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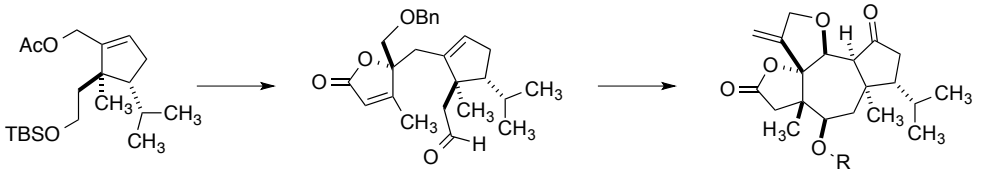


ABSTRACT: The first total synthesis of trichoaurantianolides C and D is described. An enantiocontrolled pathway leads to rapid construction of the tricyclic carbon skeleton and establishes the *trans*-dimethyl geometry of the quaternary bridgehead carbons via a reductive cyclization. Application of the π-allyl Stille cross coupling leads to a nonracemic allylic alcohol as a prerequisite for the introduction of asymmetry in the cycloheptane system. Two strategies have been examined for elaboration of the unsaturated tetrahydrofuranyl ring from a common tricyclic intermediate. These efforts reveal a number of unanticipated issues of reactivity and significant stereochemical requirements for a novel acyloin rearrangement as well as the elimination and cyclodehydration of chiral α-hydroxyketones. Key reactions leading to completion of the synthesis include the stereoselective addition of isopropenyllithium TMEDA complex and a facile chemoselective oxidation with selenium dioxide.

INTRODUCTION

Trichoaurantianolides A–D were isolated from fruiting bodies of mushrooms of *Tricholoma aurantium* and *Tricholoma fracticum* in 1995, and were independently characterized by the studies of Vidari[1] and Steglich.[2] These metabolites were assigned as

structures **1**–**4** (Figure 1) on the basis of extensive NMR studies and were presented as a previously unknown class of diterpenes described as neodolastanes. A confirmation of relative stereochemistry was achieved by an X-ray crystallographic analysis of **2**.[2]

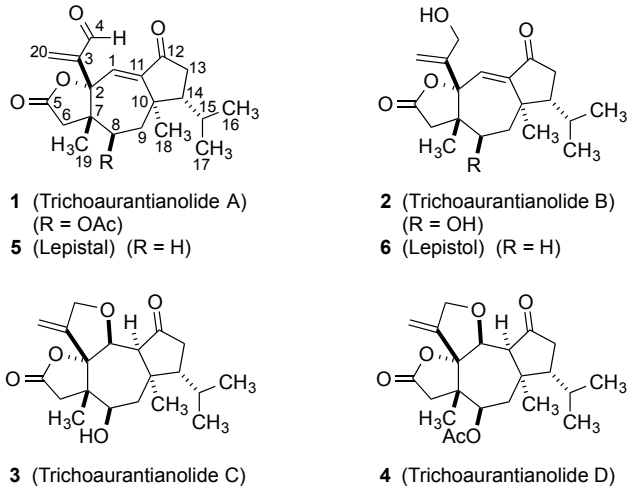
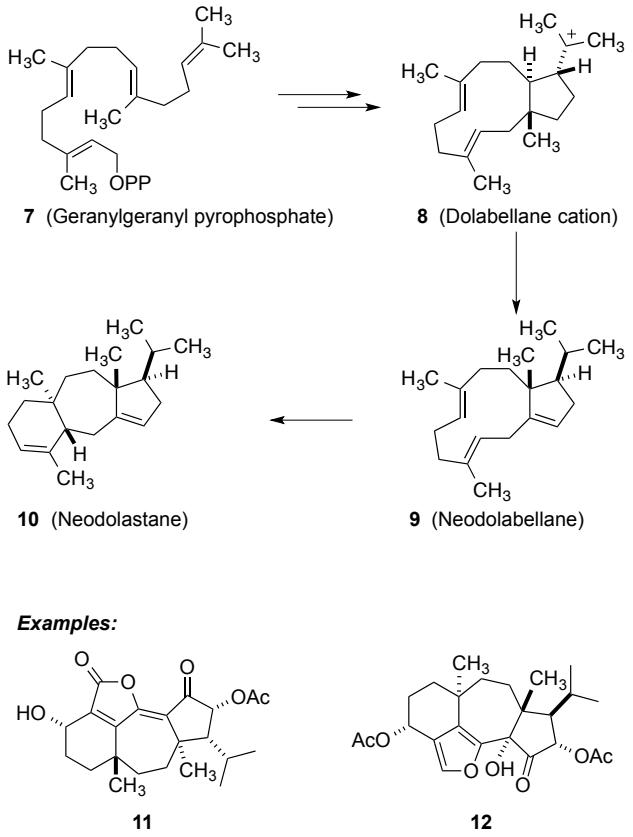


Figure 1. Trichoaurantianolides A–D and related metabolites.

Steglich and coworkers[2] also assigned the absolute stereochemistry of trichoaurantianolide B (**2**) using Hamilton's applications of linear-hypothesis testing of crystallographic data, which proved to be in agreement with the proposed configuration advanced by Vidari's assessment of the observed Cotton effects. Shortly thereafter, Sterner and coworkers[3] reported the isolation of lepistal (**5**) and lepistol (**6**), corresponding to the deoxygenated C_8 compounds of **1** and **2**, respectively. In 2003, Ohta and coworkers[4] characterized the related neodolastanes, tricholomalides A, B, and C, and concluded that these fungal metabolites had the opposite absolute configuration of the trichoaurantianolides based on their studies of circular dichroism. The latter claim is surprising since the body of evidence suggests that related diterpenes from a common biogenetic pathway in algae, fungi, liverworts, and higher plants are enantiomeric to the metabolites isolated from species of marine invertebrates.[5] Although the carbon

framework of the trichoaurantianolides and related substances differs substantially from previously known examples of the tricyclic dolastanes, it was recognized that these neodolastanes would originate from an enzymatic cyclization of geranylgeranyl pyrophosphate producing the nonracemic dolabellane cation **8** (Scheme 1). A branch of this biosynthetic pathway leads to a stereospecific backbone migration to account for

Scheme 1. Biosynthesis of neodolastanes



translocation of the bridgehead methyl substituent.[6] This event directly forms the neodolabellanes **9**, which are [9.3.0]-bicyclic diterpenes frequently isolated from various species of coral, albeit in the enantiomeric series.[7] The initiation of a transannular reaction of the neodolabellanes (**9**) yields the corresponding 5-7-6 tricyclic neodolastanes (**10**).[8] Guanacastepenes, such as **11**,[9] and heptemerones, such as **12**,[10] are primary examples of the 5-7-6 neodolastane family. Trichoaurantianolides **1**–**4** result from

subsequent oxidations and cleavage of the cyclohexenyl ring of **10** leading to the formation of novel cis-fused butyrolactones.

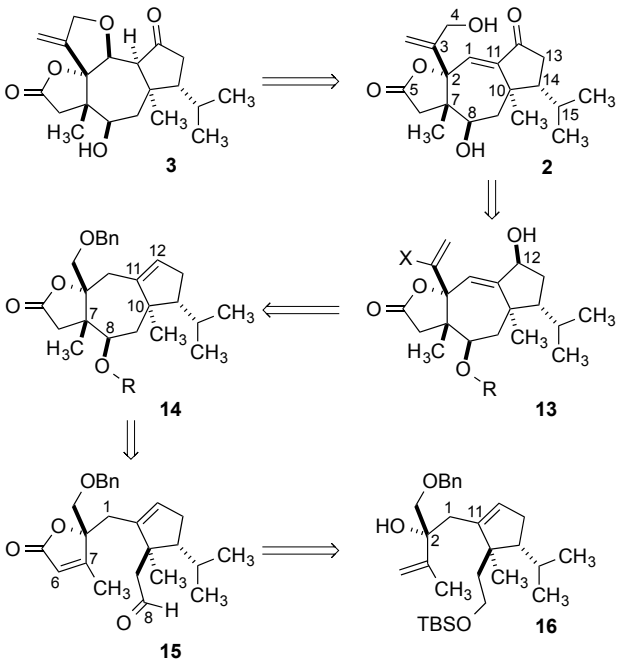
Notable biological activity has been reported for these substances. Vidari has described the antibiotic activity of **1** against *Bacillus subtilis* and *Staphylococcus aureus*.[1] Similarly, antibacterial activity is recorded for lepistal (**5**) against *Streptomyces sp.* ATCC23836 and *Bacillus subtilus* as well as antifungal activity against *Rhodotorula glutinis* and *Saccharomyces cerevisiae* S288c.[3] Initial studies of the guanacastepenes showed promising antibiotic activity against several drug-resistant strains of *Staphylococcus aureus* and *Enterococcus faecalis*,[11] but interest diminished as subsequent experimentation indicated that these compounds were responsible for lysis of red blood cells. On the other hand, the tricholomalides A–C were found to induce neurite outgrowth in rat pheochromocytoma cells at micromolar concentrations.[4] These significant biological properties enticed Danishefsky and coworkers to undertake studies leading to the total synthesis of racemic tricholomalides A and B.[12] These efforts also led to a structural revision of these natural products. Herein, a full account of our studies describe an enantiocontrolled pathway for the first total synthesis of trichoaurantianolides C and D. Our investigations have explored an intramolecular reductive cyclization strategy for construction of the central cycloheptane by tethering two nonracemic five-membered ring components. A notable application of the π-allyl Stille cross coupling provides for the efficient formation of a tetrasubstituted olefin directly leading to a Sharpless asymmetric epoxidation for the installation of the critical C-2 stereochemistry. Efforts to advance these studies have examined two strategies for stereocontrolled elaboration toward the unsaturated oxacycle of **3** and **4**. Unanticipated results are

described in these investigations, which led us to uncover several notable tactical solutions with broad implications for synthetic chemistry. Our efforts have revealed valuable insights of novel reactivity for the synthesis of similarly functionalized polycyclic systems.

RETROSYNTHETIC ANALYSIS

The densely functionalized skeleton of trichoaurantianolides C and D presents a significant challenge for synthesis. The framework contains seven contiguous asymmetric carbons, six of which are found within the seven-membered ring. In addition, three of these sites of chirality are fully substituted, and the bridgehead positions at C-7 and C-10 are quaternary carbon centers. We devised an initial strategy for the synthesis of **3** and **4** as illustrated in Scheme 2. Our retrosynthetic analysis presumed that the formation of trichoaurantianolide B (**2**) would permit studies of the intramolecular conjugate addition leading to the bridging furanyl ether in **3**. Furthermore, this prospect suggests that the stereochemistry at C-11 of **3** results by protonation of an intermediate arising from this 1,4-addition. However, conditions for the thermodynamic interconversion of the natural metabolites **2** and **3** were undefined. We rationalized that a cross coupling reaction of **13** (X = $SnBu_3$; I; or triflate) would permit conversion to the corresponding allylic ether (X = CH_2OPMB) for oxidation at C-12 and mild deprotection for studies of the final ring closure. The C=C double bond of **14** was considered as a reasonable precursor to **13**, and the removal of benzyl protection in **14** would also allow for elaboration to the activated alkenyl species.

Scheme 2. Retrosynthetic Analysis

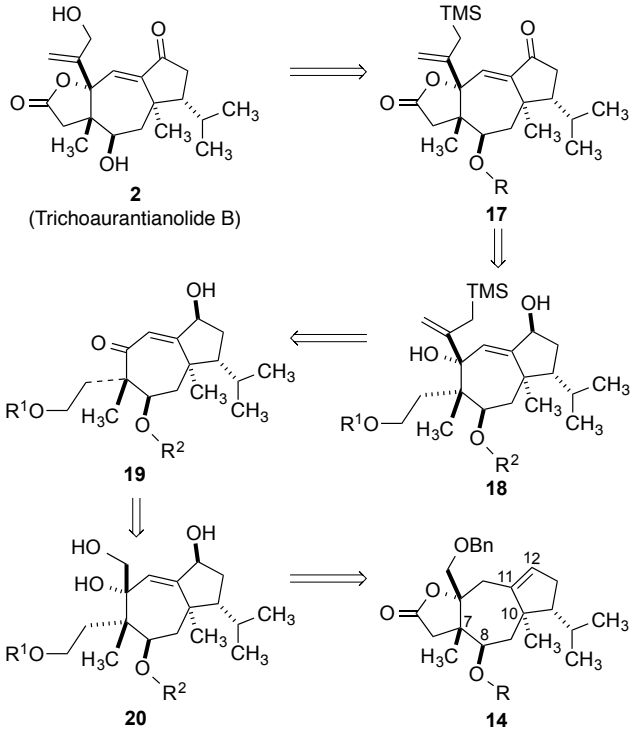


An important feature of our plan requires the introduction of the desired *anti* stereochemistry for the two chiral, fully substituted carbons at C_7 and C_{10} within the cycloheptane framework of **14**. The plan for developing the central seven-membered ring led us to explore the intramolecular reductive cyclization of **15** to give the *cis*-fused butyrolactone. The proposal would use the intact five-membered rings of **15**, incorporating crucial elements of chirality at C-2, C-10, and C-14, and our modeling predicted a minimization of steric interactions in the cyclization leading to the *anti*-dimethyl arrangement. The synthesis of butenolide **15** is envisioned by the formation of an acrylate ester of the tertiary alcohol in **16**, and the application of ring-closing metathesis (RCM).

An alternative sequence for the installation of the allylic alcohol appendage of **2** is shown in Scheme 3, and this plan envisions a stereocontrolled nucleophilic addition to the enone **19**. A known Grignard reagent, obtained from (2-bromoallyl)trimethylsilane,

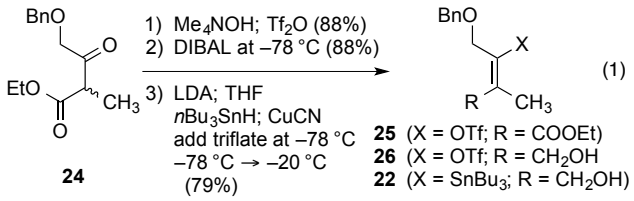
provides for 1,2-addition to **19** to yield the allylsilane **18** for an oxidation leading to butyrolactone and enone formation in the penultimate intermediate **17**. Subsequent epoxidation of **17**, followed by facile desilylation under basic or acidic conditions, would then afford a mild conversion to the allylic alcohol of **2**. The cycloheptenone **19** is available by cleavage of the 1,2-diol of **20**, which intersected with our analysis of Scheme 2 via straightforward manipulations of the key intermediate **14**. By comparison, Scheme 2 requires careful execution of steps leading to alkene **13** and a challenging cross coupling reaction to yield **2**. Scheme 3 relies on successful stereoselective addition to the functionalized enone **19**. In either case, the stereochemistry of the accessible nonracemic C-2 alcohol in **16** of Scheme 2 is effectively transferred in the construction of the quaternary C-7 and C-8 stereogenicity. Thus, our studies initially sought pathways for convenient preparation of the chiral alcohol **16**.

