of CH_2PPh_3 in refluxing THF to give the corresponding alkene. The large excess of ylide was required to avoid epimerization of the stereocenter adjacent to the aldehyde prior to the Wittig olefination. The carboxylic acid resulting from Jones oxidation of the primary alcohol was refluxed with 2 N HCl (1:1) for 2 h to give bicyclic lactone **13** (89%, 2 steps). Ozonolysis of **13** followed by a reductive work-up gave aldehyde **3** which was treated in situ with (*E*)-crotyl tri-*n*-butyl stannane[19] and BF_3•OEt_2 at −78 °C[20] to give a 1:8 ratio of the homoallylic alcohols **14** and **15 (**correct C-7 configuration) in 74% overall yield. Crotylboration of aldehyde **3**, using (*Z*)-2−butenylboronic acid pinacol cyclic ester,[21] gave a 2:1 ratio of **14** and **15,** respectively. Homoallylic alcohol **15** was treated with triethylsilyl trifluoromethanesulfonate (TESOTf) in pyridine to give the corresponding TES ether. Lactone deprotonation using LiHMDS/HMPA in THF at −78 °C followed by quenching the enolate with allyl bromide at −78 °C gave diene **16** (90%). At this point, we envisioned that the key formation of the bridging eight-membered ring would be more facile from the C-3 epimer of **16**. However, we were unable to achieve efficient epimerization of the allyl side chain. In spite of the many recent advances in ring-closing metathesis there was no literature precedent to suggest that diene **16** would cyclize. We proceeded with reaction of diene **16**, even though, conformational analyses indicated that the alkene moieties were far removed from one another. Remarkably, ring-closing metathesis of **16** was achieved using 50 mol% of the ruthenium catalyst **20**[22] in refluxing methylene chloride (0.007M) for 24 h to give the 'inside-outside' tricycle **17** (92%). The relative stereochemistry of **17** was confirmed by ^1H NMR nOe experiments. To our knowledge this is the first example of an eight-membered ring bearing an 'in-out'-intrabridgehead stereochemical relationship[6,23] to be synthesized by ring-closing metathesis.



a, DIBAL-H, toluene, −78 °C (96%); b, $MePPh_3Br$ (10 equiv), *n*-Bu-Li, THF, reflux, 20 min (89%); c, i. Jones' reagent/acetone, ii. *i*-PrOH, 2 N HCl, reflux, 2 h (89%); d, i. O_3/CH_2Cl_2, −78 °C, ii. Me_2S, iii. (*E*)-crotyl Sn^nBu_3, CH_2Cl_2, −78 °C, BF_3•Et_2O (74%; **15**/**14**, 8:1); e, TESOTf, pyridine, 0 °C (87%); f, i. LiHMDS/HMPA, −78 °C, THF, ii. allyl bromide (90%); g, 50 mol% [**20**, $(PPh_3)_2Cl_2Ru(CHPh)$], 0.007M CH_2Cl_2, reflux, 24 h (92%); h, TBAT, CH_3CN, reflux, 29 h (62% of **19**); (i) H_2, 10 mol% Pd/C, EtOH (93%); j, $^nPr_4NRuO_4$/NMO, CH_2Cl_2 (100%).

Scheme 3

Desilylation of **17** with tetrabutylammonium (triphenylsilyl)difluorosilicate[24] (TBAT) (6 equivalents) in refluxing acetonitrile for 29 hours gave alcohols **18** (30%) and **19** (62%). When alcohols **18** and **19** were individually resubjected to reaction with TBAT in refluxing acetonitrile a 2:1 equilibrium mixture of **19**: **18** was obtained. All attempts to deprotonate/reprotonate lactone **18** under kinet-

ic conditions failed. Molecular Mechanics calculations[25] for **18** and **19** showed a 0.5 Kkcal difference in energy in favor of alcohol **19**. Tricycle **19** was hydrogenated over Pd/C in EtOH to give the corresponding saturated tricyclic lactone in quantitative yield. Oxidation of the secondary alcohol with tetrapropylammonium perruthenate and NMO in methylene chloride[26] gave asteriscanolide (**1**), which was identical to the natural product[1] by ^{1}H NMR analysis (satisfactory spectral data: IR, MS, ^{13}C, ^{1}H NMR nOe comparison and combustion analysis were also obtained).

Our strategy for the synthesis of asteriscanolide allows for the stereocontrolled introduction of the C-7 methyl group and takes advantage of two transition metal-mediated carbocyclic ring forming reactions as key elements. In these investigations, we have further developed the applications of the intermolecular Pauson−Khand reaction with polarized alkynes. Furthermore, we have shown that ring-closing metathesis can be used to form an eight-membered ring with 'in-out'-intrabridgehead stereochemistry. The synthesis of asteriscanolide has been achieved in 19 steps and 12% overall yield**.** Investigations into the synthesis of other medium-sized rings with 'in-out'-intrabridgehead stereochemistry are underway and these results will be reported in due course.

(Ethyl 5-*tert*-butyldimethylsilyloxy-2-pentynoate)hexacarbonyldicobalt (5)

IR: ν = 2096, 2058, 2034, 1999, 1701 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.08 (s, 6H, Si(CH_3)$_2$), 0.90 (s, 9H, Si-C(CH_3)$_3$), 1.31 (t, 3H, *J* = 7.1 Hz, $CO_2CH_2CH_3$), 3.07 (t, 2H, *J* = 7.1 Hz, C≡C-CH_2), 3.90 (t, 2H, *J* = 7.1 Hz, CH_2-OSi), 4.40 (q, 2H, *J* = 7.1 Hz, $CO_2CH_2CH_3$).

^{13}C NMR (75 MHz): δ = −5.7, 13.8, 18.1, 25.6, 36.4, 60.1, 61.6, 63.3, 79.2, 94.9, 169.9, 198.0−200.0 (m).

