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Toward the Total Synthesis of (±)-Andrastin C†

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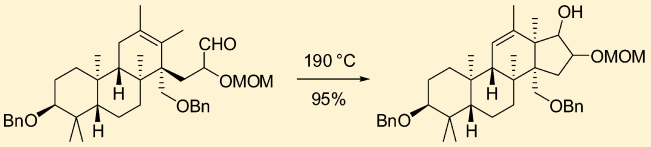
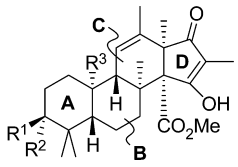
Supporting Information

ABSTRACT: An efficient approach to generate a fully functionalized cyclopenta[*a*]phenanthrene **34**, the basic carbon framework of andrastin C (**1c**), is described. The present synthetic route features a stereoselective intramolecular Diels–Alder reaction of triene **12** and an intramolecular carbonyl ene reaction of 3-phenanthrenyl-2-(methoxymethoxy)propanal **31**.



INTRODUCTION

Andrastins A–D (**1a–d**), the naturally occurring ras farnesyltransferase inhibitors, were discovered in 1996 in cultures of *Penicillium* sp. FO-3929.[1] Since farnesylation is essential for the activation of ras oncogene proteins, andrastins are anticipated to be promising anticancer drugs.[2] A key structural feature of andrastins (**1**) is the sterically hindered *cis*-hydrindane ring system possessing vicinal quaternary carbons at the bridgehead positions of the CD ring system (Figure 1).



Andrastin A (**1a**): R^1=OAc, R^2=H, R^3=CHO
Andrastin B (**1b**): R^1=OAc, R^2=H, R^3=CH_2OH
Andrastin C (**1c**): R^1=OAc, R^2=H, R^3=Me
Andrastin D (**1d**): R^1=R^2=O, R^3=CHO

Figure 1. Structures of andrastins A–D (**1a–d**).

Despite the interesting bioactivity and unique structure of andrastins (**1**), no general strategy for their synthesis has been developed, and to the best of our knowledge, no total synthesis of **1** has been reported since their original isolation.[3]

Although a wide variety of procedures for the synthesis of angularly substituted hydrindanes have been reported by means of transition metal catalyzed cyclizations,[4] Diels–Alder reactions,[5] Brønsted acid promoted transannular enol alkylations,[6] radical cyclizations,[7] carbene reactions,[8] and intramolecular Hosomi–Sakurai reactions,[9] the construction of angularly substituted *cis*-hydrindanes is still a challenging field.

We became interested in the use of the intramolecular carbonyl ene reaction as a key step for the assembly of the CD ring system of andrastins (**1**).

RESULTS AND DISCUSSION

Our strategy is outlined in Scheme 1. We anticipated that an intramolecular carbonyl ene reaction of aldehyde **3** would provide cyclopenta[*a*]phenanthrene **2**, which is convertible to andrastin C (**1c**). We believed that tricyclic aldehyde **3** would be obtained through functional group manipulations using tetracyclic compound **4**, which would be synthesized stereoselectively by means of an intramolecular Diels–Alder reaction on triene **5**. Finally, triene **5** would be constructed from (±)-**6**[10] by stereoselective introduction of the diene and dienophile substituents. Although the intramolecular carbonyl ene reaction has been studied extensively,[11] to the best of our knowledge its application to the unique challenges represented by this type of highly congested skeleton has not been described.

Our approach begins with the preparation of the perhydrophenanthrene framework, the ABC ring system, of andrastin C (**1c**). Namely, ketone **6** was subjected to Baeyer–Villiger oxidation with magnesium monoperoxyphthalate hexahydrate (MMPP) to afford lactone **7**, in 94% yield, which was treated with sodium methoxide to give hydroxy ester **8** (86%) (Scheme 2). Dehydration of **8** using phosphorus oxychloride in the presence of pyridine provided olefinic ester **9**, which was reduced with one equivalent of diisobutylaluminium hydride (DIBALH) at −78 °C to furnish aldehyde **10** in 91% yield. The Horner–Wadsworth–Emmons reaction of **10** gave rise to unsaturated enone **11** as a 4:1 mixture of diastereoisomers. After purification of **11** by silica gel flash column chromatography, enone **11** was subjected to silylation with TBSOTf and triethylamine at −78 °C to give cross conjugate silyl enol ether **12** in 98% yield.

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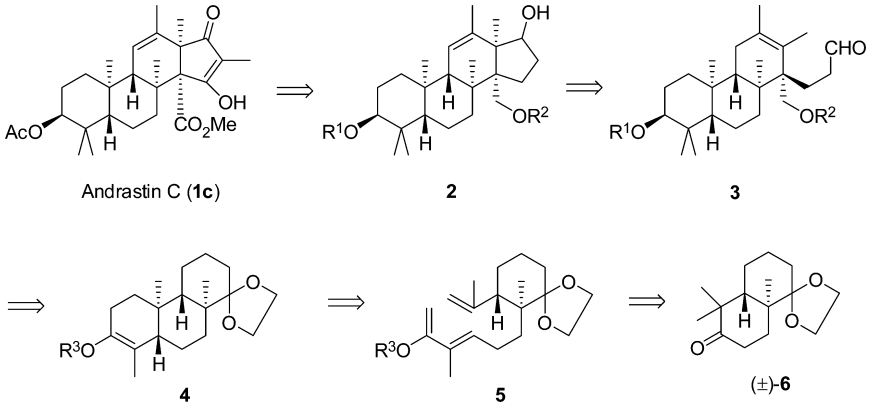
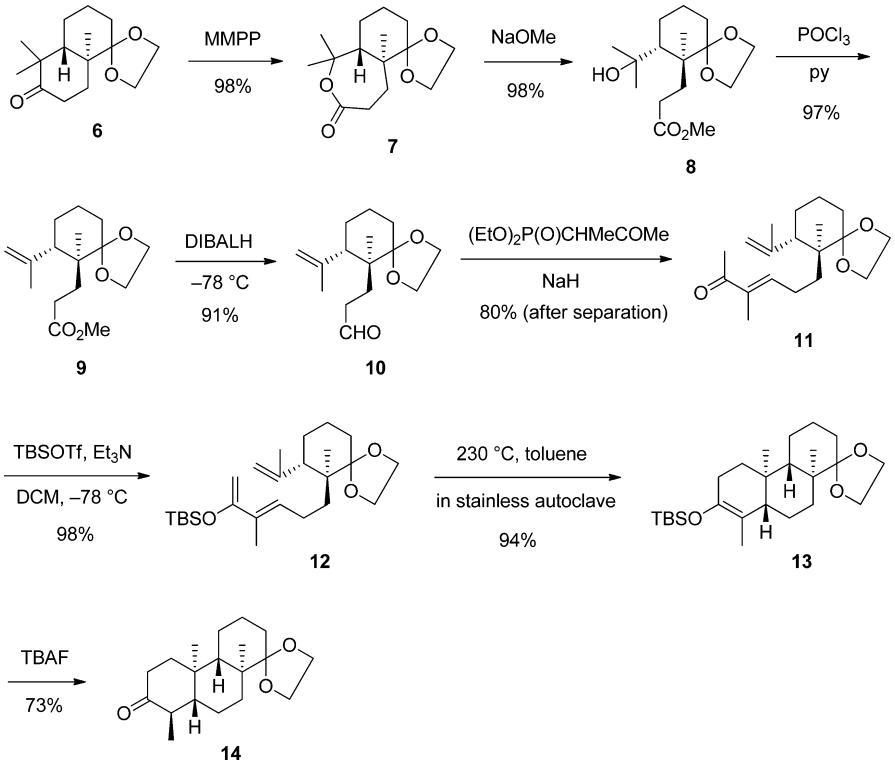
Scheme 1. Retrosynthetic Analysis of Andrastin C



Scheme 2. Preparation of Perhydrophenanthrene 13



With the requisite triene **12** for the first key reaction in hand, the intramolecular Diels–Alder reaction of **12** was performed next. Heating **12** at 230 °C in toluene in a stainless autoclave produced the desired tetracyclic compound **13** (87%) as a single stereoisomer. To confirm the relative stereochemistry of **13**, silyl enol ether **13** was transformed into ketone **14** using tetra-n-butylammonium fluoride (TBAF) in tetrahydrofuran (THF) at room temperature. All protons and carbons of ketone **14** were assigned by $^{1}H-^{1}H$ correlation spectroscopy (COSY) and $^{1}H-^{13}C$ COSY experiments. The relative stereochemistry of **14** was established on the basis of Nuclear Overhauser effect spectroscopy (NOESY) correlations between the following proton pairs: 4-H/10-Me, 8-Me/10-Me, and the coupling constant (J_{HaHb} = 12.0 Hz) as depicted in Figure 2.

The high stereoselectivity observed for this Diels–Alder reaction might be attributed to the fixed conformation of the isopropenyl group (dienophile), in which the 1,3-allylic strain is minimized in both conformers **A** and **B** in Figure 3.[12] However,

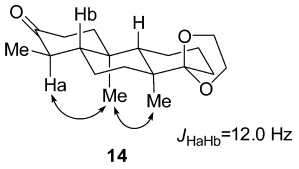


Figure 2. Significant NOESY correlations in **14**.

the nonbonding interaction of the methyl group on the diene substituent with the axial hydrogen of the methylene would disfavor conformer **B**. By contrast, this interaction is absent in conformer **A**, which provides the desired cycloadduct **13**. Conversely, conformers **C** and **D** suffer from the severe nonbonding interactions shown in Figure 3.