Scheme 3. An Alternative Plan for Formation of 2



RESULTS AND DISCUSSION

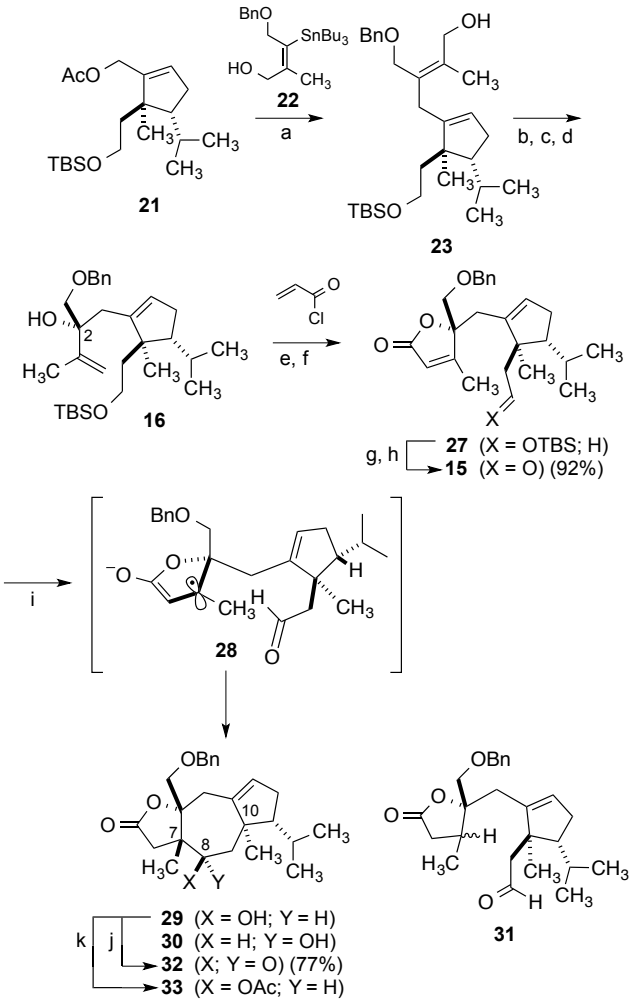
To address the issue of stereocontrol in the formation of the C-2 tertiary alcohol of **16**, our efforts developed a noteworthy π-allyl Stille cross coupling[9b,13] of the nonracemic acetate **21**[14] (Scheme 4) with the *E*-alkenyl stannane **22** to give the nonconjugated diene **23** (88%). The reaction proceeds in the presence of the unprotected allylic alcohol and yields the tetrasubstituted alkene with complete retention of olefin geometry. This protocol provides a general route for the synthesis of configurationally defined *E*- and *Z*-trisubstituted and tetrasubstituted alkenes. In fact, it has proven to be very useful in the stereocontrolled preparations of skipped 1,4-dienes as shown by additional examples reported in our preliminary studies related to this work.[13a] The stannane **22** is readily obtained from ethyl 4-benzyloxy-2-methylacetoacetate (**24**)[15] in three steps by stereocontrolled formation of the triflate **25**,[16] reduction, and replacement of the vinylic triflate of **26** with a higher-order stannylcuprate reagent.[17] The cross



coupling product **23** (Scheme 4) allows for the introduction of the desired C-2 stereochemistry by the application of a Sharpless asymmetric epoxidation (dr 87:13), and conversion of the resulting primary alcohol to the bromide for reductive elimination using *n*-BuLi at –78 °C. Alcohol **16** is purified by silica gel chromatography and alkoxide formation at 0 °C is followed by dropwise addition of acryloyl chloride. The desired acrylate (74%) is purified by flash chromatography, with the recovery of a small amount of starting alcohol (12–18%) which is subsequently resubmitted for acylation. RCM

using the Grubbs II catalyst[18] in toluene at 70 °C yields butenolide **27** (99%), and the key aldehyde intermediate **15** is then readily achieved upon TBS deprotection and Dess–Martin oxidation.[19]

Scheme 4. Synthesis of the tricyclic skeleton of 2[a]



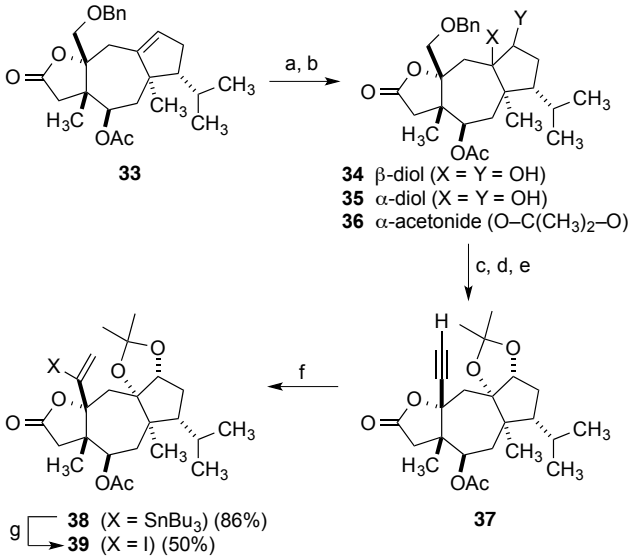
[a](a) **22**, $Pd(PPh_3)_4$ (cat), LiCl, CuCl, DMSO, 88%; (b) $Ti(O^iPr)_4$, D-DIPT, ^{t}BuOOH, 4 Å MS; 75%; (c) CBr_4, PPh_3, imid, 82%; (d) *n*-BuLi, –78 °C, 99%; (e) ^{i}PrMgCl, ClC(O)CHCH$_2$, 74%; (f) Grubbs II cat, tol, 70 °C, 99%; g) HF, MeCN, 96%; h) DMP, $NaHCO_3$, CH_2Cl_2, 92%; i) SmI_2, HMPA, THF, ^{t}BuOH, 63% (dr 66:34); j) DMP, $NaHCO_3$, CH_2Cl_2, 77%; k) Ac_2O, pyr, DMAP, CH_2Cl_2, 98%.

Studies for the formation of the seven-membered ring have focused on the use of SmI_2, which has been generally described for intramolecular reductive cyclizations to afford five- and six-membered systems.[20] In our case, preliminary studies have explored conditions for successful cyclizations to occur with HMPA as an additive in THF solutions of samarium diiodide at 22 °C by the inclusion of small quantities of *tert*-butanol.[13a,21] The C-8 diastereomeric alcohols **29** and **30** (dr 67:33) are isolated in 63% yield and are individually characterized after preparative HPLC. The coordination of additives with SmI_2 alters the oxidation potential of the *in situ* reagent[22] and may dramatically affect the course of the reduction. For example, our reactions produce substantial amounts of the reduced lactone **31** in the absence of *tert*-butanol, and no reaction is observed without the inclusion of HMPA. The tethered arrangement of the ketyl radical **28** presents a conformational bias for facial selectivity. Thus, both **29** and **30** possess 7,10-*anti*-dimethyl substitution as a result of a minimization of steric interactions leading to the *cis*-fused lactones. In large-scale reactions, the direct conversion of this mixture to the corresponding acetate or benzoate esters or TBS ethers facilitates the chromatographic separation of the major isomer **29** as a protected secondary alcohol. Oxidation of the mixture of alcohols affords a single ketone **32** as a crystalline solid (mp 94 °C–95.5 °C), and subsequent X-ray studies have unambiguously confirmed the *anti* stereochemistry of the critical quaternary chiral centers (C_7 and C_{10}).[23]

From this point, our retrosynthetic analysis of Scheme 2 incorporates a proposed oxidation of the C_{11}–C_{12} double bond for conversion to the allylic alcohol moiety of **13**. A number of strategies were examined to carry out this transformation without success. For example, epoxidation of the cyclopentene of suitably protected derivatives of **29** (R =

Ac, Bz, or TBS) was followed by typical reagents for isomerization of the epoxide to an allylic alcohol, and these attempts produced a facile backbone migration of the bridgehead methyl substituent. Subsequent efforts employed a dihydroxylation of the acetate **33** (Scheme 5) which required DMAP to activate OsO_4.[24] The procedure gave a separable mixture of β-diol **34** (75%) and α-diol **35** (25%), and each diastereomer was separately advanced to simplify our NMR analyses of reaction products. The production of diol diastereomers seemed to be of no consequence for our planned conversion to the conjugated enone **2** of Scheme 2, and we arbitrarily selected these diol isomers to investigate methodology for the elaboration of the bridgehead benzyloxymethylene substituent into the desired allylic alcohol. For example, the efficient formation of the acetonide **36** was followed by hydrogenation, Dess–Martin oxidation,[19] and reaction with the Gilbert–Seyferth reagent[25] to yield the terminal alkyne

Scheme 5. Preparation of Stille reaction precursors.[a]



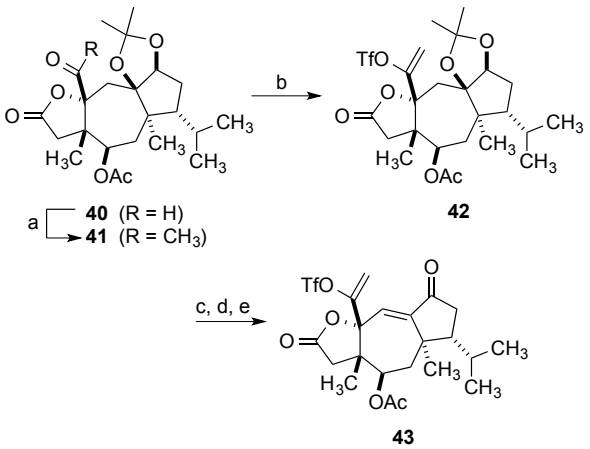
[a](a) OsO_4, DMAP, ^{t}BuOH, H_2O, 34 °C, 99% (dr 75:25); (b) $Me_2C(OMe)_2$, CSA (cat), 0 °C, 95%; (c) H_2, 10% Pd-C (cat), MeOH, 100%; (d) DMP, CH_2Cl_2, 99%; (e) $HCN_2P(O)(OMe)_2$, THF, –78 °C, 96%; (f) *fac*-

$Mo(CO)_3(CN^tBu)_3$, $n$$Bu_3SnH$, THF, hydroquinone, 55 °C, 86%; (g) I_2, CH_2Cl_2, 50%.

37. A highly regioselective, molybdenum-catalyzed hydrostannylation of the alkyne **37** was observed with *fac*-$Mo(CO)_3(CN^tBu)_3$.[26] This noteworthy stannylation proceeded in high yield, and the preparation of **38** also permitted conversion to the corresponding iodide **39** for subsequent use in Stille carbonylation reactions[27] or with a cross-coupling partner X–CH_2–OPMB (X = halide or $SnBu_3$).[28]

We utilized the β-acetonide, originating from **34** of Scheme 5, in efforts for synthesis of the analogous vinyl triflate **42** as summarized in Scheme 6. The sensitive aldehyde **40**, derived from hydrogenolysis and Dess–Martin oxidation of the β-acetonide, selectively reacted with trimethylalane in CH_2Cl_2 to produce a mixture of alcohol diastereomers (97% (dr 90:10)) for immediate oxidation to the methyl ketone **41**. Kinetic

Scheme 6. Formation of vinyl triflates 42 and 43.[a]



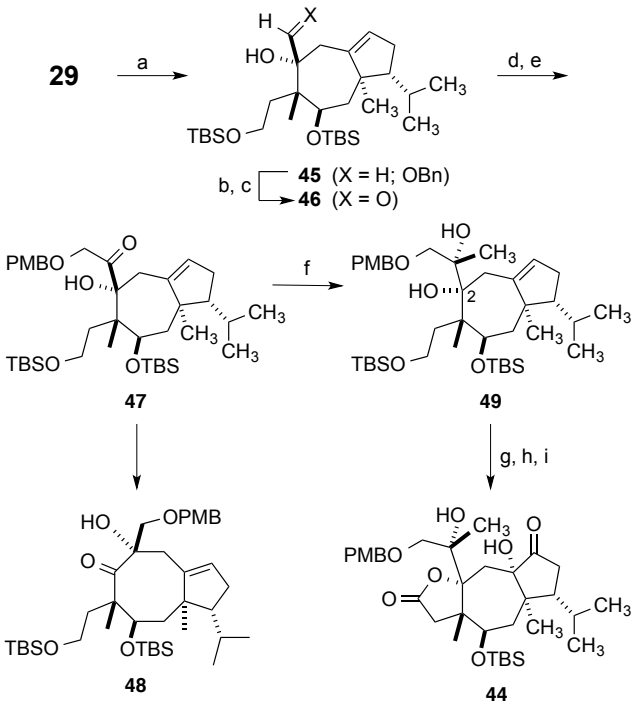
[a](a) $AlMe_3$, CH_2Cl_2, 97%, then DMP, $NaHCO_3$, CH_2Cl_2, 90%; (b) NaHMDS, THF, –78 °C, $PhNTf_2$, 56%; (c) $FeCl_3$, CH_2Cl_2, 0 °C, 63%; (d) IBX, DMSO, 50%; (e) $SOCl_2$; pyr, 50 °C, 90%.

deprotonation at –78 °C led to the unstable triflate **42**, and a portion of the material was also transformed into the enone **43** by hydrolysis of the acetonide, oxidation and elimination. With considerable efforts, we subsequently attempted cross-coupling and carbonylation reactions of **38**, **39**, **42**, and **43** using a variety of palladium catalysts in order to execute the late-stage transformations of Scheme 2. However, these studies consistently produced rapid decomposition to many polar byproducts which lacked the presence of the butyrolactone moiety.

To circumvent this difficulty, the strategy outlined in the retrosynthetic analysis of Scheme 2 was amended to feature the formation of diol **44** of Scheme 7 for a proposed double elimination to install a cyclic enone as well as the desired terminal alkene. Our plans for a selective nucleophilic addition to ketone precursors, such as **41**, could not be achieved in the presence of the carbonyl of the butyrolactone. Thus, a reduction of **33** ($LiAlH_4$; Et_2O) followed by TBS protection (TBSOTf; 2,6-lutidine; CH_2Cl_2) yielded the tertiary alcohol **45** (Scheme 7). Reductive debenzylation and Swern oxidation[29] gave the α-hydroxy aldehyde **46** which was converted to ketone **47** in two steps. First, the formation and addition of the lithium reagent generated by transmetalation of $PMBOCH_2SnBu_3$ was carried out at –78 °C to avoid the Wittig rearrangement of this reactive carbanion, and subsequent oxidation uneventfully gave **47**. Reactions of the hindered ketone **47** with excess methylmagnesium bromide (5.0 equiv) proceeded very slowly at room temperature and led to the isolation of varying amounts of the acyloin rearrangement product **48** as a single diastereomer along with the desired **49** as well as the recovered ketone. The use of methylcerium reagent (CH_3Li; $CeCl_3$) favored formation of the eight-membered ketone **48**, which is produced by a selective migration of the

neighboring methylene. In principle, the reversible isomerization of the α-ketol of **47** to the eight-membered cyclooctane **48** should reflect the relative stabilities of these cyclic systems. In practice, the resubmission of **48** to the reaction conditions led to the recovery of starting material and no evidence for the formation of **47** or the corresponding alcohol **49**.

Scheme 7. Double elimination approach. [a]



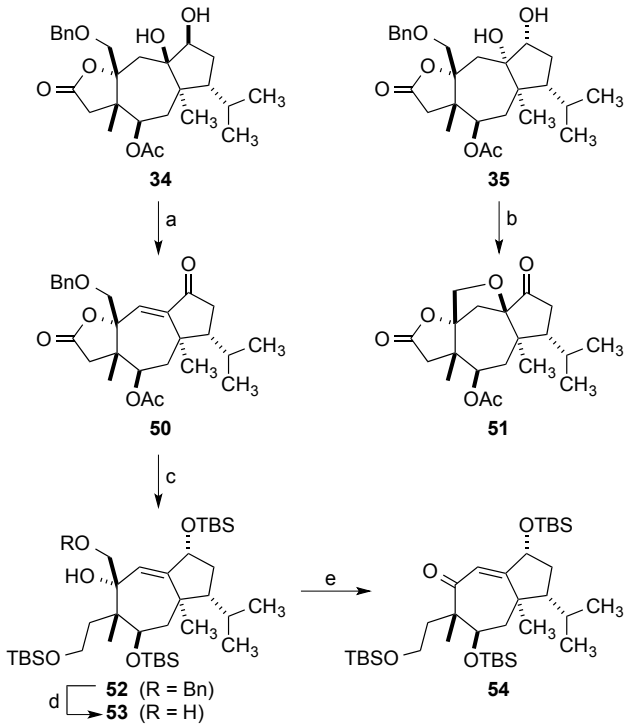
[a](a) $LiAlH_4$, Et2O, then TBSOTf, 2,6-lutidine, CH_2Cl_2 (85%); b) Na, NH_3, THF, –78 °C, 93%; (c) $(COCl)_2$, DMSO, CH_2Cl_2, then Et_3N at –55 °C, 98%; (d) $PMBOCH_2SnBu_3$, *n*BuLi, THF, –78 °C, 68% (dr 95:5, 82% brsm); (e) $(COCl_2)$, DMSO, CH_2Cl_2, then Et_3N at –55 °C, 93%; (f) MeLi, Et_2O, –78 °C to rt, 40% (83% brsm); (g) OsO_4, DMAP, ^{t}BuOH, H_2O, 80% (dr 84:16); (h) TBAF, AcOH (2.5:1) in THF, 90%; (i) TEMPO, NaOCl, KBr, $NaHCO_3$, 84%.