(Ethyl 5-hydroxy-2-pentynoate)hexacarbonyldicobalt

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.34 (t, 3H, *J* = 6.0 Hz, OCH_2CH_3), 3.18 (t, 2H, *J* = 5.4 Hz, C≡C-CH_2), 3.23 (br t, 1H, *J* = 6.0 Hz, CH_2OH), 3.89 (dq, 2H, *J* = 6.0, 5.4 Hz, CH_2CH_2OH), 4.33 (q, 2H, *J* = 6.0 Hz, OCH_2CH_3).

2-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-3-ethoxycarbonyl-5-methyl-2-cyclopentenone (7)

To a solution of (ethyl 5-*t*-butyldimethylsilyloxy-2-pentynoate)hexacarbonyldicobalt (**5**, 101 mg, 0.19 mmol) in CH_2Cl_2 (1.0 mL) in a 15 mL capacity resealable tube cooled to −78 °C was condensed propene (~1.0 mL, bp −50 °C) resulting in a 0.2 M solution of (ethyl 5-*t*-butyldimethylsilyloxy-2-pentynoate)hexacarbonyldicobalt in 1:1 propene/CH_2Cl_2. *N*-methylmorpholine *N*-oxide monohydrate ($NMO.H_2O$, obtained from 15% aq solution (Aldrich) and recrystallized twice from acetone, 2 equiv, 50 mg, 0.37 mmol) was added to the mixture, after which the tube was sealed and allowed to warm to r.t. The mixture was stirred at r.t. for 15 min after which it was cooled to −78 °C and $NMO.H_2O$ (2 equiv) were added, a total of 6 equiv were added. The reaction was complete after a total time of 2.5 h. The mixture was cooled to −78 °C, CH_2Cl_2 (1 mL) was added and the tube was loosely capped to allow propene to evaporate. The mixture was then run through a plug of silica gel (EtOAc/hexane, 1:6). Flash chromatography (EtOAc/hexane, 1:15) yielded enones 2-[2-(*t*-butyldimethylsilyloxy)ethyl]-3-ethoxycarbonyl-5-methyl-2-cyclopentenone (**7)**, and 2-[2-(*t*-butyldimethylsilyloxy)ethyl]-3-ethoxycarbonyl-4-methyl-2-cyclopentenone in 89% yield (50 mg) and >30:1 ratio by integration of resonances in the ^{1}H NMR (500 MHz) spectrum. When the reaction was scaled up (1.3 g expected yield using 45 mL capacity tube and 2.5 g expected yield using the 100 mL capacity tube), $NMO.H_2O$ (a total of 8 equiv) was added to the reaction mixtures (2 equiv added for every 30 min of reaction time) and the reaction was worked up after total reaction times not exceeding 12 h.

IR (film): ν = 1704, 1457, 1092 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.03 (s, 6H, Si(CH_3)$_2$), +0.03 (s, 9H, Si-C(CH_3)$_3$), 1.18 (d, 3H, *J* = 7.1 Hz, 5-C-CH_3), 1.33 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 2.34 (br dt, 1H, *J* = 18.7, 2.7 Hz, 4-C*H*H), 2.42 (ddq, 1H, *J* = 2.8, 7.1, 7.1 Hz, 5-C*H*), 2.79 (br t, 2H, *J* = 6.6 Hz, 2-C-CH_2), 3.01 (br dd, 1H, *J* = 18.7, 7.1 Hz, 4-CH*H*), 3.67 (t, 2H, *J* = 6.6 Hz, CH_2-OSi), 4.29 (q, 2H, *J* = 7.1 Hz, OCH_2CH_3).

^{13}C NMR (75 MHz): δ = 13.9, 15.9, 18.0, 25.7, 27.6, 35.6, 39.4, 61.0, 146.8, 155.1, 165.8, 212.3, 216.3.

EIMS: *m*/z = 326 (M^+), 269 (100), 75.

Anal. Calcd for $C_{17}H_{30}O_4Si$: C, 62.54; H, 9.27. Found: C, 62.72; H, 9.37.

2-[2-(*tert*−Butyldimethylsilyloxy)ethyl]-3-ethoxycarbonyl-5,5-dimethyl-2-cyclopentenone (4)

IR (film): ν = 1704, 1248 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 6H, Si(CH_3)$_2$), 0.83 (s, 9H, SiC(CH_3)$_3$), 1.11 (s, 6H, 5-C(CH_3)$_2$), 1.35 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 2.63 (t, 2H, *J* = 1.1 Hz, 4-CH_2), 2.81 (tt, 2H, *J* = 6.6, 1.1 Hz, 2-C-CH_2CH$_2$-O), 2.81 (t, 2H, *J* = 6.6 Hz, 2-C-CH$_2$CH_2-O), 4.30 (q, 2H, *J* = 7.1 Hz, OCH_2CH_3).

^{13}C NMR (75 MHz): δ = 13.40, 17.97, 24.75, 25.66, 27.62, 42.82, 43.61, 60.99, 145.43, 153.68, 165.78, 214.19.

EIMS: *m*/z = 340 (M^+), 283 (100).

Anal. Calcd for $C_{18}H_{32}O_4Si$: C, 63.49; H, 9.48. Found: C, 63.21; H, 9.45.

2-[2-Hydroxyethyl]-3-ethoxycarbonyl-5,5-dimethyl-2-cyclopentenone (8)

IR (film): ν = 3604, 2872, 1714, 1704 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 (s, 6H, 2 × CH_3), 1.36 (t, 3H, *J* = 7.2 Hz, CH$_2$CH_3), 2.33 (br t, 1H, *J* = 5.4 Hz, CH$_2$O*H*), 2.67 [t, 2H, *J* = 1.3 Hz, CH_2C(CH$_3$)$_2$], 2.86 (tt, 2H, *J* = 6.0, 1.3 Hz, CH_2CH$_2$OH), 3.75 (q, 2H, *J* = 5.6 Hz, CH_2OH), 4.32 (q, 2H, *J* = 7.2 Hz, CH_2CH$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 24.7, 27.8, 43.1, 43.6, 61.3, 61.4, 146.1, 154.2, 166.0, 215.1.

MS (CI isobutane): *m*/z = 226 (M^+).

Anal. Calcd for $C_{12}H_{18}O_4.0.2\ H_2O$: C, 62.70, H, 8.07. Found C, 62.53, H, 7.93.