Having assembled the requisite skeletal framework, our synthetic efforts were focused on the functional group adjustments of **13**. After a cyclopropanation reaction (83%),[13] the resulting compound **15** was subjected to partial hydrolysis

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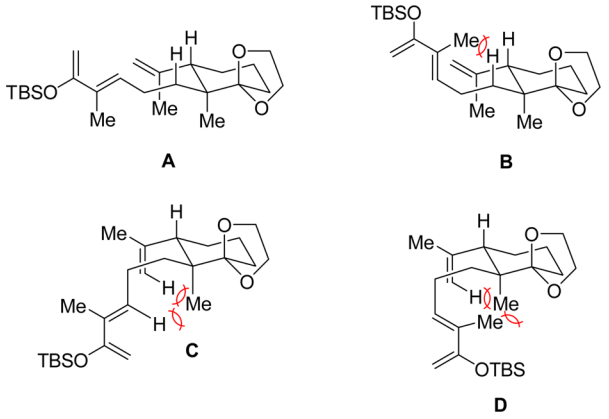


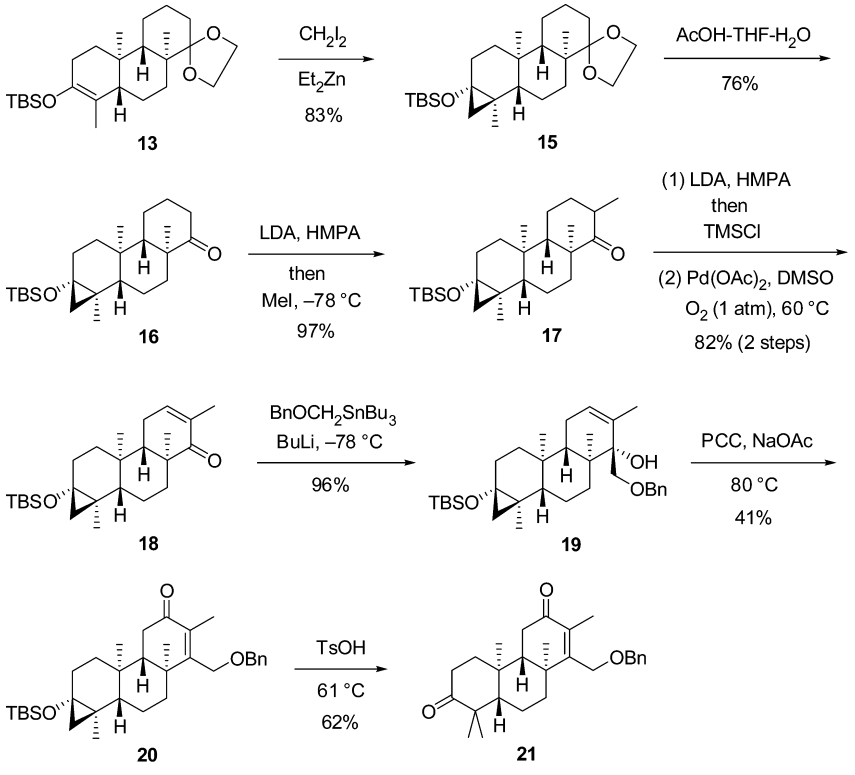
Figure 3. Plausible conformations for the intramolecular Diels–Alder reaction.

using aqueous acetic acid to afford the desired ketone **16** in 76% yield. Then a methyl group was introduced to **16** in the presence of lithium diisopropylamide (LDA) at −78 °C, and the diastereomeric mixture **17** was converted to enone **18**[14] in 82% total yield over two steps by silyl enol ether formation followed by a catalytic Ito–Saegusa reaction.[15] Addition of [(benzyloxy)methyl]lithium[16] to **18** produced tertiary alcohol **19**, which was oxidized at 80 °C with pyridinium chlorochromate (PCC) in the presence of sodium acetate to furnish enone **20** in 41% yield (Scheme 3). Cyclopropane ring cleavage of **20** was performed under acidic conditions to lead to ketone **21** in 62% yield.

With the stereoselective synthesis of ketone **21** realized, the stage was now set for the formation of a quaternary carbon on the C ring system (Scheme 4). Reduction of both carbonyl groups of **21** with lithium aluminum hydride (LAH) followed by allylic oxidation gave alcohol **22** in 72% total yield over two steps. After protection of **22** with benzyl trichloroacetimidate using a catalytic amount of triflic acid,[17] the resulting compound was reduced by applying a Luche reduction[18] to yield allylic alcohol **23** as a single stereoisomer. At this stage, we expected the stereochemistries of the benzyloxy group at the C7 position and the hydroxy group of **23** to be as depicted in Scheme 4. The stereochemistry of **23** was eventually established after conversion to **34**. Of particular note was the highly stereoselective hydride reduction of **21** and **22**. The high preference for a hydride ion to add to **21** and **22** can be explained by the Cieplak effect.[19] Inversion of the stereochemistry of the hydroxyl group in **23** was achieved via a modified Mitsunobu reaction followed by hydrolysis to yield **24**.[20] Johnson–Claisen rearrangement[21] of **24** using trimethyl orthoactate in the presence of a catalytic amount of *p*-methoxybenzoic acid gave rise to the corresponding ester, which was then reduced with LAH to produce alcohol **25** in 48% total yield over two steps. A hydroboration–oxidation reaction[22] of **25** gave alcohol **26**, in 58% yield, which was subjected to protection (99%) followed by Ley–Griffith oxidation[23] (86%) to provide ketone **27** as the sole product. At this stage, the stereochemistry of the hydroxyl group in **27** was not determined because the stereochemistry would disappear in **28** (Scheme 5).

With the required ketone **28** in hand, we turned to the next phase of our scheme. Aldehyde **32,** needed for the second key reaction of the synthesis, was constructed as shown in Scheme 5. Introduction of a methyl group to **27** with methyllithium (33%) followed by dehydration using the Martin reagent[24] gave rise to **28** in 93% yield. Fortunately, the most thermodynamically stable tetrasubstituted olefin **28** was obtained under these reaction conditions as a single diastereoisomer. After

Scheme 3. Synthesis of Enone 20



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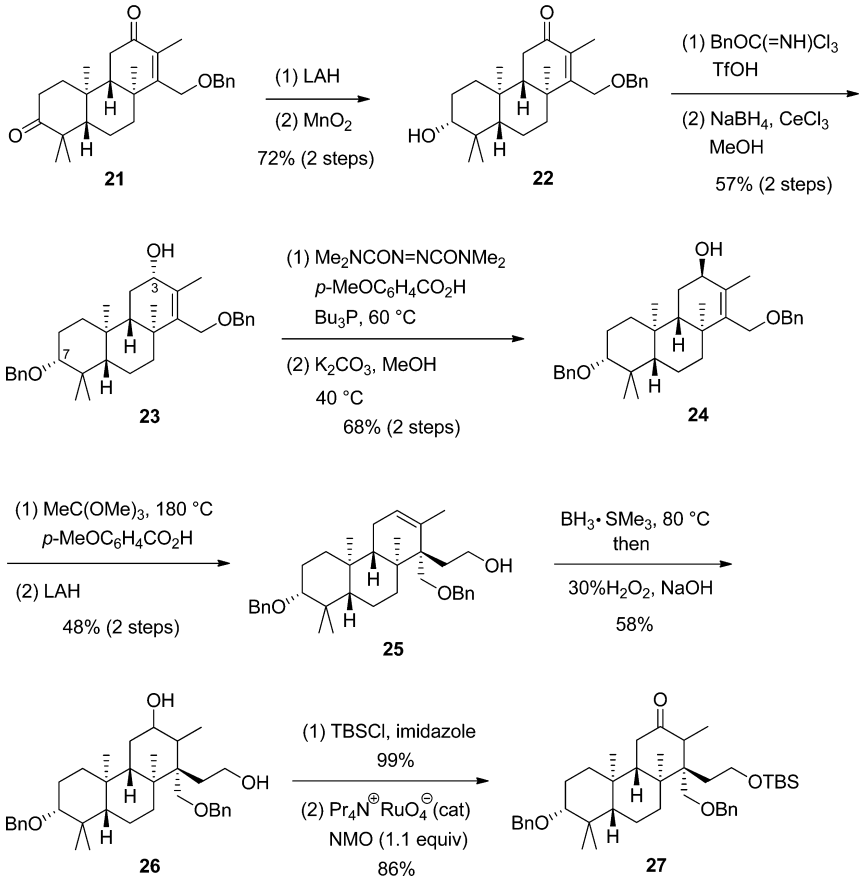
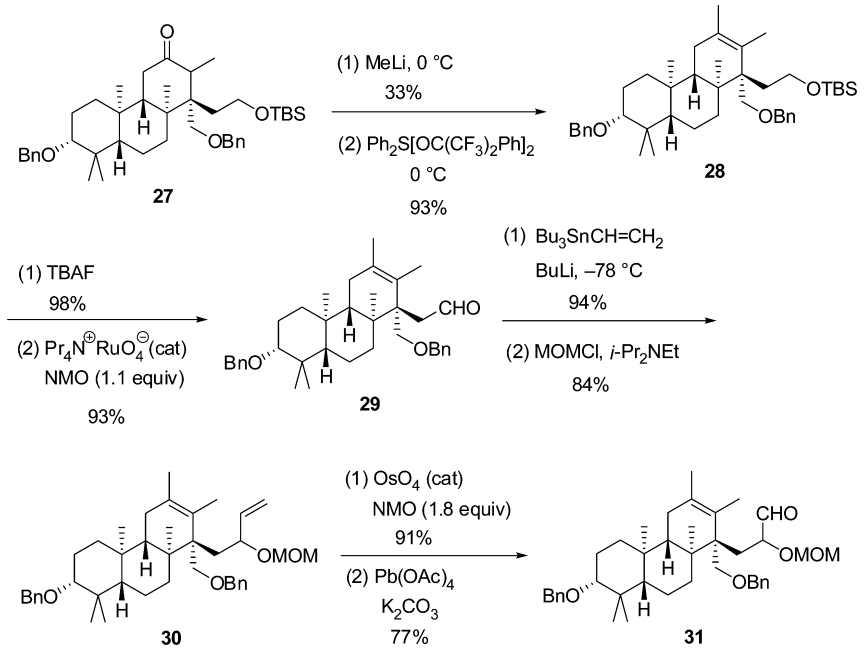
Scheme 4. Construction of Ketone 27



Scheme 5. Preparation of Aldehyde 31



deprotection of the silyl ether in **28** with TBAF (98%), the resulting alcohol was oxidized by Ley–Griffith oxidation to afford aldehyde **29**, which was subjected to 1,2-addition of a vinyl group. The resulting allylic alcohol (94%), as an approximately 1:1 mixture of stereoisomers, which was protected to furnish methoxymethyl (MOM) ether **30** (84%). Compound **30** was transformed into aldehyde **31** by dihydroxylation using a catalytic amount of osmium tetroxide[25] (91%) followed by oxidative cleavage of the diol by means of lead(IV) acetate[26] (77%; Scheme 5)

With the requisite aldehyde **31** in hand, heating of **31** in toluene at 190 °C for 17 h in a stainless autoclave gave rise to

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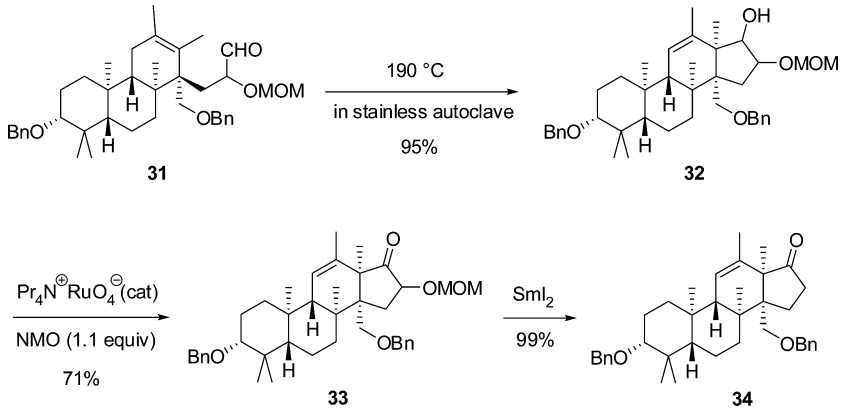
Scheme 6. Construction of Potential Intermediate 34 for the Synthesis of Andrastin C (1c)



cyclization product **32** in 95% yield. Finally, **32** was converted to ketone **34** via **33** by applying Ley–Griffith oxidation (71%) and reductive removal of alkoxy group with samarium diiodide[27] (99%) as depicted in Scheme 6.

