JOC The Journal of Organic Chemistry

Article

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Anionic Polycyclization Entry to Tricycles Related to Quassinoids and Terpenoids: A Stereocontrolled Total Synthesis of (+)-Cassaine

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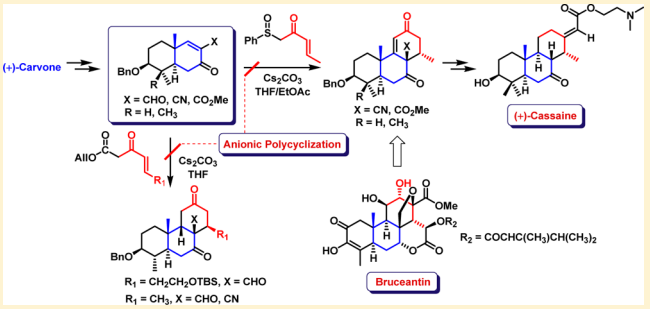
Supporting Information

ABSTRACT: A full account of our anionic polycyclization approach to access highly functionalized tricycles related to quassinoids and terpenoids from several optically active bicyclic enone systems and Nazarov reagents is presented. (+)-Carvone is the only chiral source used to fix the entire stereochemistry of all of the tricycles, and the stereochemical outcome of this process was unambiguously determined by X-ray crystallographic analysis. The utility of this strategy was demonstrated by the stereocontrolled construction of advanced tricycles related to the highly potent anticancer natural product bruceantin, a member of quassinoid family, and the total synthesis of the cardioactive terpenoid (+)-cassaine, a nonsteroidal inhibitor of Na^+-K^+-ATPase.



INTRODUCTION

Terpenoids constitute the largest group of natural products and are known to exhibit a wide range of biological activities against cancer, malaria, inflammation, and a variety of infectious diseases.[1] Quassinoids are highly oxygenated natural products formed by oxidative degradation of terpene derivatives, isolated as bitter principles of plants of the *Simaroubaceae* family,[2] which have been used for many years in the folk medicine of Asia and Africa. Currently, more than 150 quassinoids have been isolated and classified on the basis of their biological activities and structural features. Many molecules are known to display inhibitory effects in vitro and/or in vivo, including anti-inflammatory, antiviral, antimalarial, and antiproliferative effects on various tumor cell types.[3] The most well-known members of the quassinoid family are quassin (**1**) and bruceantin (**2**) (Figure 1). Bruceantin was first isolated from *Brucea antidysenterica,* a tree widely used in Ethiopia for the treatment of cancer and known to possess activities against B16 melanoma, colon 38, and L1210 and P388 leukemia in mice.[3,4] Phase I and II clinical trials of **2** were then initiated, but no objective tumor regressions were observed in humans, whereas relative toxicity was observed (nausea, vomiting, and hypotension at low doses and thrombocytopenia at higher doses).[1−3] A semisynthetic analogue of bruceantin, NBT-272 (**3**) (Figure 1), was shown to be up to 10-fold more potent than the parent molecule in inhibiting the cellular proliferation of variety cancer cell lines and also arrested tumor growth in a xenograft model of neuroblastoma cells with coinciding reduction of MYC expression and ERC activation in treated tumors.[5] Investigations into the preparation of more potent and less toxic analogues of **2** and other quassinoids via structural modification of the parent molecules seems the best possible choice to develop novel anticancer drugs of this class, and thus, there is a large unmet need to develop a practical synthetic route for these natural products. The highly oxygenated pentacyclic framework with many consecutive chiral centers of **2**, coupled with its remarkable biological profile and lowest natural abundance, makes it an attractive target in organic synthesis. Since its isolation in 1973,[6] several groups have reported synthetic approaches for the construction of highly

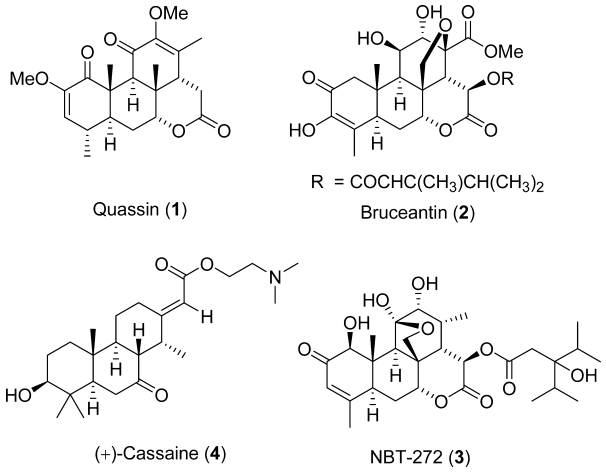
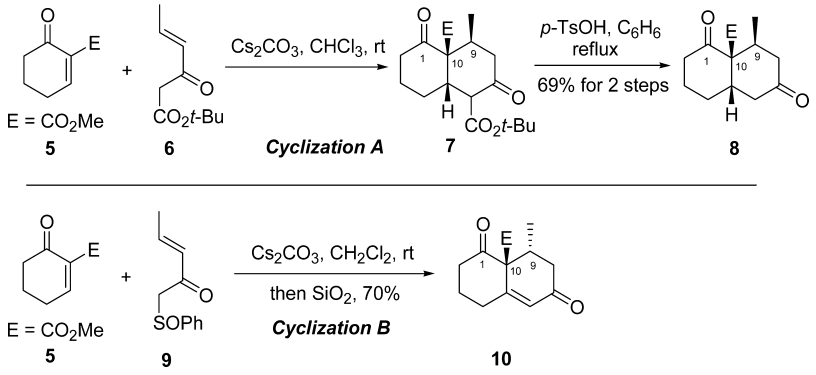


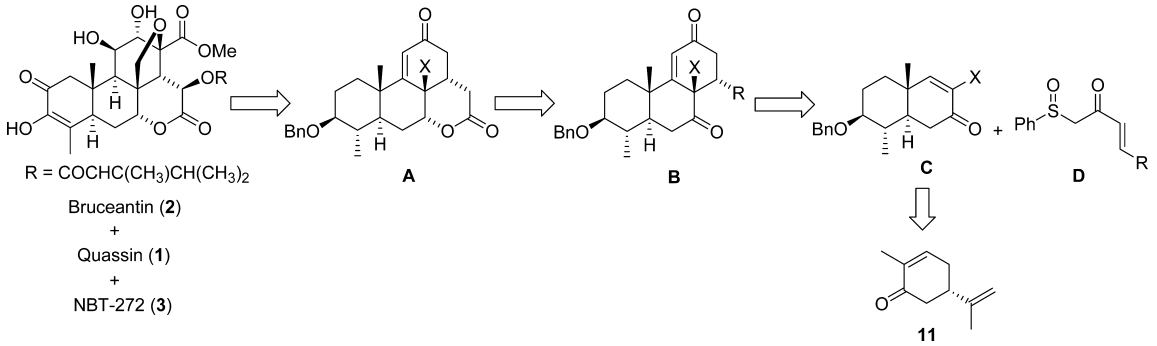
Figure 1. Chemical structures of quassin (**1**), bruceantin (**2**), NBT-272 (**3**), and (+)-cassaine (**4**).

Received: May 21, 2014
Published: July 24, 2014

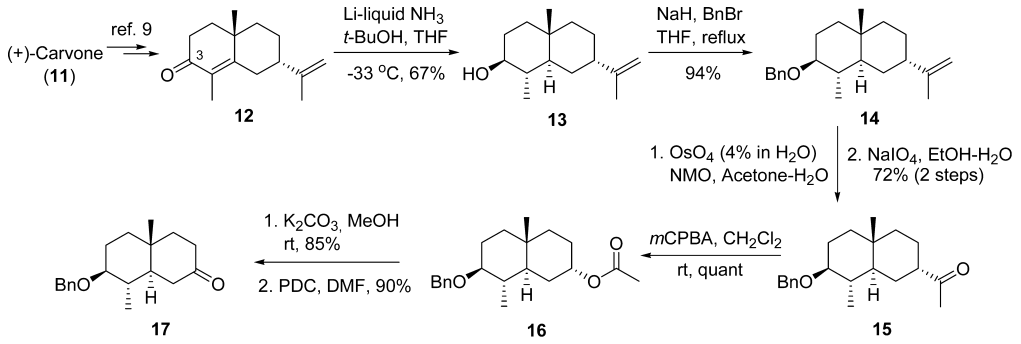
Scheme 1. Representative Examples of Anionic Polycyclization



Scheme 2. Retrosynthetic Analysis of Bruceantin (2), Quassin (1), and NBT-272 (3)



Scheme 3. Synthesis of Bicyclic Ketone 17



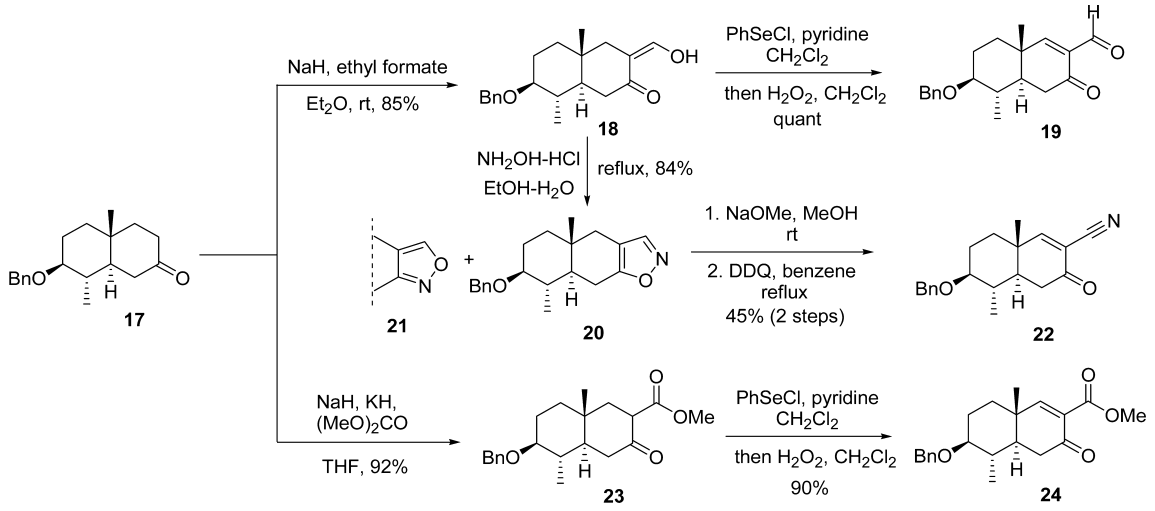
functionalized intermediates.[7] A relay synthesis of **2** was reported by Takahashi in 1990,[8] and this was followed by the first total synthesis in 1993 by Grieco and co-workers.[9]

More than two decades ago, we reported the stereocontrolled synthesis of *cis*-decalin **8** from the condensation of 2-carbomethoxy-2-cyclohexenone (**5**) with the enolate of enone ester **6** (Nazarov reagent) in nonpolar solvent via *β*-keto ester **7** (cyclization A, Scheme 1).[10] This anionic polycyclization process can be viewed as the result of two successive Michael additions or a Diels–Alder cycloaddition.[11,12] We used this reaction as the basic strategy for the construction of racemic 13-*α*-methyl-14-*α*-hydroxy[13] and 13-*β*-methyl-14-*β*-hydroxy[14,15] steroids related to batrachotoxin, ouabain, and other sterols. This powerful reaction also allowed us to report the first stereocontrolled total synthesis of ouabain, a highly potent cardioactive glycoside.[16] In addition, Petrovic and Bruckner[17] reported the synthesis of densely functionalized octalindiones from acceptor-substituted benzoquinone monoketals and various substituted Nazarov reagents using this anionic polycyclization.

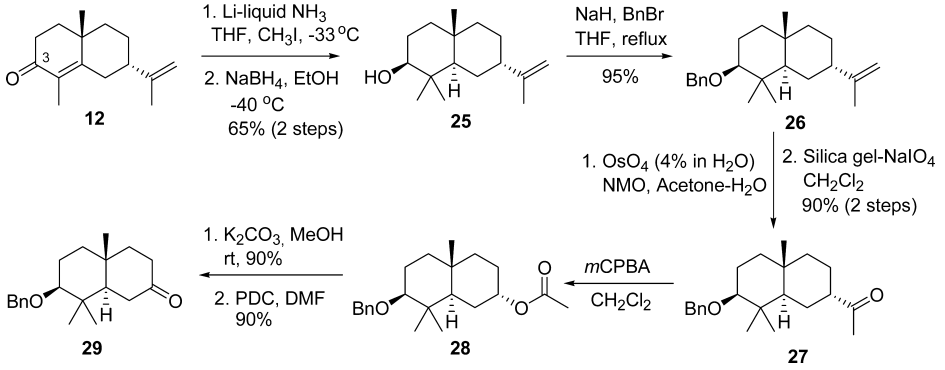
In addition to the above cycloaddition, we also discovered that the reaction of activated enone **5** with the enolate of enone sulfoxide **9** under similar conditions directly gives the unsaturated decalin **10** with the stereocenter at C9 opposite to that observed in **8** (cyclization B, Scheme 1).[18] This stereocontrolled process, which was never exploited, can in principle be used for the total synthesis of natural products. Recently,[19] we disclosed a versatile anionic polycyclization methodology using bicyclic activated enones and acyclic enone sulfoxide reagents to prepare various tricycles related to **2** (quassinoids) and terpenoids. We also reported the stereocontrolled total synthesis of (+)-cassaine (**4**) (Figure 1) utilizing this strategy.[20] Herein we give a full account of our most recent efforts toward the synthesis of various tricycles related to bruceantin and other quassinoids and its application in the stereocontrolled total synthesis of **4**.

dx.doi.org/10.1021/jo501122k | J. Org. Chem. 2014, 79, 7979–7999

Scheme 4. Synthesis of Activated Bicyclic Enones 19, 22, and 24



Scheme 5. Synthesis of Bicyclic Ketone 29



RESULTS AND DISCUSSION

In the retrosynthetic analysis described in Scheme 2, we envisioned the synthesis of bruceantin (**2**), quassin (**1**), and NBT-272 (**3**) from the suitable tetracycle **A** obtained from tricycle **B**, which can be formed via anionic polycyclization of suitably activated enone **C** (X = CHO, CN, CO_2Et) and appropriately substituted enone sulfoxide reagent **D**. (+)-Carvone (**11**) was considered the best choice of chiral starting material to prepare various diastereomerically pure tricycles via bicyclic activated enone **C**.

In order to identify the suitably activated enones **C** and reagent **D** to yield the desired tricycles **B** with requisite stereochemistry and substitution patterns related to **1**–**3**, we prepared various bicyclic enones and Nazarov reagents whose suitability for the anionic polycyclization reaction was tested. (+)-Carvone (**11**) was selected as the appropriate chiral starting material for the diastereoselective synthesis of various activated bicyclic enone intermediates possessing CN, CHO, and CO_2Et groups as activators at the α-position of the ketone functionality. Primarily, bicyclic ketone intermediate **17** was prepared from enone **12**, which can be readily obtained from **11** (via Birch reduction, Robinson annulation with ethyl vinyl ketone, and dehydration) using a well-precedented literature procedure.[19,21] Thus, enone **12** was reduced to the C3 equatorial alcohol **13** bearing a C4 equatorial methyl group,[22] which was then protected as its benzyl ether **14** using standard reaction conditions (NaH, BnBr) (Scheme 3). Having served its diastereomeric control purpose in the annulation reaction, the isopropenyl group was then subjected to dihydroxylation followed by $NaIO_4$ cleavage to provide methyl ketone **15**. Baeyer–Villiger oxidation of **15** using *m*CPBA in anhydrous CH_2Cl_2 provided acetate **16**. Saponification (K_2CO_3, MeOH) of acetate **16** followed by PDC oxidation gave the desired bicyclic ketone **17**, which was used as a key building block for the synthesis of various activated bicyclic enone partners for the anionic polycyclization reaction.

Formylation of ketone **17** using NaH and ethyl formate furnished the enol form of β-keto aldehyde **18**, and subsequent phenylselenation (PhSeCl, pyridine) and oxidative elimination (H_2O_2, CH_2Cl_2) of benzeneselenic acid afforded α-formyl enone **19** (Scheme 4).[23] Condensation of β-keto aldehyde **18** with $NH_2OH{\cdot}HCl$ gave a 9:1 mixture of isoxazoles[24] **20** and **21**, and the major isomer **20** was treated with NaOMe in MeOH to give the cyano ketone, which was subsequently treated with DDQ to give cyano enone **22**.[23,25] Bicyclic ketone **17** was converted to substituted α-carbomethoxy enone **24** via carbomethoxylation[26] using NaH and dimethyl carbonate followed by phenylselenation and oxidative elimination of phenylselenic acid.[23]

Using a synthetic sequence similar to that described in Scheme 4, we prepared the C4-dimethyl-substituted analogues **31**, **33**, and **35** starting from enone **12** via ketone **29**. These C4-dimethyl analogues (whose structures are shown in Scheme 6) are related to the A/B ring system of (+)-cassaine (**4**) and various terpenoid natural products. Accordingly, enone **12** was subjected to reductive methylation (Li, liquid NH_3, MeI)

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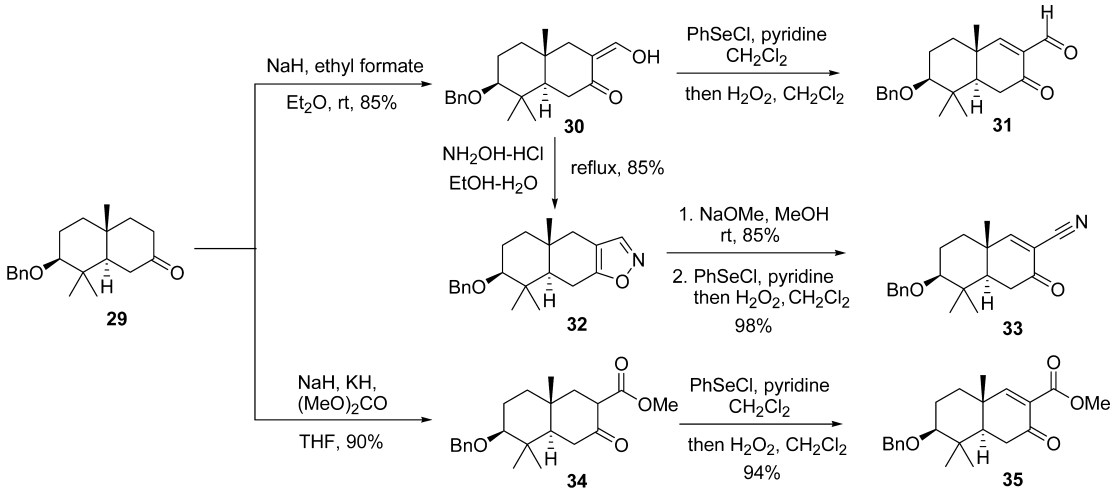
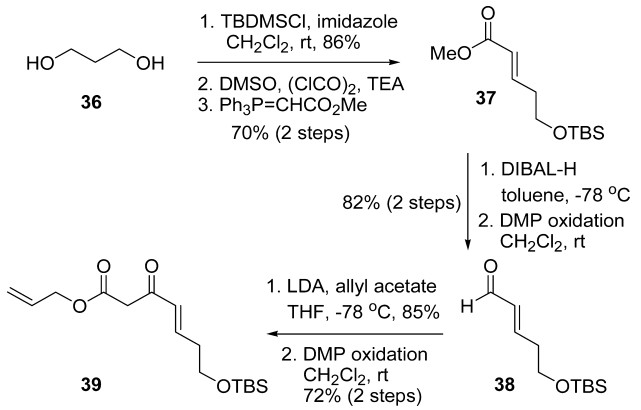
Scheme 6. Synthesis of Activated Bicyclic Enones 31, 33, and 35



followed by stereocontrolled reduction of the C3 ketone functionality using $NaBH_4$ to give the desired alcohol **25**,[27] which was then transformed into ketone **29** as illustrated in Scheme 5. Starting from bicyclic ketone **29**, we then prepared various activated bicyclic enone intermediates **31**, **33**, and **35** using the previously described series of reactions (Scheme 6).

Then we turned our attention to the preparation of suitable substituted Nazarov reagents for the construction of key intermediates for the synthesis of bruceantin and quassinoids. Monoprotection of 1,3-propanediol (**36**) followed by Swern oxidation and Wittig olefination furnished the α,β-unsaturated ester **37**. DIBAL-H reduction of **37** to give the allyl alcohol followed by Dess–Martin periodinane (DMP) oxidation gave the corresponding aldehyde **38**. Addition of allyl acetate anion (generated using LDA) to aldehyde **38** followed by DMP oxidation gave the desired Nazarov reagent **39** (Scheme 7).[19]

Scheme 7. Synthesis of Nazarov Reagent 39



Having several activated bicyclic enone intermediates (**19**, **22**, **24**, **31**, **33**, and **35**) and Nazarov reagent **39** in hand, we first studied the Cs_2CO_3-mediated anionic polycyclization of α-formyl enone **19** and Nazarov reagent **39** in anhydrous THF at room temperature, which gave tricycle **40** in 65% yield (Scheme 8). As we observed in our earlier reports, the stereochemistry at C9 (β-H) is directly influenced by the C10 angular methyl group, which forces the Nazarov reagent to approach from the α-face of enone **19** and directs the stereochemical outcome of tricycle **40**. The C9 hydrogen and C8 substituent (CHO) are *cis* to the C10 methyl group, and the stereochemistry at C14 results from the exclusive *exo* approach of the Nazarov reagent. Dealkoxycarbonylation of **40** using $Pd(PPh_3)_4$ and morpholine provided tricycle **41**. Similarly, cyclization of the analogous Nazarov reagent **42** with **19** furnished the corresponding tricycle **43**, and subsequent $Pd(PPh_3)_4$-catalyzed dealkoxycarbonylation of **43** provided the crystalline tricycle **44**. The expected stereochemistry of tricycle **44** was unambiguously confirmed by single-crystal X-ray diffraction analysis.[19] We then decided to examine the reactivity of cyano enone **22** in anionic polycyclization using Nazarov reagent **42**, which cleanly furnished the expected tricycle **45**. The stereochemistry of **45** was assigned on the basis of the analogy to the data for tricycle **43**. The dealkoxycarbonylation using $Pd(PPh_3)_4$ and morpholine furnished tricycle **46**.

We next turned our attention to an examination of the effect of the known compound 1-phenylsulfinyl-3-penten-2-one (**9**) in anionic polycyclization. Thus, the cyclization of enone sulfoxide **9** with formyl enone **19** using Cs_2CO_3 in EtOAc at room temperature directly furnished diastereomerically pure **47** in a low yield of 23% via the elimination of phenyl sulfoxide and formyl groups (Scheme 9). Similarly, C4-dimethyl formyl enone **31** reacted with **9** to give tricycle **49** in a low yield of 25%, which could be due to the instability of the aldehyde functionality under these reaction conditions.