This result indicates an unexpected thermodynamic preference for the highly substituted cyclooctane system. Subsequently, we found that the use of newly purchased bottles of methyllithium in ether (15 equiv) afforded modest yields of the desired diol **49** as a single

diastereomer (40% yield; 83% brsm) without formation of the ketone **48**.[30] The three-step conversion to the desired α-ketol **44** was achieved by the recycling of ketone **47** through this problematic transformation as well as a noteworthy improvement in the stereoselectivity of the dihydroxylation of the C-11/C-12 olefin (dr 84:16). We were poised to examine the final stages of our total synthesis by the elimination of two equivalents of water from **44**. However, various procedures for effecting dehydration, including the use of the Martin sulfurane,[31] Burgess reagent,[32] thionyl chloride or mesyl chloride, led to a multitude of products.

Problems encountered in these elimination attempts led us to investigate the stereochemistry of the C-11/C-12 diol and its implications in subsequent reactions. Experiments independently examined β-diol **34** and α-diol **35**, as shown in Scheme 8.

Scheme 8. Studies leading to ketone 52.[a]



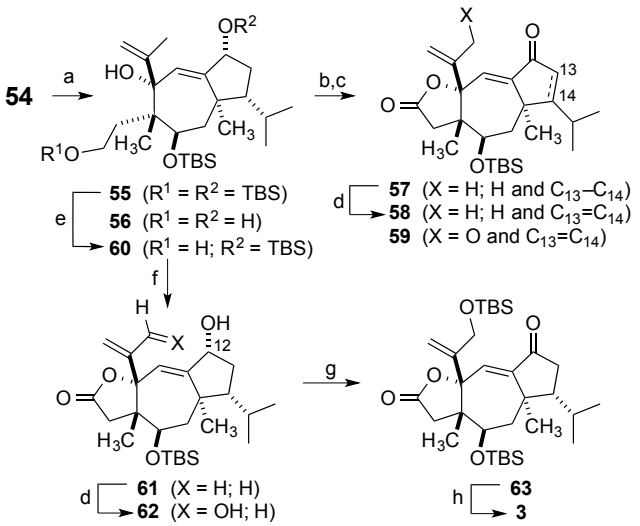
[a](a) TEMPO, NaOCl, KBr, $NaHCO_3$, 90%, then $SOCl_2$, pyr, 55 °C, 64%; (b) TEMPO, NaOCl, KBr, $NaHCO_3$, 82%, then $SOCl_2$, pyr, 55 °C, 50%; (c) Red-Al, tol –78 °C □ +65 °C, then: TBSOTf, CH_2Cl_2, 2,6-lutidine, 82%; (d) LiDBB, THF, –78 °C, 77%; (e) $Pb(OAc)_4$, K_2CO_3, CH_2Cl_2, 0 °C, 89%.

TEMPO oxidation[33] of **34** led to the *syn*-elimination of the α-hydroxyketone using thionyl chloride to afford the enone **50**. However, application of these conditions to diastereomeric **35** resulted in formation of the bridging ether of the *trans*-fused ketone **51**. Formation of **51** was minimized by adaptation of a published procedure for reaction of the starting ketol with 1,1′-thiocarbonyldiimidazole followed by *syn*-elimination in *o*-dichlorobenzene at reflux.[8a] The elevated temperature and prolonged reaction time gave only modest yields of **50** with considerable decomposition using this diastereomer. Nevertheless, sufficient quantities of the desired enone **50** were available from the major diol **34**, and the enone **50** was advanced using the reduction and protection conditions as previously described in Scheme 7 to produce **52**. Although the Birch conditions for removal of the benzyl ether of **52** resulted in reductive cleavage of the allylic silyl ether, our use of the radical anion of 4,4′-di-*tert*-butylbiphenyl (LiDBB)[34] gave the desired diol **53**. Subsequently, an efficient oxidative cleavage in CH_2Cl_2 using lead tetraacetate yielded the seven-membered enone **54** in 89% yield.

In response to the difficulties encountered in our attempts to functionalize three contiguous, fully-substituted carbons as illustrated in **44** of Scheme 7 (C-2, C-3, and C-7) we devoted increasing attention to the proposed strategy of Scheme 3. This approach allowed for direct introduction of a functionalized allylic alcohol equivalent into the C-2 carbonyl of the cycloheptenone precursor. However, the diastereofacial selectivity of the anticipated nucleophilic addition was our primary concern. In the event, our studies of

nucleophilic addition using an excess of Grignard reagent (20 equiv) derived from (2-bromoallyl)trimethylsilane completely failed to produce a reaction with enone **54** at elevated temperatures (50 °C), whereas the addition of 2-propenyllithium (15 equiv) to **54** at –78 °C provided a mixture of C-2 diastereomers in modest yield (dr 2:1). Fortunately, significant improvement of this reaction was achieved by precomplexation with tetramethylethylenediamine (TMEDA)[35] in ether at –78 °C leading to the desired C-2 tertiary alcohol **55** (90% yield (dr 95:5)) (Scheme 9). Deprotection gave an intermediate triol **56** which afforded the lactone **57** upon oxidation. Thus, a single allylic

Scheme 9. Completion of the total synthesis.[a]



[a](a) isopropenylbromide, ^{t}BuLi, Et_2O, TMEDA (1 eqiv) at –78 C, 90% (dr 95:5); (b) TBAF, AcOH (2.5:1), THF, 87%; (c) TPAP, NMO, CH_2Cl_2, 80%; (d) sublimed SeO_2, dioxane, 65 °C, 60% (93% brsm); (e) TBAF, AcOH (1:1), THF, 96%; (f) TPAP, NMO, 90%, then, TBAF, AcOH (2.5:1), 88%; (g) TBSCl, Et_3N, CH_2Cl_2, 62% (84% brsm), then, TPAP, NMO, 92%; h) TAS-F, DMF, 75%.

hydroxylation was required to accomplish our goals.[36] Unfortunately, the completion of the total synthesis was confounded by a facile SeO_2 reaction of **57** which readily introduced the cyclopentenone unsaturation of **58**. A selective reaction could not be

achieved since formation of the C_{13}–C_{14} double bond occurred at a faster rate than the allylic hydroxylation. The observed dehydrogenation of **57** is particularly effective because of the ease of enolization of the starting ketone, as well as the resulting stereochemistry of the intermediate selenoxide that allows for an efficient *syn*-elimination. Further oxidation to the C-4 aldehyde **59** also proceeded at a comparable rate. Alternatively, attempts to effect the desired allylic oxidation using singlet oxygen failed.[37] Moreover, reasonable alternatives for elaboration of **54** using the lithium reagent derived from 3-trimethylsilyl-2-bromo-1-propene with TMEDA complexation did not proceed.

We overcame these difficulties by the selective cleavage of the primary OTBS ether of **55** to give **60** of Scheme 9 followed by oxidation to produce the butyrolactone which was immediately treated with TBAF to yield allylic alcohol **61**. The SeO_2 oxidation of **61** gave the desired **62** together with the related aldehyde (X = O). These reactions were halted prior to the observation of a slower oxidation leading to formation of the C-12 ketone. In practice, our reactions were quenched with a Luche reduction,[38] which provided the diol **62** in 60% yield (93% brsm) after flash column chromatography with an additional 33% of recovered **61**.

Trichoaurantianolide C (**3**) is cleanly produced by the provisional TBS protection of the primary allylic alcohol of **62** and oxidation to give the enone **63**. Our initial plan to explore conditions which trigger the internal conjugate addition for interconversions of trichoaurantianolides B (**2**) and C (**3**) did not develop as expected. Indeed, global deprotection with TAS-F[39] led exclusively to the ring-closed natural product, trichoaurantianolide C (**3**). Trichoaurantiolide D (**4**) was obtained from synthetic **3** by

acetylation (Ac_2O; DMAP; CH_2Cl_2 (80%)). The total synthesis of **3** and **4** was confirmed by comparisons of proton and carbon NMR data and optical rotations with reported characterizations of the authentic natural metabolites.[40]

CONCLUSION

In summary, the first enantiocontrolled total synthesis of trichoaurantianolides C and D has been achieved. Trichoaurantianolide C (**3**) was obtained in 21 steps from the known allylic acetate **21**, and these efforts confirm the original assignment of absolute configuration by Steglich and Vidari. The stereocontrolled route features a samarium diiodide reductive cyclization to establish the *anti*-dimethyl configuration at C_7 and C_{10} quaternary carbons. Studies demonstrate a facile π-allyl Stille coupling for efficient stereocontrolled preparation of tetrasubstituted alkenes in skipped 1,4-dienes. Our investigations have also uncovered several aspects of unexpected reactivity in the formation and reactivity of α-ketols in synthesis, including stereoselective elimination reactions to yield the corresponding enones, and nucleophilic addition reactions of α-hydroxy aldehyde and α-hydroxy ketone substrates, as well as a stereoselective acyloin rearrangement for ring expansion to yield a highly substituted cyclooctanone. Our results demonstrate improved diastereoselectivity by precomplexation with TMEDA in the course of nucleophilic addition of an alkenyllithium reagent. Overall, these efforts provide new insights for the synthesis of polycyclic terpenes.

EXPERIMENTAL SECTION

General Methods. All reactions were performed in flame-dried or oven-dried glassware under argon atmosphere. All non-volatile samples were pumped to constant weight at ambient temperature (0.2-0.1 mmHg) following removal of solvents by rotary

evaporation. Non-aqueous reagents were transferred using syringe techniques under argon atmosphere. Bulk grade hexanes and ethyl acetate for chromatography were distilled prior to use. Tetrahydrofuran (THF), dimethylformamide (DMF), toluene, acetonitrile, diethyl ether (Et_2O) and dichloromethane (DCM) were obtained anhydrous by degassing with argon and then passing through activated alumina columns to remove water. Triethylamine (Et_3N) and diisopropylethylamine (DIPEA) were distilled from CaH_2 under dry argon immediately before use. Commercial reagents were used as obtained unless otherwise specified. Air-sensitive reagents were handled inside a glove box under a dry argon atmosphere.

Reactions were monitored by standard thin-layer chromatography (TLC) techniques using silica gel 60 F254 pre-coated plates (0.25 mm thickness). Following the run, TLC plates were visualized under UV light and/or by appropriate stains (p-anisaldehyde or cerric ammonium nitrate or potassium permanganate). Flash column chromatography was performed with flash silica gel (ultra-pure 40–63 μm)

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on 400 MHz and 500 MHz instruments. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were measured using 101 MHz and 125 MHz instruments. NMR coupling constants and signal patterns are reported as *J* values in Hz and δ values in parts per million (ppm). ^{1}H and ^{13}C NMR spectra are internally referenced to residual solvent signals ($CDCl_3$ referenced to δ 7.26 and 77.16 ppm respectively). The following abbreviations were used to indicate the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. High resolution mass measurements (HRMS) were obtained using ESI time-of-flight (TOF) instrumentation. Optical rotation data were obtained on a polarimeter and are reported in

terms of degree of rotation of plane-polarized light. IR spectra were recorded on a FT-spectrometer and are reported in terms of frequency of absorption (cm^{-1}).

*(E)-ethyl-4-(benzyloxy)-2-methyl-3-(tributylstannyl)but-2-enoate (**25**).* To a 3-neck round-bottom flask with stir bar, ethyl 4-(benzyloxy)-2-methyl-3-oxobutanoate[15] (2.05g, 8.19 mmol), hexanes (41 mL), and water (11 mL) were added. The resulting solution was cooled to 5 °C (internal temp) and tetramethylammonium hydroxide (25 wt % in water, 14.7 mL, 41 mmol) was added dropwise. The reaction was vigorously stirred for 10 min. Triflic anhydride (3.44 mL, 20.48 mmol) was then added dropwise, taking care to maintain an internal temperature of +5 to +15 °C. After 25 min, water (10 mL) was added and the reaction was warmed to rt. The organic layer was separated and the aqueous layer was washed with EtOAc (3 x 20 mL). The combined organic layers were washed with water (40 mL), brine (30 mL), dried over $MgSO_4$, and concentrated *in vacuo* to provide a yellow oil. The crude product was purified by flash column chromatography (Hexanes/EtOAc (15:1)) to afford **25** (2.85 g, 88%) as a clear colorless oil: R_f 0.26 (Hexanes/EtOAc (10:1)); IR (film) 3066, 2984, 2872, 1724, 1663, 1455, 1419, 1283, 1213, 1140, 1069, 930, 853, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.30 (m, 5H), 4.58–4.57 (m, 2H), 4.55 (s, 2H), 4.21 (q, J = 7.2 Hz, 2h), 2.05 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 152.4, 137.1, 128.4, 127.9, 125.9, 118.4 (q, J = 3.2 Hz), 72.7, 66.2, 61.9, 14.0, 13.9; HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $C_{15}H_{17}O_6SF_3Na$ 405.0596; found, 405.0581.

*(E)-4-(benzyloxy)-2-methyl-3-(tributylstannyl)but-2-en-1-ol (**26**).* A solution of **25** (9.70 g, 25.4 mmol) in THF (508 mL) was cooled to –78 °C and was treated with a dropwise addition of DIBAL-H (1M in hexanes, 63.4 mL, 63.4 mmol). After 90 min, the

reaction was allowed to warm to 0 °C. The reaction was then recooled to –78 °C and an additional portion of DIBAL-H (1M in hexanes, 15.2 mL, 15.2 mmol) was introduced. After 30 min, the reaction was allowed to warm to 0 °C, quenched with saturated aqueous Rochelle's salt (100 mL) and warmed to rt. After stirring for 2 h, the organic layer was separated and the aqueous layer was washed with CH_2Cl_2 (100 mL), and Et_2O (3 x 100 mL). The organic extracts were then combined, washed with brine (50 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to provide a yellow oil. The crude product was purified by flash column chromatography (gradient elution Hexanes/EtOAc (7:3 to 1:1)) to afford **26** (7.63 g, 88%) as a clear colorless oil: R_f 0.20 (Hexanes/EtOAc (4:1)); IR (film) 3413, 2929, 2873, 1689, 1410, 1211, 1141, 1068, 918, 821 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.32 (m, 5H), 4.54 (s, 2H), 4.26 (s, 2H), 4.15 (d, J = 6.4 Hz, 2H), 1.95 (s, 3H), 1.82 (t, J = 6.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.1, 136.8, 134.6, 128.6, 128.2, 128.0, 118.4 (q,–CF_3), 72.7, 65.9, 62.2, 15.1; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{13}H_{15}O_5SF_3Na$ 363.0490; found, 363.0480.

*(E)-4-(benzyloxy)-2-methyl-3-(tributylstannyl)but-2-en-1-ol (**22**).* A solution of diisopropylamine (8.55 mL, 60.8 mmol) in THF (168 mL) was cooled to –78 °C and treated with dropwise addition of *n*BuLi (2.46M in hexanes, 24.7 mL, 60.8 mmol). After 1 h, nBu$_3$SnH (13.7 mL, 51.48 mmol) was added dropwise via syringe. After 30 min, anhydrous CuCN (2.31 g, 25.9 mmol) was added in one portion and the cold bath was removed. Within ten min, the cloudy yellow suspension became a clear orange solution, and the reaction was cooled back to –78 °C. Vinyl triflate **26** (4.00 g, 11.7 mmol) in THF (8 mL) was added dropwise over 15 min, and the reaction was allowed to warm slowly to –20 °C over 1.5 h. The reaction was quenched at –20 °C with a solution of 90% saturated

aqueous NH_4Cl/10% NH_4OH (200 mL), and the reaction was warmed to rt, and stirred for 30 min. Et_2O (100 mL) was added and the organic layer was separated. The aqueous extract was washed with Et_2O (3 x 100 mL), and the organic extracts were combined, washed with brine (75 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to provide a yellow oil. The crude product was purified by flash column chromatography (gradient elution Hexanes/EtOAc (8:1 to 5:1)) to afford **22** (4.45 g, 79%) as a clear colorless oil: R_f 0.5 (Hexanes/EtOAc (4:1); IR (film) 3374, 2954, 2870, 2853, 1615, 1454, 1376, 1100, 1070, 1028 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.26 (m, 5H), 4.49 (s, 2H), 4.17 (t, J_{Sn-H} = 23.5 Hz, 2H), 4.11 (d, J = 6.1 Hz, 2H), 2.02 (t, J = 6.1 Hz, 1H), 1.94–1.91 (m, 3H), 1.52–1.28 (m, 12H), 0.99–0.86 (m, 15H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.0, 138.8, 138.1, 128.3, 127.8, 127.6, 72.4, 71.1, 62.7, 29.1, 27.4, 24.3, 13.7, 10.8; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{24}H_{42}O_2SnNa$ 505.2104; found, 505.2101.