The relative stereochemistry of ketone **34** was established on the basis of the NOESY correlations shown in Figure 4.

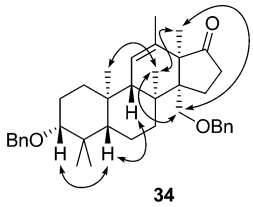


Figure 4. Significant NOESY correlations in **34**.

CONCLUSION

We have developed a novel process to construct highly functionalized cyclopenta[*a*]phenanthrene **34**, a potential intermediate for the synthesis of the new protein farnesyltransferase inhibitors, andrastins (**1**). Although some product yields were moderate, the intramolecular Diels–Alder reaction of triene **12** provided the desired cycloadduct **13** as a single stereoisomer, and the intramolecular carbonyl ene reaction of 3-phenanthrenyl-2-(methoxymethoxy)propanal **31** turned out to be effective for the construction of a sterically hindered *cis*-hydrindane ring system (*e.g.*, **32**) possessing vicinal quaternary carbons at the bridgehead positions.

EXPERIMENTAL SECTION

General Methods. Unless otherwise noted, all reactions were performed in oven-dried glassware sealed with a rubber septum under an atmosphere of argon. Anhydrous THF, CH_2Cl_2, and Et_2O were purchased. Chloroform, MeCN, pyridine, and $^iPr_2NH$ were distilled from CaH_2 prior to use. DMSO and HMPA were distilled from CaH_2 under reduced pressure. TMSCl was distilled and used immediately. Unless otherwise mentioned, materials were obtained from commercial suppliers and used without further purification. Flash column chromatography was carried out using Cica silica gel 60 N (spherical/40–50 μm) silica gel. Reactions and chromatography fractions were analyzed employing precoated silica gel 60 F_{254} plates. Compounds were visualized using an ultraviolet lamp (254 nm) and/or by staining with *p*-anisaldehyde (in EtOH), phosphomolybdic acid (in EtOH), ammonium molybdate (in 10% H_2SO_4). ^1H and ^{13}C NMR spectra were recorded on 300 or 400 MHz spectrometers. ^1H NMR spectra were recorded with tetramethylsilane (δ 0), $CHCl_3$ (δ 7.26), or C_6H_6 (δ 7.16) as an internal standard. ^{13}C NMR spectra were recorded with $CDCl_3$ or acetone-d_6 as an internal standard.

(5a*S,9a*R**)-6,6-Ethylenedioxy-1,1,5a-trimethyl-4,5,5a,6,7,8,9,9a-octahydro-2-benz[*c*]oxepin-3-one (7).** To a solution of ketone **6** (200.2 mg, 0.793 mmol) in MeOH (4 mL) and H_2O (2 mL) were added magnesium monoperoxyphthalate hexahydrate (589 mg, 0.953 mmol) and $NaHCO_3$ (80.3 mg, 0.956 mmol) at rt. The mixture was stirred at rt for 17.5 h. After addition of saturated aqueous $NaHCO_3$ solution (8 mL), the resulting mixture was extracted three times with EtOAc. The organic layers were washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by flash column chromatography on silica gel. Elution with a 5:1 mixture of hexanes–EtOAc afforded lactone **7** (209.8 mg, 98%) as colorless crystals: mp 131–132 °C; IR ($CHCl_3$) 1721 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.99–3.86 (4H, m), 2.72–2.67 (2H, m), 2.20 (1H, dd, J = 10.8, 3.0 Hz), 1.94 (1H, ddd, J = 14.8, 9.9, 4.1 Hz), 1.73–1.40 (7H, m), 1.44 (6H, s), 1.22 (3H, s); ^{13}C (75 MHz, $CDCl_3$) δ 175.5, 112.5, 85.2, 64.5, 64.2, 49.6, 45.0, 33.1, 31.4, 29.1, 27.3, 24.0, 23.8, 21.9, 16.4; LRMS m/z 268 (M^+). Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01. Found: C, 67.17; H, 9.01.

Methyl 3-[(1*S,6*R**)-6-(1-Hydroxy-1-methylethyl)-2,2-(ethylenedioxy)-1-methylcyclohexyl]propanoate (8).** To a stirred solution of sodium (105 mg, 4.57 mmol) in anhydrous MeOH (4 mL) was added dropwise a solution of lactone **7** (18.4 mg, 0.404 mmol) in ahhydrous MeOH (1 mL) at rt. After being stirred at rt for 1 h, the solvent was removed and then saturated aqueous NH_4Cl solution (5 mL) was added. The resulting mixture was extracted four times with Et_2O, and the combined ethereal layers were washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and concentrated to give an oil, which was purified by flash column chromatography on silica gel. Elution with a 4:1 mixture of hexanes–EtOAc provided ester **8** (110.1 mg, 98%) as a colorless oil: IR (neat) 3517, 1716 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.97–3.89 (4H, m), 3.65 (3H, s), 2.70–2.58 (2H, m), 2.16–2.12 (1H, m), 2.00–1.92 (2H, m),1.64–1.43 (7H, m), 1.31 (3H, s), 1.25 (3H, s), 1.16 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 114.1, 74.5, 64.0, 63.7, 51.0, 48.0, 45.7, 33.7, 31.5, 31.2, 30.2, 28.0, 25.2, 22.0, 19.4; LRMS m/z 300 (M^+). Anal. Calcd for $C_{16}H_{28}O_5$: C, 63.97; H, 9.40. Found: C,63.89; H, 9.28.

Methyl 3-[(1*S,6*S**)-6-Isopropenyl-2,2-(ethylenedioxy)-1-methylcyclohexyl]propanoate (9).** To a solution of ester **8** (197.0 mg, 0.656 mmol) in anhydrous pyridine (6.8 mL) was added $POCl_3$ (0.3 mL, 3.27 mmol) at 0 °C. The mixture was then stirred at rt for 3 days. The mixture was poured into a mixture of ice and saturated aqueous $NaHCO_3$ solution. The resulting mixture was extracted with Et_2O, and then the ethereal layer was washed with saturated aqueous $KHSO_4$ solution and brine, dried over $MgSO_4$, and evaporated. The residue was purified by flash column chromatography on silica gel. Elution with a 4:1 mixture of hexanes–EtOAc furnished olefinic ester **9** (179.0 mg, 97%) as a colorless oil: IR (neat) 1732 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.86–4.81 (1H, m), 4.76–4.72 (1H, m), 3.99–3.90 (4H, m), 3.64 (3H, s), 2.47–2.38 (2H, m), 2.31 (1H, dd, J = 12.6, 3.0 Hz), 1.78–1.74 (3H, m), 1.84–1.41 (8H, m), 1.07 (3H, s); ^{13}C

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NMR (75 MHz, $CDCl_3$) δ 174.1, 146.6, 113.0, 112.6, 63.8, 63.0, 50.3, 50.0, 43.2, 29.8, 29.4, 27.0, 23.2, 21.8, 14.8; LRMS m/z 282 (M^+). Anal. Calcd for $C_{16}H_{26}O_4$: C,68.06; H, 9.28. Found: C, 68.14; H, 9.41.

(*E*)-6-[(1*S,6*S**)-6-Isopropenyl-2,2-(ethylenedioxy)-1-methylcyclohexyl]-3-methyl-3-hexen-2-one (11).** To a stirred solution of ester **9** (263.5 mg, 2.21 mmol) in CH_2Cl_2 (3 mL) was added dropwise DIBALH (1.0 M solution in hexane, 2.43 mL, 2.43 mmol) at −78 °C. After being stirred at −78 °C for 30 min, saturated aqueous NH_4Cl solution (2.24 mL) was slowly added at −78 °C. The resulting mixture was allowed to warm to rt over a period of 30 min and dried over $MgSO_4$. The suspension was filtered through Celite. The filtrate was concentrated to yield an oil, which was purified by flash column chromatography on silica gel. Elution with a 5:1 mixture of hexanes−EtOAc gave aldehyde **10** (508.7 mg, 91%) as an oil: IR (neat) 1724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.70 (1H, t, J = 2.0 Hz), 4.85−4.83 (1H, m), 4.75−4.73 (1H, m), 4.00−3.86 (4H, m), 2.54 (2H, ddd, J = 8.8, 8.0, 2.0 Hz), 2.36 (1H, dd, J = 12.8, 3.6 Hz), 1.80 (1H, ddd, J = 14.4, 8.0, 8.0 Hz), 1.75 (3H, br s), 1.72−1.36 (7H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.0, 147.4, 114.0, 113.6, 64.6, 63.8, 51.1, 44.0, 41.0, 30.1, 27.8, 27.0, 24.1, 22.7, 16.2; LRMS m/z 252 (M^+). This compound was used in the next step without further purification. To a stirred suspension of NaH (60% in oil, 82.4 mg, 2.06 mmol) in THF (3 mL) was added dropwise a solution of diethyl 2-oxobutane-3-phosphonate (414.4 mg, 1.990 mmol) at 0 °C. A solution of the above aldehyde **10** (242.5 mg, 0.961 mmol) was added dropwise over 10 min. The resulting reaction mixture was poured into a stirred suspension of silica gel (5 g) in a 1:1 mixture of hexanes and EtOAc (30 mL) at rt. The mixture was filtered through Celite and concentrated to produce an oil, which was purified by flash column chromatography on silica gel. Elution with a 10:1 mixture of hexanes−EtOAc afforded enone **11** (234.6 mg, 80%) as a colorless oil: IR (neat) 1667 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.56 (1H, t, J = 6.4 Hz), 4.85−4.83 (1H, m), 4.47−4.74 (1H, m), 4.03−3.92 (4H, m), 2.30 (3H, s), 2.37−2.29 (3H, m), 1.77 (3H, br s), 1.73 (3H, br s), 1.79−1.34 (8H, m), 11.13 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.9, 147.5, 145.5, 136.7, 113.6, 113.4, 64.3, 63.6, 51.0, 44.2, 33.8, 29.8, 27.4, 25.3, 25.1, 23.6, 22.4, 15.5, 10.7; LRMS m/z 306 (M^+). Anal. Calcd for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C,74.84; H, 9.66.