We then examined the cyclization of cyano enone **22** with enone sulfoxide **9** to furnish tricycle **50**. Here the sulfoxide group was eliminated upon silica gel column chromatography to give the crystalline tricycle **50**, which has all of the stereochemical requirements for the synthesis of bruceantin. The stereochemistry of tricycle **50** was rigorously confirmed by single-crystal X-ray diffraction studies.[19] The stereochemistry of the C14 methyl group was confirmed as *axial*, which is *trans* to the C8 cyano group and very difficult to obtain by other methods. As we observed in our earlier studies,[18] the stereochemical outcome of **50** at C14 resulted from an exclusive *endo* approach of the enone sulfoxide reagent. Tricycle **50** was readily converted to enone tricycle **47** using SmI_2/HMPA-THF-mediated elimination of the nitrile group[28] with concomitant olefin migration, and this in turn confirmed the structure of enone tricycle **47**, which was obtained from the cyclization of **19** and **9**. Similarly, cyclization of cyano enone **33**

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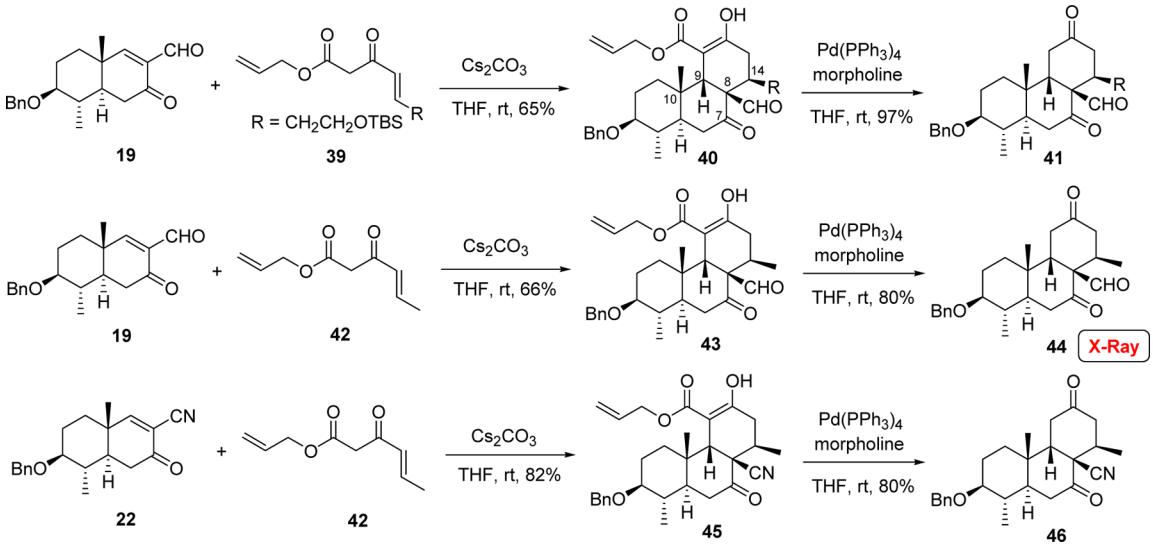
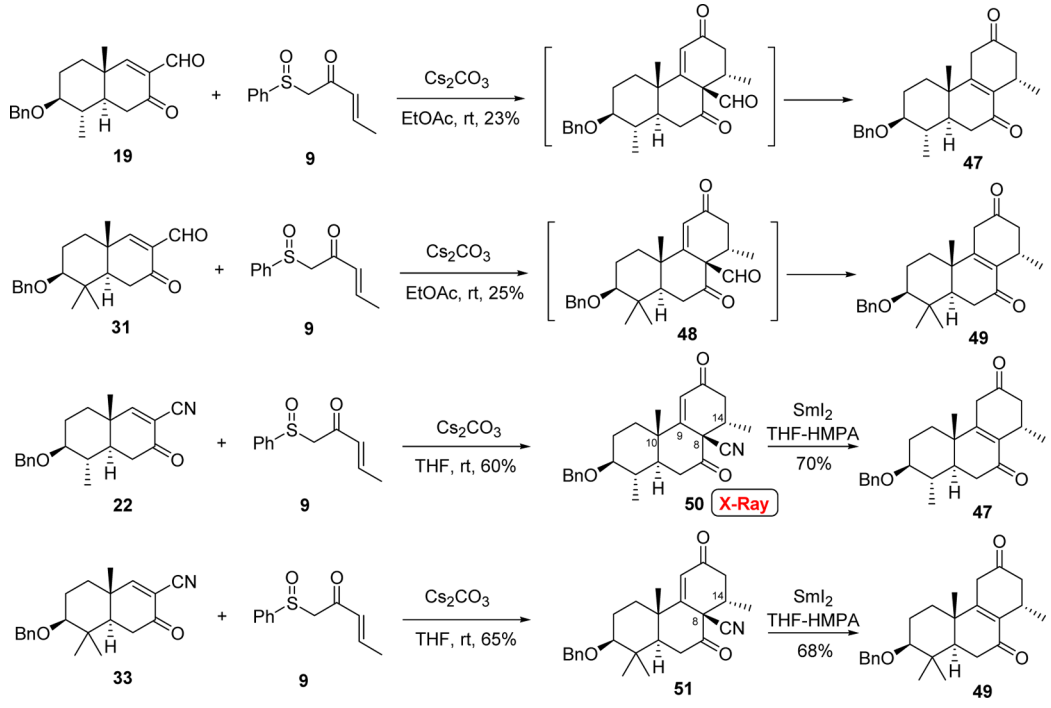
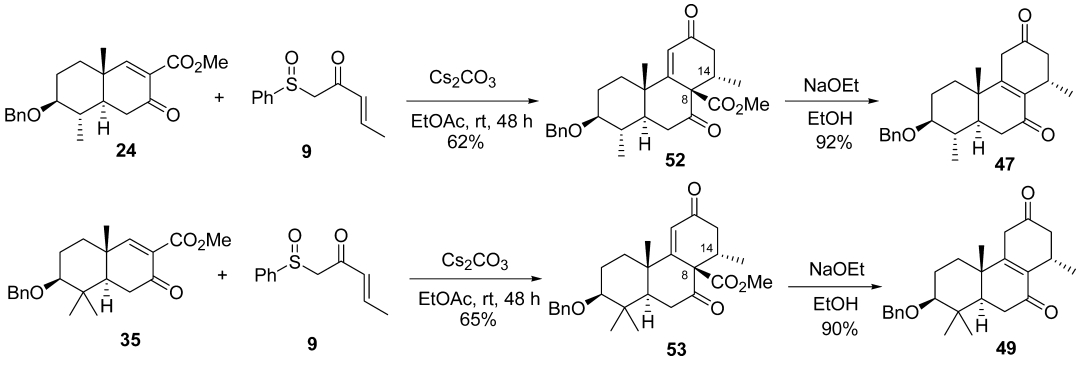
Scheme 8. Synthesis of Tricycles 41, 44, and 46



Scheme 9. Synthesis of Tricycles 50, 51, 47, and 49



Scheme 10. Synthesis of Tricycles 52, 53, 47, and 49



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with Nazarov reagent **9** furnished the expected tricycle **51**, which provided the corresponding enone tricycle **49** upon exposure to SmI_2 in HMPA-THF (Scheme 9).

Next, we carried out the anionic polycyclization of α-carbomethoxy enone **24** and enone sulfoxide reagent **9** to furnish tricycle **52** possessing the same stereochemistry at C8 and C14 as observed in tricycle **50**, in which the C8 β-ester group can be used for the construction of natural products related to bruceantin and other quassinoids. Then we performed the cyclization reaction of the analogous α-carbomethoxy enone **35** and Nazarov reagent **9** to furnish the corresponding tricycle **53** without altering the stereochemistry as observed in the earlier analogous tricycle **52**. Tricycles **52** and **53** were converted to tricycles **47** and **49** using NaOEt in EtOH to facilitate the decarbomethoxylation with concomitant olefin migration (Scheme 10). Tricycle **49** is closely related to the skeleton of (+)-cassaine (**4**).

The results described in Schemes 8−10 confirm our previous discovery[18] that the enolate of the enone sulfoxide reacts with activated cyclohexenones (E = CHO, COOMe, CN) in a stereocontrolled manner but produces the opposite stereochemistry for the alkyl substituents in comparison with the enolate of the enone ester (i.e., the Nazarov reagent). This a priori surprising behavior may be due to a difference in mechanism. In the case of the enone sulfoxide, the corresponding enolate ion would react as a diene in a Diels−Alder reaction taking place through an *endo* transition state (*endo* to the ring carbonyl group) of the activated cyclohexanone (cf. **E** → **F** → **G** in Figure 2). On the other hand, the

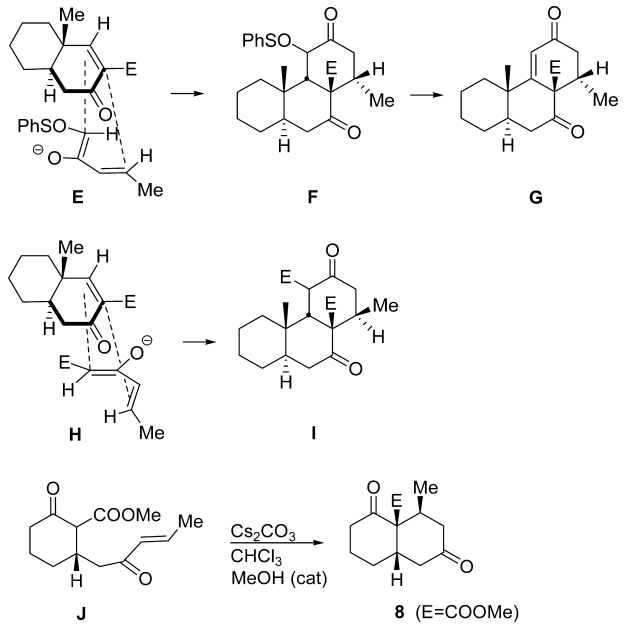


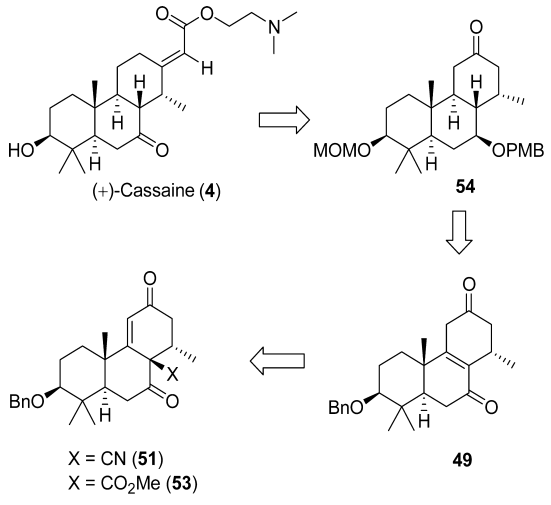
Figure 2. Plausible mechanism for the synthesis of *cis,cis*-decalin systems.

enolate of the enone ester would undergo a reversible double Michael addition through an *exo* approach, leading to the more stable equatorial isomer (**H** → **I**). This is supported by the fact that the intramolecular Michael addition of **J** with Cs_2CO_3 in nonpolar solvent containing a catalytic amount of MeOH gives *cis,cis*-decalin **8** (Figure 2).[29]

After the successful synthesis of nine new tricycles (**41**, **44**, **45**, **47**, **49**, **50**, **51**, **52**, and **53**) related to quassinoids and terpenoids (Schemes 8, 9 and 10) utilizing the anionic polycyclization method, we were interested in proving the efficiency of this strategy in the total synthesis of biologically active natural products. As the retrosynthetic analysis in Scheme 2 illustrates, tricycles **50** and **52** can serve as prominent precursors for the synthesis of bruceantin and various quassinoids, as these key tricycles possess adequate functionalities for completing the quassinoid framework and introducing a variety of oxygenated groups at various positions, such as those characteristic of quassinoids (Schemes 9 and 10). On the other hand, tricycles **51** and **53** can be used as starting materials for the synthesis of (+)-cassaine (**4**), a cardioactive terpenoid natural product (Scheme 11).

In 1935, the Dalma group isolated **4**, an *Erythrophleum* alkaloid, from the bark of *Erythrophleum guineense*.[30] It is a nonsteroidal inhibitor of Na^+-K^+-ATPase and is known to possess remarkable pharmacological action similar to that of digitalis glycosides such as digitoxin, even though the chemical structure are quite different.[31] **4** is an *N,N*-dimethylaminoethoxycarbonyl-tethered diterpenoid whose structural elucidation[32] and first relay total synthesis[33] were reported by Turner and co-workers. In light of the interesting structural features and biological activity of **4**, we previously reported its stereoselective total synthesis by means of a transannular Diels−Alder reaction.[34] Herein we report our first application of anionic polycyclization involving acyclic β-keto sulfoxide **9** in the stereocontrolled total synthesis of natural product **4** starting from tricycles **51** and **53** via enone tricycle **49** and *trans*−*antitrans* (TAT) tricycle **54** (Scheme 11).

Scheme 11. Retrosynthetic Analysis of (+)-Cassaine (4)



As described in Schemes 9 and 10, tricycles **51** and **53** were converted into enone tricycle **49** using SmI_2/HMPA-THF-mediated cleavage and NaOEt/EtOH-induced decarbomethoxylation, respectively. Selective reduction of diketone **49** using $NaBH_4$ at −78 °C gave alcohol **55**, which was protected as its TBS ether **56** using TBSCl and imidazole in anhydrous CH_2Cl_2 (Scheme 12). Palladium-catalyzed hydrogenolysis of benzyl ether **56** (Pd/C, 15 psi H_2, 24 h) gave the corresponding alcohol **57** in 90% yield without affecting the enone functionality. Then we aimed to convert tricycle **57** into alcohol **60** possessing TAT stereochemistry. Unprecedentedly, Pd/C-catalyzed hydrogenation of enone **57** (20 psi H_2, 48 h; route A in Scheme 12) furnished the desired ketone **58** having

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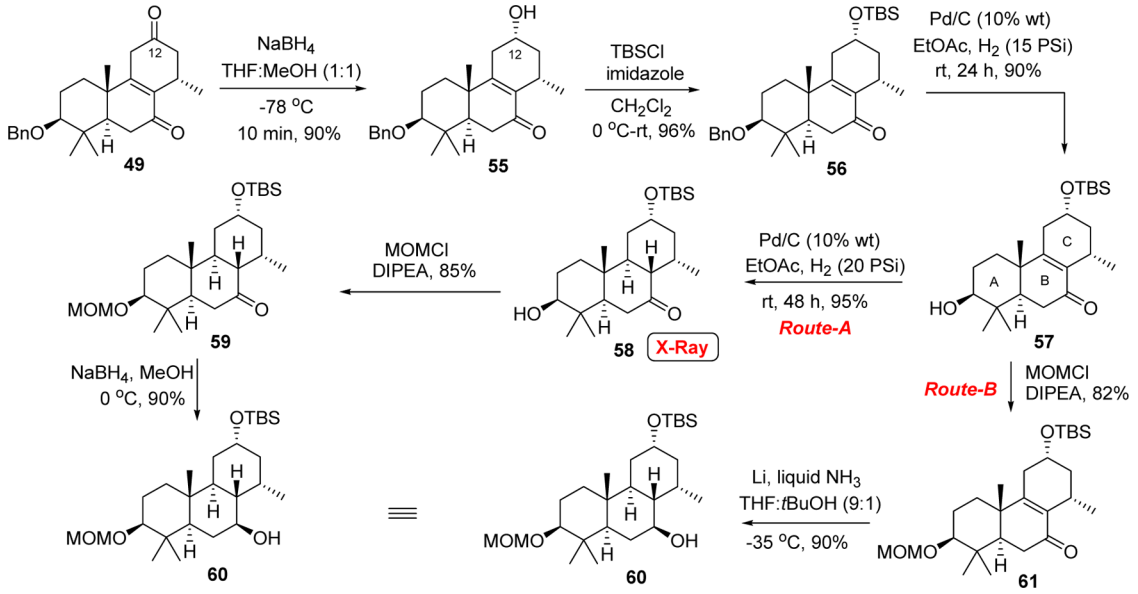
Scheme 12. Synthesis of TAT Tricycle 60



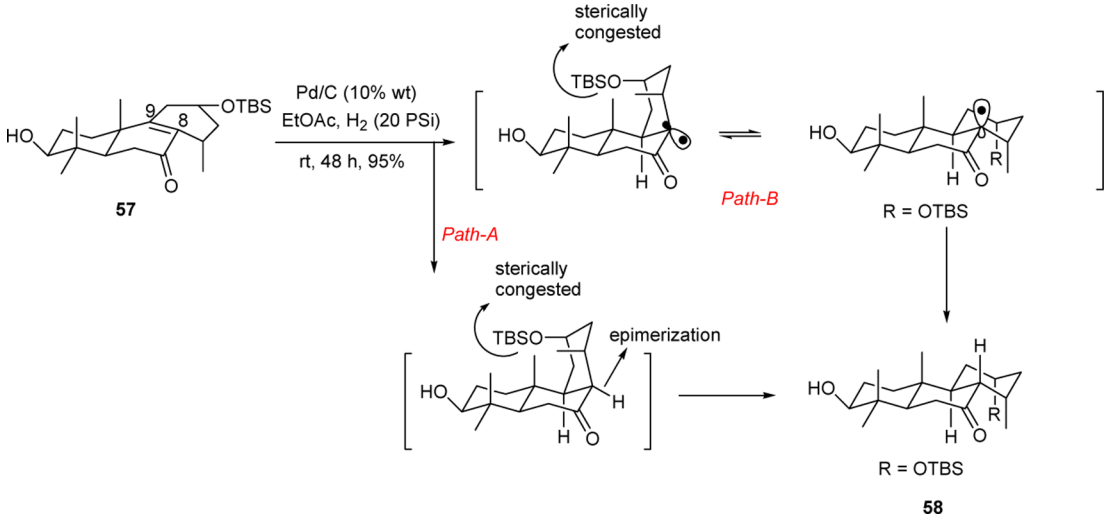


Figure 3. Plausible mechanisms for the conversion of enone **57** into **58**.

the *trans* B/C ring junction. The stereochemistry of tricycle **58** was confirmed by single-crystal X-ray diffraction analysis.[20] MOM protection of alcohol **58** followed by highly stereoselective reduction of the ketone using $NaBH_4$ gave the alcohol **60** in 90% yield. Alcohol **60** could also be prepared from enone **57** by an alternative route: conversion of **57** into its MOM ether **61** followed by stereoselective Birch reduction[35] (Li, liquid NH_3, *t*BuOH-THF) furnished the desired alcohol **60** in 90% yield (route B in Scheme 12).

The unexpected catalytic hydrogenation of enone **57** to yield tricycle **58** possessing the *trans* B/C ring junction might be due to initial reduction to give the *cis* B/C ring junction followed by Pd/C-promoted epimerization at C8 (Figure 3, path A) or stepwise reduction of the enone double bond with the α addition of a hydrogen at C9 followed by the sterically less congested β-addition of a hydrogen at C8 (path B).

Having secured TAT tricycle **60**, our attention was directed toward the installation of the exocyclic (*E*)-vinyl triflate at C13 in **67** via ketone **54** (Scheme 13). Hence, PMB protection of alcohol **60** furnished PMB ether **62**. TBS deprotection of **62** using TBAF in anhydrous THF gave the corresponding alcohol, which was oxidized with PDC to provide the desired ketone **54**. Selective carbomethoxylation[26] of ketone **54** at C13 followed by selective reduction using $NaBH_4$ furnished β-hydroxy ester **63**, which was subsequently converted to the α,β-unsaturated ester **64** using $SOCl_2$/pyridine-mediated dehydration.[36] Attempts to reduce α,β-unsaturated ester **64** to give **65** using Stryker's reagent ($[(PPh_3)CuH]_6$), $NaBH_4/Cu_2Cl_2$, and $NaBH_4/CuCl_2$ proved to be unfruitful. Using excess $NaBH_4$ in combination with $NiCl_2{\cdot}6H_2O$ with a longer reaction time (3 days at rt) showed only 20% conversion. Pleasingly, reduction of **64** by magnesium in MeOH was found to be suitable for this conversion, giving the desired ester **65** in 96% yield as a mixture of diastereomers.[37] DIBAL-H reduction of ester **65** furnished the corresponding alcohols, which were converted to aldehydes **66** using Dess–Martin periodinane. Attempts to synthesize (*E*)-vinyl triflate **67** from aldehyde **66** under various conditions, including Tf_2O/2,6-di-*tert*-butylpyridine, Tf_2O/Et_3N, and Tf_2O/DIPEA at 0 °C and room temperature, were unsuccessful, revealing the high sensitivity of the substrate to

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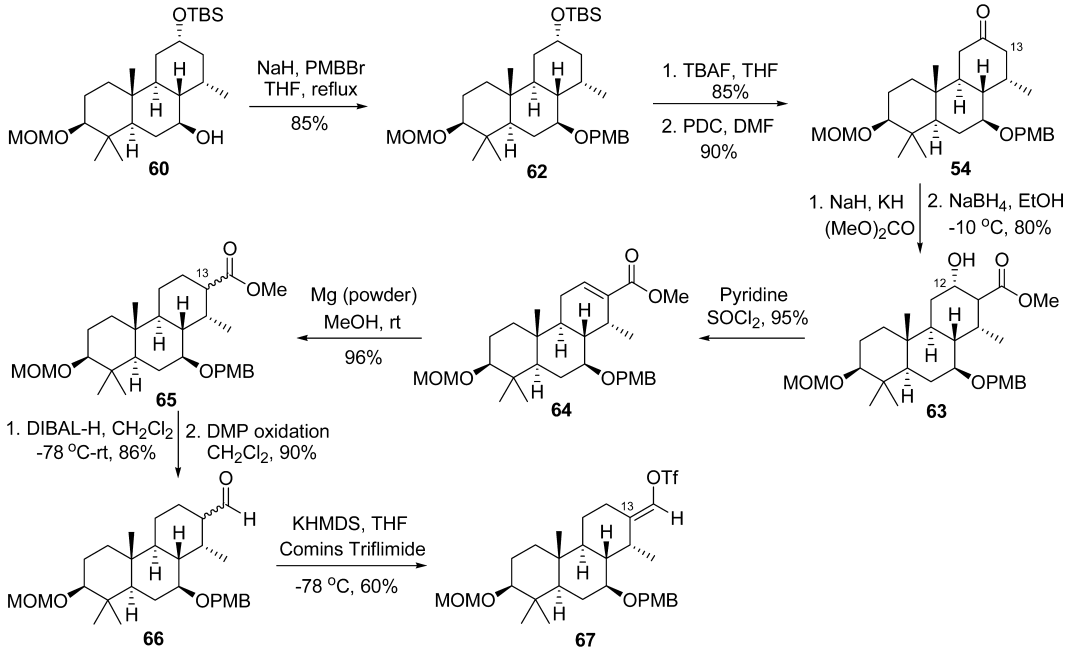
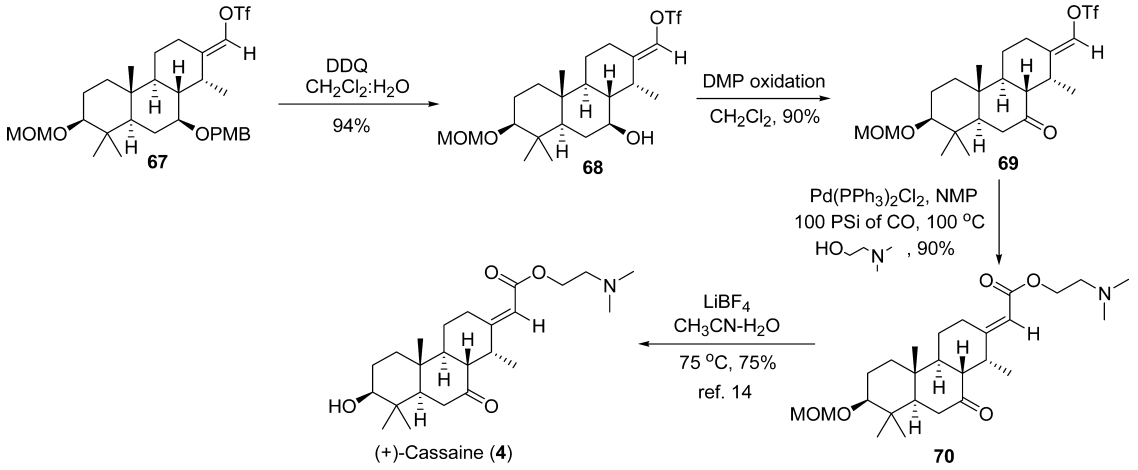
Scheme 13. Synthesis of (*E*)-Vinyl Triflate 67



Scheme 14. Synthesis of (+)-Cassaine (4)



those conditions, and we were unable to recover the starting aldehyde after the reaction. Gratifyingly, the Comins protocol[38] using *N*-(5-chloro-2-pyridyl)triflimide and KHMDS at −78 °C furnished the desired (*E*)-vinyl triflate **67** in 60% yield.