*((2R,3S)-3-((benzyloxy)methyl)-3-(((4R,5R)-5-(2-((tert-butyldimethylsilyl)oxy)ethyl)-4-isopropyl-5-methylcyclopent-1-en-1-yl)methyl)-2-methyloxiran-2-yl)methanol (**23**).* To a 200 mL round-bottom flask, LiCl (511 mg, 12.1 mmol) was added and flame-dried under vacuum. Once cooled the flask was charged with $Pd(PPh_3)_4$ (232 mg, 0.2 mmol) and CuCl (671 mg, 10.1 mmol). After flushing the flask with argon for five min, a solution of allylic acetate **21**[14] (712 mg, 2.61 mmol) in dry DMSO (20.2 mL) was added followed by vinyl stannane **22** (1.26 g, 2.61 mmol) in DMSO (20 mL). The resulting reaction mixture was degassed (3x) by the freeze-pump-thaw method. The reaction was stirred for one h at rt, and then heated at 50 °C for 36 h. After cooling to rt, water (400 mL) and Et_2O (200 mL) were added, and the organic

extracts were separated. The aqueous layer was extracted with Et_2O (2 x 200 mL) and the combined organic layers were washed with brine (40 mL) and dried over Na_2SO_4. Concentration *in vacuo* provided a brown oil. The crude product was purified by flash column chromatography (Hexanes/EtOAc/Et_3N (85:10:5)) to afford **23** (861 mg, 88%) as a clear colorless oil: R_f 0.37 (Hexanes/EtOAc (4:1)); $[\alpha]_D^{20}$ –1.4 (*c* 0.4, $CHCl_3$); IR (film) 3421, 2955, 2857, 1472, 1255, 1092, 1006, 935, 775 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40–7.28 (m, 5H), 5.11 (s, 1H), 4.51 (d, *J* = 12.5 Hz, 1H), 4.47 (d, *J* = 12.5 Hz, 1H), 4.16–4.06 (m, 2H), 4.00 (d, *J* = 10.0 Hz, 1H), 3.91 (d, *J* = 10.0 Hz, 1H), 3.71 (td, *J* = 9.7, 6.5 Hz, 1H), 3.47 (td, *J* = 10.0, 4.7 Hz, 1H), 2.73 (d, *J* = 17.0 Hz, 1H), 2.66 (d, *J* = 16.5 Hz, 1H), 2.25–2.16 (m, 1H), 2.04 (t, *J* = 6.2 Hz, 1H), 1.87–1.62 (m, 5H), 1.78 (s, 3H), 1.01 (d, *J* = 6.0 Hz, 3H), 0.89 (s, 9H), 0.88 (s, 3H), 0.86 (d, *J* = 6.1 Hz, 3H), 0.04 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.3, 138.0, 137.0, 132.1, 128.4, 127.9, 127.7, 123.3, 72.7, 69.7, 64.0, 61.0, 51.4, 50.0, 40.6, 34.5, 30.2, 29.4, 26.0, 22.6, 22.3, 19.8, 18.4, 17.6, –5.1, –5.2; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{30}H_{50}O_3SiNa$ 509.3427; found, 509.3412.

*(Z)-4-(benzyloxy)-3-(((4R,5R)-5-(2-((tert-butyldimethylsilyl)oxy)ethyl)-4-isopropyl-5-methylcyclopent-1-en-1-yl)methyl)-2-methylbut-2-en-1-ol (**23a**).* A heterogeneous solution of D–DIPT (231 mg, 0.986 mmol), CH_2Cl_2 (16 mL) and 4Å powdered molecular sieves (400 mg) was cooled to –20 °C and treated with $Ti(O^iPr)_4$ (243 µl, 0.822 mmol) dropwise. After 1 h, ^{t}BuOOH (457 µl, 3.6M in toluene, 1.64 mmol) was added dropwise. After 1 h, the reaction was cooled to –40 °C and a solution of **23** (400 mg, 0.822 mmol) in CH_2Cl_2 (3 mL) was introduced via syringe followed by a CH_2Cl_2 (3 mL) syringe wash. The reaction was allowed to stir for 40 h, then warmed to –

35 °C, and quenched with a 30% aqueous NaOH solution saturated with NaCl (1.3 mL) followed by H_2O (10 mL). The reaction mixture was warmed to rt, with stirring for 1.5 h. The mixture was then filtered through Celite, and the filtrate was diluted with H_2O (50 mL) and CH_2Cl_2 (50 mL). The organic layer was then separated and the aqueous layer was washed with CH_2Cl_2 (2 x 50 mL). The organic extracts were combined, washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to provide a cloudy yellow oil. The product was purified by flash column chromatography (Hexanes/EtOAc (5:1)) to provide **23a** (331 mg, 75%) as a 87:13 mixture of inseparable epoxy alcohol diasteromers. R_f 0.30 (Hexanes/EtOAc (4:1)); $[\alpha]_D^{20}$ –0.6 (*c* 3.62, $CHCl_3$); IR (film) 3454, 2955, 2896, 1472, 1256, 1090, 835, 775 cm^{-1}. The major diastereomer was characterized as follows: ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.29 (m, 5H), 5.41 (s, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.43 (d, *J* = 12.0 Hz, 1H), 3.80–3.54 (m, 6H), 3.43 (td, *J* =9.7, 4.8, 1H), 2.49 (d, *J* = 17.9 Hz, 1H), 2.42 (d, *J* = 8.9, 4.5 Hz, 1H), 2.13 (dd, 17.1, 1.9 Hz, 1H), 1.95–1.90 (m, 1H), 1.83–1.60 (m, 4H), 1.45 (s, 3H), 1.02 (d, *J* = 6.1 Hz, 3H), 0.89–0.86 (m, 15H), 0.03 (s, 6H); ^{13}C (126 MHz, $CDCl_3$) δ 145.3, 137.3, 128.5, 128.0, 127.9, 124.9, 73.7, 72.0, 66.6, 65.5, 64.2, 60.5, 50.8, 49.9, 40.5, 35.0, 29.9, 29.3, 26.0, 22.6, 22.4, 19.5, 18.3, 17.0, –5.2; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{30}H_{50}O_4SiNa$ 525.3376; found, 525.3370.

*(2-((1R,5R)-2-(((2S,3S)-2-((benzyloxy)methyl)-3-(bromomethyl)-3-methyloxiran-2-yl)methyl)-5-isopropyl-1-methylcyclopent-2-en-1-yl)ethoxy)(tert-butyl)dimethylsilane **(23b)**.* To a solution of epoxyalcohol **23a** (1.18 g, 2.35 mmol) in CH_2Cl_2 (47 mL) at 0 °C was added imidazole (959 mg, 14.1 mmol), and PPh_3 (2.34 g, 7.05 mmol) followed by CBr_4 (2.34 g, 7.05 mmol). The reaction flask was protected from light and stirred for 30

min at which time the solvent was then removed *in vacuo* to provide a white solid. The crude product was purified by flash column chromatography (Hexanes/EtOAc (20:1)) affording bromide **23b** (1.06 g, 82%) as a 87:13 mixture of inseparable diastereomers as a clear, yellow oil. R_f 0.41 (Hexanes/EtOAc (10:1)); $[\alpha]_D^{20}$ –18.7 (*c* 2.97, $CHCl_3$); IR (film) 2955, 2857, 1470, 1373, 1255, 1092 cm^{-1}; The major diastereomer was characterized as follows: ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.28 (m, 5H), 5.57 (s, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 3.91 (d, *J* = 11.0 Hz, 1H), 3.71–3.63 (m, 1H), 3.56 (d, *J* = 10.4 Hz, 1H), 3.48 (d, *J* = 11.0 Hz, 1H), 3.44–3.37 (m, 1H), 3.39 (d, *J* = 10.5 Hz, 1H), 2.82 (d, *J* = 17.4 Hz, 1H), 2.36–2.25 (m, 1H), 1.95–1.90 (m, 1H), 1.86 (d, *J* = 17.5 Hz, 1H), 1.84–1.58 (m, 4H), 1.52 (s, 3H), 1.02 (d, *J* = 5.9 Hz, 3H), 0.89–0.88 (m, 15H), 0.03 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.2, 137.8, 128.3, 127.7, 127.6, 124.0, 73.3, 69.0, 67.8, 62.6, 60.6, 50.7, 50.1, 40.6, 36.4, 35.1, 29.3, 28.7, 26.0, 22.5, 22.4, 19.5, 18.3, 17.3, –5.2, –5.3; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{30}H_{49}O_3SiBrNa$ 587.2532; found, 587.2533.

*(R)-1-(benzyloxy)-2-(((4R,5R)-5-(2-((tert-butyldimethylsilyl)oxy)ethyl)-4-isopropyl-5-methylcyclopent-1-en-1-yl)methyl)-3-methylbut-3-en-2-ol (**16**).* A solution of bromide **23b** (2.66 g, 4.71 mmol) in THF (79 mL) was cooled to –100 °C in a hexanes/N_2 (l) bath and treated by the dropwise addition of *n*BuLi (2.86 mL, 2.47 M in hexanes, 7.05 mmol). The reaction was stirred for 25 min with a cooling bath temperature no higher than –85 °C. The reaction was then allowed to warm to –78 °C and then was quenched with pH 7 buffer (22 mL) and warmed to rt. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were dried with Na_2SO_4, and concentrated *in vacuo* to provide a clear, colorless oil.

Purification by flash column chromatography (Hexanes/EtOAc (10:1)) provided **16** (1.85 g) and a second fraction of **16** and ***epi*-16** (406 mg) as a 1:1 mixture of C-2 alcohol diastereomers as clear colorless oils which were resubjected to chromatography to obtain additional quantities of pure **16**. Overall yield of **16** and ***epi*-16:** 99%. This purification also afforded a small amount of pure ***epi*-16** for characterization purposes. Data for characterization of **16**: R_f 0.44 (Hexanes/EtOAc (10:1)); $[\alpha]_D^{20}$ –18.7 (*c* 0.34, $CHCl_3$); IR (film) 2953, 3928, 2856, 1462, 1255, 1091 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.26 (m, 5H), 5.67 (s, 1H), 5.15 (s, 1H), 4.97 (s, 1H), 4.57 (s, 2H), 3.67 (td, *J* = 9.8, 6.2 Hz, 1H), 3.50–3.45 (m, 1H), 3.47 (d, *J* = 9.0 Hz, 1H), 3.42 (d, *J* = 9.0 Hz, 1H), 2.62 (s, 1H), 2.29–2.20 (m, 2H), 2.18–2.14 (d, *J* = 16.2 Hz, 1H), 1.91–1.83 (m, 1H), 1.82–1.74 (m, 1H), 1.72 (s, 3H), 1.71–1.58 (m, 3H), 1.00 (d, *J* = 5.9 Hz, 3H), 0.88 (s, 9H), 0.87–0.83 (m, 6H), 0.03 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.4, 144.3, 138.1,128.4, 127.7, 124.1, 112.3, 76.9, 76.5, 73.5, 60.5, 50.5, 50.3, 40.7, 35.0, 32.4, 29.2, 26.0, 22.7, 22.2, 20.0, 19.9, 18, –5.2; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{30}H_{50}O_3SiNa$ 509.3427; found, 509.3404. Data for characterization of ***epi*-16**: R_f 0.40 (Hexanes/EtOAc (10:1)); $[\alpha]_D^{20}$ +12.9 (*c* 0.35, $CHCl_3$); IR (film) 2953, 2929, 2857, 1462, 1365, 1255, 1091 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 5H), 5.65 (s, 1H), 5.18 (s, 1H), 4.98 (s, 1H), 4.58 (s, 2H), 3.67 (td, *J* = 9.7, 6.3 Hz, 1H), 3.45 – 3.40 (m, 1H), 3.46 (d, *J* = 9.2 Hz, 1H), 3.41 (d, *J* = 9.2 Hz, 1H), 2.51 (s, 1H), 2.30–2.19 (m, 2H), 1.96–1.85 (m, 1H), 1.83–1.55 (m, 5H), 1.77 (s, 3H), 1.00 (d, *J* = 6.0 Hz, 3H), 0.92–0.82 (m, 15H), 0.03 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.9, 144.7, 138.2, 128.4, 127.6, 124.0, 112.3, 76.8, 76.5, 73.5,60.7, 50.7, 50.3, 40.7,35.1, 32.4, 29.3, 26.0,22.7, 22.3, 20.1, 19.9, 18.4, –5.2 (2 C); HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{30}H_{50}O_3SiNa$ 509.3427; found, 509.3422.

*(R)-1-(benzyloxy)-2-(((4R,5R)-5-(2-((tert-butyldimethylsilyl)oxy)ethyl)-4-isopropyl-5-methylcyclopent-1-en-1-yl)methyl)-3-methylbut-3-en-2-yl acrylate (**16a**).* A solution of alcohol **16** (643 mg, 1.32 mmol) in THF (13 mL) was cooled to 0 °C and was treated by dropwise addition of isopropylmagnesium chloride (1.5M in Et_2O, 1.06 mL, 1.59 mmol) over five min and then allowed to warm to rt. After 1 h, acryloyl chloride (644 µl, 7.92 mmol) was added dropwise which turned the solution from colorless to a clear yellow color, and this mixture was stirred for an additional 16 h at rt. The reaction was cooled to 0 °C and quenched with saturated aqueous $NaHCO_3$ (10 mL). After warming to rt, CH_2Cl_2 (10 mL) and water (10 mL) were added and the layers were separated. The aqueous layer was washed with CH_2Cl_2 (2 x 15 mL), and the organic layers were combined. The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to provide a clear yellow oil. Purification by flash column chromatography (Hexanes/EtOAc (30:1)) provided the corresponding acrylate **16a** (526 mg, 74%, 90% brsm) as a clear colorless oil and the recovered allyl alcohol **16** (117 mg, 18%)). Data for characterization of the ester **16a**: R_f 0.45 (Hexanes/EtOAc (10:1)); $[\alpha]_D^{20}$ –6.9 (*c* 0.29, $CHCl_3$); IR (film) 2955, 2855, 1725, 1472, 1195, 1090 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.24 (m, 5H), 6.34 (m, 1H), 6.10 (m, 1H), 5.77 (m, 1H), 5.52 (s, 1H), 5.10 (s, 1H), 5.06 (s, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 3.98 (d, *J* = 10.0 Hz, 1H), 3.93 (d, *J* = 9.6 Hz, 1H), 3.66 (td, *J* = 9.8, 6.4, 1H), 3.44 (td, *J* = 9.7, 5.1, 1H), 2.79 (dd, *J* = 17.5, 2.2 Hz, 1H), 2.52 (d, *J* = 17.6 Hz, 1H), 2.24–2.18 (m, 1H), 1.88–1.56 (m, 8H), 0.99 (d, *J* = 6.0 Hz, 3H), 0.88 (s, 9H), 0.86 (s, 3H), 0.83 (d, *J* = 6.0 Hz, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 144.4, 143.5, 138.3, 130.0, 129.6, 128.2, 127.5, 127.5, 123.9,

113.1, 85.9, 73.3, 71.6, 60.5, 50.9, 50.1, 40.8, 35.0, 29.9, 29.2, 26.0, 22.7, 22.1, 19.8, 19.7, 18.3, –5.2; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{33}H_{52}O_4SiNa$ 563.3533; found, 563.3511.