(*E*)-5-[(1*S,6*S**)-6-Isopropenyl-2,2-(ethylenedioxy)-1-methylcyclohexyl]-3-methyl-2-[(*tert*-butyldimethylsilyl)oxy]-1,3-hexadiene (12).** To a solution of enone **11** (180.3 mg, 0.588 mmol) and Et_3N (0.16 mL, 1.14 mmol) in DCM (10 mL) was added dropwise TBSOTf (0.20 mL, 0.853 mmol) at −78 °C. After stirring at −78 °C for 2.5 h, saturated aqueous $NaHCO_3$ solution was added at −78 °C. The resulting mixture was allowed to warm to rt and extracted with Et_2O. The ethereal layer was washed with brine, dried over K_2CO_3, and evaporated to leave an oil, which was purified by flash column chromatography on silica gel. Elution with a 40:1:01 mixture of hexanes−EtOAc−Et_3N yielded silyl enol ether **12** (242.2 mg, 98%) as a colorless oil: IR (neat) 2930, 2860 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 6.38 (1H, br t, J = 7.2 Hz), 4.89−4.87 (1H, m), 4.84−4.82 (1H, m), 4.52 (1H, s), 4.41 (1H, s) 3.58−3.47 (4H, m), 2.58 (1H, dd, J = 12.4, 3.6 Hz), 2.51−2.34 (2H, m), 1.87 (1H, ddd, J = 14.0, 11.6, 6.0 Hz), 1.83 (3H, s), 1.73 (3H, s), 1.70−1.35 (7H, m), 1.20 (3H, s), 1.04 (9H, s), 0.19 (6H, s); ^{13}C (100 MHz, C_6D_6) δ 158.2, 148.1, 130.9, 130.4, 113.8, 113.5, 91.1, 64.8, 64.0, 51.6, 45.1, 35.9, 30.8, 28.1, 26.1, 25.1, 24, 3, 23.1, 18.6, 16.1, 13.5, −4.4; LRMS m/z 420 (M^+); HRMS calcd for $C_{25}H_{44}O_3Si$ (M^+) 420.3060, found 420.3050.

[(4a*R,4b*S**,8a*S**,10a*S**)-2-(*tert*-Butyldimethylsiloxy)-8,8-(ethylenedioxy)-1,4a,8a-trimethyl-3,4,4a,4b,5,6,7,8,8a,9,10,10a-dodecahydrophenanthrene (13).** A solution of triene **12** (111.3 mg,0.058 mmol) and Et_3N (2 drops) in toluene (4 mL) was heated at 230 °C in a stainless autoclave for 96 h. After removal of the solvent, the residue was purified by flash column chromatography on silica gel. Elution with a 100:4:0.5 mixture of hexanes−EtOAc−Et_3N yielded cycloadduct **13** (104.8 mg, 94%) as a white solid: mp 93−96 °C; IR (neat) 2933, 2861, 1195, 1174, 1065, 839 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 3.60−3.46 (4H, m), 2.18−1.95 (3H, m), 1.78−1.47 (12H, m), 1.41−0.98 (4H, m), 1.24 (3H, s), 1.05 (9H, s), 0.81 (3H, s), 0.15 (3H, s), 0.145 (3H, s); ^{13}C NMR (100 MHz, C_6D_6) δ 142.5, 113.6, 112.7, 65.4, 64.9, 50.3, 48.8, 43.8, 36.2, 36.1, 32.0, 31.0, 28.3, 26.2, 23.6, 21.2, 20.6, 18.5, 18.3, 13.03, 13.02, −3.31, −3.62; LRMS m/z 420 (M^+). Anal. Calcd for $C_{26}H_{44}O_3Si$: C, 71.37; H, 10.54. Found: C, 71.33; H, 10.29.

(1*R,4a*R**,4b*S**,8a*S**,10a*R**)-8,8-(Ethylenedioxy)-1,4a,8a-trimethyl-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-tetradecahydrophenanthrene-2-one (14).** To a stirred solution of cycloadduct **13** (104.8 mg, 0.249 mmol) in THF 5 mL) was added dropwise TBAF (1.0 M solution in THF, 0.5 mL, 0.5 mmol) at 0 °C, and then the mixture was allowed to warm to rt. To the reaction mixture was added a 1:1 mixture of saturated aqueous NaCl solution and hexanes. The organic layer was separated. The aqueous layer was extracted with hexanes, and the combined organic layers were washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and concentrated to produce an oil, which was purified by flash column chromatography on silica gel. Elution with a 10:1 mixture of hexanes−EtOAc furnished ketone **14** (56.0 mg, 73%) as a colorless crystal: IR (neat) 2950, 2771, 1708, 1216, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.92−3.75 (4H, m), 2.39 (1H, dddd, J = 14.8, 13,6 6.8, 0.8 Hz), 2.30−2.18 (2H, m), 2.01−1.95 (1H, ddd, J = 13.2, 6.8, 2.4 Hz), 1.68−1.20 (10H, m), 1.14 (1H, ddd, J = 12.4, 12.4, 2.8 Hz), 1.07 (3H, s), 0.99 (3H, s), 0.95 (3H, d, J = 6.4 Hz); ^{13}C NMR (100 Hz, $CDCl_3$) δ 213.6, 113.3, 65.4, 64.9, 53.0, 51.0, 44.7, 43.3, 39.9, 37.4, 36.8, 30.8, 30.5, 23.0, 21.8, 20.5, 17.4, 13.7, 11.7; LRMS m/z 306 (M^+); HRMS calcd for $C_{19}H_{30}O_3$ (M^+) 306.2195, found 306.2196.

(4a*R,4b*S**,8a*S**,10a*S**)-2-[(*tert*-Butyldimethylsilyl)oxy]-8,8-(ethylenedioxy)-1,4a,8a-trimethyl-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-tetradecahydrocyclopenta[*a*]-phenanthrene (15).** To a stirred solution of **13** (1.808 g, 4.294 mmol) in toluene (26 mL) was added Me_2Zn (1.0 M solution in hexane, 13 mL, 13 mmol) at 0 °C. After the solution was stirred at 0 °C for 10 min, CH_2I_2 (2.1 mL, 26 mmol) was added dropwise, and then the mixture was allowed to warm to rt. After being stirred at the same temperature for 6 h, the mixture was poured into saturated aqueous NH_4Cl solution, and then the resulting mixture was extracted three times with hexanes. The organic layer was washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and concentrated to leave an oil, which was purified by flash column chromatography on silica gel. Elution with a 10:1 mixture of hexanes−EtOAc provided **15** (1.559 g, 83%) as a colorless crystal: mp 142−144 °C; IR (neat) 2953, 2932, 1215, 772 cm^{-1}; 1H NMR (400 MHz, $CDCl_3$) δ 3.94−3.79 (4H, m), 2.06 (1H, ddd, J = 13.6, 6.0, 1.6 Hz), 1.90 (1H, ddd, J = 14.0, 14.0, 7.2 Hz), 1.71−1.31 (10H, m), 1.22 (1H, dddd, J = 12.4, 12.4, 12.4, 3.2 Hz), 1.12 (1H, dd, J = 12.4, 2.0 Hz), 1.09 (3H, s), 1.03 (3H, s), 0.86−0.81 (1H, m), 0.85 (9H, s), 0.79 (3H, s), 0.59 (1H, ddd, J = 13.2, 13.2, 6.4 Hz), 0.47 (1H, dd, J = 5.2, 0.8 Hz), 0.22 (1H, d, J = 5.2 Hz), 0.10 (3H, s), 0.04 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 113.7, 65.4, 64.9, 58.6, 54.1, 49.8, 43.3, 35.8, 35.5, 31.3, 30.7, 29.5, 29.0, 26.0, 23.4, 22.3, 22.0, 20.3, 18.1, 17.6, 15.7, 12.6, −2.9, −3.6; LRMS m/z 434 (M^+). Anal. Calcd for $C_{26}H_{46}O_3Si$: C, 71.83; H, 10.67. Found: C,72.12; H, 10.35.

(1a*R,1b*S**,3a*S**,7a*S**,7b*R**,9a*S**)-9a-[(*tert*-Butyldimethylsilyl)oxy]-1,2,3,4,4a,4b,5,6,7,8,8a,9,10,10a-tetradecahydro-1a,3a,7b-trimethylcyclopropa[*a*]phenanthren-4-one (16).** To a stirred solution of **15** (400.9 mg, 0.922 mmol) in a 2:1 mixture of THF−H_2O (45 mL) was added dropwise AcOH (1.5 mL) at rt, and the resulting mixture was heated at 80 °C. After being stirred at 80 °C for 24 h, an additional AcOH (0.5 mL) was added at rt, and the mixture was heated at 90 °C for 48 h. A mixture of hexanes (10 mL) and saturated aqueous $NaHCO_3$ solution (50 mL) was added, and then the organic layers were separated. The aqueous layer was washed three times with Et_2O, and the combined organic layers were washed with saturated aqueous $NaHCO_3$ solution, dried over $MgSO_4$, and evaporated to give an oil, which was purified by flash column chromatography on silica gel. Elution with a 25:1 mixuture of hexanes−EtOAc afforded ketone **16** (272.1 mg, 76%) as colorless crystals: mp 159−162 °C; IR (neat) 2926, 2859, 1708, 1255, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.58 (1H, ddd, J = 14.0, 14.0, 7.2 Hz), 2.20−2.00 (3H, m), 1.93 (1H, ddd, J = 13.2, 13.2, 7.2 Hz), 1.79−1.44 (8H, m), 1.19 (3H, s), 1.04 (3H, s), 0.89 (3H, s), 0.86 (9H, s), 0.87−0.75 (2H, m), 0.55 (1H, ddd, J = 13.2, 13.2, 6.8 Hz), 0.51

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(1H, d, J = 5.2 Hz), 0.23 (1H, d, J = 5.2 Hz), 0.11 (3H, s), 0.05 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.1, 58.4, 54.1, 54.0, 48.9, 37.6, 36.6, 35.9, 33.8, 29.4, 29.1, 26.4, 25.9, 22.2, 21.8, 20.5, 19.6, 18.1, 15.6, 13.0, −2.9, −3.6; LRMS m/z 390 (M^+); HRMS calcd for $C_{24}H_{42}O_2Si$ (M^+) 390.2954, found 390.2952.