Bicyclic Hydroxy Lactone 9

To a stirred solution of hydroxy ketone **8** (1.95 g, 8.62 mmol) and cerium trichloride heptahydrate (6.42 g; 17.24 mmol) in absolute EtOH (45 mL) at 0 °C was carefully added $NaBH_4$ (655 mg, 17.24 mmol). After the reaction was complete according to TLC, 2 N HCl (50 mL) was carefully added to the solution and the reaction was stirred overnight. The reaction mixture was poured into a separatory funnel and extracted with CH_2Cl_2 (2 x 100 mL). The organic layers were combined and dried ($MgSO_4$). Removal of solvent in vacuo gave the crude product which was chromatographed on silica gel (hexane/EtOAc, 1:4) to give the product **9** as a colorless oil (1.40 g; 89%).

IR (film): ν = 3418, 2957, 1704, 1468, 1123, 1084 cm^{-1}.

^1H NMR (500 MHz, C_6D_6): δ = 0.78 (s, 3H, CH_3), 0.82 (s, 3H, CH_3), 1.60 (AB, dddd, 1H, J_{AB} = 18.2, J = 9.6, 7.5, 3.9, 2.1 Hz, C*H*HCH$_2$O), 1.79 (AB, dddd, 1H, J_{AB} = 18.2, J = 8.1, 5.7, 3.0, 0.9 Hz, CH*H*CH$_2$O), 2.15 [AB, ddd, 1H, J_{AB} = 15.8 Hz, J = 3.6, 1.8, 1.8 Hz, C*H*HC(CH$_3$)$_2$], 2.31 [AB, ddd, 1H, J_{AB} = 15.8, J = 2.1, 2.1, 2.0, CH*H*C(CH$_3$)$_2$], 3.67 (br s, 1H, CHO*H*), 3.71 (AB, dd, 1H, J_{AB} = 11.1, J = 9.3, 5.1 Hz, C*H*HOCO), 3.75 (AB, dd, 1H, J_{AB} = 11.1, J = 11.1, 5.4 Hz, CH*H*OCO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8, 22.8, 27.2, 42.5, 42.7, 67.2, 85.2, 129.0, 158.3, 164.7.

MS (CI, isobutane): *m*/z = 183 (MH^+).

Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.91, H, 7.74. Found C, 65.99, H, 7.81.

Bicyclic Lactone 10

IR ($CHCl_3$): ν = 2958, 2859, 1716, 1213, 1115 cm^{-1}.

^1H NMR (500 MHz, C_6D_6): δ = −0.11 (s, 3H, SiCH_3), −0.05 (s, 3H, SiCH_3), 0.87 (s, 3H, CH_3), 0.89 (s, 9H, SiC(CH_3)$_3$), 0.92 (s, 3H, CH_3), 1.67 (AB, dddd, 1H, J_{AB} = 17.9, J = 9.6, 7.6, 4.0, 1.9 Hz, C*H*HCH$_2$OCO), 1.88 (AB, dddd, 1H, J_{AB} = 17.9, J = 6.9, 4.6, 2.2, 1.0 Hz, CH*H*CH$_2$OCO), 2.18 [AB, ddd, 1H, J_{AB} = 15.8, J = 4.2, 2.1, 2.1 Hz, C*H*HC(CH$_3$)$_2$], 2.39 [AB, ddd, 1H, J_{AB} = 15.7, J = 1.8, 1.8, 1.8 Hz, CH*H*C(CH$_3$)$_2$], 3.75 (AB, dd, 1H, J_{AB} = 11.1, J = 9.9, 4.8 Hz, C*H*HOCO), 3.83 (AB, dd, 1H, J_{AB} = 11.1, J = 5.7, 4.8 Hz, CH*H*OCO), 3.94 (ddd, J = 3.0,1.9, 1.9, 1H,C*H*OTBS).

^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.7, −4.6, 17.9, 22.4, 23.3, 25.6, 27.0, 42.6, 43.6, 67.0, 85.3, 128.0, 159.2, 164.7.

MS (CI, isobutane): *m*/z = 297 (MH^+).

Anal. Calcd. for $C_{16}H_{28}O_3Si$: C, 64.82, H, 9.52. Found C, 64.76, H, 9.56.

Lactones 11 and 12

11: mp 64−65 °C (hexane/EtOAc).

IR (film): ν = 2956, 1740, 1472, 1389, 1257, 1162, 1096, 1073 cm^{-1}.

^1H NMR (500 MHz, C_6D_6): δ = 0.04 (s, 3H, SiCH_3), 0.06 (s, 3H, SiCH_3), 0.90 (s, 12H, SiC(CH_3)$_3$, α-CH_3), 0.99 (s, 3H, β-CH_3), 1.55 (dddd, 1H, J = 14.0, 10.6, 10.1, 3.4 Hz, $H_{6\beta}$), 1.73 (dd, 1H, J = 13.5, 9.9 Hz, $H_{3\beta}$), 1.96 (dd, 1H, J = 13.5, 9.3 Hz, $H_{3\alpha}$), 2.14 (dddd, 1H, J = 14.0, 7.0, 4.7, 2.1 Hz, $H_{6\alpha}$), 2.42 (dddd, 1H, J = 12.4, 8.8, 8.3, 7.5 Hz, $H_{5\alpha}$), 2.96 (ddd, 1H, J = 12.2, 9.6, 9.6 Hz, $H_{4\alpha}$), 3.35 (d, 1H, J = 8.6 Hz, $H_{1\beta}$), 4.16 (ddd, 1H, J = 11.5, 10.4, 2.1 Hz, $H_{7\alpha}$), 4.36 (ddd, 1H, J = 11.2, 4.4, 3.6 Hz, $H_{7\beta}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.5, −4.2, 17.8, 20.2, 25.6, 26.4, 28.2, 37.1, 40.0, 41.1, 41.4, 67.2, 86.2, 175.6.

MS (CI, isobutane): *m*/z = 299 (MH^+).

Anal. Calcd for $C_{16}H_{30}O_3Si$: C, 64.38, H, 10.13. Found C, 64.23, H, 10.05.