Now the stage was set for the completion of the synthesis of (+)-cassaine (**4**) (Scheme 14). Deprotection of the PMB ether of **67** followed by DMP oxidation furnished ketone **69**. Heck-type coupling of *N*,*N*-dimethylethanolamine, carbon monoxide, and (*E*)-vinyl triflate **69** using the Pd(II) catalyst bis-(triphenylphosphine)dichloropalladium, K_2CO_3, and 1-methyl-2-pyrrolidinone (NMP) afforded the known MOM-cassaine **70**, which upon MOM deprotection with $LiBF_4$ in acetonitrile and water furnished the natural product **4**. The analytical data for MOM-cassaine **70** and (+)-cassaine (**4**) were in good agreement with the data reported in the literature.[20,33,39]

■ CONCLUSION

We have demonstrated the reactivity of six new activated bicyclic enones (**19**, **22**, **24**, **31**, **33**, and **35**) with reagents **39**, **42**, and **9** in Cs_2CO_3-mediated anionic polycyclization reactions and prepared nine new tricycles (**41**, **44**, **46**, **47**, **49**, **50**, **51**, **52**, and **53**) related to quassinoids and terpenoids. We have also proven the efficacy of this strategy by the stereocontrolled total synthesis of (+)-cassaine (**4**) starting from tricycles **51** and **53** via **49**. The crucial groundwork has been established to attempt the asymmetric total synthesis of bruceantin (**2**) by the stereoselective construction of suitably functionalized tricycles **50** and **52**, and developments in this regard will be reported in due course.

■ EXPERIMENTAL SECTION

General Procedures. All reactions were performed under an argon atmosphere with oven (80 °C)- or flame-dried glassware. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium/benzophenone under an argon atmosphere immediately prior to use. Dichloromethane, toluene, *N*,*N*-dimethylformamide, and acetonitrile were freshly distilled over calcium hydride under an argon atmosphere. For the NMR spectral assignments, the following abbreviations were used: s, singlet; d, doublet; t, triplet; q, quartet; m,

dx.doi.org/10.1021/jo501122k | J. Org. Chem. 2014, 79, 7979−7999

multiplet, ABq, AB quartet; br, broad. Chemical shifts are reported in parts per million relative to the solvent used ($CHCl_3$: 7.26 ppm for ^1H NMR and 77.0 ppm for ^{13}C NMR) as an internal standard. Optical rotations were measured at the sodium D line (589 nm) using a cell with a path length of 1.00 dm. Infrared spectra were recorded as neat liquid films, and only the most significant absorption bands (in cm^{-1}) are reported. HRMS data were obtained on a TOF mass spectrometer with electrospray ionization (ESI). The IUPAC nomenclature is used in the Experimental Section, and the names of all compounds were generated using ChemDraw Ultra 12.0 software. Experimental procedures for all of the new compounds and the known compounds without published experimental procedures are described below. Compounds that are not presented in the main text are numbered starting from **S1**.

(1*S*,2*S*,4a*S*,7*S*,8a*S*)-1,4a-Dimethyl-7-(prop-1-en-2-yl)-decahydronaphthalen-2-ol (13). Lithium (33 mg, 4.81 mmol) was washed with hexanes and placed in a flask topped with a dry ice condenser. The entire system was flushed with argon. The flask was cooled to −78 °C, and the condenser was filled with a dry ice/acetone mixture. Ammonia was condensed until no further lithium was seen and bronze globules (golden liquid) started to appear. The cooling bath was removed, and the mixture was allowed to equilibrate to the refluxing temperature (−33 °C). THF (5 mL) was added to disperse the newly formed reagent, followed by slow addition of a solution of crude (4a*S*,7*S*)-1,4a-dimethyl-7-(prop-1-en-2-yl)-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one (**12**) (504 mg, 2.29 mmol) and *t*-BuOH (169 mg, 2.29 mmol) in THF (5 mL). The reaction mixture was then stirred at −33 °C for 2 h. Ethanol followed by a saturated aqueous NH_4Cl solution was added to quench the excess unreacted lithium, and ammonia was allowed to evaporate under a stream of air. The mixture was extracted with CH_2Cl_2, and the organic layer was washed with water, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (30% EtOAc/hexanes) to furnish 339 mg (67% yield over two steps) of the title compound **13** as a white solid. IR (neat/NaCl) ν (cm^{-1}) 3341, 2969, 2926, 1640, 1457, 1018, 884; mp 60−62 °C; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 4.89 (s, 1H), 4.80 (s, 1H), 3.10 (td, J = 4.8, 10.2 Hz, 1H), 2.34 (br s, 1H), 1.96−1.89 (m, 1H), 1.85−0.9 (m, 12H), 1.72 (s, 3H), 0.97 (d, J = 6.4 Hz, 3H), 0.89 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 147.1, 110.7, 76.9, 43.2, 39.9, 39.2, 38.9, 37.1, 33.8, 30.9, 26.0, 23.1, 22.8, 16.7, 14.8; LRMS m/z (relative intensity) 222 (M^+, 35), 179 (34), 161 (59), 122 (88), 107 (79), 81 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_{15}H_{26}O$ 222.1984, found 222.1979.

(1*S*,2*S*,4a*S*,7*S*,8a*S*)-2-(Benzyloxy)-1,4a-dimethyl-7-(prop-1-en-2-yl)decahydronaphthalene (14). Compound **13** (12.5 g, 56.4 mmol) predissolved in anhydrous THF (10 mL) was added to a suspension of NaH (6.77 g, 169.2 mmol) in THF (200 mL) at 0 °C. Benzyl bromide (16.5 mL, 141.0 mmol) was then added, followed by TBAI (10.4 g, 128.2 mmol), and the reaction mixture was allowed to stir at room temperature overnight and for 5 h at reflux. The mixture was cooled to 0 °C and quenched by careful addition of cold water. The resulting mixture was extracted with EtOAc, and the organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography (2% EtOAc/hexanes) to furnish 17.5 g (94% yield) of the title compound **14**. IR (neat/NaCl) ν (cm^{-1}) 2939, 1447, 1088; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 7.35−7.25 (m, 5H), 4.88 (br s, 1H), 4.80 (br s, 1H), 4.63 (d, J = 11.4 Hz, 1H), 4.41 (d, J = 11.4 Hz, 1H), 2.88 (td, J = 4.9, 10.2 Hz, 1H), 2.34 (br s, 1H), 1.95−1.90 (m, 2H), 1.79−1.73 (m, 2H), 1.72 (s, 3H), 1.42−1.12 (m, 8H), 0.98 (d, J = 6.3 Hz, 3H), 0.89 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 147.6, 128.3, 127.8, 127.4, 110.6, 84.0, 70.8, 43.6, 39.8, 38.9, 37.4, 37.0, 26.5, 26.1, 23.1, 22.9, 16.6, 15.1; LRMS m/z (relative intensity) 312 (M^+, 10), 221 (63), 204 (49), 109 (77), 91 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_{22}H_{32}O$ 312.2453, found 312.2462 ± 0.0009.

1-((2*S*,4a*S*,7*S*,8*S*,8a*S*)-7-(Benzyloxy)-4a,8-dimethyldecahydronaphthalen-2-yl)ethanone (15). NMO (16.5 g, 141.0 mmol) and OsO_4 (3.58 mL, 0.56 mmol, 4% in water) were added to a solution of **14** (18.6 g, 56.4 mmol) in a 4:1 mixture of acetone and water (150 mL). The reaction mixture was stirred at room temperature overnight. A 10% sodium bisulfite aqueous solution was introduced, and the mixture was stirred for 15 min. The reaction mixture was extracted with ethyl acetate, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The crude diol (20.5 g, quant.) was directly used for the next step.

The crude diol was dissolved in ethanol (350 mL) and water (150 mL), and sodium periodate (24.1 g, 112.8 mmol) was slowly added to the vigorously stirred solution. The reaction mixture was stirred for 1 h at room temperature. After filtration, the solution was extracted with ethyl acetate, and the organic phase was washed with water and brine. The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (5% EtOAc/hexanes) to afford 13.5 g (72% yield over two steps) of the title compound **15**. IR (neat/NaCl) ν (cm^{-1}) 2933, 1702, 1066; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 7.38−7.25 (m, 5H), 4.62 (d, J = 11.4 Hz, 1H), 4.40 (d, J = 11.4 Hz, 1H), 2.87 (td, J = 4.9, 10.2 Hz, 1H), 2.61 (br s, 1H), 2.21−2.08 (m, 1H), 2.13 (s, 3H), 2.00−1.94 (m, 2H), 1.75−1.03 (m, 8H), 1.00 (d, J = 6.3 Hz, 3H), 0.87 (s, 3H), 0.83−0.74 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 128.4, 128.3, 127.8, 127.6, 127.4, 83.7, 72.1, 71.0, 47.4, 45.2, 39.4, 37.8, 37.4, 27.8, 26.5, 25.0, 21.4, 16.2, 15.0; LRMS m/z (relative intensity) 314 (M^+, 2), 223 (79), 206 (39), 167 (85), 107 (66), 91 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_{21}H_{30}O_2$ 314.2246, found 314.2258 ± 0.0009.

(2*S*,4a*S*,7*S*,8*S*,8a*S*)-7-(Benzyloxy)-4a,8-dimethyldecahydronaphthalen-2-ol (S1). To a solution of **15** (2.47 g, 7.89 mmol) in anhydrous CH_2Cl_2 (10 mL) was added *m*-CPBA (4.08 g, 23.6 mmol), and the resulting reaction mixture was stirred at room temperature for 32 h. The reaction was monitored by ^1H NMR spectroscopy, following the decrease of the 2.6 ppm signal and the increase of the 5.1 ppm signal. The reaction mixture was washed with a saturated aqueous $NaHCO_3$ solution, water, and brine. The combined organic layers were dried over anhydrous $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude (2*S*,4a*S*,7*S*,8*S*,8a*S*)-7-(benzyloxy)-4a,8-dimethyldecahydronaphthalen-2-yl acetate (**16**) (2.61 g, quant.) was directly used for the next step.

Compound **16** (2.61 g, 7.89 mmol) was dissolved in methanol (20 mL), and potassium carbonate (3.28 g, 23.69 mmol) was added at room temperature. The reaction mixture was stirred at room temperature overnight. The mixture was extracted with EtOAc, and the organic layer was washed with a 1 N HCl solution, water, and brine, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20% EtOAc/hexanes) to give 2.07 g (92% yield) of the title compound **S1**. IR (neat/NaCl) ν (cm^{-1}) 3429, 2922, 1639; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 7.37−7.25 (m, 5H), 4.64 (d, J = 11.4 Hz, 1H), 4.42 (d, J = 11.4 Hz, 1H), 4.13−4.11 (m, 1H), 2.93 (td, J = 4.9, 10.2 Hz, 1H), 2.04−1.14 (m, 13H), 0.95 (d, J = 6.3 Hz, 3H), 0.86 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 128.3, 127.8, 127.4, 84.0, 71.0, 66.5, 41.9, 39.5, 37.3, 35.1, 33.5, 31.8, 28.4, 26.6, 15.7, 15.1; LRMS m/z (relative intensity) 197 ($[M - Bn]^+$, 26), 123 (66), 91 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_{19}H_{28}O_2$ 288.2089, found 288.2082.

(4a*R*,7*S*,8*S*,8a*S*)-7-(Benzyloxy)-4a,8-dimethyloctahydronaphthalen-2(1*H*)-one (17). PDC (5.22 g, 13.8 mmol) was added in one portion at room temperature to a DMF (15 mL) solution of **S1** (2.06 g, 6.94 mmol). The reaction mixture was stirred at room temperature for 2 h and then poured into a 1:1 mixture of diethyl ether and water. The mixture was extracted with Et_2O, and the combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (15% EtOAc/hexanes) to furnish 1.78 g (90% yield) of the title compound **17** as a low-melting solid. IR (neat/NaCl) ν (cm^{-1}) 2927, 1705, 1092; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 7.35−7.25 (m, 5H), 4.65 (d, J = 11.4 Hz, 1H), 4.43 (d, J = 11.4 Hz, 1H), 2.94 (td, J = 4.9, 10.2 Hz, 1H), 2.45−1.19 (m, 12H), 1.09 (s, 3H), 0.95 (d, J = 6.4 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 138.7, 128.4, 127.8, 127.6, 83.0, 77.2, 71.2, 48.8, 41.4, 40.2, 38.4,

dx.doi.org/10.1021/jo501122k | J. Org. Chem. 2014, 79, 7979−7999

38.2, 37.6, 32.9, 26.4, 16.0, 14.9; LRMS m/z (relative intensity) 286 (M^+, 2), 195 (61), 91 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_{19}H_{26}O_2$ 286.1933, found 286.1927.

(4a*R*,7*S*,8*S*,8a*S*,*Z*)-7-(Benzyloxy)-3-(hydroxymethylene)-4a,8-dimethyloctahydronaphthalen-2(1*H*)-one (18). A solution of **17** (250 mg, 1.04 mmol) and ethyl formate (3.36 mL, 41.6 mmol) in diethyl ether (3 mL) was slowly added to a suspension of NaH (124 mg, 3.12 mmol) in anhydrous diethyl ether (5 mL). The reaction mixture was stirred at room temperature for 5 h, and a saturated aqueous NH_4Cl solution was then added cautiously. The mixture was extracted with EtOAc, and the combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography (15% EtOAc/hexanes) to afford 275 mg (85% yield) of the title compound **18** as a slightly orange low-melting solid. IR (neat/NaCl) ν (cm^{-1}) 3423, 2927, 2842, 1636, 1583, 1097; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 14.37 (d, J = 3.2 Hz, 1H), 8.58 (d, J = 3.2 Hz, 1H), 7.35−7.25 (m, 5H), 4.66 (d, J = 11.4 Hz, 1H), 4.43 (d, J = 11.4 Hz, 1H), 2.93 (td, J = 4.9, 10.2 Hz, 1H), 2.51 (dd, J = 5.5, 19.2 Hz, 1H), 2.13−1.15 (m, 9H), 1.01 (d, J = 6.3 Hz, 3H), 0.86 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 187.4, 184.2, 128.4, 127.8, 127.5, 107.4, 82.8, 77.2, 71.0, 43.9, 39.3, 38.5, 38.2, 33.3, 32.6, 26.4, 16.6, 15.1; no characteristic peaks were observed in the MS analysis with different samples and different ionization methods.

(4a*S*,5*S*,6*S*,8a*S*)-6-(Benzyloxy)-5,8a-dimethyl-3-oxo-3,4,4a,5,6,7,8,8a-octahydronaphthalene-2-carbaldehyde (19). To a solution of **18** (50 mg, 0.16 mmol) in anhydrous dichloromethane (1.5 mL) was added pyridine (15 μL, 0.19 mmol) followed by a solution of phenylselenium chloride (PhSeCl) (33.5 mg, 0.17 mmol) in dichloromethane (1.5 mL) at room temperature. The resulting mixture was stirred for 2 h at room temperature. After completion of the reaction, the mixture was washed with 1 N HCl and water, and 35% hydrogen peroxide (1 mL) was then added to the organic layer, which was vigorously stirred for 15 min until complete disappearance of the yellow color. The mixture was washed with water, and the organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Careful evaporation of the organic solvent was done in order to avoid decomposition of the title compound **19**. Crude **19** was used as such for the next step without further purification by column chromatography.

(4a*R*,7*S*,8*S*,8a*S*)-7-(Benzyloxy)-4a,8-dimethyl-4,4a,5,6,7,8,8a,9-octahydronaphtho[2,3-*d*]isoxazole (20) and Its Isomer (4a*R*,7*S*,8*S*,8a*S*)-7-(Benzyloxy)-4a,8-dimethyl-4,4a,5,6,7,8,8a,9-octahydronaphtho[2,3-*c*]isoxazole (21). Compound **18** (30 mg, 0.095 mmol) was dissolved in ethanol (3 mL). Hydroxylamine hydrochloride (69 mg, 0.95 mmol) was dissolved in a minimum amount of water, and this solution was added to the above reaction mixture at room temperature. The mixture was refluxed for 1.5 h. Ethanol was removed under reduced pressure, and the residue was dissolved in EtOAc. The organic layer was washed with a saturated aqueous $NaHCO_3$ solution, water, and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (15% EtOAc/hexanes) to afford 24.5 mg (84% yield) of a 9:1 mixture of the title compounds **20** and **21**, respectively. Major isomer **20**: IR (neat/NaCl) ν (cm^{-1}) 2931, 2847, 1452, 1090, 732; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 8.02 (s, 1H), 7.36−7.28 (m, 5H), 4.68 (d, J = 11.4 Hz, 1H), 4.45 (d, J = 11.4 Hz, 1H), 3.01−2.92 (m, 2H), 2.23−2.05 (m, 4H), 1.74−1.52 (m, 3H), 1.39−1.31 (m, 2H), 1.09 (d, J = 6.3 Hz, 3H), 0.83 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 166.7, 159.7, 153.3, 149.6, 138.7, 128.3, 127.8, 127.5, 113.9, 110.8, 82.9, 71.0, 45.8, 45.4, 39.3, 38.9, 38.6, 38.4, 35.8, 34.7, 33.7, 26.4, 24.3, 22.7, 17.0, 15.3; LRMS m/z (relative intensity) 311 (M^+, 2), 268 (11), 220 (36), 91 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_{20}H_{25}NO_2$ 311.1885, found 311.1888 ± 0.0009. Minor isomer **21**: ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 8.08 (s, 1H), 7.38−7.25 (m, 5H), 4.68 (d, J = 11.4 Hz, 1H), 4.46 (d, J = 11.4 Hz, 1H), 3.09 (dd, J = 5.4, 17.3 Hz, 1H), 2.98 (td, J = 4.5, 10.3 Hz, 1H), 2.45 (d, J = 15.6 Hz, 1H), 2.25−2.05 (m, 3H), 1.73−1.49 (m, 4H), 1.36−1.25 (m, 3H), 1.10 (d, J = 6.3 Hz, 3H), 0.82 (s, 3H).

(4a*S*,5*S*,6*S*,8a*S*)-6-(Benzyloxy)-5,8a-dimethyl-3-oxo-3,4,4a,5,6,7,8,8a-octahydronaphthalene-2-carbonitrile (22). Sodium metal (221 mg, 9.63 mmol) was washed with hexanes and added in pieces to anhydrous MeOH (8 mL) at 0 °C (gas evolution) under an argon atmosphere. A solution of compounds **20** and **21** (100 mg, 0.32 mmol) in anhydrous MeOH (2 mL) was added to the above freshly prepared NaOMe solution in MeOH, and the reaction mixture was stirred for 1 h at room temperature. After completion of the reaction, the mixture was diluted with EtOAc, and the organic layer was washed with 1 N HCl, a saturated aqueous sodium bicarbonate solution, water, and brine. The organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was directly used for the next step without any purification.

To the above crude α-cyanoketone (100 mg, 0.32) in anhydrous benzene was added DDQ (87 mg, 0.38 mmol) in one portion at room temperature. The resulting mixture was refluxed for 15 min, cooled to room temperature, and then filtered and concentrated. The residue was purified by silica gel column chromatography (15% EtOAc/hexanes) to afford 44 mg (45% yield over two steps) of the title compound **22** as a colorless oil. IR (neat/NaCl) ν (cm^{-1}) 2935, 2232, 1694, 1452, 1355, 1098, 750; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 7.48 (s, 1H), 7.36−7.25 (m, 5H), 4.65 (d, J = 11.3 Hz, 1H), 4.44 (d, J = 11.3 Hz, 1H), 3.05−2.90 (m, 1H), 2.70 (dd, J = 3.4, 17.7 Hz, 1H), 2.28−2.04 (m, 2H), 1.79−1.51 (m, 5H), 1.17 (s, 3H), 1.01 (d, J = 5.9 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 192.1, 171.2, 138.2, 128.4, 127.8, 127.7, 115.4, 113.9, 81.9, 71.4, 45.3, 37.0, 36.9, 34.9, 29.7, 26.1, 16.8, 14.5. LRMS m/z (relative intensity) 309 (M^+, 2), 253 (7), 218 (6), 92 (56), 91 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_{20}H_{23}NO_2$ 309.1729, found: 309.1735 ± 0.0009.

(4a*S*,5*S*,6*S*,8a*R*)-Methyl 6-(Benzyloxy)-5,8a-dimethyl-3-oxodecahydronaphthalene-2-carboxylate (23). A THF solution of compound **17** (300 mg, 1.04 mmol) was added to a suspension of NaH (131 mg, 3.14 mmol, 60% in mineral oil) and KH (12 mg, 0.104 mmol, 35% in mineral oil) in anhydrous THF at 0 °C. Then dimethyl carbonate (236 mg, 2.62 mmol) was added at 0 °C. The reaction mixture was allowed to reflux for 2 h and then was cooled to 0 °C, neutralized by slow addition of 3 M aqueous AcOH solution, and extracted with Et_2O. The organic layers were washed with water and brine solution. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude product by silica gel chromatography (12% EtOAc/hexanes) afforded 332 mg (92% yield) of the title compound **23**. TLC (20% EtOAc/hexanes) R_f = 0.63, visualized with anisaldehyde and ceric ammonium molybdate (CAM); $[\alpha]_D^{20}$ −24.6 (c 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, δ ppm) 12.1 (s, 1H), 7.4−7.24 (m, 5H), 4.67 (d, J = 11.3 Hz, 1H), 4.44 (d, J = 11.3 Hz, 1H), 3.75 (s, 3H), 2.94 (td, J = 10.9, 4.6 Hz, 1H), 2.47−2.37 (m, 1H), 2.2−1.1 (m, 9H), 1.03 (d, J = 6.2 Hz, 3H), 0.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 173.2, 171.3, 139.1, 128.5, 128, 127.7, 96.2, 83.2, 71.2, 51.6, 44.6, 38.9, 38.7, 38.6, 32.4, 31.3, 26.7, 17.2, 15.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{29}O_4$ 345.2060, found 345.2065.

(4a*S*,5*S*,6*S*,8a*S*)-Methyl 6-(Benzyloxy)-5,8a-dimethyl-3-oxo-3,4,4a,5,6,7,8,8a-octahydronaphthalene-2-carboxylate (24). Pyridine (94 μL, 1.16 mmol) was added to a solution of compound **23** (200 mg, 0.581 mmol) in anhydrous dichloromethane (2 mL) at 0 °C. The mixture was stirred for 15 min, and then phenylselenium chloride (166 mg, 0.872 mmol) in dichloromethane (2 mL) was added in one portion at 0 °C. The reaction mixture was stirred for 2 h at room temperature and then placed into a separatory funnel and washed with 1 N HCl followed by water. The organic layer was treated with 35% hydrogen peroxide (1 mL) and vigorously stirred for 15 min until complete disappearance of the yellow color. The mixture was then washed twice with water, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude product by silica gel column chromatography (25% EtOAc/hexanes) furnished 179 mg (90% yield) of the title compound **24**. TLC (20% EtOAc/hexanes) R_f = 0.22, visualized with UV and CAM; $[\alpha]_D^{20}$ +34.4 (c 0.75, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$, δ ppm) 7.45 (s, 1H),

dx.doi.org/10.1021/jo501122k | J. Org. Chem. 2014, 79, 7979−7999

7.37−7.23 (m, 5H), 4.65 (d, J = 11.3 Hz, 1H), 4.43 (d, J = 11.3 Hz, 1H), 3.78 (s, 3H), 2.98−2.89 (m, 1H), 2.67−2.58 (m, 1H), 2.3−2.07 (m, 2H), 1.80−1.41 (m, 5H), 1.13 (s, 3H), 1.01 (d, J = 5.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 194.8, 165.9, 165.5, 138.7, 130.3, 128.6, 128.1, 127.9, 82.6, 71.5, 52.5, 45.7, 38.6, 37.3, 36.7, 35.5, 26.5, 17.1, 14.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{27}O_4$ 343.1904, found 343.1908.