(1a*R,1b*S**,3a*S**,7a*S**,7b*R**,9a*S**)-9a-[(*tert*-Butyldimethylsilyl)oxy]-1,1a,1b,2,3,3a,7,7a,7b,8,9,9a-dodecahydro-1a,3a,5,7b-tetramethylcyclopropa[*a*]phenanthren-4-one (18).** To a stirred solution of LDA, prepared from diisopropylamine (0.1 mL, 0.7 mmol) and BuLi (1.62 M solution in hexanes, 0.4 mL, 0.64 mmol), in THF (5 mL) was added dropwise a THF solution (1 mL) of ketone **16** (178.5 mg, 0.457 mmol) and HMPA (0.1 mL, 0.56 mmol) at −78 °C. The mixture was allowed to warm to 0 °C and stirred at the same temperature for 30 min. The reaction mixture was cooled to −78 °C, and then MeI (0.1 mL, 1.58 mmol) was added at −78 °C. The mixture was allowed to warm to rt, and saturated aqueous NH_4Cl solution was added at 0 °C. The reaction mixture was extracted three times with Et_2O, and the combined ethereal layers were washed with saturated aqueous NaCl solution, dried over $MgSO_4$, and evaporated to leave an oil, which was purified by flash column chromatography on silica gel. Elution with a 20:1 mixture of hexanes−EtOAc provided **17** (179.2 mg, 97%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.71−2.60 (0.32H, m), 2.50−2.40 (0.68 H, m), 2.12−1.04 (1H, m), 1.99−1.44 (9H, m), 1.31−1.24 (1H, m), 1.2−1.07 (4H, m), 1.04 (3H, s), 1.03 (2.04H, d, J = 6.8 Hz), 0.96 (0.96H, d, J = 6.0 Hz), 0.89 (3H, s), 0.86 (9H, s), 0.77 (1H, dd, J = 12.8, 3.2 Hz), 0.58 (1H, ddd, J = 13.2, 13.2, 6.0 Hz), 0.51 (1H, d, J = 5.2 Hz), 0.22 (1H, d, J = 5.2 Hz), 0.11 (2.04 H, s), 0.10 (0.96 H, s), 0.05 (2.04H, s), 0.04 (0.96H, s); LRMS m/z 404 (M^+); HRMS calcd for $C_{25}H_{44}O_2Si$ (M^+) 404.3111, found 404.3103.

To a stirred solution of LDA, prepared from diisopropylamine (0.2 mL, 1.42 mmol) and BuLi (1.62 M solution in hexane, 0.4 mL, 0.64 mmol), in THF (5.0 mL) was added dropwise a solution of ketone **17** (179.2 mg, 0.443 mmol) and HMPA (0.1 mL, 0.56 mmol) in THF (6.0 mL) at −78 °C. After being stirred at −78 °C for 30 min, the resulting mixture was stirred at 0 °C for 30 min and then recooled to −78 °C. After addition of TMSCl (0.15 mL, 1.17 mmol) at −78 °C, the mixture was allowed to warm to rt. After addition of saturated aqueous $NaHCO_3$ solution, the mixture was extracted with hexanes. The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over $MgSO_4$, and concentrated to yield an oil (220.7 mg), which was used in the next reaction without purification.

To a stirred solution of the above silyl enol ether (220 mg) in DMSO (15 mL) was added $Pd(OAc)_2$ (10.0 mg, 0.0445 mmol) at rt, and then the resulting mixture was stirred at 60 °C for 70 h under an atmosphere of O_2. After addition of saturated aqueous NaCl solution, dried over $MgSO_4$, and concentrated to give an oil, which was purified by flash column chromatography on silica gel. Elution with a 20:1 mixture of hexanes−EtOAc gave rise to enone **18**[a] (173.5 mg, 82% total yield over two steps) as colorless crystals: IR (neat) 2952, 2923, 2857, 1679 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66−6.62 (1H, m), 2.32−2.14 (2H, m), 2.09 (1H, dd, J = 13.6, 6.0 Hz), 1.97−1.86 (2H, m), 1.82−1.75 (1H, m), 1.75 (3H, br s), 1.65 (1H, dd, J = 13.2, 7.2 Hz), 1.58−1.44 (1H, m), 1.42−1.30 (2H, m), 1.05 (3H, s), 1.04 (3H, s), 0.93 (3H, s), 0.85 (9H, s), 0.80 (1H, dd, J = 12.4, 2.8 Hz), 0.56 (1H, ddd, J = 13.2, 13.2, 6.4 Hz), 0.51 (1H, d, J = 5.2 Hz), 0.23 (1H, d, J = 5.2 Hz), 0.10 (3H, s); ^{13}C NMR (75 MHz) δ 206.1, 143.6, 133.1, 58.4, 54.0, 50.1, 44.8, 35.9, 35.3, 34.0, 29.1, 26.0, 24.122.1, 21.9, 18.3, 18.1, 16.5, 15.7, 13.3, −2.9, −3.7; LRMS m/z 402 (M+); HRMS calcd for $C_{25}H_{42}O_2Si$ (M^+) 402.2954, found 402.2946. The above spectral data of enone **18** were in agreement with those reported in the literature.[14]

(1a*R,1b*S**,3a*S**,4*S**,7a*S**,7b*R**,9a*S**)-4-[(Benzyloxy)-methyl]-9a-[(*tert*-butyldimethylsilyl)oxy]-1a,1b,2,3,3a,4,7,7a,7b,8,9,9a-dodecahydro-1a,3a,5,7b-tetramethylcyclopropa[*a*]phenanthren-4-ol (19).** To a solution of Bu_3SnCH_2OBn (1.96 g, 4.77 mmol) in THF (15 mL) was added dropwise BuLi (1.65 M solution in hexane, 2.0 mL, 3.30 mmol) at −78 °C. The mixture was stirred at −78 °C for 1 h. To the mixture was slowly added a solution of enone **18** (292.8 mg, 0.727 mmol) in THF (6.0 mL) at −78 °C. After the mixture was stirred at the same temperature for 1 h, H_2O was added at −78 °C, and then the resulting mixture was allowed to warm to rt. The mixture was extracted with $CHCl_3$, and the organic layer was washed with brine, dried over $MgSO_4$, and evaporated to furnish an oil, which was purified by flash column chromatography on silica gel. Elution of a 100:3 mixture of hexane−EtOAc afforded alcohol **19** (366.1 mg, 96%) as colorless crystals: IR (KBr) 3530, 2926 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.28 (5H, m), 5.43 (1H, br s), 4.58 (1H, d, J = 12.2 Hz), 3.73 (1H, d, J = 9.8 Hz), 3.23 (1H, d, J = 9.8 Hz), 2.10−2.04 (1H, m), 1.95−1.78 (3H, m), 1.70 (3H, br s), 1.73−1.60 (3H, m), 1.58−1.44 (2H, m), 1.22−1.12 (1H, m), 1.07 (3H, s), 1.02 (3H, s), 0.90 (3H, s), 0.88 (9H, s), 0.78−0.74 (1H, m), 0.56−0.47 (1H, m), 0.52 (1H, d, J = 5.6 Hz), 0.25 (1H, d, J = 5.6 Hz), 0.12 (3H, s), 0.07 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 136.5, 127.7, 127.6, 124.2, 77.7, 73.4, 71.8, 58.5, 54.4, 45.5, 40.8, 35.9, 33.1, 29.0, 28.8, 25.8, 23.5, 22.2, 22.1, 18.5, 17.9, 15.8, 15.6, 12.7, −3.0, −3.8; LRMS m/z 524 (M^+). Anal. Calcd for $C_{33}H_{52}O_3Si$ (M^+): C, 75.52; H, 9.99. Found: C, 75.32; H, 9.87.

(1a*R,1b*S**,3a*S**,7a*S**,7b*S**,9a*S**)-4-[(Benzyloxy)methyl]-9a-(*tert*-butyldimethyl)-1,1a,1b,2,3,3a,7,7a,7b,8,9,9a-dodecahydro-1a,3a,5,7b-tetramethylcyclopropa[*a*]phenanthren-6-one (20).** To a stirred solution of **19** (312.0 mg, 0.594 mmol) in DCE (15.0 mL) were added NaOAc (99.6 mg, 1.12 mmol), Florisil (551.2 mg), and PCC (615.1 mg, 2.80 mmol) at rt. After being stirred at 80 °C for 70 min, the suspension was cooled to rt and diluted with Et_2O. The reaction mixture was filtered through Celite, and the filtrate was concentrated to give an oil, which was purified by flash column chromatography on silica gel. Elution with a 10:1 mixture of hexanes−EtOAc provided enone **20** (125.8 mg, 41%) as colorless crystals: IR (KBr) 2930, 1668 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.26 (5H, m), 4.56 (2H, s), 4.11 (1H, d, J = 9.9 Hz), 4.05 (1H, d, J = 9.9 Hz), 2.47 (1H, dd, J = 18.6, 4.7 Hz), 2.35 (1H, dd, J = 18.6, 13.1 Hz), 2.10 (1H, dd, J = 13.1, 4.7 Hz), 1.98−1.86 (2H, m), 1.83−1.77 (1H, m), 1.78 (3H, s), 1.70−1.48 (4H, m), 1.13 (3H, s), 0.89−0.83 (1H, m), 0.88 (3H, s), 0.87 (9H, s), 0.59−0.49 (1H, m), 0.53 (1H, d, J = 5.1 Hz), 0.23 (1H, d, J = 5.1 Hz), 0.12 (3H, s), 0.05 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.8, 160.5, 137.6, 133.2, 128.3, 127.9, 127.8, 73.3, 65.6, 58.1, 53.6, 50.5, 39.4, 35.9, 35.2, 35.0, 34.8, 29.0, 28.8, 25.7, 22.0, 21.8, 19.2, 17.8, 15.3, 11.9, 11.3, −3.1, −3.; LRMS m/z 522 (M^+); HRMS calcd for $C_{33}H_{50}O_3Si$ (M^+) 522.3529, found 522.3527.

(4a*S,4b*S**,8a*S**,10a*S**)-8-[(Benzyloxy)methyl]-4,4a,4b,5,8a,9,10,10a-octahydro-1,1,4a,7,8a-pentamethylphenanthrene-2,6-dione (21).** To a stirred solution of enone **20** (109.7 mg, 0.21 mmol) in $CHCl_3$ (10 mL) was added p-TsOH·H_2O (32.7 mg, 0.172 mmol), and the mixture was heated at reflux for 24 h. The reaction mixture was poured into saturated aqueous $NaHCO_3$ solution at 0 °C. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated to give an oil, which was purified by flash column chromatography on silica gel. Elution with a 3:1 mixture of hexanes−EtOAc afforded ketone **21** (53.5 mg, 62%) as colorless crystals: IR ($CHCl_3$) 2936, 1703, 1666 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.28 (5H, m), 4.56 (1H, d, J = 11.6 Hz), 4.51 (1H, d, J = 11.6 Hz), 4.12 (1H, d, J = 10.0 Hz), 4.07 (1H, d, J = 10.0 Hz), 2.56−2.38 (4H, m), 2.03−1.96 (1H, m), 1.86 (1H, ddd, J = 13.2, 8.2, 4.2 Hz), 1.79 (3H, s), 1.73 (1H, dd, J = 8.2, 8.0 Hz), 1.66−1.61 (3H, m), 1.49−1.36 (2H, m), 1.13 (3H, s), 1.09 (3H, s) 1.04 (3H, s), 1.03 (3H, s), 1.01 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.3, 199.8, 159.6, 137.4, 133.1, 128.2, 127.7, 127.6, 73.2, 65.4, 53.9, 53.1, 46.9, 39.6, 37.8, 36.2, 35.8, 34.3, 33.4, 26.3, 20.7, 19.0, 18.5, 15.2, 11.1; LRMS m/z 408 (M^+). Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.20; H, 8.76.