*(R)-5-((benzyloxy)methyl)-5-(((4R,5R)-5-(2-((tert-butyldimethylsilyl)oxy)ethyl)-4-isopropyl-5-methylcyclopent-1-en-1-yl)methyl)-4-methylfuran-2(5H)-one (**27**).* A solution of acrylate ester **16a** (660 mg, 1.22 mmol) in toluene (61 mL) was heated to 70 °C and a solution of Grubbs II catalyst (103.5 mg, 0.122 mmol) was introduced in toluene (12.2 mL) *via* a syringe pump over 6 h. After an additional 90 min of stirring, the reaction was cooled to rt, and the solvent was removed *in vacuo* to provide a tan oil. The product was purified by flash column chromatography (Hexanes/EtOAc (10:1)) to provide the butenolide **27** (622 mg, 99%) as a light brown solid: R_f 0.63 (Hexanes/EtOAc (2:1)); $[\alpha]_D^{20}$ +2.4 (*c* 0.83, $CHCl_3$); IR (film) 2955, 2859, 1759, 1650, 1471, 1364, 1292, 1255, 1094, 954 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.26 (m, 5H), 5.83 (d, *J* = 1.4 Hz, 1H), 5.48 (s, 1H), 4.57 (d, *J* = 12.5 Hz, 1H), 4.48 (d, *J* = 12.5 Hz, 1H) 3.67–3.62 (m, 3H), 3.45 (td, *J* = 9.8, 5.1 Hz, 1H), 2.52 (dd, *J* = 16.9, 1.7 Hz, 1H), 2.26–2.21 (m, 1H), 2.17 (d, *J* = 16.9 Hz, 1H), 2.00 (d, *J* = 1.4 Hz, 3H), 1.91–1.85 (m, 1H), 1.81–1.74 (m, 1H), 1.72–1.63 (m, 2H), 1.61–1.54 (m, 1H), 0.98 (d, *J* = 6.0 Hz, 3H), 0.88 (s, 9H), 0.86 (s, 3H), 0.84 (d, *J* = 6.0 Hz, 3H), 0.03 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.5, 128.4, 127.8, 127.6, 126.2, 118.4, 90.4, 73.8, 72.3, 60.3, 50.6, 50.3, 40.8, 34.7, 29.5, 29.1, 26.0, 22.7, 22.0, 20.2, 18.3, 13.9, –5.2 (2 C); HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{31}H_{48}O_4SiNa$ 535.3220; found, 535.3247.

*(R)-5-((benzyloxy)methyl)-5-(((4R,5R)-5-(2-hydroxyethyl)-4-isopropyl-5-methylcyclopent-1-en-1-yl)methyl)-4-methylfuran-2(5H)-one (**27a**).* To a solution of

butenolide **27** (198 mg, 0.386 mmol) in CH_3CN (3.9 mL) was added HF (19.3 µl, 52% in H_2O, 0.579 mmol), and the mixture was stirred for 15 min. The reaction was then poured into saturated aqueous $NaHCO_3$ (15 mL) and stirred for five min. EtOAc (10 mL) was added and the layers were separated. The aqueous layer was washed with EtOAc (2 x 15 mL), the organic layers were combined. The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to provide a clear light amber oil. The crude product was purified by flash column chromatography (Hexanes/EtOAc (1:1)) to provide the primary alcohol **27a** (148 mg, 96%) as a clear colorless viscous oil: R_f0.14 (Hexanes/EtOAc (2:1)); $[\alpha]_D^{20}$ –2.3 (*c* 1.15, $CHCl_3$); IR (film) 3418, 2955, 1743, 1648, 1455, 1293, 1100, 957 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.25 (m, 5H), 5.83 (d, *J* = 1.4 Hz, 1H), 5.46 (s, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 12.0 Hz. 1H), 3.74–3.61 (m, 3H), 3.54–3.46 (m, 1H), 2.55 (d, *J* = 16.6 Hz, 1H), 2.30–2.16 (m, 2H), 2.03 (d, *J* = 1.4 Hz, 3H), 1.93–1.77 (m, 2H), 1.72–1.59 (m, 2H), 1.49–1.47 (m 1H), 0.97 (d, *J* = 4.3 Hz, 3H),0.87 (s, 3H), 0.84 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 170.1, 142.0, 137.4, 128.5, 127.9, 127.7, 126.7, 118.4, 90.4, 73.8, 72.3, 59.8, 50.6, 50.2, 40.6, 34.8, 29.2, 29.1, 22.6, 21.9, 20.3, 13.9; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{25}H_{34}O_4Na$ 421.2355; found, 421.2343.

*2-((1R,5R)-2-(((R)-2-((benzyloxy)methyl)-3-methyl-5-oxo-2,5-dihydrofuran-2-yl)methyl)-5-isopropyl-1-methylcyclopent-2-en-1-yl)acetaldehyde (**15**).* A solution of the primary alcohol **27a** (40.8 mg, 0.102 mmol) in CH_2Cl_2 (1 mL) was cooled to 0 °C and was treated with $NaHCO_3$ (26 mg, 0.306 mmol) and Dess–Martin periodinane (DMP) (56.4 mg, 0.133 mmol), and the cold bath was removed. After 2 h the reaction was quenched with mixture of saturated aqueous $NaHCO_3$ (2 mL) and saturated aqueous

$Na_2S_2O_3$ (2 mL), diluted with CH_2Cl_2 (5 mL) and stirred for 20 min. The organic layer was separated and the aqueous layer was washed with CH_2Cl_2 (2 x 8 mL). The combined organic extracts were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to provide a clear colorless oil. The crude product was purified by flash column chromatography (Hexanes/EtOAc (4:1)) to provide aldehyde **15** (37.3 mg, 92%) as a clear, colorless oil: $[\alpha]_D^{20}$ –7.6 (*c* 0.25, $CHCl_3$); R_f 0.46 (Hexanes/EtOAc (2:1)); IR (film) 2958, 2870, 1754, 1717, 1650, 1454, 1291, 1098, 954 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.71 (dd, *J* = 3.7, 2.1 Hz, 1H), 7.39–7.22 (m, 5H), 5.83 (d, *J* = 1.4 Hz, 1H), 5.58 (s, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 3.67 (d, *J* = 10.0 Hz, 1H), 3.60 (d, *J* = 10.0 Hz, 1H), 2.61– 2.52 (m, 2H), 2.44 (dd, *J* = 16.0, 2.1 Hz, 1H), 2.37–2.30 (m, 1H), 2.24 (d, *J* = 17.9 Hz, 1H), 2.16 (d, *J* = 1.4 Hz, 3H), 2.03–1.95 (m, 1H), 1.80–1.70 (m, 2H), 0.99 (s, 3H), 0.98 (d, *J* = 6.2 Hz, 3H), 0.86 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.7, 172.1, 170.0, 141.0, 137.3, 128.5, 128.1, 127.9, 127.7, 118.4, 90.1, 73.8, 71.8, 52.8, 51.5, 50.7, 34.7, 29.9, 29.1, 22.8, 21.7, 19.7, 13.9; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{25}H_{32}O_4Na$ 419.2198; found, 419.2183.

*(3aS,4R,5aR,6R,9aR)-9a-(benzyloxymethyl)-4-hydroxy-6-isopropyl-3a,5a-dimethyl-3a,4,5,5a,6,7,9,9a-octahydroazuleno[5,6-b]furan-2(3H)-one (**29**)*. To a solution of SmI_2 (9.2 mL, 0.1 M in THF, 0.918 mmol) at rt was added anhydrous HMPA (639 µl, 3.67 mmol) dropwise. After 2 min, aldehyde **15** (178 mg, 0.449 mmol) in a solution of THF: *t*-BuOH (46 mL, 100:1 by volume) was added dropwise over seven min. The reaction became yellow in color and an additional amount of SmI_2 (1.6 mL, 0.1 M in THF, 0.16 mmol) was introduced to the reaction mixture. After five min the reaction was quenched by the addition of a volume of 20 mL of silica gel. The suspension was washed

through a short plug of silica gel with ethyl acetate. The solution was concentrated *in vacuo* to provide a clear yellow oil. The crude product was purified by flash column chromatography (Hexanes/EtOAc (4:1)) to provide **29** and **30** (113 mg, 63%) as a 66:34 mixture of C–8 diastereomers. The diastereomers were separated by HPLC using a Supelco Ascentis Si Column, (Hexanes/Isoprop (98:2)) to provide **29** (73 mg) t_R: 40.2 min and **30** (36 mg) t_R: 33.6 min as clear colorless oils. Characterization data for alcohol **29**: $[\alpha]_D^{20}$ –20.3 (*c* 1.40, $CHCl_3$); R_f 0.35 Hexanes/EtOAc (2:1)); IR (film) 3479, 2955, 2870, 1771, 1454, 1418, 1236, 1103, 1070 953 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.27 (m 5H), 5.34 (s, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.14–4.08 (m, 1H), 3.77 (d, *J* = 10.0 Hz, 1H), 3.48 (d. *J* = 10.0 Hz, 1H), 3.11 (d, *J* = 18.1 Hz, 1H), 2.64 (d, *J* = 13.9 Hz, 1H), 2.62 (d, *J* = 18.1 Hz, 1H), 2.39 (d, *J* = 14.1 Hz, 1H), 2.29 (ddd, *J* = 16.2, 7.8, 2.6 Hz, 1H), 1.98–1.84 (m, 3H), 1.76–1.65 (m, 2H), 1.51 (dd, *J* = 18.1, 9.5 Hz, 1H), 1.15 (s, 3H), 1.01 (s, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.1, 144.2, 137.7, 128.4, 128.2, 127.6, 127.5, 88.6, 74.0, 73.7, 69.0, 60.4, 49.3, 48.2, 48.0, 42.3, 36.1, 33.4, 29.5, 22.8, 22.7, 20.1, 16.1 Hz; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{25}H_{34}O_4Na$ 421.2355; found, 421.2341. Characterization data for *(3aS,4S,5aR,6R,9aR)-9a-((benzyloxy)methyl)-4-hydroxy-6-isopropyl-3a,5a-dimethyl-3a,4,5,5a,6,7,9,9a-octahydroazuleno[5,6-b]furan-2(3H)-one* ***(30)****:* $[\alpha]_D^{20}$ –1.9 (*c* 0.7, $CHCl_3$); R_f 0.35 Hexanes/EtOAc (2:1)); IR (film) 3467, 2956, 2869, 1763, 1417, 1238, 1104, 1096, 956 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 5H), 5.45 (s, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 12.0 Hz. 1H), 3.75 (d, *J* = 10.9 Hz, 1H), 3.74–3.71 (m, 1H), 3.57 (d, *J* = 10.8 Hz, 1H), 2.85 (d, *J* = 13.4 Hz, 1H), 2.76 (d, *J* = 17.3 Hz, 1H), 2.54 (d, *J* = 13.3 Hz, 1H), 2.49 (d, *J* = 17.3 Hz, 1H), 2.29 (ddd,

J = 16.0, 7.7, 2.5 Hz, 1H), 2.01–1.89 (m, 3H), 1.81–1.69 (m, 1H), 1.63–1.58 (m, 2H), 1.18 (s, 3H), 1.01 (d, *J* 6.5 Hz, 3H), 0.99 (s, 3H), 0.90 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.0, 144.6, 137.9, 128.4, 127.6, 127.4 (2 C), 89.7, 75.3, 73.4, 72.4, 57.1, 49.0, 48.7, 45.1, 40.6, 35.9, 31.6, 29.6, 22.9, 22.8, 21.3, 21.1; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{25}H_{34}O_4Na$ 421.2355; found, 421.2343.

*(3aR,5aR,6R,9aR)-9a-((benzyloxy)methyl)-6-isopropyl-3a,5a-dimethyl-3,3a,5,5a,6,7,9,9a-octahydroazuleno[5,6-b]furan-2,4-dione (**32**).* To a solution containing a 67:33 mixture of alcohols **29** and **30** (4.4 mg, 11 μmol) in CH_2Cl_2 (1 mL) was added $NaHCO_3$ (2.8 mg, 33 μmol) and DMP (14.6 mg, 14.3 μmol). The reaction mixture was stirred for 50 min and quenched with a solution of saturated aqueous $NaHCO_3$ (2 mL) and saturated aqueous $Na_2S_2O_3$ (2 mL). After 20 min the layers were separated and the aqueous layer was washed with CH_2Cl_2 (2 x 4 mL). The organic layers were combined, dried over Na_2SO_4, and concentrated *in vacuo* to provide a clear colorless oil. Purification via flash chromatography (Hexanes/EtOAc (5:1)) provided **32** (3.4 mg, 77%) as a white crystalline solid: mp 94–95.5 °C; $[\alpha]_D^{20}$ +60.3 (*c* 1.22, $CHCl_3$); R_f 0.62 (Hexanes/EtOAc (2:1)); IR (film) 2960, 2870, 1783, 1697, 1497, 1454, 1378, 1233, 1117, 1068, 957 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.27 (m, 5H), 5.51 (bs, 1H), 4.56 (d, *J* = 11.5 Hz, 1H), 4.53 (d, *J* = 11.5 Hz, 1H), 3.80 (d, *J* = 11.0 Hz, 1H), 3.70 (d, *J* = 11.0 Hz, 1H), 3.13 (d, *J* = 17.8 Hz, 1H), 2.92 (d, *J* = 11.2 Hz, 1H), 2.76 (d, *J* = 14.2 Hz, 1H), 2.55 (d, *J* = 11.1 Hz, 1H), 2.45 (d, *J* = 17.8 Hz, 1H), 2.33 (ddd, *J* = 16.3, 7.9, 2.9 Hz, 1H), 2.22–2.14 (m, 1H), 1.99–1.87 (m, 1H), 1.79–1.66 (m, 1H), 1.57–1.48 (m, 1H), 1.40 (s, 3H) , 0.95 (d, *J* = 6.6 Hz, 3H), 0.94 (s, 3H), 0.89 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.0, 174.0, 143.5, 137.4, 129.3, 128.4, 127.8, 127.7, 86.3,

73.9, 72.6, 59.6, 57.2, 52.3, 49.2, 39.8, 35.7, 35.5, 29.4, 22.7, 22.6, 20.5, 19.3, 18.5; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{25}H_{32}O_4Na$ 419.2198; found, 419.2186.

*(3aS,4R,5aR,6R,9aR)-9a-((benzyloxy)methyl)-6-isopropyl-3a,5a-dimethyl-2-oxo-2,3,3a,4,5,5a,6,7,9,9a-decahydroazuleno[5,6-b]furan-4-yl acetate (**33**).* A solution of **29** (29.5 mg, 0.074 mmol) in CH_2Cl_2 (1 mL) was cooled to 0 °C and treated with Ac_2O (21 µl, 0.222 mmol), pyridine (48 µl, 0.592 mol) and DMAP (1 mg, 8.18 µmol). The cold bath was removed, and after stirring for 1.5 h, the reaction was quenched with saturated aqueous NH_4Cl (2 mL), and diluted with CH_2Cl_2 (3 mL). The organic layer was removed, and the aqueous layer was washed with CH_2Cl_2 (3 x 3 mL). The organic extracts were combined, washed with brine (4 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to provide a clear colorless oil. The crude product was purified by flash column chromatography (Hexanes/EtOAc (5:1)) to provide the acetate **33** (31.8 mg, 98%) as a clear colorless oil: $[\alpha]_D^{20}$ –31.5 (*c* 0.39, $CHCl_3$); R_f 0.46 (Hexanes/EtOAc (2:1)); IR (film) 2958, 1778, 1742, 1455, 1240, 1105, 1020, 958, 753 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.27 (m, 5H), 5.39 (s, 1H), 5.34 (d, *J* = 9.6 Hz, 1H), 4.48 (d, *J* = 11.5 Hz, 1H), 4.45 (d, *J* = 11.5 Hz, 1H), 3.70 (d, *J* = 10.0 Hz, 1H), 3.45 (d, *J* = 10.0 Hz, 1H), 2.72–2.47 (m, 4H), 2.28 (ddd, *J* = 16.2, 7.9, 2.7 Hz, 1H), 2.05 (s, 3H), 1.93–1.80 (m, 3H), 1.75–1.68 (m, 1H), 1.45 (dd, *J* = 18.1, 10 Hz, 1H), 1.23 (s, 3H), 1.06 (s, 3H), 0.93 (d, *J* = 6.5, 3H), 0.88 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 169.7, 144.1, 137.6, 128.5, 128.4, 127.7, 127.5, 88.4, 73.7 (2 C), 72.5, 60.3, 48.0, 47.2, 45.0, 42.8, 35.9, 33.8, 29.4, 22.8, 22.7, 21.2, 19.4, 17.3; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{27}H_{36}O_5Na$ 463.2460; found, 463.2446.