(2*S*,4a*S*,7*S*,8a*R*)-1,1,4a-Trimethyl-7-(prop-1-en-2-yl)-decahydronaphthalen-2-ol (25). Small pieces of lithium metal (1.10 g, 183.48 mmol) were placed in a flask topped with a dry ice condenser. The system was flushed with argon. The flask was cooled to −78 °C, and the condenser was filled with a dry ice/acetone mixture. Ammonia was condensed until no further lithium was seen. The cooling bath was removed, and the system was allowed to equilibrate to the refluxing temperature (−33 °C) for 15 min. Anhydrous THF (20 mL) was added to disperse the newly formed reagent, followed by slow addition of a solution of compound **12** (10 g, 45.87 mmol) in anhydrous THF (80 mL). After 2 h, methyl iodide (28.43 mL, 458 mmol) was added cautiously, and the reaction mixture was stirred at −33 °C for 1 h. Solid NH_4Cl was added to quench the excess of lithium, and ammonia was allowed to evaporate at room temperature. The reaction mixture was diluted with water and extracted with Et_2O, and the organic layer was washed with water and brine solution, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude ketone was directly used for the next step.

The above crude ketone was dissolved in absolute ethanol (100 mL), and $NaBH_4$ (3.47 g, 91.74 mmol) was added at −40 °C. The reaction mixture was allowed to stir at −40 °C for 1 h and then at −10 °C for an additional 1 h. The resulting solution was poured into ice-cold water and Et_2O was added. The mixture was extracted with Et_2O (3 × 100 mL), dried over anhydrous $MgSO_4$, filtered using a sintered funnel, and concentrated under reduced pressure. Purification of the crude product by silica gel column chromatography (6% EtOAc/hexanes) afforded 7.036 g (65% yield over two steps) of the title compound **25**. TLC (20% EtOAc/hexanes) R_f = 0.45, visualized with anisaldehyde; $[\alpha]_D^{20}$ −16.9 (c 0.6, $CHCl_3$); IR (neat/NaCl) ν (cm^{-1}) 3258, 2934, 1636, 1456, 1439, 1384, 1361, 1027, 994; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 4.9 (s, 1H), 4.8 (s, 1H), 3.21 (dd, J = 16, 7.8 Hz, 1H), 2.39 (s, 1H), 1.91−1.65 (m, 4H), 1.72 (s, 3H), 1.64−1.44 (m, 2H), 1.43−1.33 (m, 1H), 1.32−1.2 (m, 1H), 1.19−1.0 (m, 4H), 0.97 (s, 3H), 0.95 (s, 3H), 0.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 147.2, 110.8, 79.4, 46.3, 40.8, 40.3, 39.4, 38.8, 34.7, 27.7, 23.7, 23.5, 23.0, 19.3, 15.1; HRMS (ESI) m/z $[M + H - H_2O]^+$ calcd for $C_{16}H_{27}$ 219.2107, found 219.2112.

(2*S*,4a*S*,7*S*,8a*R*)-2-(Benzyloxy)-1,1,4a-trimethyl-7-(prop-1-en-2-yl)decahydronaphthalene (26). Compound **25** (6.0 g, 25.4 mmol) predissolved in anhydrous THF (30 mL) was slowly added to a suspension of NaH (3.16 g, 76.27 mmol) in anhydrous THF (50 mL) at room temperature under an argon atmosphere. Benzyl bromide (9.05 mL, 72.27 mmol) was then added, followed by TBAI (18.76 g, 50.8 mmol), and the reaction mixture was stirred overnight at room temperature and for 5 h at reflux temperature. The mixture was cooled to 0 °C, and ice−water was added carefully. The mixture was extracted with EtOAc, and the organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (2% EtOAc/hexanes) to afford the title compound **26** (7.87 g, 95% yield). TLC (10% EtOAc/hexanes) R_f = 0.75, visualized with anisaldehyde; $[\alpha]_D^{20}$ +35.73 (c 0.75, $CHCl_3$); IR (neat/NaCl) ν (cm^{-1}) 2968, 2934, 2848, 1639, 1454, 1362, 1097, 1027, 668, 733, 686; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.44−7.23 (m, 5H), 4.94−4.91 (m, 1H), 4.85−4.83 (m, 1H), 4.69 (d, J = 11.7 Hz, 1H), 4.45 (d, J = 11.7 Hz, 1H), 2.97 (dd, J = 11.7, 4.3 Hz, 1H), 2.42 (s, 1H), 1.95−1.77 (m, 3H), 1.75 (s, 3H), 1.74−1.68 (m, 1H), 1.65−1.51 (m, 2H), 1.48−1.41 (m, 1H), 1.33−1.19 (m, 2H), 1.16−1.04 (m, 2H), 1.02 (s, 3H), 1.01 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 147.3, 139.7, 128.4, 127.7, 127.4, 110.8, 87.1, 71.6, 46.8, 40.9, 40.3, 39.5, 39.0, 34.7, 28.0, 23.6, 23.4, 23.0, 19.4, 16.1; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{23}H_{34}NaO$ 349.2502, found 349.2524.

1-((2*S*,4a*S*,7*S*,8a*R*)-7-(Benzyloxy)-4a,8,8-trimethyldecahydronaphthalen-2-yl)ethanone (27). Compound **26** (19.41 g, 59.5 mmol) was dissolved in 4:1 acetone/water (160 mL). NMO (17.2 g, 147.2 mmol) and OsO_4 (3.73 mL, 0.58 mmol, 4% in water) were added to the reaction mixture at room temperature. The reaction mixture was stirred at room temperature overnightm and 10% sodium bisulfite ($NaHSO_3$) aqueous solution was introduced. The mixture was stirred for 15 min at room temperature and then extracted with EtOAc, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to afford the crude diol (21.43 g), which was directly used for the next step.

To a vigorously stirred suspension of silica gel-supported $NaIO_4$ reagent (120 g, prepared according to the literature procedure) in 200 mL of CH_2Cl_2 was added a solution of the diol (21.4 g, 59.52 mmol) in 100 mL of CH_2Cl_2. The reaction was monitored by TLC, and after complete conversion, the mixture was filtered through a sintered glass funnel and the silica gel was thoroughly washed with $CHCl_3$. The solvent was removed under reduced pressure, and purification by silica gel column chromatography (8% EtOAc/hexanes) afforded the title compound **27** (17.5 g, 90% yield over two steps). TLC (10% EtOAc/hexanes) R_f = 0.6, visualized with anisaldehyde; $[\alpha]_D^{20}$ +34.63 (c 1.1, $CHCl_3$); IR (neat/NaCl) ν (cm^{-1}) 2361, 1771, 1653, 1635, 1603, 1558, 1540, 1456, 1274; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.4−7.24 (m, 5H), 4.66 (d, J = 11.7 Hz, 1H), 4.42 (d, J = 11.7 Hz, 1H), 2.92 (dd, J = 11.7, 4.3 Hz, 1H), 2.69−2.62 (m, 1H), 2.15 (s, 3H), 2.13−2.04 (m, 1H), 2.02−1.94 (m, 1H), 1.86−1.77 (m, 1H), 1.7−1.5 (m, 2H), 1.47−1.38 (m, 1H), 1.24−0.84 (m, 5H), 1.02 (s, 3H), 0.96 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 211.7, 139.6, 128.4, 127.6, 127.4, 86.6, 71.6, 48.8, 48.1, 41.6, 39.9, 38.9, 34.2, 27.8, 23.2, 22.6, 21.8, 18.9, 15.9; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{22}H_{32}NaO_2$ 351.2295, found 351.2299.

(2*S*,4a*S*,7*S*,8a*R*)-7-(Benzyloxy)-4a,8,8-trimethyldecahydronaphthalen-2-ol (S2). Compound **27** (20 g, 60.97 mmol) was dissolved in anhydrous CH_2Cl_2 (150 mL), and powdered $NaHCO_3$ (15.3 g, 182 mmol) followed by anhydrous *m*-chloroperoxybenzoic acid (13.6 g, 79.2 mmol) in CH_2Cl_2 (50 mL) was added at room temperature. The reaction mixture was stirred at room temperature for 16 h under an argon atmosphere and then washed with 10% Na_2SO_3 aqueous solution and a saturated aqueous solution of $NaHCO_3$. The organic layers were dried over anhydrous $MgSO_4$, filtered using a sintered funnel, and concentrated under reduced pressure. The crude (2*S*,4a*S*,7*S*,8a*R*)-7-(benzyloxy)-4a,8,8-trimethyldecahydronaphthalen-2-yl acetate (**28**) (17.14 g, 85% yield) was used as such for the next reaction.

Crude **28** (17.14 g, 49.82 mmol) was dissolved in methanol (150 mL), and anhydrous K_2CO_3 (20.65 g, 149.47 mmol) was added in one portion. The reaction mixture was stirred vigorously at room temperature for 16 h and then neutralized with aqueous 3 N HCl solution and extracted with EtOAc (3 × 125 mL). The organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered using a sintered funnel, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (20% EtOAc/hexanes) to afford the title compound **S2** (13.53 g, 90% yield). TLC (20% EtOAc/hexanes) R_f = 0.25, visualized with anisaldehyde; $[\alpha]_D^{20}$ +23.3 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.41−7.23 (m, 5H), 4.69 (d, J = 11.7 Hz, 1H), 4.45 (d, J = 11.7 Hz, 1H), 4.19−4.13 (m, 1H), 3.0 (dd, J = 11.7, 4.3 Hz, 1H), 1.9−1.8 (m, 1H), 1.77−1.35 (m, 8H), 1.31−1.05 (m, 2H), 0.98 (s, 3H), 0.94 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 139.6, 128.4, 127.7, 127.4, 86.9, 71.6, 66.9, 45.2, 40.0, 38.9, 38.6, 34.3, 29.2, 28.8, 27.9, 23.3, 18.5, 16.2; HRMS (ESI) m/z $[M + H - H_2O]^+$ calcd for $C_{20}H_{29}O$ 285.2213, found 285.2221.

(4a*R*,7*S*,8a*R*)-7-(Benzyloxy)-4a,8,8-trimethyloctahydronaphthalen-2(1*H*)-one (29). PDC (24.89 g, 66.17 mmol) was added to a DMF (100 mL) solution of compound **S2** (10 g, 33.08 mmol) at room temperature under an argon atmosphere in small portions. The reaction mixture was stirred at room temperature for 2 h and then poured into a mixture of Et_2O and water. The reaction mixture was extracted with ether, and the combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure.

dx.doi.org/10.1021/jo501122k | J. Org. Chem. 2014, 79, 7979−7999

The crude product was purified by silica gel column chromatography (15% EtOAc/hexanes) to afford 8.93 g (90% yield) of the title compound **29**. TLC (20% EtOAc/hexanes) R_f = 0.55, visualized with anisaldehyde and $KMnO_4$; $[\alpha]_D^{20}$ +31.6 (*c* 1.0, $CHCl_3$); IR (neat/NaCl) ν (cm^{-1}) 3066, 3063, 1942, 1864, 1602, 1584, 1495, 1360, 1212, 1113, 858, 814, 693, 679; ^1H NMR (400 MHz, $CDCl_3$, δ ppm) 7.39−7.25 (m, 5H), 4.68 (d, *J* = 11.7 Hz, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 2.97 (dd, *J* = 11.3, 4.3 Hz, 1H), 2.50−2.24 (m, 4H), 1.96−1.87 (m, 1H), 1.69−1.57 (m, 3H), 1.46−1.29 (m, 2H), 1.27−1.17 (m, 1H), 1.15 (s, 3H), 0.96 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 212.7, 139.3, 128.5, 127.6, 127.5, 86.2, 71.8, 52.1, 43.5, 39.3, 38.9, 38.8, 37.9, 33.7, 27.6, 23.2, 18.6, 15.5; HRMS (ESI) *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{29}O_2$ 301.2162, found 301.2154.

(4a*R*,7*S*,8a*R*,*Z*)-7-(Benzyloxy)-3-(hydroxymethylene)-4a,8,8-trimethyloctahydronaphthalen-2(1*H*)-one (30). A solution of compound **29** (300 mg, 1.0 mmol) and ethyl formate (3.23 mL, 40.0 mmol) in anhydrous diethyl ether (10 mL) was slowly added to a suspension of NaH (166 mg, 4.0 mmol) in anhydrous diethyl ether (6 mL). The reaction mixture was stirred at room temperature for 16 h, and a saturated aqueous NH_4Cl solution was then added to quench the reaction. The reaction mixture was extracted with EtOAc, and the combined organic layers were dried over anhydrous $MgSO_4$, filtered using a sintered funnel, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (12% EtOAc/hexanes) to provide 278 mg (85% yield) of the title compound **30**. TLC (20% EtOAc/hexanes) R_f = 0.65, visualized with anisaldehyde; ^1H NMR (400 MHz, $CDCl_3$, δ ppm) 8.49 (d, *J* = 2.7 Hz, 1H), 7.41−7.25 (m, 5H), 4.7 (d, *J* = 11.7 Hz, 1H), 4.45 (d, *J* = 11.7 Hz, 1H), 2.99 (dd, *J* = 11.3, 4.3 Hz, 1H), 2.47−2.28 (m, 2H), 2.12−1.83 (m, 3H), 1.74−1.54 (m, 2H), 1.4−1.21 (m, 3H), 1.01 (s, 3H), 0.92 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 186.4, 186.1, 139.4, 128.5, 127.7, 127.6, 107.6, 86.4, 71.7, 47.1, 42.7, 39.0, 38.7, 33.4, 30.1, 27.8, 23.1, 19.1, 15.5; HRMS (ESI) *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{29}O_3$ 329.2111, found 329.2113.

(4a*R*,7*S*,8a*R*)-7-(Benzyloxy)-4a,8,8-trimethyl-4,4a,5,6,7,8,8a,9-octahydronaphtho[2,3-*d*]isoxazole (32). Compound **30** (600 mg, 1.82 mmol) was dissolved in 10 mL of absolute ethanol. Hydroxylamine hydrochloride salt (1.27 g, 18.28 mmol) dissolved in a minimum amount of water was added to the reaction mixture at room temperature, and then mixture was stirred at reflux for 2 h. Ethanol was removed under reduced pressure, and the residue was dissolved in 10 mL of EtOAc. The organic layer was washed with a saturated aqueous $NaHCO_3$ solution, water, and brine, and the combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (15% EtOAc/hexanes) to give 505 mg (85% yield) of the title compound **32**. TLC (20% EtOAc/hexanes) R_f = 0.55, visualized with anisaldehyde and CAM; IR (neat/NaCl) ν (cm^{-1}) 2932, 1716, 1613, 1455, 1409, 1362, 1273, 1096, 1062, 741, 698; ^1H NMR (400 MHz, $CDCl_3$, δ ppm) 8.01 (s, 1H), 7.42−7.24 (m, 5H), 4.71 (d, *J* = 11.7 Hz, 1H), 4.47 (d, *J* = 11.7 Hz, 1H), 3.03 (dd, *J* = 11.7, 3.9 Hz, 1H), 2.86 (dd, *J* = 17.1, 4.7 Hz, 1H), 2.62−2.51 (m, 1H), 2.17 (s, 2H), 1.95−1.24 (m, 5H), 1.08 (s, 3H), 1.01 (s, 3H), 0.9 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 167.5, 149.8, 139.3, 128.5, 127.7, 127.6, 110.7, 86.5, 71.8, 49.3, 39.4, 39.2, 39.1, 34.4, 28.2, 23.1, 20.7, 19.4, 16.3; HRMS (ESI) *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{28}NO_2$ 326.2115, found 326.2105.

(4a*R*,6*S*,8a*R*)-6-(Benzyloxy)-5,5,8a-trimethyl-3-oxodecahydronaphthalene-2-carbonitrile (S3). Sodium (812 mg, 36.92 mmol) in small pieces was added to anhydrous MeOH (10 mL) at 0 °C in portions over 4 h. A methanolic solution of **32** (400 mg, 1.23 mmol) was added to the above freshly prepared NaOMe solution, and the reaction mixture was stirred for 1 h at room temperature. Excess base was neutralized with 1 N HCl solution, and the reaction mixture was extracted with ethyl acetate and washed with a sufficient amount of water and aqueous $NaHCO_3$ solution. The organic layers were dried over anhydrous $MgSO_4$ and filtered using a sintered funnel, and the solvent was removed under reduced pressure. Purification of the crude product by silica gel column chromatography (20% EtOAc/hexanes) gave the title compound **S3** (340 mg, 85% yield). TLC (20% EtOAc/hexanes) R_f = 0.3, visualized with anisaldehyde and CAM; ^1H NMR (400 MHz, $CDCl_3$, δ ppm) 7.39−7.25 (m, 5H), 4.68 (d, *J* = 11.7 Hz, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 3.63 (dd, *J* = 13.6, 5.4 Hz, 1H), 2.97 (dd, *J* = 11.7, 4.3 Hz, 1H), 2.56 (dd, *J* = 14.8, 3.51 Hz, 1H), 2.41−2.3 (m, 1H), 2.05 (dd, *J* = 12.8, 5.4 Hz, 1H), 1.99−1.9 (m, 1H), 1.79−1.56 (m, 3H), 1.39 (dd, *J* = 14.1, 3.5 Hz, 1H), 1.29−1.21 (m, 1H), 1.2 (s, 3H), 0.97 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 200.6, 139.0, 128.5, 127.7, 116.7, 85.4, 71.9, 52.4, 47.8, 40.4, 39.33, 38.0, 37.9, 34.2, 27.6, 22.9, 18.7, 15.6; HRMS (ESI) *m*/*z* [M + NH_4]$^+$ calcd for $C_{21}H_{31}N_2O_2$ 343.2380, found 343.2371.

(4a*R*,6*S*,8a*R*)-6-(Benzyloxy)-5,5,8a-trimethyl-3-oxo-3,4,4a,5,6,7,8,8a-octahydronaphthalene-2-carbonitrile (33). Compound **S3** (300 mg, 0.92 mmol) was dissolved in anhydrous dichloromethane under an argon atmosphere. Pyridine (0.110 mL, 1.38 mmol) dissolved in dichloromethane (5 mL) followed by phenylselenium chloride (212 mg, 1.10 mmol) in dichloromethane (3 mL) was added at room temperature. The reaction mixture was allowed to stir for 2 h at room temperature and then was washed with 1 N HCl and water. The organic layers were treated with 35% hydrogen peroxide (2 mL) and vigorously stirred for 20 min until complete disappearance of the yellow color. The mixture was then washed twice with water, and the organic layer was dried over anhydrous $MgSO_4$ and filtered. The solvents were removed under reduced pressure, and the crude product was purified by silica gel column chromatography (30% EtOAc/hexanes) to furnish the title compound **33** (292 mg, 98% yield). TLC (20% EtOAc/hexanes) R_f = 0.3 (same as reactant), visualized with anisaldehyde and CAM; IR (neat/NaCl) ν (cm^{-1}) 2944, 2248, 1715, 1453, 1413, 1265, 1065, 897, 738, 697; ^1H NMR (400 MHz, $CDCl_3$, δ ppm) 7.36 (s, 1H), 7.35−7.25 (m, 5H), 4.68 (d, *J* = 11.7 Hz, 1H), 4.45 (d, *J* = 11.7 Hz, 1H), 3.01 (dd, *J* = 11.7, 4.3 Hz, 1H), 2.64 (dd, *J* = 17.9, 3.5 Hz, 1H), 2.5−2.41 (m, 1H), 2.06−1.98 (m, 1H), 1.82−1.47 (m, 4H), 1.2 (s, 3H), 1.01 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 193.5, 171.7, 138.8, 128.5, 127.8, 127.7, 114.5, 114.2, 84.8, 71.9, 48.5, 38.9, 38.2, 35.5, 34.7, 27.5, 22.9, 18.1, 16.1; HRMS (ESI) *m*/*z* [M + NH_4]$^+$ calcd for $C_{21}H_{29}N_2O_2$ 341.2224, found 341.2214.

(4a*R*,6*S*,8a*R*)-Methyl 6-(Benzyloxy)-5,5,8a-trimethyl-3-oxodecahydronaphthalene-2-carboxylate (34). To a suspension of KH (40 mg, 1.0 mmol) and NaH (1.25 g, 30 mmol, 60% in mineral oil) in anhydrous THF were added compound **29** (3.0 g, 10.0 mmol) and dimethyl carbonate (2.25 g, 25 mmol) at 0 °C under an argon atmosphere. The reaction mixture was allowed to reflux for 2 h. After completion of the reaction, the mixture was cooled to 0 °C and treated with 3 M aqueous AcOH solution slowly. The reaction mixture was extracted with Et_2O, and the organic layers were washed with water and brine solution. The combined organic layers were dried over anhydrous $MgSO_4$ and filtered using a sintered funnel, and the solvent was removed under reduced pressure to give the crude product, which was purified by silica gel column chromatography (12% EtOAc/hexanes) to afford 3.221 g (90% yield) of the title compound **34**. TLC (20% EtOAc/hexanes) R_f = 0.65, visualized with anisaldehyde and CAM; $[\alpha]_D^{20}$ −6.2 (*c* 1.0, $CHCl_3$); IR (neat/NaCl) ν (cm^{-1}) 2936, 2851, 1659, 1619, 1490, 1441, 1358, 1283, 1242, 1217, 1100, 1055, 820, 735; ^1H NMR (400 MHz, $CDCl_3$, δ ppm) 12.11 (s, 1H), 7.39−7.25 (m, 5H), 4.69 (d, *J* = 11.7 Hz, 1H), 4.45 (d, *J* = 11.7 Hz, 1H), 3.74 (s, 3H), 2.98 (dd, *J* = 11.7, 3.9 Hz, 1H), 2.33−2.66 (m, 2H), 2.1−2.03 (m, 1H), 1.92−1.83 (m, 2H), 1.72−1.53 (m, 2H), 1.36−1.16 (m, 2H), 1.01 (s, 3H), 0.93 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 172.9, 171.6, 139.2, 128.2, 127.4, 127.3, 95.7, 86.3, 71.5, 51.4, 47.4, 41.8, 38.9, 38.4, 32.8, 27.7, 27.2, 22.9, 19.1, 15.6; HRMS (ESI) *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{31}O_4$ 359.2217, found 359.2240.