(4a*S,4b*S**,7*R**,8a*S**,10a*S**)-1-[(Benzyloxy)methyl]-4,4a,5,6,7,8,8a,9,10,10a-decahydro-7-hydroxy-2,4b,8,8,10a-pentamethylphenanthren-3-one (22).** To a stirred suspension of LAH (716.8 mg, 15.1 mmol) in THF (20 mL) was added dropwise a solution of **21** (1.10 g, 0.249 mmol) in THF (20 mL) at 0 °C. The reaction mixture was allowed to warm to rt. After the mixture was stirred at rt for 7 h, the reaction was quenched by successive addition

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of H_2O (0.72 mL), 15% aqueous NaOH solution (0.72 mL), and H_2O (2.16 mL) at 0 °C. After being stirred at rt for 30 min, the mixture was dried over $MgSO_4$. The mixture was filtered through Celite, and the filtrate was concentrated to yield an oil, which was used in the next reaction without purification.

To a stirred solution of the above diol (722.0 mg) in DCM (200 mL) was added MnO_2 (10.8 g, 124.2 mmol) at rt. After being stirred at rt for 23 h, the suspension was diluted with Et_2O. The resulting mixture was filtered through Celite, and the filtrate was concentrated to yield an oil, which was purified by flash column chromatography on silica gel. Elution with 2:3 mixture of hexanes−EtOAc lead to alcohol **22** (798.2 mg, 72% total yield over two steps) as colorless crystals: IR ($CHCl_3$) 3464, 2926, 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.28 (5H, m), 4.56 (1H, d, J = 11.8 Hz), 4.52 (1H, d, J = 11.8 Hz), 4.10 (1H, d, J = 10.0 Hz), 4.04 (1H, d, J = 10.0 Hz), 3.18 (1H, dd, J = 11.8, 4.6 Hz), 2.48−2.33 (2H, m), 2.01−1.93 (1H, m), 1.78 (3H, s), 1.71−1.43 (8H, m), 1.08 (3H, s), 0.98 (3H, s), 0.91 (3H, s), 1.10−0.84 (2H, m), 0.79 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 160.2, 137.7, 133.4, 128.4, 128.0, 127.9, 78.5, 73.5, 65.6, 54.7, 54.1, 39.8, 38.7, 37.5, 36.9, 36.8, 34.3, 27.8, 27.0, 19.2, 18.1, 15.7, 15.3, 11.4; LRMS m/z 410 (M^+). Anal. Calcd for $C_{27}H_{38}O_3$: C, 78.98; H, 9.33. Found: C, 79.16; H, 9.30.

(3*S,4a*S**,4b*S**,7*R**,8a*S**,10a*S**)-7-(Benzyloxy)-1-[(benzyloxy)methyl]-3,4,4a,4b,5,6,7,8,8a,9,10,10a-dodecahydro-2,4b,8,8,10a-pentamethylphenanthren-3-ol (23).** To a stirred solution (1 mL) of alcohol **22** (8.9 mg, 0.0217 mmol) and benzyl 2,2,2-trichloroacetimidate (0.006 mL, 0.032 mmol) in a 1:1 mixture of DCM and cyclohexane was added TfOH (0.1 μL, 1.13 μmol) at 0 °C. After being stirred at rt for 30 min, the reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ solution at 0 °C. The organic layer was separated and washed with brine, dried over $MgSO_4$, and evaporated to give an oil (10.9 mg), which was used in the next step without purification.

To a stirred solution of the above product (10.9 mg) and $CeCl_3{\cdot}7H_2O$ (11.8 mg, 0.032 mmol) in MeOH (3.0 mL) was added $NaBH_4$ (1.2 mg, 0.032 mmol) at 0 °C. After the solution was stirred at 0 °C for 15 min, H_2O was added at 0 °C. The reaction mixture was evaporated, and the residue was diluted with H_2O. The mixture was extracted with $CHCl_3$, and the organic layer was washed with brine, dried over $MgSO_4$, and concentrated to leave an oil, which was purified by flash column chromatography on silica gel. Elution with a 3:1 mixture of hexanes−EtOAc yielded benzyl ether **23** (6.1 mg, 57% total yield over two steps) as a colorless oil: IR (neat) 3402, 2936, 2853 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35−7.17 (10H, m), 4.65 (1H, d, J = 11.8 Hz), 4.51 (1H, d, J = 11.8 Hz), 4.46 (1H, d, J = 11.8 Hz), 4.41 (1H, d, J = 11.8 Hz), 4.08−4.01 (1H, m), 3.91 (1H, d, J = 9.9 Hz), 3.76 (1H, d, J = 9.9 Hz), 2.88 (1H, dd, J = 11.8, 4.2 Hz), 2.02 (1H, dd, J = 11.8, 7.0 Hz), 1.86−1.70 (3H, m), 1.73 (3H, s), 1.65−1.50 (3H, m), 1.46−1.32 (3H, m), 1.13−1.06 (1H, m), 0.98 (3H, s), 0.97 (3H, s), 0.89−0.75 (2H, m), 0.85 (3H, s), 0.83 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 139.4, 138.3, 135.0, 128.3, 128.1, 128.0, 127.6, 127.3, 127.1, 86.5, 73.2, 71.4, 65.6, 55.5, 53.8, 39.0, 38.9, 37.9, 37.7, 36.6, 28.7, 28.1, 22.8, 21.5, 18.0, 16.3, 16.2, 14.8; LRMS m/z 484 (M^+ − 18, H_2O); HRMS calcd for $C_{34}H_{44}O_2$ (M^+ − 18) 484.3341, found 484.3344.

(3*R,4a*S**,4b*S**,7*R**,8a*S**,10a*S**)-7-(Benzyloxy)-1-[(benzyloxy)methyl]-3,4,4a,4b,5,6,7,8,8a,9,10,10a-dodecahydro-2,4b,8,8,10a-pentamethylphenanthren-3-ol (24).** To a stirred solution of alcohol 23 (163.9 mg, 0.326 mmol) in anhydrous C_6H_6 (6 mL) were added PBu_3 (0.2 mL, 0.779 mmol), *p*-methoxybenzoic acid (125.3 mg, 0.825 mmol), and tetramethylazodicarboxamide (102.5 mg, 0.595 mmol) at rt. After the mixture was stirred at 60 °C for 1 h, H_2O was added at rt, and the resulting mixture was extracted with Et_2O. The ethereal layer was washed with brine, dried over $MgSO_4$, and evaporated to leave an oil (246 mg), which was used in the next reaction without purification.

To a stirred solution of the above benzoate (246 mg) in MeOH (100 mL) and DCE (1 mL) was added K_2CO_3 (1.108 g, 8.01 mmol) at rt, and the mixture was heated at 45 °C for 96 h. The resulting mixture was cooled to rt and evaporated. The residue was diluted with H_2O, and the mixture was extracted with $CHCl_3$. The organic layer was separated, and washed with brine, dried over $MgSO_4$, and concentrated to afford an oil, which was purified by flash column chromatography on silica gel. Elution with a 3:1 mixture of hexanes−EtOAc yielded alcohol 24 (11.9 mg, 68% total yield over two steps) as a colorless oil: IR (neat) 3300, 2936, 2868 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.10 (10H, m), 4.66 (1H, d, J = 11.8 Hz), 4.52 (1H, d, J = 11.8 Hz), 4.47 (1H, d, J = 11.8 Hz), 4.42 (1H, d, J = 11.8 Hz), 3.98−3.89 (1H, m), 3.92 (1H, d, J = 10.2 Hz), 3.84 (1H, d, J = 10.2 Hz), 2.89 (1H, dd, J = 11.8, 4.2 Hz), 1.86−1.30 (10H, m), 1.77 (3H, s), 1.24 (1H, br s), 1.00−0.81 (2H, m), 0.97 (3H, s), 0.92 (3H, s), 0.86 (3H, s), 0.82 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 139.5, 138.3, 133.4, 128.4, 128.2, 128.0, 127.7, 127.4, 127.2, 86.4, 73.1, 71.5, 70.3, 65.4, 55.6, 50.2, 39.0, 38.9, 38.0, 37.4, 36.5, 28.1, 27.5, 22.8, 19.7, 18.2, 17.1, 16.4, 16.2; LRMS m/z 484 (M^+ − 18, H_2O); HRMS calcd for $C_{34}H_{44}O_2$ (M^+ − 18) 484.3341, found 484.3345.

2-(1*S,4a*S**,4b*S**,7*R**,8a*S**,10a*S**)-7-(Benzyloxy)-1-[(benzyloxy)methyl]-1,4,4a,4b,5,6,7,8,8a,9,10,10a-dodecahydro-1-(2-hydroxyethyl)-2,4,4b,8,8,10a-pentamethylphenanthrene (25).** A solution of alcohol **24** (335.1 mg, 0.667 mmol) and *p*-methoxybenzoic acid (6.6 μL, 1.0 mmol) in triethyl orthoacetate (6.0 mL, 32.7 mmol) was heated at 180 °C in a stainless autoclave for 12 h. After the mixture was cooled to rt, the mixture was evaporated to give an oil (521 mg), which was used in the next step without purification.

To a stirred suspension of LAH (111.1 mg, 2.93 mmol) in THF (20 mL) was added dropwise a solution of the above ester (521 mg) in THF (15 mL) at 0 °C. After being stirred at rt for 1 h, the reaction was quenched by successive addition of H_2O (0.12 mL), 15% aqueous NaOH solution (0.12 mL), and H_2O (0.36 mL) at 0 °C. The mixture was dried over $MgSO_4$ and filtered through Celite. The filtrate was concentrated to give an oil, which was purified by flash column chromatography on silica gel. Elution with a 3:1 mixture of hexanes−EtOAc furnished alcohol **25** (169.7 mg, 48% total yield over two steps) as a colorless oil: IR (neat) 3418, 2934, 2872 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.12 (10H, m), 5.46 (1H, br s), 4.64 (1H, d, J = 12.0 Hz), 4.48−4.40 (3H, m), 3.71−3.67 (2H, m), 3.49 (2H, br s), 2.91 (1H, dd, J = 12.0, 4.4 Hz), 2.51 (1H, br s), 1.92−1.60 (8H, m), 1.72 (3H, br s), 1.68−1.35 (4H, m), 0.99−0.74 (2H, m), 0.98 (3H, s), 0.93 (3H, s), 0.88 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4, 137.9, 135.5, 128.3, 128.1, 127.6, 127.5, 127.4, 127.2, 124.5, 86.2, 73.5, 73.4, 71.3, 61.3, 55.6, 48.8, 47.7, 40.5, 38.8, 38.7, 38.2, 37.2, 34.7, 28.2, 22.8, 22.6, 18.4, 17.3, 16.6, 15.9; LRMS m/z 530 (M^+); HRMS calcd for $C_{36}H_{50}O_3$ (M^+) 530. 3760, found 530.3751.