12: IR (film): ν = 2955, 1740, 1471, 1388, 1255, 1161, 1095 cm^{-1}.

^1H NMR (500 MHz, C_6D_6): δ = −0.11 (s, 3H, SiCH_3), −0.06 (s, 3H, SiCH_3), 0.65 (s, 3H, α-CH_3), 0.93 (s, 3H, β-CH_3), 0.94 (s, 9H, SiC(CH_3)$_3$), 1.08 (dddd, 1H, J = 14.0, 8.3, 2.8, 1.8 Hz, $H_{6\beta}$), 1.47 (dd, 1H, J = 13.2, 6.7 Hz, $H_{3\beta}$), 1.65 (dddd, 1H, J = 14.0, 12.5, 10.9, 3.6 Hz, $H_{6\alpha}$), 2.05 (dddd, 1H, J = 11.4, 11.2, 8.0, 4.9 Hz, $H_{5\beta}$), 2.25 (ddd, 1H, J = 11.7, 9.3, 6.8 Hz, $H_{4\beta}$), 2.40 (dd, 1H, J = 13.2, 6.7 Hz, $H_{3\alpha}$), 3.13 (d, 1H, J = 4.9 Hz, $H_{1\beta}$), 3.43 (ddd, 1H, J = 12.4, 10.6, 1.6 Hz, $H_{7\beta}$), 3.79 (ddd, 1H, J = 10.9, 3.9, 3.1 Hz, $H_{7\alpha}$).

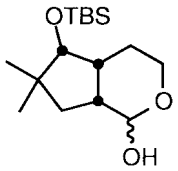
^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.6, −4.4, 17.9, 23.4, 23.8, 25.7, 26.8, 39.1, 39.7, 40.9, 43.2, 67.2, 80.9, 175.7.

MS (CI, isobutane): *m*/z = 299 (MH^+).

Anal. Calcd for $C_{16}H_{30}O_3Si$: C, 64.38, H, 10.13. Found C, 64.62, H, 10.10.

Bicyclic Lactone 13

To a stirred solution of lactone **12** (1.55 g; 5.2 mmol) in dry toluene (26 mL) at −78 °C was added dropwise DIBAL-H (6.9 mL, 10.4 mmol, 1.3 M solution in toluene). The resulting solution was stirred at −78 °C for 20 min and monitored by TLC. Upon completion, the reaction was quenched at −78 °C with sat. sodium potassium tartrate and warmed to r.t. The reaction mixture was partitioned between CH_2Cl_2 and H_2O. The aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL) and the combined organic extracts were dried ($MgSO_4$). Removal of solvent in vacuo gave the crude lactol as a mixture of diastereoisomers (1.52 g, 97%) which was used immediately for the next step without further purification.



To a suspension of $MePPh_3Br$ (12.73 g, 35.6 mmol) in dry THF (71 mL) under N_2 at 0 °C was added *n*-BuLi (21.14 mL, 33.82 mmol, 1.6 M solution in hexanes). The ice bath was removed and the resulting orange solution was stirred for 15 min. A solution of crude lactol (1.06 g, 3.56 mmol) in dry THF (17.8 mL) was added and the reaction mixture was refluxed for 30 min. The reaction was complete and the solution was cooled to r.t. The excess ylide was quenched by dropwise addition of H_2O and the reaction mixture was partitioned between EtOAc and H_2O. The aqueous layer was extracted with EtOAc (2 x 100 mL) and the combined organic extracts were washed with brine and dried ($MgSO_4$). Removal of solvent in vacuo gave the crude product, which was filtered through a plug of silica gel eluting with hexane/EtOAc (3:1). Final purification by flash chromagraphy on silica gel using hexane/EtOAc (first 6:1 followed by 3:1) gave the corresponding hydroxy alkene as a pale yellow oil (940 mg, 89%).

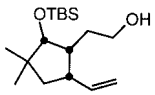
IR (film): ν = 3338.3, 2954.4, 1638.4, 1471.4, 1254.7 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.059 (s, 3H, Si CH_3), 0.062 (s, 3H, Si CH_3), 0.94 (s, 9H, SiC(CH_3), 0.98 (s, 3H, CH_3), 0.99 (s, 3H, CH_3), 1.50 (dd, 1H, J = 13.2, 7.0 Hz, $H_{3\alpha}$), 1.62 (dddd, 1H, J = 13.9, 8.6, 7.0, 6.0 Hz, C*H*HCH$_2$OH), 1.68 (obscured dd, 1H, J = 13.4, 8.2 Hz, $H_{3\beta}$), 1.68 (obscured dddd, 1H, J = 14.5, 7.2, 7.2, 5.1 Hz, CH*H*CH$_2$OH), 2.24 (dddd, 1H, J = 8.5, 8.5, 4.8, 4.8 Hz, $H_{5\beta}$), 2.66 (dddd, 1H, J = 8.2, 8.1, 8.2, 8.2 Hz, $H_{4\beta}$), 3.58 (partly obscured ddd, 1H, J = 10.3, 7.0, 7.0 Hz, C*H*HOH), 3.59 (partly obscured d, 1H, J = 4.2 Hz, $H_{1\beta}$), 3.66 (ddd, 1H, J = 10.3, 7.3, 5.8 Hz, CH*H*OH), 4.87 (ddd, 1H, J = 16.7, 2.1, 0.9 Hz, CH = CHH_{trans}), 4.89 (ddd, 1H, J = 10.5, 2.2, 0.4 Hz, CH = CH_{cis}H), 5.91 (ddd, 1H, J = 16.7, 10.3, 9.4 Hz, C*H* = CH$_2$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.3, −4.3, 18.1, 25.3, 26.0, 29.2, 29.5, 42.3, 43.5, 43.8, 45.2, 62.2, 84.2, 113.5, 143.2.

MS (CI, isobutane): *m*/z = 299 (MH^+).

Anal. Calcd for $C_{17}H_{34}O_2Si$: C, 68.39, H, 11.48. Found C, 68.34, H, 11.55.