(4a*R*,6*S*,8a*R*)-Methyl 6-(Benzyloxy)-5,5,8a-trimethyl-3-oxo-3,4,4a,5,6,7,8,8a-octahydronaphthalene-2-carboxylate (35). To a solution of compound **34** (3.6 g, 10 mmol) in anhydrous dichloromethane (20 mL) was added pyridine (1.624 mL, 20 mmol) at 0 °C. The mixture was stirred for 15 min under an argon atmosphere, and then phenylselenium chloride (2.8 g, 15 mmol) dissolved in dichloromethane (10 mL) and was added dropwise at 0 °C. The reaction mixture was allowed to stir for 2 h at room

dx.doi.org/10.1021/jo501122k | *J. Org. Chem.* 2014, 79, 7979−7999

temperature and then placed into a separatory funnel and washed with 1 N HCl followed by water. The organic layer was placed into a round-bottom flask, treated with 35% hydrogen peroxide (10 mL), and vigorously stirred for 15 min until complete disappearance of the yellow color. The mixture was then washed with water, dried over anhydrous $MgSO_4$, and filtered, and the solvent was removed under reduced pressure. The crude product was purified by silica gel column chromatography (25% EtOAc/hexanes) to give 3.37 g (94% yield) of the title compound **35**. TLC (20% EtOAc/hexanes) R_f = 0.25, visualized with UV and CAM; $[\alpha]_D^{20}$ +24.3 (*c* 1.0, $CHCl_3$); IR (neat/NaCl) ν (cm^{-1}) 2988, 2870, 1743, 1683, 1613, 1496, 1454, 1436, 1260, 1235, 1100, 1068, 737; ^1H NMR (400 MHz, $CDCl_3$, δ ppm) 7.34 (s, 1H), 7.33−7.24 (m, 5H), 4.67 (d, *J* = 11.7 Hz, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 3.78 (s, 3H), 3.0 (dd, *J* = 11.3, 4.3 Hz, 1H), 2.6−2.4 (m, 2H), 2.02−1.95 (m, 1H), 1.79−1.63 (m, 3H), 1.54−1.44 (m, 1H), 1.15 (s, 3H), 0.99 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 195.5, 166.1, 165.3, 138.8, 128.9, 128.2, 127.5, 127.4, 85.1, 71.6, 52.2, 48.5, 38.6, 37.0, 35.8, 35.7, 27.4, 22.9, 17.8, 15.9; HRMS (ESI) *m*/*z* $[M + H - H_2O]^+$ calcd for $C_{22}H_{27}O_3$ 339.1955, found 339.1963.

3-((*tert*-Butyldimethylsilyl)oxy)propan-1-ol (36a). To a solution of compound **36** (19 mL, 263.9 mmol) in anhydrous dichloromethane (250 mL) were addded TBDMSCl (7.9 g, 52.6 mmol) and imidazole (3.6 g, 52.6 mmol) at room temperature. The resulting mixture was stirred at room temperature for 20 h and then washed four times with water. The combined organic layers were dried over anhydrous $MgSO_4$ and filtered, and the solvent was removed under reduced pressure to give 8.73 g (86% yield) of 3-((*tert*-butyldimethylsilyl)oxy)propan-1-ol (**36a**). The crude compound was directly used for the next step without any further purification.

(*E*)-Methyl 5-((*tert*-Butyldimethylsilyl)oxy)pent-2-enoate (37). Oxalyl chloride (1.76 mL, 20.8 mmol) was slowly added to a solution of DMSO (2.25 mL, 31.2 mmol) in anhydrous dichloromethane (30 mL) at −78 °C, and the mixture was stirred for 15 min. A solution of compound **36a** (2.0 g, 10.4 mmol) in dichloromethane (2 mL) was then added to the reaction mixture, which was stirred for 1 h at −78 °C. Triethylamine (6.06 mL, 41.6 mmol) was added to the mixture and it was allowed to reach to room temperature over 1 h. Methyl (triphenylphosphoranylidene)acetate (Ph_3PCHCO_2Me) (6.95 g, 20.8 mmol) was added, and the reaction mixture was stirred at room temperature overnight and then filtered through a plug of silica gel using a sintered funnel and washed with 10% EtOAc/hexanes. The residue was purified by flash chromatography (5% EtOAc/hexanes) to afford 1.79 g (70% yield over two steps) of the title compound **37** as slightly yellow oil. IR (neat/NaCl) ν (cm^{-1}) 2957, 2853, 1725, 1658, 1256, 1097, 829, 768; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 6.97 (dt, *J* = 15.7, 7.1 Hz, 1H), 5.87 (m, 1H), 3.73 (s, 3H), 3.72 (t, *J* = 6.4 Hz, 2H), 2.41 (dq, *J* = 6.4, 1.5 Hz, 2H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 166.9, 146.2, 122.5, 61.5, 51.4, 35.7, 25.9, −6.2; LRMS *m*/*z* (relative intensity) 243 (M^+, 1), 229 (2), 213 (6), 187 (46), 119 (34), 89 (100); HRMS (ESI) *m*/*z* $[M - H]^-$ calcd for $C_{12}H_{24}O_3Si$ 243.1416, found 243.1421.

(*E*)-5-((*tert*-Butyldimethylsilyl)oxy)pent-2-enal (38). To a solution of compound **37** (560 mg, 2.29 mmol) in anhydrous toluene (10 mL) was added DIBAL-H (1.5 M in toluene, 3.82 mL, 5.73 mmol) slowly at −78 °C, and the reaction mixture was stirred for 1 h at −78 °C. Cautious addition of MeOH was followed by introduction of a 1 M sodium hydroxide solution. The mixture was extracted with CH_2Cl_2, and the organic layer was washed with water, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude alcohol (490 mg, quant.) was directly used for the next step.

The crude alcohol (490 mg, 2.29 mmol) was dissolved in anhydrous dichloromethane (10 mL), and to this solution was added Dess−Martin periodinane (1.42 g, 3.44 mmol) at 0 °C. The reaction mixture was stirred for 1 h at room temperature and then filtered through a plug of silica gel. The solvent was evaporated under reduced pressure, and the crude product was purified by silica gel column chromatography (5% EtOAc/hexanes) to give 400 mg (82% yield over two steps) of the title compound **38** as a colorless oil. IR (neat/NaCl) ν (cm^{-1}) 2951, 2926, 2853, 1697, 1107, 848; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 9.51 (d, *J* = 7.9 Hz, 1H), 6.88 (dt, *J* = 15.7, 6.9 Hz, 1H), 6.16 (dt, *J* = 7.9, 1.4 Hz, 1H), 3.78 (t, *J* = 6.2 Hz, 2H), 2.54 (dq, *J* = 6.5, 1.4 Hz, 2H), 0.88 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 193.9, 155.5, 134.3, 61.2, 36.1, 25.8, 18.2; LRMS *m*/*z* (relative intensity) 199 ($[M - CH_3]^+$, 1), 173 (11), 157 (60), 127 (100); HRMS (ESI) *m*/*z* $[M - CH_3]^+$ calcd for $C_{10}H_{19}O_2Si$ 199.1154, found 199.1158.

(*E*)-Allyl 7-((*tert*-Butyldimethylsilyl)oxy)-3-oxohept-4-enoate (39). An LDA solution was prepared by adding *n*-butyllithium (1.6 M in hexanes, 0.81 mL, 1.29 mmol) to a solution of diisopropylamine (0.2 mL, 1.41 mmol) in anhydrous THF (10 mL) at 0 °C. After complete addition, the mixture was brought to −78 °C, and allyl acetate (0.14 mL, 1.29 mmol) was added. The reaction mixture was stirred for 45 min at −78 °C, and a solution of compound **38** (251 mg, 1.17 mmol) in THF (1 mL) was added. After 1 h of stirring at −78 °C, a saturated aqueous NH_4Cl solution was introduced, and the mixture was extracted with EtOAc. The combined organic layers were washed with water, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The crude alcohol was directly used for the next step.

To a solution of the crude alcohol (369 mg, 1.17 mmol) in anhydrous dichloromethane (10 mL) was added Dess−Martin periodinane (545 mg, 1.29 mmol) at 0 °C. The resulting reaction mixture was allowed to stir for 30 min at room temperature and then filtered through a plug of silica gel. The solvent was removed under reduced pressure, and the crude product was purified by silica gel column chromatography (10% EtOAc/hexanes) to furnish 264 mg (72% yield over two steps) of the title compound **39** as a colorless oil (isolated as a mixture of keto and enol forms). IR (neat/NaCl) ν (cm^{-1}) 2930, 2859, 1662, 1594, 1420, 1222, 1143, 837; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 11.75 (d, *J* = 1.5 Hz, fraction), 6.89 (dt, *J* = 15.7, 6.9 Hz, fraction), 6.65 (dt, *J* = 15.7, 6.9 Hz, fraction), 6.21 (dt, *J* = 15.9, 1.5 Hz, fraction), 6.01−5.82 (m, 1H), 5.37−5.22 (m, 1H), 4.66−4.62 (m, 2H), 3.76−3.69 (m, 2H), 3.61 (s, 1H), 2.48−2.36 (m, 2H), 0.88 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 191.8, 146.8, 137.8, 131.6, 131.0, 125.9, 118.7, 118.3, 89.9, 65.9, 64.7, 61.9, 61.3, 46.6, 36.1, 36.0, 25.8, 18.2; LRMS *m*/*z* (relative intensity) 255 ($[M - C_3H_5O]^+$, 26), 197 (71), 74 (100); HRMS (ESI) *m*/*z* $[M - C_3H_5O]^+$ calcd for $C_{13}H_{23}O_3Si$ 255.1416, found 255.1430.

Tricycle 40. Cesium carbonate (136 mg, 0.42 mmol) was added to a solution of the compounds **39** (62 mg, 0.21 mmol) and **19** (65 mg, 0.21 mmol) in anhydrous THF (4 mL) in one portion at room temperature, and the mixture was stirred at room temperature for 1 h, filtered through a plug of silica gel, and washed with 15% EtOAc/hexanes. The solvent was removed under reduced pressure, and the crude product was purified by silica gel column chromatography using 30% EtOAc/hexanes to afford 82 mg (65% yield) of tricycle **40** as a colorless oil. IR (neat/NaCl) ν (cm^{-1}): 2929, 2846, 1735, 1694, 1646, 1612, 1289, 1200, 1090, 836; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 12.30 (s, 1H), 9.57 (d, *J* = 1.93 Hz, 1H), 7.60−7.25 (m, 5H), 6.90−5.88 (m, 1H), 5.40−5.23 (m, 1H), 4.72−4.66 (m, 1H), 4.62 (d, *J* = 11.5 Hz, 1H), 4.40 (d, *J* = 11.5 Hz, 1H), 3.72−3.52 (m, 2H), 3.35 (s, 1H), 2.90−1.25 (m, 16H), 1.03 (s, 3H), 0.96 (d, *J* = 6.4 Hz, 3H), 0.86 (s, 9H), 0.02 (d, *J* = 2.1 Hz, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 213.7, 199.5, 172.1, 171.9, 138.5, 131.3, 128.4, 127.8, 127.7, 127.6, 119.6, 96.4, 81.6, 70.9, 65.6, 64.0, 59.5, 43.0, 41.8, 41.0, 39.4, 38.2, 33.8, 33.7, 30.8, 26.5, 26.0, 21.7, 15.4, −5.3, −5.4; LRMS *m*/*z* (relative intensity) 595 ($[M - CHO]^+$, 2), 567 ($[M - C_4H_9]^+$, 10), 509 (29), 312 (26), 197 (48), 74 (100); HRMS (ESI) *m*/*z* $[M - CHO]^+$ calcd for $C_{35}H_{51}O_6Si$ 595.3455, found 595.3458.

Tricycle 41. To a solution of tricycle **40** (25 mg, 0.04 mmol) in anhydrous THF (3 mL) were added tetrakis(triphenylphosphine)-palladium (1 small spatula tip) and morpholine (5 drops). The resulting mixture was stirred for 1 h at room temperature and then filtered through a plug of silica gel. The solvent was removed under reduced pressure, and the crude reaction mixture was purified by silica gel column chromatography (15% EtOAc/hexanes) to give 21 mg (97% yield) of tricycle **41** as a colorless oil. IR (neat/NaCl) ν (cm^{-1}): 2923, 2851, 1723, 1097; ^1H NMR (300 MHz, $CDCl_3$, δ ppm) 9.95 (s, 1H), 7.37−7.24 (m, 5H), 4.65 (d, *J* = 11.4 Hz, 1H), 4.42 (d, *J* = 11.4

dx.doi.org/10.1021/jo501122k | J. Org. Chem. 2014, 79, 7979−7999

Hz, 1H), 3.76−3.47 (m, 2H), 2.91−1.24 (m, 17H), 0.99 (d, J = 6.3 Hz, 3H), 0.88 (s, 3H), 0.86 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 211.0, 210.3, 202.2, 139.2, 128.4, 127.8, 127.6, 81.9, 71.0, 63.4, 59.6, 44.5, 41.0, 40.4, 39.9, 39.7, 38.5, 36.7, 35.5, 33.2, 32.0, 26.0, 25.9, 20.2, 15.3, −5.3, −5.4; LRMS m/z (relative intensity) 522 ($[M - CH_3]^+$, 3), 483 ($[M - C_4H_9]^+$, 36), 453 (19), 91 (100); HRMS (ESI) m/z $[M - C_4H_9]^+$ calcd for $C_{28}H_{39}O_5Si$ 483.2567, found 483.2577 ± 0.0014.

(*E*)-Allyl 3-Oxohex-4-enoate (42). A THF solution of LDA was prepared by adding *n*-butyllithium (1.6 M in hexanes, 8.46 mL, 13.5 mmol) to a solution of diisopropylamine (1.99 mL, 14.2 mmol) in THF (10 mL) at 0 °C. After complete addition, the mixture was cooled to −78 °C, and then allyl acetate (0.92 mL, 8.55 mL) was added. The reaction mixture was stirred for 45 min at −78 °C, and crotonaldehyde (99.9% *trans*, 500 mg, 7.13 mmol) was added. After 1 h of stirring at −78 °C, a saturated aqueous NH_4Cl solution (10 mL) was added, and the mixture was extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed with water, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20% EtOAc/hexanes) to afford 1.04 g (86% yield) of a colorless alcohol.

To a solution of the above alcohol (75 mg, 0.44 mmol) in anhydrous dichloromethane (10 mL) at 0 °C was added Dess−Martin periodinane (224 mg, 0.53 mmol). The reaction mixture was stirred for 30 min at room temperature and then filtered through a short pad of silica gel. The solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (10% EtOAc/hexanes) to furnish 53 mg (72% yield) of the title compound **42** as a colorless oil (isolated as a mixture of keto and enol forms). IR (neat/NaCl) ν (cm^{-1}) 2936, 1744, 1667, 1229, 1148; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 11.76 (d, J = 1.5 Hz, fraction), 6.94−6.82 (m, fraction), 6.16 (dq, J = 15.7, 1.6 Hz, 1H), 5.94−5.76 (m, 1H), 5.33−5.19 (m, 2H), 4.63−4.59 (m, 2H), 3.58 (s, 1H), 1.92−1.89 (m, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 191.7, 145.3, 136.3, 132.1, 131.6, 131.1, 125.6, 118.6, 118.1, 89.5, 65.8, 64.6, 46.6, 18.3, 18.2; LRMS m/z (relative intensity) 168 (M^+, 44), 153 (50), 111 (92), 84 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_9H_{12}O_3$ 168.0786, found 168.0793 ± 0.0005.

(1*R*,4a*S*,4b*S*,7*S*,8*S*,8a*S*,10a*S*)-Allyl 7-(Benzyloxy)-10a-formyl-3-hydroxy-1,4b,8-trimethyl-10-oxo-1,2,4a,4b,5,6,7,8,8a,9,10,10a-dodecahydrophenanthrene-4-carboxylate (43). To a solution of compound **19** (60 mg, 0.19 mmol) in anhydrous THF (4 mL) was added a THF solution of compound **42** (32 mg, 0.19 mmol) followed by cesium carbonate (123 mg, 0.38 mmol) in one portion at room temperature. The resulting reaction mixture was stirred for 1 h at room temperature and then filtered through a short pad of silica gel and washed with 15% EtOAc/hexanes solution. The residue was purified by silica gel column chromatography (15% EtOAc/hexanes) to give 61 mg (66% yield) of the title compound **43** as a colorless oil (enol form only). IR (neat/NaCl) ν (cm^{-1}) 2938, 1721, 1700, 1647, 1273, 1220; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 12.24 (s, 1H), 9.67 (s, 1H), 7.35−7.30 (m, 5H), 6.07−5.82 (m, 1H), 5.41−5.28 (m, 1H), 4.69−4.60 (m, 3H), 4.39 (d, J = 11.5 Hz, 1H), 3.46 (s, 1H), 2.85−2.55 (m, 3H), 2.41−2.32 (m, 2H), 2.15−2.04 (m, 2H), 1.66−1.39 (m, 6H), 1.04−0.95 (m, 9H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 213.3, 199.3, 172.1, 171.5, 138.5, 131.4, 128.3, 127.8, 127.5, 119.4, 96.8, 81.5, 70.8, 65.5, 64.3, 56.1, 42.0, 41.2, 40.9, 39.6, 38.1, 33.9, 31.6, 26.5, 21.1, 16.0, 15.4; LRMS m/z (relative intensity) 465 ($[M - Me]^+$, 1), 451 ($[M - CHO]^+$, 18), 393 (100), 91 (90); HRMS (ESI) m/z $[M - CHO]^+$ calcd for $C_{28}H_{35}O_5$ 451.2484, found 451.2489 ± 0.0013.

(1*S*,2*S*,4a*S*,4b*S*,8*R*,8a*S*,10a*S*)-2-(Benzyloxy)-1,4a,8-trimethyl-6,9-dioxotetradecahydrophenanthrene-8a-carbaldehyde (44). To a solution of **43** (60 mg, 0.13 mmol) in anhydrous THF (4 mL) was added tetrakis(triphenylphosphine)palladium (1 spatula tip) followed by morpholine (5 drops). The reaction mixture was stirred for 16 h at room temperature and then filtered through a plug of silica gel. The solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (30% EtOAc/hexanes) to afford 41 mg (80% yield) of the title compound **44** as a crystalline white solid. IR (neat/NaCl) ν (cm^{-1}) 2961, 2931, 2873, 1717, 1097, 1069, 746; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 9.92 (s, 1H), 7.35−7.24 (m, 5H), 4.64 (d, J = 11.3 Hz, 1H), 4.42 (d, J = 11.3 Hz, 1H), 2.88−2.04 (m, 10H), 1.68−1.11 (m, 5H), 1.07 (d, J = 7.3 Hz, 3H), 0.99 (d, J = 6.3 Hz, 3H), 0.94 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 209.9, 209.1, 202.6, 138.4, 128.4, 127.8, 127.6, 81.9, 71.1, 63.7, 45.2, 44.2, 40.7, 40.4, 39.0, 38.5, 36.9, 34.8, 32.9, 26.1, 20.0, 15.4, 15.2; LRMS m/z (relative intensity) 404 ($[M + NH_4]^+$, 92), 397 ($[M + H]^+$, 100), 368 (63), 91 (52); HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{33}O_4$ 397.2379, found 397.2371 ± 0.0012.

(1*R*,4a*S*,4b*S*,7*S*,8*S*,8a*S*,10a*S*)-Allyl 7-(Benzyloxy)-10a-cyano-3-hydroxy-1,4b,8-trimethyl-10-oxo-1,2,4a,4b,5,6,7,8,8a,9,10,10a-dodecahydrophenanthrene-4-carboxylate (45). Cesium carbonate (92 mg, 0.28 mmol) was added in one portion to a solution of **42** (23 mg, 0.14 mmol) and cyclohexenone **22** (44 mg, 0.14 mmol) in THF (4 mL). The reaction mixture was stirred for 1 h at room temperature and then filtered through a plug of silica gel. The residue was purified by flash chromatography (20% EtOAc/hexanes) to afford 55 mg (82% yield) of the title compound **45** as a colorless oil (enol form only). IR (neat/NaCl) ν (cm^{-1}) 2940, 2242, 1721, 1655, 1611, 1271, 1218, 1063, 750; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 12.35 (s, 1H), 7.37−7.25 (m, 5H), 6.01−5.87 (m, 1H), 5.41−5.29 (m, 2H), 4.72−4.64 (m, 2H), 4.61 (d, J = 11.5 Hz, 1H), 4.38 (d, J = 11.5 Hz, 1H), 3.39 (s, 1H), 2.87−2.70 (m, 2H), 2.67−2.52 (m, 2H), 2.29−2.16 (m, 2H), 2.04−1.89 (m, 2H), 1.62−1.36 (m, 3H), 1.31−1.10 (m, 1H), 1.08 (d, J = 6.5 Hz, 3H), 1.07 (s, 3H), 0.97 (d, J = 6.3 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 204.5, 171.8, 170.2, 138.4, 131.0, 128.4, 127.8, 127.7, 120.2, 117.3, 96.4, 81.1, 70.8, 66.0, 57.4, 49.3, 43.0, 39.4, 39.3, 38.8, 33.5, 33.3, 29.3, 26.3, 22.2, 18.0, 15.5; LRMS m/z (relative intensity) 477 (M^+, 8), 328 (15), 310 (28), 219 (28), 167 (52), 91 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_{29}H_{35}NO_5$ 477.2515, found 477.2528 ± 0.0014.

(1*S*,2*S*,4a*S*,4b*S*,8*R*,8a*S*,10a*S*)-2-(Benzyloxy)-1,4a,8-trimethyl-6,9-dioxotetradecahydrophenanthrene-8a-carbonitrile (46). To a solution of compound **45** (32 mg, 0.06 mmol) in anhydrous THF (2 mL) was added tetrakis(triphenylphosphine)palladium (1 spatula tip) followed by morpholine (5 drops) at room temperature. The reaction mixture was stirred for 16 h at room temperature and then filtered through a plug of silica gel. The residue was purified by silica gel column chromatography (40% EtOAc/hexanes) to afford 20 mg (80% yield) of the title compound **46** as a colorless oil. IR (neat/NaCl) ν (cm^{-1}) 2966, 2930, 2873, 2234, 1719, 1456, 1090, 729; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 7.35−7.25 (m, 5H), 4.65 (d, J = 11.4 Hz, 1H), 4.41 (d, J = 11.4 Hz, 1H), 2.88 (td, J = 4.9, 10.2 Hz, 1H), 2.72−2.26 (m, 8H), 2.12−2.04 (m, 1H), 1.74−1.55 (m, 3H), 1.39−1.24 (m, 2H), 1.32 (s, 3H), 1.11 (d, J = 6.7 Hz, 3H), 1.01 (d, J = 6.2 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 208.1, 203.1, 138.3, 128.4, 127.8, 127.7, 119.2, 81.6, 71.1, 53.6, 50.6, 43.6, 41.8, 39.7, 39.5, 38.6, 37.4, 33.4, 33.2, 25.7, 20.5, 16.9, 15.3; LRMS m/z (relative intensity) 393 (M^+, 22), 285 (16), 226 (23), 167 (77), 92 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_{25}H_{31}NO_3$ 393.2304, found 393.2313 ± 0.0011.