(1*S,2*S**,3*S**,4a*S**,4b*S**,7*R**,8a*S**,10a*S**)-7-(Benzyloxy)-1-[(benzyloxy)methyl]tetradecahydro-1-(2-hydroxyethyl)-2,4b,8,8,10a-pentamethylphenanthren-3-ol (26).** A solution of olefinic alcohol **25** (286.3 mg, 0.539 mmol) and $BH_3{\cdot}SMe_2$ (10 M solution in THF, 2.0 mL, 20.0 mmol) in THF (4 mL) was heated at 80 °C in a stainless autoclave for 80 min. After the reaction mixture was cooled to 0 °C, to the mixture were successively added 15% aqueous NaOH solution (1 mL) and 30% aqueous H_2O_2 solution (2 mL). The mixture was allowed to warm to rt and then extracted with $CHCl_3$. The organic layer was washed with brine, dried over $MgSO_4$, evaporated to leave an oil, which was purified by column chromatography on silica gel. Elution with a 1:1 mixture of hexanes−EtOAc gave rise to diol **26** (172.3 mg, 58%) as a colorless oil: IR (neat) 3246, 2936, 2872 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.18 (10H, m), 4.66 (1H, d, J = 12.0 Hz), 4.48−4.38 (3H, m), 3.89−3.83 (3H, m), 3.57 (1H, d, J = 9.6 Hz), 3.41 (1H, d, J = 9.6 Hz), 3.00−2.60 (1H, m), 2.91 (1H, dd, J = 10.8, 4.0 Hz), 2.23−2.15 (3H, m) 1.83−1.37 (12H, m), 1.07 (3H, s), 1.06−0.78 (7H, m), 0.90 (3H, s), 0.82 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 138.2, 128.3, 128.1, 127.5, 127.4, 127.3, 127.1, 86.3, 73.9, 73.7, 73.3, 71.4, 59.7, 56.0, 44.4, 44.3, 41.9, 38.7, 37.4, 37.0, 36.4, 36.0, 28.1, 24.6, 22.9, 19.0, 17.8, 17.2, 16.9, 16.4; LRMS m/z 530 (M^+ − 18, H_2O); HRMS calcd for $C_{36}H_{50}O_3$ (M^+ − 18) 530.3760, found 530.3755.

(1*R,4a*S**,4b*S**,7*R**,8a*S**,10a*S**)-7-(Benzyloxy)-1-[(benzyloxy)methyl]-1-[2-[(*tert*-butyldimethylsilyl)oxy]ethyl]-1,4,4a,4b,5,6,7,8,8a,9,10,10a-dodecahydro-2,3,4b,8,8,10a-hexamethylphenanthrene (28).** To a solution of diol **26** (71.1 mg, 0.130 mmol) and imidazole (20.7 mg, 0.304 mmol) in DMF (4 mL)

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was added TBSCl (25.4 mg, 0.164 mmol) at rt, and then the mixture was stirred at the same temperature for 2 h. The reaction mixture was poured into saturated aqueous $NaHCO_3$ solution, and then the resulting mixture was extracted with Et_2O. The ethereal layer was washed with brine, dried over $MgSO_4$, and evaporated to give an oil, which was purified by flash column chromatography on silica gel. Elution with a 3:1 mixture of hexanes−EtOAc provided the corresponding mono TBS ether (84.8 mg, 99%) as a colorless oil. *Data for this product*: IR (neat) 3425, 2961, 2586 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.22 (10H, m), 4.66 (1H, d, J = 11.8 Hz), 4.49−4.27 (3H, m), 3.81−3.74 (3H, m), 3.63 (1H, d, J = 9.9 Hz), 3.26 (1H, d, J = 9.9 Hz), 2.92 (1H, dd, J = 11.8, 4.0 Hz), 2.33−2.10 (3H, m), 1.86−1.75 (3H, m) 1.64−1.31 (3H, m) 1.09−0.78 (6H, m), 1.07 (3H, s), 0.96 (3H, s), 0.88 (9H, s), 0.82 (3H, s), 0.72−0.71 (1H, m) 0.02 (3H, s) 0.00 (3H, s); LRMS m/z 603 ($M^+ - 59$, C_4H_{11}); HRMS calcd for $C_{38}H_{55}O_4Si$ ($M^+ - 59$) 603.3870, found: 603.3866.

To a stirred solution of the above alcohol (84.8 mg, 0.128 mmol) in DCM (10 mL) were added tetrapropylammonium perruthenate (25.3 mg, 0.0698 mmol) and NMO (169.3 mg, 1.40 mmol) at rt. After being stirred at rt for 1 h, the reaction mixture was filtered through Celite, and the filtrate was concentrated to yield an oil, which was purified by flash column chromatography on silica gel. Elution with a 6:1 mixture of hexanes−EtOAc afforded ketone **27** (73.1 mg, 86%) as colorless crystals: IR (neat) δ 2932, 2855, 1705 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.18 (10H, m), 4.54 (1H, d, J = 12.0 Hz), 4.43 (1H, d, J = 12.0 Hz), 4.39 (2H, s), 3.82−3.76 (2H, m), 3.47 (1H, d, J = 9.6 Hz), 3.38 (1H, d, J = 9.6 Hz), 2.92 (1H, dd, J = 16.0, 4.2 Hz), 2.66−2.58 (1H, m), 2.44−2.34 (1H, m), 2.26−2.18 (1H, m), 2.06−1.97 (1H, m), 1.85−1.40 (8H, m), 1.12−0.78 (18H, m), 0.87 (9H, s), 0.06 (0.17H, s), 0.05 (0.17H, s), 0.03 (2.83H, s), 0.02 (2.83H, s); LRMS m/z 660 (M^+); HRMS calcd for $C_{42}H_{64}O_4Si$ (M^+) 660.4574, found 660.4577.

To a stirred solution of ketone **27** (73.1 mg, 0.111 mmol) in Et_2O (4 mL) was added MeLi (0.98 M solution in Et_2O, 4.0 mL, 3.92 mmol) at 0 °C. After the solution was stirred at 0 °C for 2 h, saturated aqueous NH_4Cl solution was added at 0 °C, and then the resulting mixture was extracted with Et_2O. The ethereal layer was washed with brine, dried over $MgSO_4$, evaporated to give an oil, which was purified by flash column chromatography on silica gel. Elution with a 5:1 mixture of hexanes−EtOAc gave the corresponding alcohol (23.7 mg, 33%) and starting material **27** (23.7 mg) as recovered. *Data for this product*: IR (neat) 3423, 2930, 2855 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.13 (10H, m), 4.68−4.37 (4H, m), 3.87−3.73 (2H, m), 3.42 (2H, s), 2.94−2.88 (1H, m), 2.50 (1H, br s), 1.98−1.34 (14H, m), 1.25−0.76 (28H, m), 0.06−0.00 (6H, m); LRMS m/z 658 (M^+−18, H_2O); HRMS calcd for $C_{43}H_{66}O_3Si$ (M^+−18) 658.4781, found 658.4780.

To a stirred solution of the above product (23.7 mg) in DCM (8 mL) was added $[C_6H_5C(CF_3)_2O]_2S(C_6H_5)_2$ (240.5 mg, 0.357 mmol) at 0 °C. After being stirred at 0 °C for 10 min, the suspension was diluted with MeOH. The reaction mixture was evaporated to leave an oil, which was purified by flash column chromatography on silica gel. Elution with a 20:1 mixture of hexanes−EtOAc gave rise to olefin **28** (21.4 mg, 91%) as a colorless oil: IR (neat) 2930, 2846 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.08 (10H, m), 4.55 (1H, d, J = 12.8 Hz), 4.28 (1H, d, J = 12.8 Hz), 4.26 (2H, s), 4.06−3.98 (1H, m), 3.50 (1H, d, J = 10.0 Hz), 3.46 (1H, d, J = 10.0 Hz), 2.77 (1H, dd, J = 11.2, 4.2 Hz), 2.15−1.99 (2H, m), 1.91−1.34 (9H, m), 1.74 (3H, s), 1.62 (3H, s), 1.14−0.85 (7H, m), 1.07 (3H, s), 1.00 (9H, s), 0.92 (3H, s), 0.72−0.68 (2H, m), 0.13 (3H, s), 0.12 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 139.1, 128.5, 128.4, 128.2, 128.0, 127.8, 127.7, 127.6, 127.5, 127.4, 86.4, 74.5, 73.6, 71.4, 62.8, 56.1, 50.0, 48.7, 40.9, 39.1, 37.4, 28.5, 26.3, 26.2, 23.0, 20.2, 18.8, 18.6, 17.9, 17.0, 16.3, 16.2, −4.8, −4.9; LRMS m/z 658 (M^+); HRMS calcd for $C_{43}H_{66}O_3Si$ (M^+) 658.4781, found 658. 4780.

2-[(1*R,4a*S**,4b*S**,7*R**,8a*S**,10a*S**)-7-(Benzyloxy)-1-[(benzyloxy)methyl]-1,4,4a,4b,5,6,7,8,8a,9,10,10a-dodecahydro-2,3,4b,8,8,10a-hexamethylphenanthren-1-yl]-acetaldehyde (29).** To a stirred solution of **28** (21.4 mg, 0.0325 mmol) in THF (2 mL) was added dropwise TBAF (1 M solution in THF, 2.0 mL, 2.0 mmol) at rt. After the mixture was stirred at rt for 25 h, brine was added, and then the resulting mixture was extracted with Et_2O. The ethereal layer was washed with brine, dried over $MgSO_4$, and evaporated to leave an oil, which was purified by flash column chromatography on silica gel. Elution with a 4:1 mixture of hexanes−EtOAc afforded the corresponding alcohol (17.3 mg, 98%) as a colorless oil. *Data for this product*: IR (neat) 3416, 2932, 2872 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.23 (10H, m), 4.66 (1H, d, J = 12.2 Hz), 4.45 (2H, s), 4.42 (1H, d, J = 12.2 Hz), 3.72−3.60 (2H, m), 3.47 (2H, s), 2.91 (1H, dd, J = 11.8, 4.0 Hz), 2.21 (1H, br s), 1.89−1.30 (11H, m), 1.67 (3H, s), 1.60 (3H, s), 1.16−1.07 (1H, m), 1.00−0.73 (2H, m), 0.98 (3H, s), 0.95 (3H, s), 0.85 (3H, s), 0.83 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4, 138.1, 128.5, 128.3, 128.2, 120.0, 127.9, 127.6, 127.5, 127.2, 86.3, 73.9, 73.4, 71.4, 61.6, 55.6, 49.6, 47.8, 40.6, 38.9, 38.8, 38.3, 37.1, 34.7, 30.1, 28.2, 22.8, 20.1, 18.4, 17.4, 16.6, 16.1, 15.9; LRMS m/z 544 (M^+); HRMS calcd for $C_{37}H_{52}O_3$ (M^+) 544.3916, found 544.3918.