*(3aS,4R,5aR,6R,8S,8aR,9aR)-9a-((benzyloxy)methyl)-8,8a-dihydroxy-6-isopropyl-3a,5a-dimethyl-2-oxododecahydroazuleno[5,6-b]furan-4-yl acetate (**34**).* To a solution of **33** (30 mg, 0.068 mmol) in 1:1 ^{t}BuOH: H_2O (800 µl), was added DMAP (20 mg, 0.163 mmol) and solid OsO_4 (35 mg, 0.136 mmol). The reaction mixture was stirred at 34 °C for 12 h, cooled to rt, diluted with $CHCl_3$, and quenched by flushing the reaction vessel with H_2S for 30 min. The resulting black heterogeneous mixture was flushed through a celite plug with $CHCl_3$, followed by H_2O. The aqueous layer was washed with CH_2Cl_2 (3 x 8 mL) and the organic layers were combined, dried over Na_2SO_4, filtered, and the solvent was removed *in vacuo* to provide a brown oil. The crude product was purified via flash column chromatography (Hexanes/EtOAc (2:1)) to provide β-diol **34** (24 mg, 75%) and α-diol **35** (8.4 mg, 25%) as clear colorless oils which solidified upon standing. For characterization of **34**: R_f 0.41 (Hexanes/EtOAc (1:1)); $[\alpha]_D^{20}$ –30.4 (*c* 0.89, $CHCl_3$); IR (film) 3468, 2958, 1740, 1379, 1243, 1096, 1020 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) 7.37–7.29 (m, 5H), 4.99 (dd, *J* = 11.0, 1.2 Hz, 1H), 4.54 (s, 2H), 3.86 (d, *J* = 10.1 Hz, 1H), 3.84–3.80 (m, 1H), 3.48 (d, *J* = 10.1 Hz, 1H), 3.29 (s, 1H), 2.70 (d, *J* = 18.5 Hz, 1H), 2.55 (d, *J* = 18.5 Hz, 1H), 2.23–2.13 (m, 3H), 2.05 (s, 3H), 2.03 (d, *J* = 6.2 Hz, 1H), 1.85–1.62 (m, 4H), 1.53 (s, 3H), 1.52–1.45 (m, 1H), 1.03 (s, 3H), 0.87 (d, *J* = 6.5 Hz, 3H), 0.84 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.6, 170.0, 137.2, 128.5, 127.9, 127.5, 90.1, 81.7, 76.9, 73.7, 73.6, 71.8, 51.8, 48.9, 47.1, 42.7, 38.5, 38.1, 36.8, 30.4, 23.1, 22.8, 21.3, 16.3, 16.2). HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{27}H_{38}O_7Na$ 497.2515; found, 497.2529. For characterization of *(3aS,4R,5aR,6R,8R,8aS,9aR)-9a-((benzyloxy)methyl)-8,8a-dihydroxy-6-isopropyl-3a,5a-dimethyl-2-oxododecahydroazuleno[5,6-b]furan-4-yl acetate (**35**):* R_f 0.31 (Hexanes/EtOAc (1:1));

$[\alpha]_D^{20}$ –24.8 (*c* 0.23, $CHCl_3$); IR (film) 3468, 2957, 1763, 1740, 1370, 1243, 1105, 1081, 1020 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.26 (m, 5H), 5.39 (d, *J* = 9.2 Hz, 1H), 4.56 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 3.59 (d, *J* = 10.5 Hz, 1H), 3.38 (d, *J* = 10.5 Hz, 1H), 3.46 (s, 1H), 3.41–3.37 (m, 1H), 3.22 (d, *J* = 4.3 Hz, 1H), 2.85 (d, *J* = 17.9 Hz, 1H), 2.34 (d, *J* = 18.0 Hz, 1H), 2.15–2.08 (m, 1H), 2.06 (s, 3H), 1.93 (s, 2H), 1.85 (dd, *J* = 15.0, 9.4 Hz, 1H), 1.70–1.60 (m, 2H), 1.30 (s, 3H), 1.11 (s, 3H), 1.05–0.95 (m, 1H), 0.91 (d, *J* = 6.7 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 169.6, 136.8, 128.6 128.1, 127.7, 89.1, 81.8, 78.9, 76.2, 74.1, 71.0, 52.7, 48.4, 46.9, 43.5, 42.0, 38.0, 36.0 28.5, 23.7, 22.2, 21.3, 15.7, 13.9; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{27}H_{38}O_7Na$ 497.2515; found, 497.2521.

*(3aR,5R,5aR,7R,7aS,10aR,11aS)-10a-((benzyloxy)methyl)-5-isopropyl-2,2,5a,7a-tetramethyl-9-oxodecahydro-3aH-furo[3',2':6,7]azuleno[1,8a-d][1,3]dioxol-7-yl acetate **(36)**.* To a solution of the α-diol **35** (8.4 mg, 0.018 mmol) in dimethoxypropane (3 mL) was added several crystals of camphor-10-sulfonic acid. After 30 min, the reaction was poured into a stirring solution of saturated aqueous $NaHCO_3$ (8 mL) at 0 °C. The aqueous layer was washed with Et_2O 3 x 6 mL), the organic layers were combined, dried over Na_2SO_4, filtered and the solvent was removed in vacuo to provide a white solid. The crude product was purified via flash column chromatography (Hexanes/EtOAc (5:1)) to provide acetonide **36** (8.6 mg, 95%) as a white solid: $[\alpha]_D^{20}$ –6.2 (*c* 0.17, $CHCl_3$); R_f 0.71 (Hexanes/EtOAc (1:1)); IR (film) 2984, 2870, 1768, 1743, 1454, 1371, 1240, 1210, 1115, 1092, 1022 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.45–7.29 (m, 5H), 5.16 (d, *J* = 8.7 Hz, 1H), 4.60 (d, *J* = 11.5 Hz, 1H), 4.45 (d, *J* = 12.0 Hz, 1H), 4.09 (dd, *J* = 7.9 ,4.5 Hz, 1H), 3.59 (d, *J* = 10.3 Hz, 1H), 3.38 (d, *J* = 10.3 Hz, 1H), 2.71 (d, *J* = 17.8 Hz, 1H), 2.33 (d, *J*

= 17.8 Hz, 1H), 2.14–2.06 (m, 1H), 2.04 (s, 3H), 2.00 (s, 1H), 1.94 (d, *J* = 15.5 Hz, 1H), 1.80 (dd, *J* = 14.8, 8.9 Hz, 1H), 1.67 (td, *J* = 13.6, 6.8 Hz, 1H), 1.56 (d, *J* = 15.6 Hz, 1H), 1.52–1.49 (m, 4H), 1.39 (s, 3H), 1.34–1.23 (m, 4H), 1.11 (s, 3H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.0, 169.5, 137.3, 128.5, 127.9, 127.7, 114.0, 92.6, 88.2, 87.7, 76.6, 74.0, 71.7, 57.5, 48.0, 47.0, 43.0, 42.4, 38.8, 33.1, 29.3, 26.6, 25.7, 23.0, 22.4, 21.3, 17.4, 14.6; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{30}H_{42}O_7Na$ 537.2828 found 537.2802.

*(3aR,5R,5aR,7R,7aS,10aR,11aS)-10a-(hydroxymethyl)-5-isopropyl-2,2,5a,7a-tetramethyl-9-oxodecahydro-3aH-furo[3',2':6,7]azuleno[1,8a-d][1,3]dioxol-7-yl acetate **(36a)**.* A solution of benzyl ether **36** (8.6 mg, 0.51 nmol) in MeOH (300 µl) was treated with 10% Pd/C (10mg). The reaction flask was purged with H_2 for 1 min and reacted over 16 h under a H_2 atmosphere. The mixture was filtered through celite, and the filtrate was washed with EtOAc (3 x 3 mL). The organic layers were combined, and the solvent was removed in vacuo to provide a clear colorless oil. The crude product was purified by flash column chromatography (Hexanes/EtOAc (2:1)) to afford primary alcohol **36a** (7.1 mg, 100%) as a clear colorless oil: $[\alpha]_D^{20}$ +1.4 (*c* 0.21, $CHCl_3$); R_f 0.1 (Hexanes/EtOAc (2:1)); IR (film) 3429, 2985, 2959, 1746, 1458, 1373, 1249, 1208, 1132, 1091, 1018, 886 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.17 (d, *J* = 8.7 Hz, 1H), 4.13 (dd, *J* = 7.9, 4.4 Hz, 1H), 3.77 (dd, *J* = 12.0, 5.6 Hz, 1H), 3.54 (dd, *J* = 12.0, 7.6 Hz, 1H), 2.66 (d, *J* = 18.0 Hz, 1H), 2.39 (d, *J* = 18.0 Hz, 1H), 2.19 (d, *J* = 15.8 Hz, 1H), 2.14–2.08 (m, 1H) 2.06 (s, 3H), 1.89 (d, *J* = 15.7 Hz, 1H), 1.82 (dd, *J* = 14.8, 8.9 Hz, 1H), 1.72–1.62 (m, 1H), 1.57 (d, *J* = 14.8 Hz, 1H), 1.53–1.49 (m, 4H), 1.39–1.29 (m, 7H), 1.12 (s, 3H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.9, 169.5, 113.9, 92.4,

88.8, 87.7, 71.5, 68.8, 57.5, 47.7, 47.1, 42.9, 42.2, 38.0, 33.0, 29.3, 26.5, 25.7, 23.0, 22.4, 21.3, 17.3, 14.4; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{23}H_{36}O_7Na$ 447.2359 found 447.2340.

*(3aR,5R,5aR,7R,7aS,10aS,11aS)-10a-ethynyl-5-isopropyl-2,2,5a,7a-tetramethyl-9- oxodecahydro-3aH-furo[3',2':6,7]azuleno[1,8a-d][1,3]dioxol-7-yl acetate (**37**).* A solution of alcohol **36a** (7.1 mg, 0.017 mmol) in CH_2Cl_2 (2 mL) was cooled to 0 °C and $NaHCO_3$ (21.0 mg, 0.251 mmol) and DMP (35.4 mg, 0.0835 mmol) were added. The cold bath was removed and after stirring for 30 min the reaction was quenched by addition of a mixture of saturated aqueous $NaHCO_3$ (7.5 mL) and saturated aqueous $Na_2S_2O_3$ (7.5mL), diluted with CH_2Cl_2 (5 mL) and was then stirred for 20 min. The organic layer was separated and the aqueous layer was washed with CH_2Cl_2 (2 x 8 mL). The combined organic extracts were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated in vacuo to provide the crude aldehyde as a clear colorless oil. In a separate flask, a solution of the Gilbert–Seyferth reagent (37.0 mg, 0.249 mmol) and THF (1.00 mL) was cooled to –78 °C by dropwise addition of *n*BuLi (78 µl, 1.6M in hexanes, 0.13 mmol). After 20 min, a solution of the crude aldehyde (7.1 mg, 0.017 mmol) in THF (500 µl) was added to the reaction via syringe followed by a THF (500 µl) syringe wash. The resulting mixture was warmed to 0 °C over 1. 5 h and then was quenched with saturated aqueous NH_4Cl (500 µl) and partitioned between H_2O and Et_2O. The aqueous phase was extracted with Et_2O (3 x 2mL) and the combined organic phases were dried over Na_2SO_4 and concentrated in vacuo to provide a clear colorless oil. The solvent was removed in vacuo and the crude product was purified by flash column chromatography (Hexanes/EtOAc 5:1)) to provide alkyne **37** (6.6 mg, 96%) in 94%

purity as a clear colorless oil; R_f 0.6 (Hexanes/EtOAc (1:1)); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.11 (d, *J* = 8.8 Hz, 1H), 4.17 (dd, *J* = 7.9, 4.5 Hz, 1H), 2.71 (s, 1H), 2.59 (d, *J* = 16.0 Hz, 1H), 2.57 (d, *J* = 17.5 Hz, 1H), 2.49 (d, *J* = 17.5 Hz, 1H), 2.30 (d, *J* = 15.9 Hz, 1H), 2.13 (dt, *J* = 13.9, 7.6 Hz, 1H), 2.06 (s, 3H), 1.87 (dd, *J* = 15.0, 8.9 Hz, 1H), 1.68 (td, *J* = 13.6, 6.7 Hz, 1H), 1.60 (d, *J* = 14.9 Hz, 1H), 1.51 (dd, *J* = 13.4, 4.5 Hz, 1H), 1.48 (s, 3H), 1.43 (s, 3H), 1.41 (s, 3H), 1.41–1.34 (m, 1H), 1.10 (s, 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 169.3, 114.2, 92.6, 87.5, 84.5, 82.2, 76.4, 70.3, 57.6, 49.1, 47.2, 42.9, 41.4, 32.9, 29.7, 29.1, 26.5, 25.8, 23.1, 22.3, 21.3, 17.8, 17.6; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{24}H_{34}O_6Na$ 441.2253 found 441.2234.

*(3aR,5R,5aR,7R,7aS,10aR,11aS)-5-isopropyl-2,2,5a,7a-tetramethyl-9-oxo-10a-(1-(tributylstannyl)vinyl)decahydro-3aH-furo[3',2':6,7]azuleno[1,8a-d][1,3]dioxol-7-yl acetate (**38**).* To a solution of the alkyne **37** (3.7 mg, 8.8 μmol), and hydroquinone (3 crystals) in THF (700 μl) was added a catalytic amount of $Mo(CO)_3(^tBu)_3$ (spatula tip) and nBu$_3$SnH (4 μl, 15.1 μmol). The reaction was heated to 55 °C for 1 h and then the cooled to rt. The solvent was removed in vacuo and the crude product was purified by flash column chromatography (2x (Hexanes/EtOAc (8:1)) to provide stannane **38** (5.3 mg, 86%) as a clear colorless oil: R_f 0.72 (Hexanes/EtOAc (2:1)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (s, 1H), 5.37 (s, 1H), 5.22 (d, *J* = 8.5 Hz, 1H), 4.07 (dd, *J* = 7.8, 4.5 Hz, 1H), 2.37 (d, *J* = 17.6 Hz, 1H), 2.28 (d, *J* = 17.6 Hz, 1H), 2.22–2.04 (m, 3H), 2.04 (s, 3H), 1.90 (dd, *J* = 14.9, 8.7 Hz, 1H), 1.77–1.63 (m, 1H), 1.62 (d, *J* = 14.8, 1H), 1.58–1.44 (m, 5H), 1.53 (s, 3H), 1.42–1.29 (m, 8H), 1.36 (s, 3H), 1.16 (s, 3H), 1.12 (s, 3H), 1.03–0.95 (m, 5H), 0.96–0.85 (m, 17H); LRMS-ESI calcd for $C_{36}H_{63}O_6Sn$ $[M+H]^+$ 711.4;

found, 711.4; HRMS (ESI-TOF) *m/z*: [M+H+Na–$SnBu_3$] calcd for $C_{24}H_{36}O_6Na$ 443.2410; found, 443.2423. Insufficient quantities of **38** did not permit the acquisition of carbon NMR data for this unstable compound. Note that **38** contains eight fully substituted carbons (without hydrogen substitution), which provide very weak signals that cannot be identified in the baseline noise.