(*E*)-1-(Phenylsulfinyl)pent-3-en-2-one (9). An LDA solution was prepared by adding *n*-butyllithium (2.5 M in hexanes, 1.44 mL, 3.59 mmol) to a solution of diisopropylamine (0.53 mL, 3.78 mmol) in anhydrous THF (10 mL) at 0 °C. After complete addition, the mixture was cooled to −78 °C, and a solution of phenyl methyl sulfoxide (318 mg, 2.27 mmol) in anhydrous THF (1 mL) was added. The reaction mixture was stirred for 45 min at −78 °C, and neat methyl crotonate (0.2 mL, 1.89 mmol) was added. After 1 h of stirring at −78 °C, a saturated aqueous NH_4Cl solution was slowly added, and the mixture was extracted with ethyl acetate (2 × 20 mL). The combined organic layers were washed with water, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (2% $MeOH/CH_2Cl_2$) to afford 225 mg (57% yield) of the title compound **9** as a colorless oil. IR (neat/NaCl) ν (cm^{-1}) 3053, 2969, 1726, 1665, 1625, 1441, 1291, 1086, 1044, 964, 749, 693; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 7.67−7.62 (m, 2H), 7.56−7.49 (m, 3H), 6.90 (dq, J =

dx.doi.org/10.1021/jo501122k | J. Org. Chem. 2014, 79, 7979−7999

6.8, 15.9 Hz, 1H), 6.14 (dq, J = 1.6, 15.9 Hz, 1H), 4.08 (d, J = 3.5 Hz, 1H), 1.90 (dd, J = 6.9, 1.6 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 190.5, 147.2, 143.2, 131.9, 131.5, 129.3, 124.2, 66.4, 18.6; LRMS m/z (relative intensity) 208 (M^+, 25), 193 (29), 160 (35), 125 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_{11}H_{12}O_2S$ 208.0558, found 208.0563 ± 0.0006.

(1*S*,4b*S*,7*S*,8*S*,8a*S*)-7-(Benzyloxy)-1,4b,8-trimethyl-1,2,5,6,7,8,8a,9-octahydrophenanthrene-3,10(4*H*,4b*H*)-dione (47). To a solution of compounds **9** (34 mg, 0.16 mmol) and **19** (50 mg, 0.16 mmol) in ethyl acetate (4 mL) was added cesium carbonate (104 mg, 0.32 mmol) in one portion. The resulting reaction mixture was stirred for 1 h at room temperature and then filtered through a plug of silica gel. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (30% EtOAc/hexanes) to afford 14 mg (23% yield) of the title compound **47** as a colorless oil. IR (neat/NaCl) ν (cm^{-1}) 2940, 2869, 1717, 1667, 1447, 1377, 1072, 732; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 7.34−7.25 (m, 5H), 4.65 (d, J = 11.4 Hz, 1H), 4.43 (d, J = 11.4 Hz, 1H), 3.43−3.57 (m, 1H), 3.04 (d, J = 2.3 Hz, 2H), 2.97−2.85 (m, 1H), 2.68−2.61 (m, 1H), 2.48−2.37 (m, 2H), 2.33−2.15 (m, 2H), 1.77−1.59 (m, 4H), 1.41−1.25 (m, 2H), 1.15 (s, 3H), 1.02 (d, J = 5.8 Hz, 3H), 0.92 (d, J = 7.1 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 196.4, 160.9, 138.5, 136.2, 128.4, 127.8, 127.6, 82.0, 71.1, 46.3, 45.4, 39.2, 37.5, 37.4, 33.5, 27.1, 26.3, 20.5, 17.1, 14.7; LRMS m/z (relative intensity) 380 (64), 366 (M^+, 6), 91 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_{24}H_{30}O_3$ 366.2195, found 366.2200 ± 0.0011.

(1*S*,4b*S*,7*S*,8a*R*)-7-(Benzyloxy)-1,4b,8,8-tetramethyl-1,2,5,6,7,8,8a,9-octahydrophenanthrene-3,10(4*H*,4b*H*)-dione (49). To a solution of compound **30** (50 mg, 0.15 mmol) and pyridine (15 μL, 0.18 mmol) in anhydrous dichloromethane (2.5 mL), was added phenylselenium chloride (34 mg, 0.18 mmol) in dichloromethane (2 mL) at room temperature. The reaction mixture was stirred for 2 h at room temperature and then washed with 1 N HCl and water. The organic layer was treated with 35% hydrogen peroxide (1.2 mL) at 0 °C and vigorously stirred for 25 min until complete disappearance of the yellow color. The mixture was then washed twice with water, and the organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Careful evaporation without heating the water bath was done in order to prevent decomposition of the crude product (4a*R*,6*S*,8a*R*)-6-(benzyloxy)-5,5,8a-trimethyl-3-oxo-3,4,4a,5,6,7,8,8a-octahydronaphthalene-2-carbaldehyde (**31**). This crude compound **31** was directly used for the next step without further purification.

Cesium carbonate (100 mg, 0.30 mmol) was added in one portion to a solution of Nazarov reagent **9** (38 mg, 0.18 mmol) and cyclohexenone **31** (50 mg, 0.15 mmol) in EtOAc (5 mL). The reaction mixture was stirred for 1.5 h at room temperature and then filtered through a plug of silica gel. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (30% EtOAc/hexanes) to afford 14.5 mg (25% yield) of the title compound **49**. TLC (30% EtOAc/hexanes) R_f = 0.35 or (20% EtOAc/hexanes) R_f = 0.25, visualized with anisaldehyde and CAM; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.38−7.21 (m, 5H), 4.68 (d, J = 11.7 Hz, 1H), 4.44 (d, J = 11.7 Hz, 1H), 3.54−3.42 (m, 1H), 3.08−2.92 (m, 3H), 2.62−2.31 (m, 4H), 2.02−1.92 (m, 1H), 1.81−1.57 (m, 3H), 1.42−1.30 (m, 1H), 1.16 (s, 3H), 1.03 (s, 3H), 0.96 (s, 3H), 0.91 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 209.1, 197.3, 161.1, 138.8, 135.5, 128.1, 127.4, 127.4, 84.9, 71.4, 49.5, 45.2, 39.2, 38.8, 38.6, 34.9, 34.0, 27.7, 27.2, 22.8, 20.4, 17.9, 16.0; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{33}O_3$ 381.2424, found 381.2429.

(1*S*,2*S*,4a*S*,8*S*,8a*S*,10a*S*)-2-(Benzyloxy)-1,4a,8-trimethyl-6,9-dioxo-1,2,3,4,4a,6,7,8,8a,9,10,10a-dodecahydrophenanthrene-8a-carbonitrile (50). To a solution of compounds **9** (36 mg, 0.16 mmol) and **22** (49 mg, 0.16 mmol) in anhydrous THF (4 mL) was added cesium carbonate (104 mg, 0.32 mmol) in one portion at room temperature. The reaction mixture was stirred for 2 h at room temperature and then filtered through a plug of silica gel. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (20% EtOAc/hexanes) to afford 37 mg (60% yield) of the title compound **50** as a crystalline white solid. IR (neat/NaCl) ν (cm^{-1}) 2971, 2940, 2874, 2233, 1721, 1673, 1094, 745; mp 89−91 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 7.35−7.25 (m, 5H), 6.08 (s, 1H), 4.68 (d, J = 11.4 Hz, 1H), 4.64 (d, J = 11.4 Hz, 1H), 3.14−3.04 (m, 2H), 2.92−2.86 (m, 1H), 2.81−2.73 (m, 1H), 2.50−2.40 (m, 2H), 2.26−2.23 (m, 1H), 1.94−1.89 (m, 1H), 1.65−1.56 (m, 4H), 1.41−1.31 (m, 1H), 1.34 (s, 3H), 1.01 (d, J = 6.2 Hz, 3H), 0.92 (d, J = 7.3 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$, δ ppm) 201.3, 196.1, 159.1, 138.2, 128.4, 127.8, 127.7, 124.8, 117.8, 81.2, 71.1, 50.7, 42.5, 42.4, 40.4, 39.2, 38.9, 38.5, 33.4, 25.7, 17.5, 15.0, 14.7; LRMS m/z (relative intensity) 391 (M^+, 13), 300 (9), 92 (34), 91 (100); HRMS (ESI) m/z $[M]^+$ calcd for $C_{25}H_{29}NO_3$ 391.2147, found 391.2144 ± 0.0011.

(1*S*,4b*S*,7*S*,8*S*,8a*S*)-7-(Benzyloxy)-1,4b,8-trimethyl-1,2,5,6,7,8,8a,9-octahydrophenanthrene-3,10(4*H*,4b*H*)-dione (47). To compound **50** (35 mg, 0.089 mmol) in anhydrous THF (1.0 mL) and HMPA (0.186 mL, 1.07 mmol) was added SmI_2 (5.34 mL, 0.1 M solution in THF, 0.537 mmol) dropwise at 0 °C, and then the mixture was slowly allowed to warm to room temperature and stirred for 1 h. The reaction mixture was cooled to 0 °C, and aqueous NH_4Cl solution was added. The mixture was extracted with EtOAc (2 × 10 mL), dried over anhydrous $MgSO_4$, filtered using a sintered funnel, and concentrated under reduced pressure. Purification by silica gel column chromatography (30% EtOAc/hexanes) afforded the title compound **47** (23 mg, 70% yield). TLC (30% EtOAc/hexanes) R_f = 0.5, visualized with CAM; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.43−7.22 (m, 5H), 4.66 (d, J = 11.3 Hz, 1H), 4.44 (d, J = 11.3 Hz, 1H), 3.58−3.45 (m, 1H), 3.05 (d, J = 3.9 Hz, 2H), 3.02−2.86 (m, 1H), 2.73−2.6 (m, 1H), 2.52−2.32 (m, 2H), 2.28−2.08 (m, 2H), 1.87−1.75 (m, 1H), 1.72−1.5 (m, 4H), 1.16 (s, 3H), 1.03 (d, J = 5.4 Hz, 3H), 0.93 (d, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 209.1, 196.6, 161.1, 138.7, 136.5, 128.6, 128.0, 127.9, 82.3, 71.4, 46.5, 45.6, 39.4, 38.6, 37.8, 37.7, 33.7, 27.3, 26.5, 20.7, 17.2, 14.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{31}O_3$ 367.2268, found 367.2255.

(2*S*,4a*S*,8*S*,8a*S*,10a*R*)-2-(Benzyloxy)-1,1,4a,8-tetramethyl-6,9-dioxo-1,2,3,4, 4a,6,7,8,8a,9,10,10a-dodecahydrophenanthrene-8a-carbonitrile (51). Cesium carbonate (400 mg, 1.23 mmol) was added in one portion to a solution of compounds **9** (128 mg, 0.619 mmol) and **33** (200 mg, 0.619 mmol) in anhydrous THF (4 mL). The reaction mixture was stirred for 2 h at room temperature and then filtered through a plug of silica gel. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (30% EtOAc/hexanes) to afford 162 mg (65% yield) of the title compound **51** as a white solid. TLC (20% EtOAc/hexanes) R_f = 0.3 (same as the β-keto nitrile), visualized with anisaldehyde and CAM; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.39−7.27 (m, 5H), 6.04 (s, 1H), 4.71 (d, J = 11.7 Hz, 1H), 4.46 (d, J = 11.7 Hz, 1H), 3.22−3.13 (m, 1H), 3.11−3.02 (m, 1H), 2.97 (dd, J = 11.3, 3.9 Hz, 1H), 2.91−2.79 (m, 1H), 2.72−2.62 (m, 1H), 2.51−2.42 (m, 1H), 2.14−1.91 (m, 2H), 1.77−1.53 (m, 2H), 1.43 (s, 3H), 1.42−1.36 (m, 1H), 0.99 (s, 3H), 0.98 (s, 3H), 0.91 (d, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 201.2, 196.6, 160.1, 138.8, 128.6, 127.8, 127.7, 124.4, 117.8, 84.8, 71.7, 50.7, 45.4, 42.6, 40.3, 39.8, 37.9, 37.1, 34.8, 31.8, 27.8, 22.5, 20.3, 16.0, 15.0; HRMS (ESI) m/z $[M + NH_4]^+$ calcd for $C_{26}H_{35}N_2O_3$ 423.2642, found 423.2659.

(1*S*,4b*S*,7*S*,8a*R*)-7-(Benzyloxy)-1,4b,8,8-tetramethyl-1,2,5,6,7,8,8a,9-octahydrophenanthrene-3,10(4*H*,4b*H*)-dione (49). To compound **51** (50 mg, 0.123 mmol) in anhydrous THF (1.5 mL) and HMPA (0.257 mL) was added SmI_2 (7.4 mL, 0.1 M solution in THF) dropwise at 0 °C, and then the mixture was slowly allowed to warm to room temperature and stirred for 1 h. The reaction mixture was cooled to 0 °C, and aqueous NH_4Cl solution was added. The mixture was extracted with EtOAc (2 × 10 mL), dried over anhydrous $MgSO_4$, filtered using a sintered funnel, and concentrated under reduced pressure. Purification by silica gel column chromatography afforded the title compound **49** (32 mg, 68% yield). TLC (20% EtOAc/hexanes) R_f = 0.25, visualized with anisaldehyde and CAM; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.38−7.24 (m, 5H), 4.69 (d, J = 11.7 Hz, 1H), 4.46 (d, J = 11.7 Hz, 1H), 3.54−3.43 (m, 1H), 3.11−2.92 (m, 3H), 2.63−2.31 (m, 4H), 2.06−1.89 (m, 1H), 1.86−1.52 (m,

dx.doi.org/10.1021/jo501122k | J. Org. Chem. 2014, 79, 7979−7999

3H), 1.42−1.30 (m, 1H), 1.17 (s, 3H), 1.03 (s, 3H), 0.97 (s, 3H), 0.93 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 209.1, 197.3, 161.1, 138.8, 135.4, 128.9, 127.7, 127.4, 84.8, 71.7, 49.5, 45.4, 39.3, 38.8, 38.6, 34.9, 34.1, 27.7, 27.2, 22.8, 20.4, 18.0, 16.1; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{25}H_{33}O_3$ 381.2424, found 381.2429.

(1*S*,2*S*,4a*S*,8*S*,8a*R*,10a*S*)-Methyl 2-(Benzyloxy)-1,4a,8-trimethyl-6,9-dioxo-1,2,3,4,4a,6,7,8,8a,9,10,10a-dodecahydrophenanthrene-8a-carboxylate (52). To a solution of compounds **9** (91 mg, 0.438 mmol) and **24** (150 mg, 0.438 mmol) in ethyl acetate (15 mL) was added cesium carbonate (285 mg, 0.877 mmol) in one portion at room temperature. After the mixture was stirred for 24 h at room temperature, additional cesium carbonate (285 mg, 0.877 mmol) and Nazarov reagent (91 mg, 0.438 mmol) were added. The reaction mixture was stirred for an additional 24 h at room temperature and then filtered through a plug of silica gel. The residue was purified by silica gel column chromatography (20% EtOAc/hexanes) to afford the title compound **52** (115 mg, 62% yield). TLC (30% EtOAc/hexanes) R_f = 0.43, visualized with UV and CAM; $[\alpha]_D^{20}$ +86.7 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.41−7.22 (m, 5H), 6.13 (s, 1H), 4.68 (d, J = 11.3 Hz, 1H), 4.44 (d, J = 11.3 Hz, 1H), 3.73 (s, 3H), 3.18−3.06 (m, 1H), 2.98−2.86 (m, 1H), 2.82−2.67 (m, 2H), 2.46−2.3 (m, 1H), 2.29−2.14 (m, 2H), 2.07−1.95 (m, 1H), 1.69−1.45 (m, 2H), 1.35−1.21 (m, 2H), 1.13 (s, 3H), 1.02 (d, J = 6.2 Hz, 3H), 0.92 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 203.6, 198.6, 169.1, 162.6, 138.6, 128.6, 128.1, 127.9, 126.1, 81.9, 71.4, 64.4, 53.8, 43.6, 42.1, 41.1, 39.6, 38.2, 36.2, 34.4, 26.3, 18.4, 18.2, 15.3; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{26}H_{33}O_5$ 425.2323, found 425.2327.

(1*S*,4b*S*,7*S*,8*S*,8a*S*)-7-(Benzyloxy)-1,4b,8-trimethyl-1,2,5,6,7,8,8a,9-octahydrophenanthrene-3,10(4*H*,4b*H*)-dione (47). Sodium metal (81.36 mg, 3.53 mmol) was added in small pieces to anhydrous EtOH (2 mL) at 0 °C, and the mixture was stirred until all of the metal was dissolved. A solution of compound **52** (50 mg, 0.117 mmol) in absolute EtOH (1 mL) was added to the above freshly prepared sodium ethoxide solution, and the reaction mixture was stirred for 2 h at room temperature. Excess base was neutralized by the addition of aqueous 2 N HCl solution, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered using a sintered funnel, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (30% EtOAc/hexanes) to afford the title compound **47** (40 mg, 92% yield). TLC (30% EtOAc/hexanes) R_f = 0.5, visualized with CAM; $[\alpha]_D^{20}$ +10.2 (c 0.22, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.41−7.23 (m, 5H), 4.66 (d, J = 11.3 Hz, 1H), 4.44 (d, J = 11.3 Hz, 1H), 3.54−3.44 (m, 1H), 3.05 (d, J = 3.9 Hz, 2H), 2.99−2.87 (m, 1H), 2.71−2.62 (m, 1H), 2.5−2.33 (m, 2H), 2.27−2.09 (m, 2H), 1.84−1.76 (m, 1H), 1.72−1.51 (m, 4H), 1.17 (s, 3H), 1.03 (d, J = 5.4 Hz, 3H), 0.93 (d, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 209.2, 196.6, 161.1, 138.7, 136.4, 128.6, 128.1, 127.9, 82.3, 71.4, 46.5, 45.7, 39.4, 38.6, 37.8, 37.7, 33.7, 27.3, 26.6, 20.7, 17.3, 14.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{24}H_{31}O_3$ 367.2268, found 367.2257.

(2*S*,4a*S*,8*S*,8a*R*,10a*R*)-Methyl 2-(Benzyloxy)-1,1,4a,8-tetramethyl-6,9-dioxo-1,2,3,4,4a,6,7,8,8a,9,10,10a-dodecahydrophenanthrene-8a-carboxylate (53). To a solution of compounds **9** (584 mg, 2.8 mmol) and **35** (1.0 g, 2.8 mmol) in ethyl acetate (15 mL) was added cesium carbonate (1.825 g, 5.61 mmol) in one portion under an argon atmosphere. After 24 h of reaction at room temperature, additional amounts of cesium carbonate (1.825 g, 5.61 mmol) and Nazarov reagent (584 mg, 2.8 mmol) were added. The reaction mixture was stirred for another 24 h at room temperature and then filtered through a plug of silica gel. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (20% EtOAc/hexanes) to afford the title compound **53** (763 mg, 62% yield) as a viscous light-yellow oil along with unreacted enone **35** (100 mg, 10% yield). TLC (30% EtOAc/hexanes) R_f = 0.45, visualized with UV and CAM; $[\alpha]_D^{20}$ +77.9 (c 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.37−7.24 (m, 5H), 6.05 (s, 1H), 4.68 (d, J = 11.7 Hz, 1H), 4.44 (d, J = 11.7 Hz, 1H), 3.72 (s, 3H), 3.13−3.03 (m, 1H), 2.98 (dd, J = 11.7, 3.9 Hz, 1H), 2.78 (dd, J = 17.9, 5.4 Hz, 1H), 2.73−2.57 (m, 2H), 2.19 (dd, J = 17.9, 1.5 Hz, 1H), 2.09−1.96 (m, 2H), 1.78−1.44 (m, 2H), 1.32−1.21 (m, 1H), 1.17 (s, 3H), 0.99 (s, 3H), 0.91 (s, 3H), 0.9 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 203.6, 198.7, 168.9, 163.4, 138.8, 128.3, 127.5, 127.4, 125.1, 84.8, 71.5, 64.1, 53.6, 46.1, 41.6, 40.2, 39.5, 37.9, 35.3, 35.1, 27.7, 22.6, 20.3, 18.1, 16.1; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{27}H_{35}O_5$ 439.2479, found 439.2472.

(1*S*,4b*S*,7*S*,8a*R*)-7-(Benzyloxy)-1,4b,8,8-tetramethyl-1,2,5,6,7,8,8a,9-octahydrophenanthrene-3,10(4*H*,4b*H*)-dione (49). Sodium metal (904 mg, 41.0 mmol) was added in small pieces to anhydrous EtOH (10 mL) at 0 °C and stirred at 0 °C under an argon atmosphere until all of the metal was dissolved. A solution of compound **53** (600 mg, 1.36 mmol) in absolute EtOH (5 mL) was added to the above freshly prepared sodium ethoxide solution, and the reaction mixture was stirred for 2 h at room temperature. Excess base was neutralized by the addition of aqueous 2 N HCl solution, and the aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (30% EtOAc/hexanes) to give the title compound **49** (468 mg, 90% yield). TLC (30% EtOAc/hexanes) R_f = 0.5, visualized with UV and CAM; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.39−7.23 (m, 5H), 4.68 (d, J = 11.7 Hz, 1H), 4.45 (d, J = 11.7 Hz, 1H), 3.53−3.43 (m, 1H), 3.11−2.92 (m, 3H), 2.63−2.31 (m, 4H), 2.03−1.93 (m, 1H), 1.82−1.52 (m, 3H), 1.4−1.29 (m, 1H), 1.17 (s, 3H), 1.02 (s, 3H), 0.96 (s, 3H), 0.92 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 209.1, 197.4, 161.2, 138.8, 135.5, 128.3, 127.5, 127.4, 84.8, 71.5, 49.5, 45.4, 39.1, 38.8, 38.6, 34.9, 34.1, 27.5, 26.9, 22.8, 20.4, 17.9, 16.1; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{25}H_{32}NaO_3$ 403.2244, found 403.2238.

(2*S*,4a*S*,6*R*,8*S*,10a*R*)-2-(Benzyloxy)-6-hydroxy-1,1,4a,8-tetramethyl-2,3,4,4a,5,6,7,8,10,10a-decahydrophenanthren-9(1*H*)-one (55). $NaBH_4$ (278 mg, 7.36 mmol) was added in one portion to a solution of compound **49** (1.4 g, 3.68 mmol) in THF (5 mL) and MeOH (5 mL) at −78 °C, and the resulting mixture was stirred for 10 min at −78 °C. Then aqueous saturated NaCl solution was added, and the solution was warmed to room temperature. The reaction mixture was extracted with EtOAc (3 × 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (40% EtOAc/hexanes) to afford the title compound **55** (1.26 g, 90% yield). TLC (40% EtOAc/hexanes) R_f = 0.3, visualized with CAM; $[\alpha]_D^{20}$ +104.8 (c 1.5, $CHCl_3$); IR (neat/NaCl) ν (cm^{-1}) 3420, 2933, 1703, 1603, 1456, 1366, 1106, 1025, 735, 698; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.39−7.23 (m, 5H), 4.68 (d, J = 11.7 Hz, 1H), 4.45 (d, J = 11.7 Hz, 1H), 3.7−3.58 (m, 1H), 3.01 (dd, J = 11.7, 4.3 Hz, 1H), 2.86−2.73 (m, 1H), 2.58−2.29 (m, 2H), 2.16−1.83 (m, 4H), 1.76−1.55 (m, 3H), 1.41−1.25 (m, 1H), 1.2−1.1 (m, 1H), 1.06 (d, J = 6.6 Hz, 3H), 1.03 (s, 3H), 0.99 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 198.9, 162.3, 138.9, 135.4, 128.2, 127.5, 127.4, 85.2, 71.5, 67.3, 48.3, 40.9, 39.3, 38.5, 35.1, 34.7, 33.5, 29.2, 27.5, 22.8, 21.4, 16.8, 16.0; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{25}H_{34}NaO_3$ 405.2400, found 405.2401.