To a stirred solution of the above alcohol (17.3 mg, 0.0319 mmol) in DCM (10 mL) were added tetrapropylammonium perruthenate (5.5 mg, 0.0152 mmol) and NMO (34.5 mg, 0.286 mmol) at rt. After being stirred at rt for 30 min, the reaction mixture was filtered through Celite, and the filtrate was concentrated to give an oil, which was purified by flash column chromatography on silica gel. Elution with a 6:1 mixture of hexanes−EtOAc furnished aldehyde **29** (16.1 mg, 93%) as a colorless oil: IR (neat) 2939, 2870, 1713 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.69 (1H, dd, J = 3.2, 3.2 Hz), 7.36−7.24 (10H, m), 4.65 (1H, d, J = 12.0 Hz), 4.44 (2H, s), 4.42 (1H, d, J = 12. Hz), 3.59 (1H, d, J = 9.8 Hz), 3.50 (1H, d, J = 12. Hz), 2.91 (1H, dd, J = 11.8, 4.2 Hz), 2.56 (1H, d, J = 15.6, 3.2 Hz), 2.47 (1H, dd, J = 15.6, 3.2 Hz), 1.92−1.11 (9H, m), 1.70 (3H, s), 1.62 (3H, s), 1.00−0.80 (2H, m),0.98 (3H, s), 0.95 (3H, s), 0.87 (3H, s), 0.78−0.69 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.4, 139.4, 138.1, 128.3, 128.2, 128.1, 127.51, 127.48, 127.43, 127.35, 127.2, 86.2, 73.3, 72.7, 71.5, 55.7, 50.8, 48.5, 47.7, 40.2, 38.9, 38.7, 37.2, 35.7, 29.9, 28.2, 22.8, 20.0, 18.3, 16.72, 16.70, 15.8, 15.3; LRMS m/z 542 (M^+); HRMS calcd for $C_{37}H_{50}O_3$ (M^+) 542.3760, found 542.3764.

(2*R,4a*S**,4b*S**,8*R**,8a*S**,10a*S**)-2-(Benzyloxy)-8-[(benzyloxy)methyl]-8-[2-(methoxymethoxy)-3-butenyl]-1,2,3,4,4a,4b,5,8,8a,9,10,10a-dodecahydro-1,1,4a,6,7,8a-hexamethylphenanthrene (30).** To a stirred solution of tributylvinyltin (0.025 mL, 0.0855 mmol) in THF (3 mL) was added dropwise BuLi (1.44 M solution in hexane, 0.05 mL, 0.072 mmol) at −78 °C, and then the mixture was stirred at −78 °C for 5 min. To the resulting mixture was slowly added a solution of aldehyde **29** (8.6 mg, 0.0158 mmol) in THF (3 mL) at −78 °C. After being stirred at −78 °C for 30 min, saturated aqueous NH_4Cl solution was added at −78 °C, and the mixture was allowed to warm to rt. The reaction mixture was extracted with Et_2O, and the ethereal layer was washed with brine, dried over $MgSO_4$, evaporated to leave an oil, which was purified by flash column chromatography on silica gel. Elution with a 5:1 mixture of hexane−EtOAc gave the corresponding alcohol (8.5 mg, 94%) as a colorless oil. *Data for this compound*: IR (neat) 3444, 2931, 2869 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45−7.10 (10H, m), 5.93−5.76 (1H, m), 5.05−4.98 (1H, m), 4.70−4.61 (1H, m), 4.54−4.40 (3H, m); LRMS m/z: 570 (M^+); HRMS calcd for $C_{39}H_{54}O_3$ (M^+) 570.4073, found 570.4071.

To a stirred solution of the above alcohol (37.3 mg, 0.0653 mmol) in DCM (5 mL) were slowly added diisopropylamine (1.0 mL, 5.6 mmol) and MOMCl (0.5 mL, 6.58 mmol) at 0 °C. After the solution was stirred at rt for 10 h, saturated aqueous NH_4Cl solution was added at 0 °C, and the resulting mixture was extracted with $CHCl_3$. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated to afford an oil, which was purified by flash column chromatography on silica gel. Elution with a 5:1 mixture of hexanes−EtOAc furnished ether **30** (33.9 mg, 84%) as a colorless oil: IR (neat) 2932, 2878, 1452 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.25 (10H, m), 5.65−5.53 (1H, m), 5.11−5.01 (2H, m), 4.71−4.16 (7H, m), 3.54−3.21 (2H, m), 3.33 (1.65H, s), 3.27 (1.35H, s), 2.97−2.88 (1H, m), 1.98−1.23 (18H, m), 1.06−0.75 (15H, m); LRMS m/z 614 (M^+); HRMS calcd for $C_{41}H_{58}O_4$ (M^+) 614.4335, found 614.4337.

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(3*R,5*S**,8*S**,9*S**,10*R**,13*R**,14*R**)-3-(Benzyloxy)-14-[(benzyloxy)methyl]-1,3,4,5,6,7,8,10,15,16-decahydro-4,4,8,10,12,13-hexamethylcyclopenta[*a*]phenanthren-17-one (34).** To a stirred solution of ether **30** (33.9 mg, 0.0551 mmol) in THF (1 mL) and H_2O (1 mL) were added OsO_4 (0.04 M solution in hexane, 0.5 mL, 0.02 mmol) and NMO (11.7 mg, 0.10 mmol) at rt. After the solution was stirred at rt for 5 h, saturated aqueous $Na_2S_2O_3$ solution was added at 0 °C. The resulting mixture was extracted with $CHCl_3$, and then the organic layer was washed with brine, dried over $MgSO_4$, and evaporated to leave an oil, which was purified by flash column chromatography on silica gel. Elution with a 1:1 mixture of hexanes−EtOAc gave rise to the corresponding diol (32.5 mg, 91%), as a colorless oil, which was used to next reaction.

To a stirred solution of the above product (32.5 mg, 0.051 mmol) and K_2CO_3 (153 mg, 1.11 mmol) in C_6H_6 (5 mL) was added $Pb(OAc)_4$ (109.3 mg, 0.222 mmol) at 0 °C. After the solution was stirred at rt for 30 min, saturated aqueous $NAHCO_3$ solution was added at 0 °C. The resulting mixture was extracted with $CHCl_3$. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated to provide an oil, which was purified by flash column chromatography on silica gel. Elution with a 6:1 mixture of hexanes−EtOAc produced aldehyde **31** (26.3 mg, 77%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.41 (0.55H, d, J = 2.8 Hz), 9.25 (0.45H, d, J = 2.8 Hz), 7.37−7.25 (10H, m), 4.69−4.36 (6H, m), 4.11−4.04 (1H, m), 3.58−3.34 (6H, m), 2.96−2.90 (1H, m), 2.22−2.02 (1H, m), 1.94−1.17 (15H, m), 1.04−0.76 (15H, m).

A solution of aldehyde **31** (4.0 mg, 0.00648 mmol) in toluene (2 mL) was heated at 190 °C in a stainless autoclave for 17 h. After removal of the solvent, the residue was purified by flash column chromatography on silica gel. Elution with a 4:1 mixture of hexanes−EtOAc gave rise to cyclization product 32 (3.8 mg, 95%) as a colorless oil: IR (neat) 3447, 2937, 2874 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.16 (10H, m), 5.60 (0.45H, br s), 5.42 (0.55H, br s), 4.77−4.33 (6H, m), 4.08−3.32 (4H, m), 3.38 (3H, br s), 2.99−2.88 (1H, m), 2.43 (1H, m), 2.29−1.10 (15H, m), 0.98−0.77 (15H, m).

To a solution of alcohol **32** (3.8 mg, 0.00616 mmol) in DCM (3 mL) were added tetrapropylammonium perruthenate (1.3 mg, 0.0037 mmol) and NMO (20.5 mg, 0.175 mmol) at rt, and then the resulting mixture was stirred at rt for 90 min. The mixture was filtered through Celite, and the filtrate was concentrated to yield an oil which was purified by flash column chromatography on silica gel. Elution with a 5:1 mixture of hexanes−EtOAc provided keto ether **33** (2.7 mg, 71%) as a colorless oil: IR (neat) 2936, 2872, 1747 cm^{-1}; ^{1}H NMR (400 HMz, $CDCl_3$) δ 7.38−7.19 (10H, m), 5.53 (0.45H, br s), 5.48 (0.55H, br s), 4.86−4.23 (7H, m), 3.68−3.33 (5H, m), 3.04−2.91 (1H, m), 2.54−2.23 (1H, m), 2.14−1.15 (14H, m), 1.00−0.79 (15H, m).

To a solution of keto ether **33** (2.7 mg, 0.00439 mmol) in Et_2O (3 mL) and MeOH (0.1 mL) was added SmI_2 (0.1 M solution in THF, 0.5 mL, 0.05 mmol) at rt. After being stirred at rt for 5 min, the reaction mixture was evaporated to leave an oil, which was purified by flash column chromatography on silica gel. Elution with a 20:3 mixture of hexanes−EtOAc gave rise to ketone **34** (2.4 mg, 99%) as a colorless oil: IR (neat) 2930, 2856, 1732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.18 (10H, m), 5.48 (1H, br s), 4.68 (1H, d, J = 12.1 Hz), 4.48 (1H, d, J = 12.1 Hz), 4.44 (1H, d, J = 12.1 Hz), 4.36 (1H, d, J = 12.1 Hz), 3.69 (1H, d, J = 8.6 Hz), 3.50 (1H, d, J = 8.6 Hz), 2.95 (1H, dd, J = 11.6, 4.1 Hz), 2.29−2.08 (4H, m), 1.92−1.74 (3H, m), 1.62−1.43 (4H, m), 1.62 (3H, br s), 1.31−1.24 (1H, m), 1.26 (3H, s), 0.99−0.78 (2H, m), 0.98 (3H, s), 0.97 (3H, s), 0.90 (3H, s), 0.84 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 217.6, 139.4, 138.2, 133.9, 128.3, 128.2, 127.5, 127.4, 127.2, 127.0, 125.2, 86.2, 74.1, 73.6, 71.4, 56.8, 55.3, 52.7, 52.4, 39.0, 38.2, 38.0, 36.9, 34.7, 33.7, 28.0, 25.3, 22.9, 19.0, 18.3, 17.75, 17.71, 16.9, 16.0; LRMS m/z 554 (M^+); HRMS calcd for $C_{38}H_{50}O_3$ (M^+) 554.3760, found 554.3769.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ DEDICATION

†Dedicated to the memory of Professor Robert E. Ireland.

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