To a stirred solution of hydroxy alkene (784 mg, 2.63 mmol) in acetone (26 mL) was added Jones' reagent (2.14 M) until there was a persistent orange/red color. When the reaction was complete, *i*-PrOH was added to quench the excess Jones' reagent, 2 N HCl (25 mL) was added, and the mixture was refluxed overnight. The reaction mixture was poured into a separatory funnel and partitioned between H_2O and CH_2Cl_2. The aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL) and the combined organic extracts were dried ($MgSO_4$). Removal of the solvent in vacuo gave the crude product which was chromatographed on silica gel eluting with hexane/EtOAc (4:1) to give the product **13** as a colorless oil (419 mg; 89%).

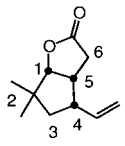
IR (film): ν = 3018, 2966, 1770, 1522, 1470, 1420 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.02 (s, 3H, β-CH_3), 1.15 (s, 3H, α-CH_3), 1.53 (obscured dd, 1H, *J* = 14.4, 4.8 Hz, $H_{3\alpha}$), 1.56 (dd, 1H, *J* = 14.4, 7.9 Hz, $H_{3\beta}$), 2.506 (d, 1H, *J* = 7.6 Hz, H_6), 2.508 (d, 1H, *J* = 6.3 Hz, $H_{6'}$), 2.96 (ddddd, 1H, *J* = 12.1, 10.6, 8.4, 1.4, 1.4 Hz, $H_{4\beta}$), 3.09 (dddd, 1H, *J* = 12.1, 7.6, 6.3, 6.3 Hz, $H_{5\beta}$), 4.40 (d, 1H, *J* = 6.1 Hz, $H_{1\beta}$), 5.05 (ddd, 1H, *J* = 17.2, 1.5, 1.5 Hz, CH = CHH_{trans}), 5.12 (ddd, 1H, *J* = 10.5, 1.3, 1.3 Hz, CH = CH_{cis}H), 5.70 (ddd, 1H, *J* = 17.2, 10.3, 7.0 Hz, C*H* = CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.3, 25.4, 30.4, 41.0, 41.8, 42.2, 42.9, 92.9, 116.6, 137.8, 177.5.

MS (CI, isobutane): *m*/z = 181 (MH^+).

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30, H, 8.95. Found C, 73.17, H, 8.94.



***syn,syn* Homoallylic Alcohol 15**

O_3 was bubbled through a stirred solution of olefinic lactone **13** (51 mg, 0.28 mmol) in CH_2Cl_2 (4 mL) at −78 °C until a blue solution was obtained. O_2 was bubbled through the solution to remove excess O_3 and N_2 was then bubbled through the solution to remove excess O_2. Dimethyl sulfide (1 mL) was added at −78 °C and the reaction was allowed to warm to r.t. and stirred for 15 h. The solvent was removed in vacuo, the crude aldehyde was redissolved in CH_2Cl_2 (3 mL), cooled to −78 °C, and (*E*)-crotyl-tri^{n}butylstannane (106 mg; 0.308 mmol) was added. To the resulting solution was added BF_3•OEt_2 (0.07 mL, 0.567 mmol) dropwise and the solution was stirred at −78 °C for 40 min. When the reaction was complete, sat. $NaHCO_3$ was added and the solution was allowed to warm to r.t. The reaction mixture was partitioned between CH_2Cl_2 and H_2O. The aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL) and the organic extracts were combined and dried ($MgSO_4$). The solvent was removed in vacuo and the crude product was chromatographed on silica gel (hexane/EtOAc, 4:1) to give the *syn,syn* homoallylic alcohol **15** as a white solid (44 mg, 66%) and the *syn,anti* alcohol **14** as a white solid (5 mg; 8%).

15: mp 108−110 °C (hexane/EtOAc).

IR ($CHCl_3$): ν = 3678, 3020, 1774, 1752, 1522, 1420 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.98 (s, 3H, β-CH_3), 1.06 (d, *J* = 6.8 Hz, 3H, CHCH_3), 1.15 (s, 3H, α-CH_3), 1.49 (dd, 1H, *J* = 12.6, 6.9 Hz, $H_{3\alpha}$), 1.51 (d, 1H, *J* = 5.3 Hz, CHO*H*), 1.66 (dd, 1H, *J* = 12.4, 12.4 Hz, $H_{3\beta}$), 2.21 (ddq, 1H, *J* = 7.2, 7.1, 6.8 Hz, C*H*CH_3), 2.43 (dddd, 1H, *J* = 12.1, 9.5, 7.1, 4.7 Hz, $H_{4\beta}$), 2.52 (dd, 1H, *J* = 18.0, 10.0 Hz, $H_{6\beta}$), 2.68 (dd, 1H, *J* = 17.9, 3.1 Hz, $H_{6\alpha}$), 3.01 (dddd, 1H, *J* = 9.5, 9.5, 6.0, 3.1 Hz, $H_{5\beta}$), 3.45 (ddd, 1H, *J* = 5.3, 5 Hz, C*H*OH), 4.33 (d, 1H, *J* = 6.0 Hz, $H_{1\beta}$), 5.07 (ddd, 1H, *J* = 10.3, 0.8, 0.8 Hz, CH = CHH_{trans}), 5.09 (ddd, 1H, *J* = 17.3, 1.4, 1.4 Hz, CH = CH_{cis}H), 5.72 (ddd, 1H, *J* = 17.3, 10.3, 7.9 Hz, C*H* = CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1, 23.2, 25.5, 31.2, 37.1, 40.4, 40.1, 41.3, 43.1, 74.1, 93.2, 115.3, 141.1, 178.4.

MS (CI, isobutane): *m*/z = 239 (MH^+).

Anal. Calcd. for $C_{14}H_{22}O_3.0.4H_2O$: C, 68.48, H, 9.36. Found C, 68.36, H, 9.21.

***syn,anti* Homoallylic Alcohol 14**

Mp: 96−97 °C (hexane/EtOAc).