(2*S*,4a*S*,6*R*,8*S*,10a*R*)-2-(Benzyloxy)-6-((*tert*-butyldimethylsilyl)oxy)-1,1,4a,8-tetramethyl-2,3,4,4a,5,6,7,8,10,10a-decahydrophenanthren-9(1*H*)-one (56). Compound **55** (800 mg, 2.09 mmol) was dissolved in anhydrous CH_2Cl_2, and the solution was cooled to 0 °C under an argon atmosphere. To this solution was added imidazole (376 mg, 6.28 mmol), DMAP (51 mg, 0.41 mmol) and TBSCl (471 mg, 3.14 mmol) at 0 °C, and the mixture was allowed to slowly warm to room temperature. The reaction mixture was stirred at rt for 3 h. The reaction mixture was quenched by addition of water, extracted with CH_2Cl_2, and washed with brine solution, and the organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude product by silica gel column chromatography (20% EtOAc/hexanes) afforded the title compound **56** (997 mg, 96% yield). TLC (20% EtOAc/hexanes) R_f = 0.55, visualized with CAM; $[\alpha]_D^{20}$ +60.4 (c 1.0, $CHCl_3$); IR (neat/NaCl) ν (cm^{-1}) 2951, 2933, 2856, 1665, 1607, 1471, 1360, 1256,

dx.doi.org/10.1021/jo501122k | J. Org. Chem. 2014, 79, 7979−7999

1206, 1111, 1087, 1029, 836, 776, 775; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.39−7.23 (m, 5H), 4.68 (d, J = 11.7 Hz, 1H), 4.45 (d, J = 11.7 Hz, 1H), 3.64−3.52 (m, 1H), 3.01 (dd, J = 11.7, 4.3 Hz, 1H), 2.84−2.7 (m, 1H), 2.53−2.28 (m, 2H), 2.14−1.83 (m, 4H), 1.76−1.46 (m, 2H), 1.38−1.07 (m, 3H), 1.05 (d, J = 6.6 Hz, 3H), 1.03 (s, 3H), 1.01 (s, 3H), 0.94 (s, 3H), 0.89 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 198.9, 162.6, 139.0, 135.4, 128.2, 127.4, 127.3, 85.2, 71.5, 68.1, 48.3, 41.1, 39.2, 38.5, 35.4, 35.0, 33.5, 31.6, 29.1, 27.5, 25.8, 22.8, 22.6, 21.5, 18.2, 16.7, 16.0, 14.1, −4.6, −4.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{31}H_{49}O_3Si$ 497.3445, found 497.3442.

(2*S*,4a*S*,6*R*,8*S*,10a*R*)-6-((*tert*-Butyldimethylsilyl)oxy)-2-hydroxy-1,1,4a,8-tetramethyl-2,3,4,4a,5,6,7,8,10,10a-decahydrophenanthren-9(1*H*)-one (57). To **56** (1.0 g, 2.01 mmol) dissolved in reagent-grade EtOAc (10 mL) in a pressure vessel was added 10% Pd/C (100 mg, 10 wt % of the substrate). The pressure vessel was evacuated three times with argon and two times with H_2 and then filled with hydrogen (15 psi), and the reaction mixture was stirred for 24 h at room temperature. After completion of the reaction, the mixture was diluted with chloroform (10 mL), filtered using a Celite-sintered funnel, and washed with chloroform. The solvent was evaporated under reduced pressure, and the crude product was purified by silica gel column chromatography (30% EtOAc/hexanes) to furnish the title compound **57** (736 mg, 90% yield). TLC (20% EtOAc/hexanes) R_f = 0.25, visualized with CAM; $[\alpha]_D^{20}$ +84.0 (c 0.5, $CHCl_3$); IR (neat/NaCl) ν (cm^{-1}) 3444, 2952, 2932, 2857, 1661, 1605, 1471, 1462, 1378, 1256, 1189, 1110, 1087, 1058, 854; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 3.61−3.5 (m, 1H), 3.28 (dd, J = 11.7, 4.3 Hz, 1H), 2.8−2.68 (m, 1H), 2.49−2.26 (m, 2H), 2.12−1.93 (m, 2H), 1.9−1.57 (m, 4H), 1.41−1.09 (m, 3H), 1.02 (d, J = 6.6 Hz, 3H), 0.98 (s, 3H), 0.97 (s, 3H), 0.86 (s, 9H), 0.83 (s, 3H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 198.9, 162.6, 135.3, 77.8, 68.1, 47.8, 41.0, 39.2, 38.4, 35.4, 35.0, 33.6, 29.1, 27.3, 27.1, 25.8, 21.4, 18.1, 16.7, 15.1, −4.6, −4.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{43}O_3Si$ 407.2976, found 407.2990.

(2*S*,4a*R*,4b*S*,6*R*,8*S*,8a*S*,10a*R*)-6-((*tert*-Butyldimethylsilyl)oxy)-2-hydroxy-1,1,4a,8-tetramethyldodecahydrophenanthren-9(1*H*)-one (58). To compound **57** (600 mg, 1.47 mmol) dissolved in anhydrous EtOAc (5 mL) in a pressure vessel was added 10% Pd/C (60 mg, 10 wt % of the substrate). The pressure vessel was evacuated three times with argon and two times with H_2 and then filled with hydrogen (20 psi). The reaction mixture was stirred at room temperature for 48 h and then diluted with $CHCl_3$ (10 mL) and filtered using a Celite-sintered funnel. The filtrate was concentrated under reduced pressure. Purification of the crude product by silica gel column chromatography (30% EtOAc/hexanes) afforded the title compound **58** (572 mg, 95% yield). TLC (20% EtOAc/hexanes) R_f = 0.3, visualized with CAM; mp 148−149 °C; IR (neat/NaCl) ν (cm^{-1}) 3453, 2952, 2855, 2708, 1694, 1462, 1426, 1371, 1343, 1307, 1252, 1144, 976, 880, 773, 737, 666; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 4.14−4.07 (m, 1H), 3.30 (dd, J = 11.3, 3.5 Hz, 1H), 2.57−2.47 (m, 1H), 2.4 (dd, J = 16.4, 3.5 Hz, 1H), 2.26 (t, J = 16.4 Hz, 1H), 1.97 (dd, J = 12.5, 3.5 Hz, 1H), 1.88−1.45 (m, 7H), 1.36−1.07 (m, 3H), 1.04 (d, J = 7.4 Hz, 3H), 0.96 (s, 3H), 0.94 (s, 3H), 0.86 (s, 9H), 0.83 (s, 3H), 0.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 211.5, 78.5, 67.6, 53.0, 50.8, 41.4, 39.0, 38.8, 38.5, 36.6, 35.3, 34.7, 27.5, 27.4, 27.1, 25.8, 17.9, 16.7, 14.9, 13.4, −4.9, −5.2; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{24}H_{44}NaO_3Si$ 431.2952, found 431.2946.

(2*S*,4a*R*,4b*S*,6*R*,8*S*,8a*S*,10a*R*)-6-((*tert*-Butyldimethylsilyl)oxy)-2-(methoxymethoxy)-1,1,4a,8-tetramethyldodecahydrophenanthren-9(1*H*)-one (59). Compound **58** (750 mg, 1.83 mmol) was dissolved in anhydrous dichloromethane (10 mL), and the solution was cooled to 0 °C. To this solution were added chloromethyl methyl ether (4.18 mL, 55.14 mmol) and diisopropylethylamine (0.958 mL, 5.51 mmol) under an argon atmosphere. The resulting mixture was stirred for 48 h at rt and then quenched with aqueous NH_4Cl solution. The mixture was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic phases were washed with brine, dried with anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure. Purification of the residue (16% EtOAc/hexanes) by silica gel column chromatography furnished the title compound **59** (706 mg, 85% yield). TLC (30% EtOAc/hexanes) R_f = 0.75, visualized with CAM; $[\alpha]_D^{20}$ +21.8 (c 0.5, $CHCl_3$); IR (neat/NaCl) ν (cm^{-1}) 3444, 2951, 2928, 2855, 1703, 1462, 1389, 1362, 1147, 1105, 1050, 917, 880, 835, 774; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 4.77 (d, J = 7 Hz, 1H), 4.62 (d, J = 7 Hz, 1H), 4.12−4.08 (m, 1H), 3.39 (s, 3H), 3.17 (dd, J = 11.7, 3.9 Hz, 1H), 2.57−2.48 (m, 1H), 2.4 (dd, J = 16.7, 3.9 Hz, 1H), 2.31−2.21 (m, 1H), 1.98 (dd, J = 12.5, 3.9 Hz, 1H), 1.87−1.46 (m, 8H), 1.37−1.16 (m, 2H), 1.05 (d, J = 7 Hz, 3H), 0.96 (s, 6H), 0.88 (s, 9H), 0.86 (s, 3H), 0.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 211.6, 95.9, 84.4, 67.6, 55.6, 53.1, 51.1, 41.4, 39.1, 38.6, 38.5, 36.6, 35.1, 34.7, 27.5, 27.4, 25.8, 23.9, 17.9, 16.7, 15.7, 13.4, −4.9, −5.0; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{49}O_4Si$ 453.3395, found 453.3381.

(2*S*,4a*R*,4b*S*,6*R*,8*S*,8a*S*,9*S*,10a*R*)-6-((*tert*-Butyldimethylsilyl)oxy)-2-(methoxymethoxy)-1,1,4a,8-tetramethyltetradecahydrophenanthren-9-ol (60). Compound **59** (500 mg, 1.10 mmol) was dissolved in methanol, and $NaBH_4$ (83.6 mg, 2.20 mmol) was added to the solution at 0 °C. The solution was stirred for 1 h at 0 °C under an argon atmosphere. After complete conversion as monitored by TLC, saturated aqueous sodium chloride solution was added, followed by EtOAc (50 mL). The mixture was extracted with ethyl acetate (2 × 50 mL), dried over anhydrous $MgSO_4$, and filtered, and the solvent was removed under reduced pressure. The crude product was purified by silica gel column chromatography (16% EtOAc/hexanes) to afford the title compound **60** (452 mg, 90% yield). TLC (30% EtOAc/hexanes) R_f = 0.6, visualized with CAM; $[\alpha]_D^{20}$ +28.54 (c 0.55, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 4.76 (d, J = 6.6 Hz, 1H), 4.62 (d, J = 6.6 Hz, 1H), 4.1−4.05 (m, 1H), 3.59−3.48 (m, 1H), 3.39 (s, 3H), 3.12 (dd, J = 11.7, 4.3 Hz, 1H), 2.27−2.16 (m, 1H), 1.91−1.83 (m, 1H), 1.8−1.22 (m, 12H), 1.08 (d, J = 7.4 Hz, 3H), 0.99 (s, 3H), 0.87 (s, 9H), 0.85 (s, 6H), 0.01 (s, 3H), 0.005 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 95.9, 84.9, 72.3, 67.8, 55.5, 51.4, 46.2, 40.0, 39.2, 38.5, 37.1, 35.9, 33.3, 30.7, 28.3, 27.1, 24.1, 25.8, 17.9, 16.7, 16.5, 14.4, −4.9, −5.0; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{26}H_{50}NaO_4Si$ 477.3371, found 477.3355.

(2*S*,4a*S*,6*R*,8*S*,10a*R*)-6-((*tert*-Butyldimethylsilyl)oxy)-2-(methoxymethoxy)-1,1,4a,8-tetramethyl-2,3,4,4a,5,6,7,8,10,10a-decahydrophenanthren-9(1*H*)-one (61). Compound **57** (300 mg, 0.73 mmol) was dissolved in anhydrous dichloromethane (8 mL), and the solution was cooled to 0 °C. Chloromethyl methyl ether (1.68 mL, 22.1 mmol) and diisopropylethylamine (0.385 mL, 2.21 mmol) were added to the above solution at 0 °C under an argon atmosphere, and the mixture was allowed to warm to room temperature. The mixture was stirred for 48 h at room temperature and then quenched with aqueous NH_4Cl solution. The mixture was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic phases were washed with brine, dried with $MgSO_4$, filtered, and evaporated. Silica gel column chromatography of the residue (20% EtOAc/Hex) afforded the title compound **61** (272 mg, 82% yield). TLC (30% EtOAc/hexanes) R_f = 0.72, visualized with CAM; IR (neat/NaCl) ν (cm^{-1}) 2951, 2930, 2856, 1665, 1608, 1256, 1204, 1148, 1110, 1087, 1047, 854, 836, 775; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 4.73 (d, J = 6.6 Hz, 1H), 4.59 (d, J = 6.6 Hz, 1H), 3.62−3.51 (m, 1H), 3.36 (s, 3H), 3.15 (dd, J = 11.7, 4.3 Hz, 1H), 2.81−2.69 (m, 1H), 2.5−2.26 (m, 3H), 2.11−1.92 (m, 2H), 1.91−1.78 (m, 2H), 1.64 (dd, J = 13.2, 4.3 Hz, 1H), 1.38−1.1 (m, 3H), 1.03 (d, J = 6.6 Hz, 3H), 1.0 (s, 3H), 0.96 (s, 3H), 0.88 (s, 3H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 198.8, 162.5, 135.4, 95.9, 83.9, 68.1, 55.5, 48.2, 41.0, 39.1, 38.2, 35.4, 35.0, 33.5, 29.1, 27.3, 25.8, 24.0, 21.5, 18.1, 16.7, 15.8, −4.6, −4.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{47}O_4Si$ 451.3238; found 451.3242.

(2*S*,4a*R*,4b*S*,6*R*,8*S*,8a*S*,9*S*,10a*R*)-6-((*tert*-Butyldimethylsilyl)oxy)-2-(methoxymethoxy)-1,1,4a,8-tetramethyltetradecahydrophenanthren-9-ol (60). Lithium pieces (53.3 mg, 8.88 mmol) were washed with hexanes and placed in a flask topped with a dry ice condenser, and the entire system was flushed with argon. The flask was cooled to −78 °C, and then ammonia was condensed until no further lithium was seen. The cooling bath was removed, and the system was allowed to equilibrate to the refluxing temperature (−33 °C). Anhydrous THF (6 mL) was added to the reaction mixture, followed

dx.doi.org/10.1021/jo501122k | J. Org. Chem. 2014, 79, 7979−7999

by slow addition of a solution of **61** (200 mg, 0.44 mmol) and *t*-BuOH (0.5 mL) in anhydrous THF (5 mL). The reaction mixture was then stirred at −33 °C for 2 h. To the reaction mixture was added ammonium chloride powder followed by triethylamine (0.5 mL), and ammonia was allowed to evaporate at room temperature. The mixture was extracted with EtOAc, and the organic layer was washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the residue by silica gel column chromatography (16% EtOAc/hexanes) gave 180 mg (90% yield) of the title compound **60**. TLC (30% EtOAc/hexanes) R_f = 0.6, visualized with CAM; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 4.75 (d, J = 6.6 Hz, 1H), 4.61 (d, J = 6.6 Hz, 1H), 4.11−4.03 (m, 1H), 3.6−3.48 (m, 1H), 3.39 (s, 3H), 3.12 (dd, J = 12.1, 4.3 Hz, 1H), 2.27−2.16 (m, 1H), 1.9−1.84 (m, 1H), 1.8−1.22 (m, 12H), 1.08 (d, J = 7.4 Hz, 3H), 0.99 (s, 3H), 0.88 (s, 3H), 0.87 (s, 9H), 0.85 (s, 3H), 0.09 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 95.9, 84.9, 72.3, 67.8, 55.5, 51.4, 46.2, 40.0, 39.2, 38.5, 37.1, 35.9, 33.3, 30.7, 28.3, 27.1, 25.8, 24.1, 17.9, 16.7, 16.5, 14.4, −4.9, −5.0. HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{26}H_{50}NaO_4Si$ 477.3371, found 477.3359.

***tert*-Butyl(((1*S*,3*R*,4a*S*,4b*R*,7*S*,8a*R*,10*S*,10a*S*)-10-((4-methoxybenzyl)oxy)-7-(methoxymethoxy)-1,4b,8,8-tetramethyltetradecahydrophenanthren-3-yl)oxy)dimethylsilane (62).** *Synthesis of 1-(Bromomethyl)-4-methoxybenzene (PMBBr).* : PMBOH (500 mg, 3.62 mmol) was dissolved into anhydrous Et_2O (10 mL), and the solution was cooled to 0 °C. PBr_3 (4.3 mL, 1.81 mmol) was added slowly dropwise under an argon atmosphere, and the reaction mixture was allowed to stir for 2 h. The mixture was cautiously poured into a mixture of saturated $NaHCO_3$ and ice. The organic layer was separated and washed twice with saturated $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered, and evaporated to give 757 mg (98% yield) of PMBBr as clear oil that was used without further purification.

Synthesis of ***62***. NaH (91.7 mg, 60 wt % in mineral oil, 2.20 mmol) and TBAI (catalytic) were suspended in anhydrous THF (8 mL) under an argon atmosphere, and the suspension was cooled to 0 °C. Alcohol **60** (500 mg, 1.10 mmol) in anhydrous THF was added, and then PMBBr (442 mg, 2.20 mmol) in THF was added dropwise to the above mixture. The reaction mixture was allowed to reflux overnight and then quenched with H_2O and diluted with Et_2O. The organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude material was purified by silica gel column chromatography (8% EtOAc/hexanes) to afford 537 mg (85% yield) of the title compound **62**. TLC (20% EtOAc/hexanes) R_f = 0.75, visualized with CAM; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.28 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 4.77 (d, J = 6.6 Hz, 1H), 4.64 (d, J = 6.6 Hz, 1H), 4.62 (d, J = 10.9 Hz, 1H), 4.35 (d, J = 10.9 Hz, 1H), 4.09−4.03 (m, 1H), 3.8 (s, 3H), 3.41 (s, 3H), 3.34−3.23 (m, 1H), 3.14 (dd, J = 11.7, 3.9 Hz, 1H), 2.38−2.27 (m, 1H), 2.15−2.06 (m, 1H), 1.8−1.2 (m, 10H), 1.7−0.8 (m, 2H), 1.02 (s, 3H), 1.01 (d, J = 7.4 Hz, 3H), 0.87 (s, 9H), 0.86 (s, 3H), 0.84 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 159.1, 131.2, 129.3, 113.7, 95.9, 85.0, 79.3, 70.1, 68.0, 55.3, 55.2, 51.2, 44.6, 40.3, 39.3, 38.7, 37.3, 37.1, 35.8, 33.6, 28.3, 27.0, 26.1, 25.8, 24.1, 17.9, 16.8, 14.4, −4.95, −4.97; HRMS (ESI) m/z $[M + NH_4]^+$ calcd for $C_{34}H_{62}NO_5Si$ 592.4392, found 592.4419.

(1*S*,3*R*,4a*S*,4b*R*,7*S*,8a*R*,10*S*,10a*S*)-10-((4-Methoxybenzyl)-oxy)-7-(methoxymethoxy)-1,4b,8,8-tetramethyltetradecahydrophenanthren-3-ol (S4). Compound **62** (400 mg, 0.69 mmol) was dissolved in anhydrous THF (3 mL), and the mixture was cooled to 0 °C. Then a solution of TBAF (1 M in THF, 1.39 mL, 1.39 mmol) was added. The reaction mixture was stirred for 3 days at rt under an argon atmosphere and then quenched with aqueous NH_4Cl solution. The reaction mixture was extracted with Et_2O (3 × 10 mL), and the organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (40% EtOAc/hexanes) to afford the title compound **S4** (272 mg, 85% yield). TLC (40% EtOAc/hexanes) R_f = 0.32, visualized with CAM; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.27 (d, J = 8.2 Hz, 2H), 6.87 (d, J = 8.2 Hz, 2H), 4.76 (d, J = 7.0 Hz, 1H), 4.68−4.59 (m, 2H), 4.34 (d, J = 10.9 Hz, 1H), 4.19−4.12 (m, 1H), 3.8 (s, 3H), 3.39 (s, 3H), 3.35−3.23 (m, 1H), 3.11 (dd, J = 12.1, 4.3 Hz, 1H), 2.42−2.3 (m, 1H), 2.17−2.09 (m, 1H), 1.8−1.45 (m, 10H), 1.41−1.16 (m, 2H), 1.04 (d, J = 7.4 Hz, 3H), 1.02 (s, 3H), 0.87 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 159.1, 131.0, 129.3, 113.7, 95.9, 85.1, 79.2, 70.2, 67.9, 55.5, 55.2, 51.2, 44.3, 40.1, 38.8, 38.6, 37.1, 35.9, 32.6, 28.4, 26.5, 26.1, 24.1, 16.8, 16.6, 14.4; HRMS (ESI) m/z $[M + NH_4]^+$ calcd for $C_{28}H_{48}NO_5$ 478.3527, found 478.3542.

(1*S*,4a*S*,4b*R*,7*S*,8a*R*,10*S*,10a*S*)-10-((4-Methoxybenzyl)oxy)-7-(methoxymethoxy)-1,4b,8,8-tetramethyldodecahydrophenanthren-3(2*H*)-one (54). PDC (408 mg, 1.08 mmol) was added to a mixture of compound **S4** (250 mg, 0.54 mmol) and pyridine (0.5 mL) in anhydrous DMF (2.5 mL) at room temperature under an argon atmosphere. The reaction mixture was stirred at rt for 3 h. After completion of the reaction, the mixture was quenched with water, extracted with Et_2O, dried over anhydrous $MgSO_4$, and filtered using a sintered funnel, and the resulting organic solvent was removed under reduced pressure. Purification of the crude product by silica gel column chromatography (30% EtOAc/hexanes) gave the title compound **54** (224 mg, 90% yield). TLC (40% EtOAc/hexanes) R_f = 0.5, visualized with CAM; IR (neat/NaCl) ν (cm^{-1}) 2950, 2926, 2881, 2851, 1713, 1611, 1586, 1513, 1464, 1389, 1366, 1248, 1146, 1045, 1010, 975, 820; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.25 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 4.73 (d, J = 7.0 Hz, 1H), 4.64 (d, J = 10.9 Hz, 1H), 4.59 (d, J = 6.6 Hz, 1H), 4.35 (d, J = 11.3 Hz, 1H), 3.77 (s, 3H), 3.37 (s, 3H), 3.26−3.16 (m, 1H), 3.07 (dd, J = 11.3, 3.9 Hz, 1H), 2.8−2.69 (m, 1H), 2.43 (dd, J = 12.8, 5.8 Hz, 1H), 2.26−2.11 (m, 3H), 2.02 (t, J = 12.8 Hz, 1H), 1.92−1.82 (m, 1H), 1.8−1.7 (m, 1H), 1.6−1.45 (m, 2H), 1.41−0.63 (m, 4H), 1.0 (s, 3H), 0.9 (s, 3H), 0.86 (s, 3H), 0.7 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 212.8, 159.2, 130.5, 129.5, 113.8, 95.9, 84.6, 78.1, 70.3, 55.5, 55.2, 51.4, 48.5, 47.5, 43.6, 40.8, 38.6, 36.6, 30.2, 28.2, 26.1, 23.9, 16.6, 14.0, 13.3; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{28}H_{43}O_5$ 459.3105, found 459.3097.

(1*R*,3*S*,4a*S*,4b*R*,7*S*,8a*R*,10*S*,10a*S*)-Methyl 3-Hydroxy-10-((4-methoxybenzyl)oxy)-7-(methoxymethoxy)-1,4b,8,8-tetramethyltetradecahydrophenanthrene-2-carboxylate (63). Compound **54** (200 mg, 0.43 mmol) and dimethyl carbonate (98.2 mg, 1.09 mmol) were added to a suspension of NaH (54.5 mg, 1.31 mmol, 60% in mineral oil) and KH (1.74 mg, 0.04 mmol) in anhydrous THF at 0 °C under an argon atmosphere. The reaction mixture was allowed to reflux for 2 h and then was cooled to 0 °C, hydrolyzed by the addition of 3 M aqueous AcOH solution, and extracted with diethyl ether. The organic layer was washed with water and brine. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product, (1*R*,4a*S*,4b*R*,7*S*,8a*R*,10*S*,10a*S*)-methyl 10-((4-methoxybenzyl)oxy)-7-(methoxymethoxy)-1,4b,8,8-tetramethyl-3-oxotetradecahydrophenanthrene-2-carboxylate (**S5**) was used in the next reaction without further purification.