*(3aR,5R,5aR,7R,7aS,10aR,11aS)-10a-(1-iodovinyl)-5-isopropyl-2,2,5a,7a-tetramethyl-9-oxodecahydro-3aH-furo[3',2':6,7]azuleno[1,8a-d][1,3]dioxol-7-yl acetate (**39**)*. A solution of stannane **38** (4 mg, 5.6 μmol) in CH_2Cl_2 (1 mL) was treated with I_2 (2.8 mg, 11.2 μmol) at 0 °C. After stirring 2 h at 0 °C, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (1 mL). The aqueous layer was washed with Et_2O (3 x 2 mL) and the combined organic layers were dried over Na_2SO_4. Removal of the solvent in vacuo and purification of the crude product by flash column chromatography (Hexanes/EtOAc 5:1)) provided the iodide **39** (2 mg, 50%) as a clear colorless oil: R_f 0.51 (Hexanes/EtOAc (2:1)); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.45 (d, *J* = 2.8 Hz, 1H), 6.18 (d, *J* = 2.8 Hz, 1H), 5.24 (d, *J* = 8.5 Hz, 1H), 4.14 (dd, *J* = 7.9, 4.4 Hz, 1H), 2.90 (d, *J* = 15.6 Hz, 1H), 2.47 (d, *J* = 17.9 Hz, 1H), 2.39 (d, *J* = 17.9 Hz, 1H), 2.19 (dt, *J* = 13.8, 7.6 Hz, 1H), 2.08–2.04 (m, 1H), 2.06 (s, 3H), 1.89 (dd, *J* = 14.9, 8.6 Hz, 1H), 1.75–1.64 (m, 1H), 1.64–1.57 (m, 1H), 1.49 (s, 3H), 1.45 (s, 3H), 1.42–1.38 (m, 1H), 1.36 (s, 3H), 1.11 (s, 3H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 3H); HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{24}H_{35}IO_6Na$ 569.1376; found, 569.1387. Insufficient quantities of **39** did not permit the acquisition of carbon NMR data for this unstable compound. Note that **39** contains nine fully substituted carbons (without hydrogen substitution), which provide very weak signals that cannot be identified in the baseline noise.

*(3aS,4R,5aR,6R,8S,8aR,9aR)-9a-(benzyloxymethyl)-8,8a-dihydroxy-6-isopropyl-3a,5a-dimethyl-2-oxododecahydroazuleno[5,6-b]furan-4-yl acetate (**34a**).* To a solution of β-diol **34** (27.6 mg, 0.06 mmol) in a mixture of acetone and Et_2O (2 mL, 1:1 by volume) at 0 °C was added several crystals of reagent-grade $AlCl_3$. The reaction was stirred at rt for 2 h and was quenched at 0 °C by dropwise addition of saturated aqueous $NaHCO_3$ (6 mL). The reaction was then allowed to warmed to rt and was extracted with CH_2Cl_2 (3 x 6 mL). The organic layers were combined, dried over Na_2SO_4, and the solvent was removed in vacuo to provide a clear colorless oil. The crude product was purified via flash column chromatography (Hexanes/EtOAc (5:1)) to provide the β-acetonide **34a** (27.0 mg, 87%) as a clear colorless oil: $[\alpha]_D^{20}$ –57.2 (*c* 0.25, $CHCl_3$); R_f 0.71 (Hexanes/EtOAc (1:1)); IR (film) 2960, 2870, 1778, 1739, 1454, 1379, 1240, 1093, 1030 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.27 (m, 5H), 5.02 (dd, *J* = 11.2, 1.8 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.17 (dd, *J* = 5.9, 3.9 Hz, 1H), 3.99 (d, *J* =10.5 Hz, 1H), 3.34 (d, *J* = 10.5 Hz, 1H), 2.87 (d, *J* = 18.2 Hz, 1H), 2.45 (d, *J* = 18.2 Hz, 1H), 2.38 (d, *J* = 16.0 Hz, 1H), 2.13 (d, *J* = 16.1 Hz, 1H), 2.04 (s, 3H), 2.01 (d, *J* = 11.4 Hz, 1H), 1.86–1.69 (m, 4H), 1.59–1.49 (m, 1H), 1.44 (s, 3H), 1.43 (s, 3H), 1.35 (s, 3H), 1.02 (s, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 170.0, 137.3, 128.5, 127.9, 127.8, 111.7, 98.1, 89.7, 84.4, 77.9, 73.8, 72.3, 52.3, 49.5, 47.4, 43.1, 39.7, 36.7, 36.6, 30.6, 29.1, 28.2, 23.3, 22.8, 21.3, 17.0, 15.1; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{30}H_{43}O_7$ 515.3009 found 515.3011.

*(3aS,5R,5aR,7R,7aS,10aR,11aR)-10a-(hydroxymethyl)-5-isopropyl-2,2,5a,7a-tetramethyl-9-oxodecahydro-3aH-furo[3',2':6,7]azuleno[1,8a-d][1,3]dioxol-7-yl acetate (**34b**).* A solution of the β-acetonide **34a** (26 mg, 0.51 nmol) in MeOH (300 μl) was

charged with 10% Pd/C (10 mg) and the reaction flask was purged with H_2 for 1 min. The reaction proceeded over 16 h under a H_2 atmosphere. The mixture was then filtered through celite, and the filtrate washed with EtOAc (3 x 3 mL). The organic phases were combined, and the solvent was removed in vacuo to provide a clear colorless oil. The crude product was purified by flash column chromatography (Hexanes/EtOAc (2:1)) to afford the primary alcohol **34b** (20 mg, 93%) as a white solid: $[\alpha]_D^{20}$ –57.5 (*c* 0.5, $CHCl_3$); R_f 0.42 (Hexanes/EtOAc (1:1)); IR (film) 3467, 2961, 1773, 1741, 1380, 1236, 1090, 1066, 1041, 1024 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.04 (dd, *J* = 11.2, 1.9 Hz, 1H), 4.22 (dd, *J* = 6.5, 3.3 Hz, 1H), 3.99 (dd, *J* = 12.1, 4.3 Hz, 1H), 3.69 (dd, *J* = 12.1, 8.8 Hz, 1H), 2.72 (d, *J* = 18.5 Hz, 1H), 2.57 (d, *J* = 14.6 Hz, 1H), 2.54 (s, 1H), 2.22–2.19 (m, 1H), 2.17 (d, *J* = 16.0 Hz, 1H), 2.06 (s, 3H), 2.06–1.99 (m, 1H), 1.90–1.81 (m, 2H), 1.78–1.72 (m, 2H), 1.55 (td, *J* = 13.4, 6.7 Hz, 1H), 1.49 (s, 3H), 1.46 (s, 3H), 1.45 (s, 3H), 1.03 (s, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.3, 170.0, 111.9, 95.1, 91.0, 84.3, 71.9, 68.4, 52.2, 49.1, 47.4, 42.8, 36.8, 36.7, 36.6, 30.4, 29.1, 28.2, 23.3, 22.8, 21.3, 17.0, 15.0; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{23}H_{36}O_7Na$ 447.2359 found 447.2380.

*(3aS,5R,5aR,7R,7aS,10aR,11aR)-10a-acetyl-5-isopropyl-2,2,5a,7a-tetramethyl-9-oxodecahydro-3aH-furo[3',2':6,7]azuleno[1,8a-d][1,3]dioxol-7-yl acetate (**41**).* A solution of the alcohol **34b** (9.0 mg, 0.021 mmol) and CH_2Cl_2 (1 mL) was cooled to 0 °C, and $NaHCO_3$ (26.7 mg, 0.32 mmol) and DMP (45 mg, 0.106 mmol) were added. The cold bath was removed, and after stirring for 2.5 h, the reaction was quenched by addition of a mixture of saturated aqueous $NaHCO_3$ (2 mL) and saturated aqueous $Na_2S_2O_3$ (2 mL), and diluted with CH_2Cl_2 (5 mL) with stirring for 20 min. The organic layer was then

separated and the aqueous layer was washed with CH_2Cl_2 (2 x 3 mL). The combined organic extracts were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated in vacuo to provide crude aldehyde **40** as a clear colorless oil. To a solution of crude aldehyde **40** (9 mg, 0.021 mmol) in CH_2Cl_2 (300 µl) at 0 °C was added $AlMe_3$ (16 µl, 2.0M in hexanes, 0.032 mmol). After 55 min, the reaction was quenched with saturated aqueous NH_4Cl (1 mL) and allowed to warm to rt. The aqueous layer was washed with EtOAc (3 x 2 mL), and the combined organic phases were dried over Na_2SO_4, filtered, and concentrated in vacuo to give a crude oil was routinely utilized in the next reaction. Flash column chromatography (Hexanes/EtOAc 2:1)) provided the secondary alcohols (9.0 mg, 97%) as a 9:1 mixture of diastereomers. Data for characterization of the major alcohol diastereomer is provided as follows: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.02 (d, J = 9.8 Hz, 1H), 4.35–4.29 (m, 1H), 4.18 (dd, J = 7.4, 1.8 Hz, 1H), 3.01 (d, J = 18.4 Hz, 1H), 2.42 (d, J = 18.4 Hz, 1H), 2.32 (d, J = 16.2 Hz, 1H), 2.21 (d, J = 16.1 Hz, 1H), 2.06 (s, 3H), 1.59 (s, 3H), 1.48 (s, 3H), 1.45 (s, 2H), 1.43 (d, J = 6.1 Hz, 3H), 0.93 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H). LRMS-ESI calcd for $C_{24}H_{39}O_7$ $[M+H]^+$ 439.3; found, 439.3. This mixture was taken on to the next step without further purification.

To a solution of the mixture of crude alcohols (5.0 mg, 11.4 µmol) and CH_2Cl_2 (500 µl) added $NaHCO_3$ (34 mg, 0.41 mmol) and DMP (58.0 mg, 13.7 µmol). The reaction mixture was stirred for 14 h and then quenched by addition of a solution of saturated aqueous $NaHCO_3$ (2 mL) and saturated aqueous $Na_2S_2O_3$ (2 mL). After 20 min the layers were separated and the aqueous layer was washed with CH_2Cl_2 (2 x 4 mL). The organic layers were combined, dried over Na_2SO_4, and concentrated in vacuo to provide a

clear colorless oil. Purification via flash chromatography (Hexanes/EtOAc (3:1)) provided methyl ketone **41** (4.4 mg, 90%) as a clear colorless oil: R_f 0.77 (Hexanes/EtOAc (1:1)); IR (film) 3360, 2920, 1770, 1728, 1472, 1060 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.01 (dd, *J* = 11.6, 2.4 Hz, 1H), 4.20 (dd, *J* = 6.9, 2.7 Hz, 1H), 2.52 (d, *J* = 17.7 Hz, 1H), 2.39 (d, *J* = 16.4 Hz, 1H), 2.33 (d, *J* = 16.4 Hz, 1H), 2.26 (s, 3H), 2.18–2.12 (m, 2H), 2.06 (s, 3H), 1.92–1.75 (m, 4H), 1.60–1.50 (m, 4H), 1.45 (s, 3H), 1.43 (s, 3H), 1.00 (s, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 207.5, 174.1, 170.0, 112.3, 95.6, 92.7, 84.8, 72.3, 52.6, 47.5, 43.0, 39.2, 36.7, 36.1, 30.3, 29.9, 29.1, 28.9, 28.7, 23.7, 22.8, 21.4, 16.3, 14.7; HRMS (ESI-TOF) *m*/*z* $[M+H]^+$ calcd for $C_{24}H_{37}O_7$ 437.2539; found, 437.2565.

*(3aS,5R,5aR,7R,7aS,10aR,11aR)-5-isopropyl-2,2,5a,7a-tetramethyl-9-oxo-10a-(1-(((trifluoromethyl)sulfonyl)oxy)vinyl)decahydro-3aH-furo[3',2':6,7]azuleno[1,8a-d][1,3]dioxol-7-yl acetate (**42**).* To a solution of ketone **41** (9.6 mg, 0.022 mmol), in THF (500 µl) at – 78 °C was added NaHMDS (26.2 µl, 1M in THF, 0.026 mmol). After 45 min, $PhNTf_2$ (55 µl, 0.6M solution in THF, 0.033 mmol) was added dropwise. After 1 h, the reaction was warmed to 0 °C and stirred for an additional 2.5 h. The reaction was quenched with saturated aqueous NH_4Cl and the aqueous layer was extracted with EtOAc (4 x 2 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated in vacuo to provide a clear colorless oil. The crude product was purified by flash column chromatography (Hexanes/ Et_2O 3:1)) to provide vinyl triflate **42** (7.0 mg, 56%) as a clear colorless oil; R_f 0.38 (Hexanes/EtOAc (4:1)); ^1H NMR (500 MHz, $CDCl_3$) δ 5.46 (d, *J* = 5.3 Hz, 1H), 5.37 (d, *J* = 5.3 Hz, 1H), 5.01 (dd, *J* = 11.7, 2.7 Hz, 1H), 4.26 (t, *J* = 4.6 Hz, 1H), 2.61 (s, 2H), 2.51 (d, *J* = 17.5 Hz, 1H), 2.47 (d, *J* = 17.0 Hz,

1H), 2.21–2.16 (m, 1H), 2.09 (s, 3H), 1.95 (dd, J = 13.5, 2.8 Hz, 1H), 1.87–1.79 (m, 3H), 1.58 (s, 3H), 1.57 (m, 1H), 1.53 (s, 3H), 1.48 (s, 3H), 1.03 (s, 3H), 0.97 (d, J = 6.7 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H); HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $C_{25}H_{35}F_3O_9SNa$ 591.1852; found, 591.1846. Note that insufficient ^{13}C NMR data was not available for **42** due to very weak signals of seven fully substituted carbons and two C=O signals that cannot be identified or assigned with confidence.

*(3aS,4R,5aR,6R,9aR)-6-isopropyl-3a,5a-dimethyl-2,8-dioxo-9a-(1-(trifluoromethylsulfonyloxy)vinyl)-2,3,3a,4,5,5a,6,7,8,9a-decahydroazuleno[5,6-b]furan-4-yl acetate (**43**).* To a solution of the vinyl triflate **42** (4.7 mg, 8.3 μmol) in CH_2Cl_2 (500 μl) at 0 °C was added a catalytic amount of $FeCl_3$ (several crystals). After 45 min, the reaction was quenched at 0 °C with saturated aqueous $NaHCO_3$ (3 mL), and the aqueous layer was extracted with Et_2O (3 x 2 mL) and EtOAc (1 x 2 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo to provide a clear colorless oil. The crude product was purified by flash column chromatography (Hexanes/EtOAc 3:1)) to provide β-diol **42a** (2.7 mg, 63%) as a clear colorless oil; R_f 0.46 (Hexanes/EtOAc (2:1)); ^1H NMR (500 MHz, $CDCl_3$) δ 5.53 (d, J = 5.1 Hz, 1H), 5.47 (d, J = 5.1 Hz, 1H), 4.99 (d, J = 9.9 Hz, 1H), 3.95 (dd, J = 9.1, 5.0 Hz, 1H), 3.04 (s, 1H), 2.64 (d, J = 18.4 Hz, 1H), 2.56 (d, J = 18.4 Hz, 1H), 2.35 (d, J = 16.5 Hz, 1H), 2.25 (dd, J = 13.4, 11.5 Hz, 1H), 2.07 (s, 3H), 1.93–1.82 (m, 2H), 1.77–1.71 (m, 2H), 1.58–1.47 (m, 4H), 1.04 (s, 3H), 0.89 (d, J = 6.5 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H). LRMS-ESI calcd for $C_{22}H_{35}F_3NO_9S$ $[M+NH4]^+$ 546.2; found, 546.3. This material was taken on to the next step without further purification and characterization.

To a solution of the diol **42a** (3.6 mg, 6.8 μmol), in DMSO (500 μl) was added IBX (3.8 mg, 0.014 mmol). After stirring for 18 h, H_2O was added (3 mL) and the aqueous layer was extracted with Et_2O (4 x 1 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated in vacuo to provide a clear colorless oil. The crude product was purified by flash column chromatography (Hexanes/EtOAc 3:1)) to provide the corresponding α-hydroxy ketone **42b** (1.8 mg, 50%) as a clear colorless oil; R_f 0.47 (Hexanes/EtOAc (2:1)); IR (film) 3400, 2935, 1775, 1745, 1452, 1373, 1098 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.41 (d, J = 5.4 Hz, 1H), 5.37 (d, J = 5.4 Hz, 1H), 5.01 (dd, J = 11.3, 1.9 Hz, 1H), 2.75–2.70 (m, 2H), 2.60 (d, J = 18.2 Hz, 1H), 2.50 (d, J = 18.2 Hz, 1H), 2.31 (s, 1H), 2.29–2.21 (m 2H), 2.10 (s, 3H), 2.08–1.94 (3 H), 1.69–1.61 (m, 1H), 1.49 (s, 3H), 1.01 (d, J = 6.6 Hz, 3H), 0.99 (s, 3H), 0.92 (d, J = 6.6 Hz, 3H); HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{22}H_{29}O_9F_3NaS$ 549.1382; found, 549.1375. This material was directly submitted for dehydration.