IR ($CHCl_3$): ν = 3569, 2967, 2874, 1767, 1637, 1469, 1371, 1194, 1161, 1042 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.99 (d, *J* = 7.0 Hz, 3H, CHCH_3), 1.00 (s, 3H, β-CH_3), 1.14 (s, 3H, α-CH_3), 1.34 (dd, *J* = 12.6, 12.6 Hz, 1H, $H_{3\alpha}$), 1.40 (dd, *J* = 12.4, 7.0 Hz, 1H, $H_{3\beta}$), 1.51 (br. s, 1H, O*H*), 2.33 (obscured dqdd, *J* = 6.6, 6.6, 6.6, 2.6, 1.5 Hz, 1H, C*H*CH_3), 2.36 (obscured dddd, *J* = 12.6, 9.9, 9.9, 7.1 Hz, 1H, $H_{4\beta}$), 2.65 (dd, *J* = 18.9, 10.3 Hz, 1H, $H_{6\beta}$), 2.89 (dd, *J* = 18.7, 2.8 Hz, 1H, $H_{6\alpha}$), 3.15 (dddd, *J* = 9.3, 9.3, 6.0, 2.8 Hz, 1H, $H_{5\beta}$), 3.46 (dd, *J* = 12.6, 2.6 Hz, 1H, $H_{1\beta}$), 4.39 (d, *J* = 5.9 Hz, 1H, $H_{1\beta}$), 5.15 (ddd, *J* = 17.4, 1.5, 1.5 Hz, 1H, CH = CHH_{trans}), 5.22 (ddd, *J* = 10.6, 1.5, 1.5 Hz, 1H, CH = CH_{cis}H), 5.88 (ddd, *J* = 17.4, 10.6, 5.7 Hz, 1H, C*H* = CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.7, 23.2, 25.1, 30.4, 39.5, 39.7, 39.8, 41.5, 42.1, 73.6, 92.9, 116.3, 141.0, 178.2.

MS (CI, isobutane): *m*/z = 239 (MH^+).

Anal. Calcd. for $C_{14}H_{22}O_3$: C, 70.56, H, 9.30. Found C, 70.51, H, 9.24.

Diene 16

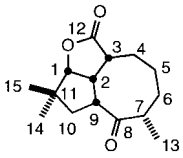
IR (film): ν = 3079, 2958, 1770, 1640, 1460, 1416, 1371, 1182, 1111 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.59 (q, 6H, *J* = 7.8 Hz, Si(C$H_2$$CH_3$)$_3$), 0.95 (t, 9H, *J* = 7.8 Hz, Si(CH_2CH_3)$_3$), 0.98 (s, 3H, β-CH_3), 0.99 (d, 3H, *J* = 6.9 Hz, CHCH_3), 1.10 (s, 3H, α-CH_3), 1.38 (dd, 1H, *J* = 12.8, 12.8 Hz, $H_{3\alpha}$), 1.55 (dd, 1H, *J* = 12.8, 5.9 Hz, $H_{3\beta}$), 2.21 (dqd, 1H, *J* = 6.8, 6.8, 1.8 Hz, C*H*CH_3), 2.36 (obscured ddd, 1H, *J* = 13.7, 8.9, 6.1 Hz, C*H*HCH = CH_2), 2.39 (obscured ddd, 1H, *J* = 12.9, 9.1, 6.1 Hz, $H_{4\beta}$), 2.50 (ddd, 1H, *J* = 13.7, 6.5, 6.5 Hz, CH*H*CH = CH_2), 2.64 (ddd, 1H, *J* = 9.7, 5.6, 4.0 Hz, $H_{6\alpha}$), 2.69 (ddd, 1H, *J* = 10.2, 6.7, 3.8 Hz, $H_{5\beta}$), 3.64 (dd, 1H, *J* = 8.9, 1.8 Hz, C*H*OSi(CH_2CH_3)$_3$), 4.30 (dd, 1H, *J* = 6.5, 0.8 Hz, $H_{1\beta}$), 5.01 (ddd, 1H, *J* = 17.2, 1.6, 1.6 Hz, $CHCH_3$CH = CHH_{trans}), 5.04 (ddd, 1H, *J* = 9.6, 1.4, 1.4 Hz, $CHCH_3$CH = CH_{cis}H), 5.17 (ddd, 1H, *J* = 11.3, 0.6, 0.6 Hz, CH_2CH = CH_{cis}H), 5.17 (ddd, 1H, *J* = 17.2, 1.4, 1.4 Hz, CH_2CH = CHH_{trans}), 5.75 (dddd, 1H, *J* = 17.4, 9.7, 7.7, 7.2 Hz, CH_2C*H* = CH_2), 5.88 (ddd, 1H, *J* = 17.4, 10.5, 7.0 Hz, $CHCH_3$C*H* = CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 5.2, 5.3, 6.8, 6.9, 12.1, 23.7, 25.7, 36.4, 40.6, 41.36, 41.6, 42.7,44.3, 91.4, 114.2, 119.2, 133.0, 142.3, 179.3.

MS (CI, isobutane): *m*/z = 393 (MH^+).

Anal. Calcd. for $C_{23}H_{40}O_3Si$: C, 70.36, H, 10.27. Found C, 70.61, H, 10.30.



3-*epi*-5,6-Dehydro-8-(dihydrotriethylsilyloxy)asteriscanolide (17)

Bis(tricyclohexylphosphine)benzylidine ruthenium(IV) dichloride $(Ph_3P)_2Cl_2Ru$ = CHPh (35 mg, 0.0423 mmol) was added to a stirred solution of diene **16** (83 mg, 0.2117 mmol) in dry CH_2Cl_2 (32 mL) and the reaction mixture was refluxed for 8 h under N_2 after which a further amount of the Grubbs' catalyst (35 mg, 0.0423 mmol) was added and the solution was refluxed for another 8 h. A final 17 mg (0.0211 mmol) was added and the reaction was refluxed for a further 8 h. The reaction was complete according to TLC and the solution was allowed to cool to r.t. and then concentrated under vacuum. The residue was loaded onto a plug of silica gel and eluted with hexane/EtOAc (9:1) to remove excess ruthenium containing compounds. The solvent was removed in vacuo and the residue was chromatographed on silica gel (hexane/EtOAc, 19:1) to give the product **17** as a pale yellow oil (70 mg, 92%).