The crude **S5** (225 mg, 0.43 mmol) was dissolved in absolute EtOH, and the solution was cooled to −10 °C, after which $NaBH_4$ (19.8 mg, 0.52 mmol) was added in one portion. After complete conversion, the reaction mixture was quenched with brine solution, and then EtOAC (20 mL) was added. The resulting mixture was extracted with EtOAc (3 × 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the crude product by silica gel column chromatography (40% EtOAc/hexanes) afforded the title compound **63** (180 mg, 80% yield). TLC (40% EtOAc/hexanes) R_f = 0.43, visualized with CAM; $[\alpha]_D^{20}$ +47.1 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.27 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 4.75 (d, J = 6.6 Hz, 1H), 4.64 (d, J = 10.9 Hz, 1H), 4.61 (d, J = 6.6 Hz, 1H), 4.37 (d, J = 10.9 Hz, 1H), 4.30−4.24 (m, 1H), 3.8 (s, 3H), 3.73 (s, 3H), 3.54 (br s, 1H), 3.39 (s, 3H), 3.35−3.25 (m, 1H), 3.1 (dd, J = 12.1, 3.9 Hz, 1H), 2.79−2.68 (m, 1H), 2.41−2.34 (m, 1H), 2.18−2.08 (m, 1H), 1.91−1.82 (m, 1H), 1.81−1.68 (m, 2H), 1.65−1.46 (m, 2H), 1.43−0.94 (m, 5H), 1.0 (s, 3H), 0.9 (d, J = 7.0 Hz, 3H), 0.68 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 176.5, 159.1, 130.8, 129.3, 113.7, 95.9, 85.0, 78.4, 70.1, 66.7, 55.5, 55.2, 51.7, 51.1, 49.7, 44.9, 39.6, 38.6, 37.0,

dx.doi.org/10.1021/jo501122k | J. Org. Chem. 2014, 79, 7979−7999

35.9, 31.1, 29.7, 28.4, 26.0, 24.1, 16.8, 14.3, 12.3; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{30}H_{46}NaO_7$ 541.3136, found 541.3142.

(1*R*,4a*S*,4b*R*,7*S*,8a*R*,10*S*,10a*S*)-Methyl 10-((4-Methoxybenzyl)oxy)-7-(methoxymethoxy)-1,4b, 8,8-tetramethyl-1,4,4a,4b,5,6,7,8,8a,9,10,10a-dodecahydrophenanthrene-2-carboxylate (64). Compound **63** (150 mg, 0.29 mmom) was dissolved in anhydrous pyridine (3 mL). This solution was cooled to 0 °C, and thionyl chloride (0.5 mL) was added. The reaction mixture was allowed to slowly warm to room temperature and stirred for 1 h at rt under an argon atmosphere. The reaction mixture was cautiously poured into ice−water and extracted with EtOAc followed by CH_2Cl_2. The organic layer was washed with water and brine, dried over magnesium sulfate, and concentrated under reduced pressure. Purification of the residue by silica gel column chromatography (30% EtOAc/hexanes) afforded the title compound **64** (137 mg, 95% yield). TLC (40% EtOAc/hexanes) R_f = 0.72, visualized with CAM; $[\alpha]_D^{20}$ +46.9 (c 0.875, $CHCl_3$); IR (neat/NaCl) ν (cm^{-1}) 2923, 2850, 1713, 1613, 1513, 1464, 1301, 1254, 1241, 1146, 1090, 1048, 820, 758; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.31 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 6.88−6.83 (m, 1H), 4.75 (d, J = 7.0 Hz, 1H), 4.65 (d, J = 10.9 Hz, 1H), 4.62 (d, J = 7.0 Hz, 1H), 4.41 (d, J = 10.9 Hz, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 3.39 (s, 3H), 3.37−3.26 (m, 1H), 3.19−3.07 (m, 2H), 2.21−1.93 (m, 3H), 1.8−1.46 (m, 5H), 1.41−1.14 (m, 3H), 1.0 (s, 3H), 0.87 (s, 3H), 0.85 (s, 3H), 0.84 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 167.4, 159.1, 138.2, 135.2, 130.8, 129.4, 113.8, 95.9, 84.9, 78.1, 69.9, 55.5, 55.3, 51.4, 51.2, 41.8, 40.9, 38.6, 37.2, 36.2, 28.3, 27.9, 25.8, 25.6, 23.9, 16.7, 14.9, 14.2; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{30}H_{44}NaO_6$ 523.3030, found 523.3033.

(1*R*,4a*S*,4b*R*,7*S*,8a*R*,10*S*,10a*S*)-Methyl 10-((4-Methoxybenzyl)oxy)-7-(methoxymethoxy)-1,4b,8,8-tetramethyltetradecahydrophenanthrene-2-carboxylate (65). Compound **64** (100 mg, 0.2 mmol) was dissolved in 5 mL of anhydrous MeOH, and then magnesium powder (48.6 mg, 2.0 mmol) was added, after which the mixture was stirred at room temperature for 5 h under an argon atmosphere. Then 3 N HCl was added carefully at room temperature until the excess magnesium was dissolved, and the mixture was extracted three times with Et_2O. The ether layer was washed with saturated aqueous NaCl solution, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (20% EtOAc/hexanes) afforded the title compound **65** as an inseparable mixture of diastereomers (96.3 mg, 96% yield). TLC (30% EtOAc/hexanes) R_f = 0.52, visualized with CAM; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm, mixture of two diastereomers): 7.32−7.24 (m, 2H), 6.92−6.84 (m, 2H), 4.78−4.72 (m, 1H), 4.67−4.57 (m, 2H), 4.41−4.34 (m, 1H), 3.79 (s, 3H), 3.66 (s, 3H), 3.38 (s, 3H), 3.25−3.13 (m, 1H), 3.12−3.03 (m, 1H), 2.87−2.7 (m, 1H), 2.45−2.28 (m, 1H), 2.14−1.89 (m, 1H), 1.8−1.63 (m, 4H), 1.62−1.4 (m, 3H), 1.38−1.15 (m, 2H), 0.98 (s, 3H), 0.85 (s, 3H), 0.83 (s, 3H), 0.66 and 0.82 (two d, J = 7.0 Hz, 3H), 1.08−0.61 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm, mixture of two diastereomers): 175.6, 175.3, 159.1, 158.9, 131.1, 130.8, 129.4, 129.2, 113.7, 113.6, 95.9, 85.0, 84.9, 78.5, 78.2, 70.0, 69.3, 55.5, 55.2, 51.5, 51.4, 51.3, 51.2, 47.3, 46.0, 45.8, 45.5, 45.2, 40.4, 38.6, 37.2, 37.1, 36.3, 36.2, 29.8, 28.8, 28.32, 28.29, 26.1, 26.0, 24.5, 24.1, 21.5, 21.47, 21.44, 16.7, 14.3, 14.0, 8.8; HRMS (ESI) m/z [M + NH$_4$]$^+$ calcd for $C_{30}H_{50}NO_6$ 520.3633, found 520.3649.

((1*S*,4a*S*,4b*R*,7*S*,8a*R*,10*S*,10a*S*)-10-((4-Methoxybenzyl)oxy)-7-(methoxymethoxy)-1,4b,8,8-tetramethyltetradecahydrophenanthren-2-yl)methanol (S6). DIBAL-H (0.250 mL, 1.0 M in THF, 0.25 mmol) was added dropwise to a solution of **65** (50 mg, 0.10 mmol) in anhydrous CH_2Cl_2 at −78 °C under an argon atmosphere. The reaction mixture was stirred for 1 h at −78 °C and for 2 h at room temperature. Then it was quenched with aqueous solution of K,Na-tartrate (0.5 M, 20 mL) at 0 °C. The mixture was vigorously stirred for 2 h at room temperature and then extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and evaporated. Purification of the residue by silica gel column chromatography (60% EtOAc/hexanes) afforded the title compound **S6** as a mixture of two diastereomers (40 mg, 86% yield). TLC (40% EtOAc/hexanes) R_f = 0.2, visualized with CAM; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm, mixture of two diastereomers): 7.26 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 4.75 (d, J = 7.0 Hz, 1H), 4.65−4.58 (m, 2H), 4.39−4.32 (m, 1H), 3.79 and 3.78 (two s, 3H), 3.68−3.46 (m, 2H), 3.39 (s, 3H), 3.29−3.16 (m, 1H), 3.12−3.04 (m, 1H), 2.44−2.24 (m, 1H), 2.13−2.05 (m, 1H), 1.78−1.41 (m, 8H), 1.4−1.17 (m, 2H), 1.13−0.57 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm, mixture of two diastereomers): 159.1, 159.1, 130.9, 130.7, 129.5, 129.5, 113.7, 95.9, 85.0, 78.9, 78.2, 70.1, 70.1, 66.3, 63.8, 55.5, 55.3, 51.28, 51.26, 46.2, 45.6, 43.0, 39.3, 38.6, 37.3, 37.1, 36.3, 28.6, 28.3, 28.3, 27.9, 26.2, 26.1, 25.1, 24.2, 22.7, 21.4, 19.9, 16.7, 16.7, 14.7, 14.3, 7.0; HRMS (ESI) m/z [M + NH$_4$]$^+$ calcd for $C_{29}H_{50}NO_5$ 492.3684, found 492.3689.

(1*R*,4a*S*,4b*R*,7*S*,8a*R*,10*S*,10a*S*)-10-((4-Methoxybenzyl)oxy)-7-(methoxymethoxy)-1,4b,8,8-tetramethyltetradecahydrophenanthrene-2-carbaldehyde (66). Dess−Martin periodinane (34.9 mg, 0.082 mmol) was added to a solution of **S6** (30 mg, 0.063 mmol) in CH_2Cl_2 (0.5 mL) at room temperature under an argon atmosphere. The reaction mixture was stirred at room temperature for 2 h and then quenched with an aqueous solution of $Na_2S_2O_3$ followed by saturated aqueous $NaHCO_3$ solution. The mixture was then extracted with CH_2Cl_2 (3 × 5 mL), and the organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the residue by silica gel chromatography (20% EtOAc/hexanes) afforded the title compound **66** as a mixture of two diastereomers (26.8 mg, 90% yield). TLC (40% EtOAc/hexanes) R_f = 0.6, visualized with CAM; ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm, mixture of two diastereomers): 9.70 and 9.65 (two s, 1H), 7.30 and 7.27 (m, 2H), 6.89 (d, J = 8.6 Hz, 2H), 4.79−4.71 (m, 1H), 4.69−4.57 (m, 2H), 4.41−4.33 (m, 1H), 3.80 (s, 3H), 3.39 and 3.38 (two s, 3H), 3.27−3.14 (m, 1H), 3.12−3.04 (m, 1H), 2.97−2.84 (m, 1H), 2.25−2.97 (m, 3H), 1.82−1.16 (m, 10H), 1.09−0.59 (m, 13H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm, mixture of two diastereomers): 205.7, 205.2, 159.2, 159.1, 130.8, 130.6, 129.5, 129.4, 113.8, 113.7, 95.94, 95.91, 84.94, 84.89, 78.4, 78.1, 70.15, 69.69, 55.5, 55.3, 54.6, 53.6, 51.24, 51.22, 45.9, 45.7, 45.3, 41.6, 38.6, 37.2, 37.1, 36.3, 28.3, 27.4, 27.3, 26.1, 25.9, 24.2, 24.1, 21.6, 19.5, 18.9, 16.7, 14.3, 14.2, 13.8, 8.9; HRMS (ESI) m/z [M + NH$_4$]$^+$ calcd for $C_{29}H_{48}NO_5$ 490.3527, found 490.3536.

(*E*)-((1*R*,4a*S*,4b*R*,7*S*,8a*R*,10*S*,10a*S*)-10-((4-Methoxybenzyl)oxy)-7-(methoxymethoxy)-1,4b,8,8-tetramethyldodecahydrophenanthren-2(3*H*)-ylidene)methyl Trifluoromethanesulfonate (67). A solution of **66** (13 mg, 0.0275 mmol) in anhydrous THF (2 mL) was added to a stirred solution of KHMDS (0.100 mL, 0.5 M in toluene, 0.055 mmol) in anhydrous THF (3 mL) at −78 °C under an argon atmosphere. After 15 min, a solution of 2-[*N*,*N*-bis(trifluoromethylsulfonyl)amino]-5-chloropyridine (21.5 mg, 0.055 mmol) in anhydrous THF (1.5 mL) was added to the above reaction mixture, and the resulting mixture was stirred for 3 h at −78 °C and then allowed to warm to 0 °C. The mixture was immediately quenched with aqueous NH_4Cl solution and extracted with Et_2O, and the organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to yield the crude product, which was purified by silica gel chromatography (6% EtOAc/hexanes) to afford the title compound **67** (10 mg, 60% yield) and 3 mg of unreacted aldehyde. TLC (30% EtOAc/hexanes) R_f = 0.65, visualized with CAM; $[\alpha]_D^{20}$ −24.2 (c 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm) 7.27 (d, J = 8.6 Hz, 2H), 6.9 (d, J = 8.6 Hz, 2H), 6.48 (s, 1H), 4.76 (d, J = 7.0 Hz, 1H), 4.7−4.57 (m, 2H), 4.34 (d, J = 10.9 Hz, 1H), 3.81 (s, 3H), 3.4 (s, 3H), 3.28−3.16 (m, 1H), 3.11 (dd, J = 12.1, 3.9 Hz, 1H), 2.85−2.73 (m, 1H), 2.67−2.56 (m, 1H), 2.2−2.02 (m, 1H), 1.9−0.65 (m, 11H), 1.01 (s, 3H), 0.9 (d, J = 7.4 Hz, 3H), 0.86 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm) 159.2, 137.7, 130.5, 129.5. 129.2, 127.7, 113.8, 95.9, 84.8, 78.0, 69.9, 55.5, 55.3, 51.2, 46.1, 45.4, 38.6, 37.2, 36.4, 32.1, 29.7, 28.3, 25.8, 25.4, 24.1, 21.1, 16.7, 14.2, 13.9; HRMS (ESI) m/z [M + NH$_4$]$^+$ calcd for $C_{30}H_{47}F_3NO_7S$ 622.3020, found 622.3028.

(*E*)-((1*R*,4a*S*,4b*R*,7*S*,8a*R*,10*S*,10a*S*)-10-Hydroxy-7-(methoxymethoxy)-1,4b,8,8-tetramethyldodecahydrophenanthren-2(3*H*)-ylidene)methyl Trifluoromethanesulfonate (68). DDQ (11.3 mg, 0.049 mmol) was added to a solution of **67** (20 mg,

dx.doi.org/10.1021/jo501122k | J. Org. Chem. 2014, 79, 7979−7999

0.033 mol) in CH_2Cl_2 (1.5 mL) and water (0.1 mL) at room temperature. The reaction mixture was stirred at room temperature for 3 h and then filtered on a pad of silica gel and washed with 30% EtOAc/hexanes. The filtrate was evaporated, and the residue was purified by silica gel column chromatography (15% EtOAc/Hex) to give the title compound **68** (15 mg, 94% yield). TLC (30% EtOAc/hexanes) R_f = 0.45, visualized with CAM; $[\alpha]_D^{20}$ −15.8 (*c* 0.5, $CHCl_3$); IR (neat/NaCl) ν (cm^{-1}) 2916, 2849, 2357, 1652, 1557, 1539, 1505, 1007; ^1H NMR (500 MHz, $CDCl_3$, δ ppm) 6.5 (s, 1H), 4.76 (d, *J* = 6.8 Hz, 1H), 4.62 (d, *J* = 6.8 Hz, 1H), 3.57−3.47 (m, 1H), 3.4 (s, 3H), 3.11 (dd, *J* = 11.9, 3.9 Hz, 1H), 2.84−2.74 (m, 1H), 2.7−2.61 (m, 1H), 1.94−0.75 (m, 12H), 1.07 (d, *J* = 7.1 Hz, 3H), 0.99 (s, 3H), 0.85 (s, 6H, 2 × CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm) 137.8, 127.7, 95.9, 84.7, 77.2, 71.6, 55.6, 51.5, 47.1, 45.9, 38.4, 37.2, 36.4, 32.2, 31.2, 28.3, 25.3, 24.1, 21.1, 16.7, 14.2, 13.8; HRMS (ESI) *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{36}F_3O_6S$ 485.2179, found 485.2183.

(*E*)-((1*R*,4a*S*,4b*R*,7*S*,8a*R*,10a*S*)-7-(Methoxymethoxy)-1,4b,8,8-tetramethyl-10-oxododecahydrophenanthren-2(3*H*)-ylidene)methyl Trifluoromethanesulfonate (69). Compound **68** (15 mg, 0.030 mmol) was dissolved in anhydrous CH_2Cl_2 (1.0 mL), and to this stirred solution was added Dess−Martin periodinane (17 mg, 0.040 mmol) at room temperature under an argon atmosphere. The reaction mixture was stirred at room temperature for 2 h and then quenched with a saturated aqueous solution of $Na_2S_2O_3$. The mixture was extracted with CH_2Cl_2 (3 × 5 mL), and the organic layers were washed with brine, dried over $MgSO_4$, filtered, and evaporated under reduced pressure. Purification of the residue by silica gel column chromatography (15% EtOAc/hexanes) afforded the title compound **69** (13.4 mg, 90% yield). TLC (30% EtOAc/hexanes) R_f = 0.65, visualized with $KMnO_4$; $[\alpha]_D^{20}$ −26.3 (*c* 0.3, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, δ ppm) 6.5 (s, 1H), 4.77 (d, *J* = 6.6 Hz, 1H), 4.63 (d, *J* = 6.6 Hz, 1H), 3.4 (s, 3H), 3.16 (dd, *J* = 11.7, 3.2 Hz, 1H), 3.07−2.98 (s, 1H), 2.76−2.67 (m, 1H), 2.44 (dd, *J* = 16.4, 2.9 Hz, 1H), 2.29 (t, *J* = 15.6 Hz, 1H), 2.1 (dd, *J* = 12.4, 3.2 Hz, 1H), 2.01−1.8 (m, 3H), 1.7−1.5 (m, 4H), 1.34−1.24 (m, 1H), 1.21−1.08 (m, 1H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.99 (s, 3H), 0.96 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm) 209.6, 136.3, 128.1, 95.9, 84.3, 77.2, 55.6, 53.4, 51.6, 47.4, 38.6, 38.5, 36.8, 35.9, 32.1, 27.6, 26.0, 23.9, 21.1, 15.7, 15.0, 13.3; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{22}H_{33}F_3NaO_6S$ 505.1842, found 505.1824.

(*E*)-2-(Dimethylamino)ethyl 2-((1*R*,4a*S*,4b*R*,7*S*,8a*R*,10a*S*)-7-(Methoxymethoxy)-1,4b,8,8-tetramethyl-10-oxododecahydrophenanthren-2(3*H*)-ylidene)acetate (70). Compound **69** (12 mg, 0.024 mmol) was dissolved in 1-methyl-2-pyrrolidinone (2 mL) at room temperature, and to this solution were added K_2CO_3 (14 mg, 0.099 mmol), LiCl (3.2 mg, 0.074 mmol), and *N*,*N*dimethylethanolamine (105 μL, 1.04 mmol). This mixture was degassed by bubbling carbon monoxide for 25 min, after which bis(triphenylphosphine)-dichloropalladium (1 mg, 1.2 μmol) was added and the bubbling of carbon monoxide was continued for 10 more min. The flask was then placed in a bomb reactor under carbon monoxide at a pressure of 100 psi, and it was heated to 100 °C for 16 h. After that, the reaction mixture was cooled to room temperature. The atmospheric pressure was re-established, and the reaction mixture was quenched with saturated aqueous NH_4Cl solution and extracted with a 1:1 mixture of Et_2O and hexanes (3 × 15 mL). The organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (10% MeOH/CH_2Cl_2) to give the title compound **70** (10 mg, 90% yield). TLC (10% MeOH/CH_2Cl_2) R_f = 0.55, visualized with UV and $KMnO_4$; $[\alpha]_D^{20}$ −46.1 (*c* 0.3, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$, δ ppm) 5.75 (s, 1H), 4.77 (d, *J* = 6.8 Hz, 1H), 4.63 (d, *J* = 6.8 Hz, 1H), 4.19 (t, *J* = 5.4 Hz, 2H), 3.79 (d, *J* = 13.9 Hz, 1H), 3.4 (s, 3H), 3.16 (dd, *J* = 11.5, 3.4 Hz, 1H), 3.1−2.95 (m, 1H), 2.61 (t, *J* = 5.6 Hz, 2H), 2.5−2.24 (m, 2H), 2.31 (s, 6H), 2.21−1.53 (m, 6H), 1.39−1.11 (m, 2H), 1.05 (d, *J* = 6.6 Hz, 3H), 1.02−0.85 (m, 2H), 0.98 (s, 3H), 0.96 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm) 210.1, 166.8, 165.6, 113.2, 95.9, 84.4, 61.5, 57.8, 55.6, 53.6, 51.7, 47.5, 45.7, 43.2, 39.4, 38.7, 38.6, 36.8, 35.9, 29.7, 27.6, 26.8, 23.9, 15.7, 14.9, 13.3; HRMS (ESI) *m*/*z* $[M + H]^+$ calcd for $C_{26}H_{44}NO_5$ 450.3214, found 450.3223.

(*E*)-2-(Dimethylamino)ethyl 2-((1*R*,4a*S*,4b*R*,7*S*,8a*R*,10a*S*)-7-Hydroxy-1,4b,8,8-tetramethyl-10-oxododecahydrophenanthren-2(3*H*)-ylidene)acetate [(+)-Cassaine (4)]. $LiBF_4$ (29 mg, 0.31 mmol) in CH_3CN (900 μL) was added to compound **70** (7 mg, 0.015 mmol) in CH_3CN (300 μL) at room temperature. Water (50 μL) was added to this mixture, and the resulting mixture was stirred for 16 h at 75 °C. The reaction mixture was cooled to room temperature, quenched with water, and extracted with Et_2O (3 × 5 mL). The organic layers were washed with water and brine and dried with anhydrous $MgSO_4$. The contents were filtered, and the solvent was evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (5% MeOH/CH_2Cl_2) to afford the title compound **4** (4.7 mg, 75% yield). TLC (10% MeOH/CH_2Cl_2) R_f = 0.45, visualized with UV and $KMnO_4$; IR (neat/NaCl) ν (cm^{-1}) 2956, 2917, 2849, 1703, 1462, 1391, 1372, 1260, 1185, 1150, 1024, 1010, 668, 601, 719, 650; ^1H NMR (500 MHz, $CDCl_3$, δ ppm) 5.73 (s, 1H), 4.31 (t, *J* = 5.8 Hz, 2H), 3.8−3.74 (dt, *J* = 14.6, 3.1 Hz, 1H), 3.3 (dd, *J* = 11.2, 4.6 Hz, 1H), 3.04 (dq, *J* = 6.9, 3.5 Hz, 1H), 2.7 (br t, 2H), 2.44 (dd, *J* = 16.2, 3.5 Hz, 1H), 2.56 (br s, 6H), 2.29 (t, *J* = 16.2 Hz, 1H), 2.05 (dd, *J* = 12.6, 3.5 Hz, 1H), 1.97−1.58 (m, 6H), 1.35−1.16 (m, 2H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.98 (s, 3H), 0.96 (s, 3H), 0.93−0.86 (m, 1H), 0.85 (s, 3H); HRMS (ESI) *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{40}NO_4$ 406.2952; found 406.2963.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Physical data; ^1H and ^{13}C spectra for all new compounds; and X-ray crystallographic data for **44**, **50**, and **58**. 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.

■ ACKNOWLEDGMENTS

We thank the Natural Sciences and Engineering Research Council (NSERC) of Canada for funding.

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