IR (film): ν = 2958, 2878, 1760, 1470, 1462, 1454 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.60 (q, 6H, *J* = 8.3 Hz, $Si(CH_2CH_3)_3$), 0.97 (t, 9H, *J* = 7.8 Hz, $Si(CH_2CH_3)_3$), 0.99 (d, 3H, *J* = 7.0 Hz, $CHCH_3$), 1.04 (s, 3H, α-CH_3), 1.07 [s, 3H, β-CH_3)], 1.36 (dd, 1H, *J* = 12.6, 12.6 Hz, $H_{10\alpha}$), 1.76 (dd, 1H, *J* = 12.8, 6.7 Hz, $H_{10\beta}$), 2.10 (dddd, 1H, *J* = 16.3, 9.9, 3.4, 2.6 Hz, $H_{4\beta}$), 2.41 (ddd, 1H, *J* = 9.7, 9.7, 1.6 Hz, $H_{3\alpha}$), 2.44 (dddd, 1H, *J* = 12.8, 9.1, 7.0, 6.1 Hz, $H_{9\beta}$), 2.65 (dqdd, 1H, *J* = 13.4, 6.0, 1.0, 0.5 Hz, $H_{7\beta}$), 2.77 (ddd, 1H, *J* = 15.8, 9.2, 1.6 Hz, $H_{4\alpha}$), 3.09 (br. ddd, 1H, *J* = 9.1, 7.9, 7.8 Hz, $H_{2\beta}$), 3.47 (dd, 1H, *J* = 9.2, 4.9 Hz, $H_{8\alpha}$), 4.35 (dd, 1H, *J* = 8.0, 0.8 Hz, $H_{1\beta}$), 5.59 (ddd, 1H, *J* = 10.5, 7.8, 2.6 Hz, H_6), 5.69 (dddd, 1H, *J* = 10.7, 9.1, 4.2, 1.4 Hz, H_5).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 4.9, 6.8, 16.4, 24.4, 28.9, 30.4, 37.2, 41.2, 41.4, 44.6, 49.6, 50.6, 80.1, 80.1, 126.8, 141.7, 179.1.

MS (CI, isobutane): *m*/z = 365 (MH^+).

Anal. Calcd. for $C_{21}H_{36}O_3Si.0.2H_2O$: C, 68.61, H, 9.98. Found C, 68.60, H, 9.95.

3-*epi*-5,6-Dehydro-8-dihydroasteriscanolide (18)

Mp: 92−94 °C (hexane/EtOAc).
IR ($CHCl_3$): ν = 3627, 2964, 1764, 1465, 1372, 1190, 1032, 1004 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.05 (s, 3H, α-CH_3), 1.08 (d, 3H, *J* = 7.1 Hz, $CHCH_3$), 1.08 (s, 3H, CH_3), 1.48 (dd, 1H, *J* = 12.6, 12.6 Hz, $H_{10\alpha}$), 1.60 (br. s, 1H, O*H*), 1.90 (dd, 1H, *J* = 12.6, 6.0 Hz, $H_{10\beta}$), 2.16 (dddd, 1H, *J* = 16.1, 9.3, 4.8, 1.8 Hz, $H_{4\beta}$), 2.37 (dddd, 1H, *J* = 12.8, 9.5, 6.6, 6.6 Hz, $H_{9\beta}$), 2.47 (ddd, 1H, *J* = 9.7, 9.7, 3.1 Hz, $H_{3\alpha}$), 2.58 (ddq, 1H, *J* = 14.1, 7.0, 7.0 Hz, $H_{7\beta}$), 2.75 (ddd, 1H, *J* = 15.9, 8.2, 3.1 Hz, $H_{4\alpha}$), 3.12 (br. ddd, 1H, *J* = 7.5, 7.5, 7.5 Hz, $H_{2\beta}$), 3.49 (dd, 1H, *J* = 9.3, 6.8 Hz, $H_{8\alpha}$), 4.37 (d, 1H, *J* = 8.1 Hz, $H_{1\beta}$), 5.58 (ddd, 1H, *J* = 11.5, 7.1, 2.2 Hz, H_6), 5.66 (dddd, 1H, *J* = 11.5, 8.2, 5.0, 1.5 Hz, H_5).

^{13}C NMR (75 MHz, $CDCl_3$): d = 16.6, 24.3, 29.0, 29.7, 37.7, 40.6, 41.1, 44.4, 48.4, 49.6, 78.7, 89.35, 126.2, 140.1, 179.0.

MS (CI, isobutane): *m*/z = 251 (MH^+).

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.97, H, 8.86. Found C, 71.71, H, 8.97.

5,6-Dehydro-8-dihydroasteriscanolide (19)

Mp: 130−132 °C (hexane/EtOAc).

IR ($CHCl_3$): ν = 3018, 1760, 1208 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.96 (s, 3H, β-CH_3), 1.16 (s, 3H, α-CH_3), 1.19 (d, 3H, *J* = 7.0 Hz, $CHCH_3$), 1.66 (dd, 1H, *J* = 12.6, 12.6 Hz, $H_{10\alpha}$), 1.69 (d, 1H, *J* = 5.4 Hz, CHO*H*), 1.77 (dd, 1H, *J* = 12.8, 7.2 Hz, $H_{10\beta}$), 2.12 (ddq, 1H, *J* = 9.6, 7.0, 7.0 Hz, $H_{7\beta}$), 2.35 (dd, 1H, *J* = 8.7, 3.5 Hz, $H_{4\beta}$), 2.37 (dd, 1H, *J* = 8.7, 8.7 Hz, $H_{4\alpha}$), 2.40 (ddd, 1H, *J* = 12.2, 10.9, 7.4 Hz, $H_{9\beta}$), 2.97 (ddd, 1H, *J* = 10.9, 8.7, 4.4 Hz, $H_{2\beta}$), 3.09 (ddd, 1H, *J* = 10.9, 8.7, 8.7 Hz, $H_{3\beta}$), 3.99 (ddd, 1H, *J* = 10.7, 10.7, 5.0 Hz, $H_{8\alpha}$), 4.28 (dd, 1H, *J* = 4.6, 0.9 Hz, $H_{1\beta}$), 5.58 (ddd, 1H, *J* = 10.7, 9.4, 8.3 Hz, H_5), 5.76 (dd, 1H, *J* = 10.7, 7.8 Hz, H_6).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.9, 22.6, 23.7, 25.1, 40.2, 43.0, 43.7, 44.8, 45.2, 46.9, 77.7, 93.0, 126.3, 135.7, 178.2.

HRMS (CI, isobutane): Calcd for $C_{15}H_{23}O_3$ (MH^+) 251.1647. Found: 251.1635.

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.97, H, 8.86. Found C, 71.81, H, 8.86.

(±)-Asteriscanolide (1)

To a solution of the unsaturated hydroxy tricycle **19** (13 mg, 0.052 mmol) in absolute EtOH (6 mL) was added palladium on carbon (4 mg) and the resulting mixture was subjected to 20 psi of H_2 for 15 h. The reaction mixture was filtered through a plug of Celite, and the solvent was removed in vacuo to give the crude product, which was chromatographed on silica gel (hexane/EtOAc, 3:1) to give 8−dihydroasteriscanolide as a white solid (12 mg, 93%), mp: 143−144 °C (hexane/EtOAc).

IR ($CHCl_3$): ν = 3850, 1760, 996 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.00 (s, 3H, β-CH_3), 1.11 (d, 3H, *J* = 6.9 Hz, $CHCH_3$), 1.17 (s, 3H, α-CH_3), 1.53 (dd, 1H, *J* = 12.7, 12.7 Hz, $H_{10\alpha}$), 1.53−1.71 (m, 5H, $H_{4\alpha}$, $H_{7\beta}$, H_5, $H_{6\alpha}$, O*H*), 1.77 (dd, 1H, *J* = 12.7, 6.9 Hz, $H_{10\beta}$), 1.94 (m, 2H, $H_{6\beta}$, $H_{5'}$), 2.08 (dddd, 1H, *J* = 10.8, 7.7, 4.8, 4.8 Hz, $H_{4\beta}$), 2.39 (dddd, 1H, *J* = 12.6, 10.6, 10.6, 6.8 Hz, $H_{9\beta}$), 2.79 (ddd, 1H, *J* = 12.2, 9.5, 6.0 Hz, $H_{3\beta}$), 3.33 (ddd, 1H, *J* = 9.8, 9.8, 5.2 Hz, $H_{2\beta}$), 3.77 (dd, 1H, *J* = 11.0, 9.0 Hz, $H_{8\alpha}$), 4.26 (dd, 1H, *J* = 5.2, 1.0 Hz, $H_{1\beta}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.7, 21.8, 22.90, 24.1, 25.4, 28.2, 40.3, 41.7, 42.9, 43.3, 44.7, 47.2, 78.6, 92.4, 179.5.

HRMS (CI, isobutane): Calcd for $C_{15}H_{25}O_3$ (MH^+) 253.1804. Found: 253.1793.

Anal. Calcd. for $C_{15}H_{24}O_3$: C, 71.39, H, 9.59. Found C, 71.23, H, 9.57.

Tetra^{n}propyl ammonium perruthenate (2 mg, 0.0022 mmol) was added to a stirred solution of 8-dihydroasteriscanolide (11 mg, 0.0436 mmol) and *N*-methylmorpholine-*N*-oxide monohydrate (9 mg, 0.0655 mmol) in dry CH_2Cl_2 (2 mL). After 2 h, the solution was filtered through a short plug of silica gel eluting with hexane/EtOAc (1:1) and the solvent was removed in vacuo to give the crude product. Final purification by flash chromatography (hexane/EtOAc, 3:1) gave the racemic natural product **1** (11 mg; 100%), mp: 142−143 °C (Et_2O).

IR ($CHCl_3$): ν = 2963, 2876, 1765, 1699, 1468, 1355, 1216, 1168 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.00 (s, 3H, β-CH_3), 1.13 (d, 3H, *J* = 6.6 Hz, $CHCH_3$), 1.20 (s, 3H, α-CH_3), 1.35 (dddd, 1H, *J* = 13.0, 10.6, 3.1, 3.1 Hz, $H_{4\beta}$), 1.39 (dd, 1H, *J* = 12.6, 6.8 Hz, $H_{10\beta}$), 1.56 (obscured m, 1H, $H_{5\alpha}$), 1.80 (dddd, 1H, *J* = 14.5, 5.0, 5.0, 2.8 Hz,

$H_{6\alpha}$), 1.93 (obscured m, 1H, $H_{5\beta}$), 1.97 (obscured dddd, 1H, J = 13.2, 8.1, 4.2, 4.2 Hz, $H_{4\alpha}$), 2.19 (dd, 1H, J = 13.0, 13.0 Hz, $H_{10\alpha}$), 2.42 (dddd, 1H, J = 15.8, 12.4, 5.0, 3.7 Hz, $H_{6\beta}$), 2.52 (ddq, 1H, J = 12.8, 10.4, 6.7 Hz, $H_{7\beta}$), 2.71 (ddd, 1H, J = 12.4, 9.5, 4.6 Hz, $H_{3\beta}$), 3.21 (ddd, 1H, J = 12.1, 12.1, 6.8 Hz, $H_{9\beta}$), 3.73 (ddd, 1H, J = 11.0, 9.7, 5.3 Hz, $H_{2\beta}$),4.27(dd, 1H, J = 5.3, 0.9 Hz, $H_{1\beta}$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.1, 22.3, 22.8, 22.8, 24.4, 27.9, 38.3, 40.7, 43.1, 45.6, 45.7, 50.2, 90.9, 178.0, 213.9.

MS (CI, isobutane): m/z = 251 (MH^+).

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 71.97, H, 8.86. Found C, 71.71, H, 8.75.

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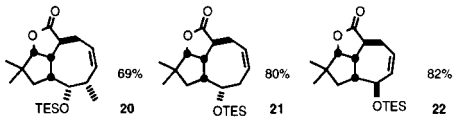

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