A solution of the intermediate α-hydroxy ketone **42b** (1.8 mg, 3.4 μmol) in pyridine (100 μl) was heated to 50 °C for 10 min after which $SOCl_2$ (7.5 μl, 0.10 mmol) was added dropwise. After stirring for 30 min the reaction was cooled to rt and quenched with H_2O. The aqueous layer was extracted with EtOAc (5 x 2 mL), and the combined organic phases were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography (Hexanes/EtOAc 3:1)) to provide enone **43** (1.6 mg, 90%) as a clear colorless oil; R_f 0.65 (Hexanes/EtOAc (1:1)); IR (film) 2970, 2932, 1776, 1730, 1660, 1375, 1068 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.43 (s, 1H), 5.59 (d, J = 5.4 Hz, 1H), 5.41 (d, J = 5.4 Hz, 1H), 5.08 (d, J = 8.5 Hz, 1H), 2.67 (d, J = 18.1 Hz, 1H), 2.55 (d, J = 18.4 Hz, 1H), 2.55–2.49 (m, 1H), 2.31–2.19 (m, 2H), 2.09–

2.06 (m, 1H), 2.06 (s, 3H), 1.85–1.79 (m, 1H), 1.57–1.53 (m, 1H), 1.27 (s, 6H), 1.03 (d, J = 6.7 Hz, 3H), 0.95 (d, J = 6.6 Hz, 3H); HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $C_{22}H_{27}O_8F_3NaS$ 531.1276; found, 531.1275. Insufficient quantities of **43** did not permit the acquisition of ^{13}C NMR data. Note that **43** presents very weak signals for six fully substituted carbons and three carbonyl carbons that could not be identified in the baseline noise.

*(1R,5R,6S,7R,8aR)-5-((benzyloxy)methyl)-7-((tert-butyldimethylsilyl)oxy)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1-isopropyl-6,8a-dimethyl-1,2,4,5,6,7,8,8a-octahydroazulen-5-ol (**45**).* The preparation of **45** was rendered from the pure acetate **33** of Scheme 4, but was more efficiently undertaken from the mixture of alcohols produced in the SmI_2 cyclization. To a solution containing a mixture of **29** and **30** (67:33 ratio) (1.00 g, 2.51 mmol) in Et_2O (50 mL), $LiAlH_4$ (5.02 mL, 5.02 mmol, 1M Et_2O) was added dropwise at 22 °C. The reaction was stirred at rt overnight, then cooled to 0 °C and quenched by careful addition of Na_2SO_4•10 H_2O (3 g). After stirring for five min, the cooling bath was removed, and the reaction was allowed to warm to rt. After vigorously stirring for 1 h, the mixture was filtered through a plug of anhydrous Na_2SO_4 and concentrated. The crude oil was dissolved in CH_2Cl_2 (50 mL) and cooled to 0 °C. To this solution was added 2,6-lutidine (1.46 mL, 12.6 mmol) followed by TBSOTf (1.44 mL, 6.28 mmol). After 30 stirring for min, the reaction was quenched with the addition of saturated aqueous $NaHCO_3$ (25 mL). The layers were separated and the aqueous layer was then extracted with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were dried with $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography (1–3% EtOAc/hexanes) provided **45** (0.833 g, 53%) and **epi-45** (0.506 g, 32%) as colorless oils.

For the characterization of **45**: R_f 0.65 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ +9.2 (*c* 0.29, $CHCl_3$); IR (film) 3582, 2954, 2928, 2855, 1578, 1541, 1470, 1388, 1254, 1078, 1029, 1002 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.29 (m, 5H), 5.27 (s, 1H), 4.54 (d, *J* = 11.5 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.03 (d, *J* = 8.8 Hz, 1H), 3.90–3.85 (m, 1H), 3.78 (d, *J* = 6.3 Hz, 1H), 3.75–3.70 (m, 1H), 3.40 (d, *J* = 8.8 Hz, 1H), 3.09 (s, 1H), 2.63 (d, *J* = 13.5 Hz, 1H), 2.40 (d, *J* = 13.9 Hz, 1H), 2.24 (ddd, *J* = 15.9, 8.1, 2.7 Hz, 1H), 2.09–2.02 (m, 2H), 1.98–1.93 (m, 1H), 1.89–1.82 (m, 2H), 1.73–1.62 (m, 2H), 1.05 (d, *J* = 6.3 Hz, 3H), 1.01 (s, 3H), 0.99 (s, 3H), 0.90 (s, 9H), 0.89 (d, *J* = 6.3 Hz, 3H), 0.87 (s, 9H), 0.12 (s, 3H), 0.06 (s, 6H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 138.8, 128.4, 127.7, 127.6, 125.1, 77.6, 77.0, 74.0, 73.2, 60.7, 56.4, 48.4, 47.8, 41.6, 38.1, 36.3, 35.0, 30.5, 26.3, 26.2, 23.0, 22.6, 22.2, 19.1, 18.4, 18.2, –2.3, –4.3, –5.1 (2C); HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{37}H_{66}O_4Si_2Na$ 653.4398 found 653.4385. This product is readily distinguished from its C-8 diastereomer, *(1R,5R,6S,7S,8aR)-5-((benzyloxy)methyl)-7-((tert-butyldimethylsilyl)oxy)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1-isopropyl-6,8a-dimethyl-1,2,4,5,6,7,8,8a-octahydroazulen-5-ol* ***(epi-45)***, which was characterized as follows: R_f 0.62 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ +28.9 (*c* 0.60, $CHCl_3$); IR (film) 3429, 1255, 1928, 2856, 1471, 1386, 1361, 1254, 1075, 1029, 1004, 937, 836, 773 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.30 (m, 5H), 5.41 (s, 1H), 4.55 (s, 2H), 3.86 (t, *J* = 7.6 Hz, 1H), 3.62 (d, *J* = 8.7 Hz, 1H), 3.51–3.48 (m, 2H), 2.98 (s, 1H), 2.59 (d, 13.2 Hz, 1H), 2.37 (d, *J* = 13.1 Hz, 1H), 2.27 (dd, *J* = 16.1, 7.6 Hz, 1H), 2.01–1.90 (m, 4H), 1.85–1.71 (m, 3H), 1.08 (d, *J* = 6.4 Hz, 3H), 1.00 (s, 3H), 0.96–0.94 (m, 15H), 0.92 (s, 9H), 0.12 (s, 9H), 0.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 138.4, 128.4, 127.6, 127.5, 125.7, 76.5, 73.4,

72.6, 72.3, 61.3, 54.8, 48.02, 47.95, 44.4, 35.1, 34.7, 33.8, 29.7, 26.2, 26.1, 23.1, 22.6, 21.9, 19.8, 18.5, 18.1, –3.3, –4.0, –5.0 (2C); HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{37}H_{66}O_4Si_2Na$ 653.4398 found 653.4387.

*(1R,5R,6S,7R,8aR)-7-((tert-butyldimethylsilyl)oxy)-6-(2-((tertbutyldimethylsilyl)oxy)ethyl)-5-hydroxy-1-isopropyl-6,8a-dimethyl-1,2,4,5,6,7,8,8a-octahydroazulene-5-carbaldehyde (**46**).* To a two-necked round-bottom flask charged with $NH_{3(l)}$ (45 mL) at –78 °C was added Na° (~0.20 g, 8.7 mmol) by introducing small pieces directly into the reaction flask to provide an inky blue solution under argon atmosphere. After stirring for 10 min, benzyl ether **45** (0.303 g, 0.48 mmol) was added in a solution of THF (5 mL, with a 5 mL syringe rinse). The reaction was stirred at –78 °C for 30 min, then iPrOH (~10 mL) was added dropwise until the blue color dissipated to provide a clear colorless solution. Saturated aqueous NH_4Cl (15 mL) was added and the cooling bath was removed and replaced with a warm water bath. The mixture was stirred for 30 min, allowed for the evaporation of $NH3_{(l)}$ and the remaining mixture was concentrated under reduced pressure to give an aqueous slurry. The aqueous slurry was extracted with CH_2Cl_2 (3 x 20 mL), and the organic extract was dried with $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography (5–10% EtOAc/hexanes) provided the expected diol **45a** (0.241 g, 93%) as a colorless oil; R_f 0.48 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ +19.6 (*c* 1.59, $CHCl_3$); IR (film) 3992, 2955, 2929, 2857, 1472, 1387, 1362, 1255, 1086, 1028, 1001, 938, 836, 772, 726 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.34 (s, 1H), 4.52 (s, 1H), 3.80–3.71 (m, 4H), 3.48 (d, *J* = 10.6 Hz, 1H), 2.49 (d, *J* = 13.7 Hz, 1H), 2.40 (d, *J* = 5.1 Hz, 1H), 2.28–2.21 (m, 2H), 1.99–1.62 (m, 6H), 1.51 (dt, *J* = 15.3, 5.2 Hz, 1H), 0.97 (d, *J* = 6.2 Hz, 3H), 0.96 (s, 3H), 0.90 (s, 3H),

0.87 (s, 9H), 0.85 (d, J = 6.2 Hz, 3H), 0.84 (s, 9H), 0.07 (s, 3H), 0.06 (s, 6H), –0.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.9, 125.6, 76.0, 75.4, 65.8, 59.9, 57.9, 48.5, 48.2, 43.4, 39.0, 36.0, 35.0, 30.0, 26.1, 25.9, 23.0, 22.7, 20.7, 18.19, 18.15, 17.9, –2.7, –4.5, –5.4, –5.5; HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $C_{30}H_{60}O_4Si_2Na$ 563.3928 found 563.3929. This diol was used for oxidation as described below.

To a solution of $(COCl)_2$ (0.25 mL, 2.95 mmol) in CH_2Cl_2 (2 mL) at –78 °C was added dry DMSO (0.31 mL, 4.43 mmol). The mixture was stirred for 10 min at –78 °C and the intermediate diol **45a** (0.160 g, 0.295 mmol) was added in a solution of CH_2Cl_2 (0.5 mL, with 0.5 mL rinse). After stirring at –78 °C for 30 min, Et_3N (1.23 mL, 8.85 mmol) was then added, and the cooling bath was removed to allow the reaction to warm to rt. The solution was diluted with water (3 mL) and the layers were separated. The aqueous layer was re-extracted with CH_2Cl_2 (3 x 2 mL), and the combined organic extracts were dried with $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography (20% EtOAc/hexanes) provided aldehyde **46** (157 mg, 98%): R_f 0.70 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ –20.7 (c 0.35, $CHCl_3$); IR (film) 3480, 2927, 1709, 1472, 1256, 1091, 835, 773 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.19 (d, J = (1.4 Hz, 1H), 5.28 (s, 1H), 3.98 (s, 2H), 3.78 (ddd, J = 10.5, 7.0, 5.1 Hz, 1H), 3.67 (ddd, J = 10.5, 7.9, 6.6 Hz, 1H), 2.75 (d, J = 14.1 Hz, 1H), 2.31–2.25 (m, 2H), 2.20 (dd, J = 16.0, 6.5 Hz, 1H), 2.14–2.07 (m, 1H), 2.03–1.69 (m, 5H), 1.06 (d, J = 6.6 Hz, 3H), 1.02 (s, 3H), 0.91 (d, J = 6.6 Hz, 1H), 0.90 (s, 9H), 0.86 (s, 9H), 0.81 (s, 3H), 0.16 (s, 3H), 0.06 (s, 6H), 0.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.6, 144.9, 127.3, 80.2, 77.6, 59.9, 56.4, 50.1, 48.3, 41.1, 36.20, 36.15, 35.6, 30.5, 26.2, 26.1, 22.9, 22.6, 22.3, 19.9, 18.3, 18.2, –

2.4, –4.3, –5.2 (2C); HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{30}H_{58}O_4Si_2Na$ 561.3771 found 561.3759.

*1-((1R,5R,6S,7R,8aR)-7-((tert-butyldimethylsilyl)oxy)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-5-hydroxy-1-isopropyl-6,8a-dimethyl-1,2,4,5,6,7,8,8a-octahydroazulen-5-yl)-2-((4-methoxybenzyl)oxy)ethanone (**47**).* To a –78 °C solution of nBu$_3$SnCH$_2$OPMB (0.98 g, 2.23 mmol) in THF (5 mL) was added nBuLi (0.80 mL, 2.00 mmol, 2.5 M in hexanes). The reaction was stirred at –78 °C for five min and aldehyde **46** (0.224 g, 0.414 mmol) was then added as a solution in THF (1 mL with a 0.5 mL syringe rinse). After stirring at –78 °C for 1 h, the reaction was quenched by the addition of saturated aqueous NH_4Cl (5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were dried with $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography (20% EtOAc/hexanes) provided the expected diol **46a** as a single diastereomer (195 mg, 68%, 82% brsm) and recovered a small amount of starting **46** (31 mg, 14%). Complete characterization of this diol **46a** is provided as follows: R_f 0.56 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ +7.7 (*c* 0.30, $CHCl_3$); IR (film) 3506, 2954, 2925, 2851, 1578, 1513, 1471, 1251, 1080, 835, 773 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.13 (s, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.46 (d, *J* = 12.0 Hz, 1H), 4.34 (dt, *J* = 7.2, 3.2 Hz, 1H), 4.19 (s, 1H), 4.08 (dd, *J* = 7.9, 3.1 Hz, 1H), 3.83 (dd, *J* = 9.7, 2.7 Hz, 1H), 3.80 (s, 3H), 3.77–3.74 (m, 2H), 3.63 (dd, 9.6, 7.3 Hz, 1H), 2.92 (d, *J* = 3.5 Hz, 1H), 2.50 (d, *J* = 15.2 Hz, 1H), 2.27 (d, *J* = 15.6 Hz, 1H), 2.22–2.19 (m, 1H), 2.02–1.80 (m, 4H), 1.73–1.65 (m, 3H), 1.07 (s, 3H), 1.01–1.00 (m, 6H), 0.90 (s, 9H), 0.89–0.88 (m, 12H), 0.12 (s, 3H), 0.07 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 147.8, 130.3,

129.5, 125.4, 113.9, 77.5, 75.1, 73.5, 72.9, 71.5, 61.0, 58.5, 55.4, 49.4, 48.4, 45.1, 39.1, 36.0, 34.3, 29.9, 26.3, 26.1, 22.9, 22.8, 20.8, 20.6, 18.4, 18.3, –2.8, –4.1, –5.2, –5.3; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{39}H_{70}O_6Si_2Na$ 713.4609 found 713.4606. This material was taken forward for oxidation as described below.

To a solution of $(COCl)_2$ (0.17 mL, 1.93 mmol) in CH_2Cl_2 (1.3 mL) at –78 °C was added dry DMSO (0.21 mL, 2.90 mmol). The mixture was stirred for 10 min and the diol **46a** (0.134 g, 0.193 mmol) was added at –78 °C as a solution in CH_2Cl_2 (0.5 mL, with a 0.5 mL syringe rinse). After stirring at –78 °C for one h, Et_3N (0.54 mL, 3.86 mmol) was introduced, the cooling bath was removed, and the reaction was allowed to warm to rt. The solution was diluted with water (2 mL), the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic extracts were dried with $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography (3–5% EtOAc/hexanes) provided ketone **47** (0.127 g, 93%) as a colorless oil: R_f 0.68 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ +20.7 (*c* 0.05, $CHCl_3$); IR (film) 3303, 2954, 2920, 2854, 1727, 1514, 1471, 1251, 1058, 835, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 5.95 (s, 1H), 5.20 (s, 1H), 4.56–4-42 (m, 4H), 4.24 (dd, *J* = 11.1, 2.1 Hz, 1H), 3.87 (t, 9.7 Hz, 1H), 3.80 (s, 3H), 3.69–3.56 (m, 1H), 2.57 (br s, 2H), 2.25–2.08 (m, 2H), 1.97–1.60 (m, 5H), 1.16 (s, 3H), 1.06 (s, 3H), 1.02 (d, *J* = 6.5 Hz, 3H), 0.92 (s, 9H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.85 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.9, 159.4, 148.4, 130.2, 129.6, 125.8, 114.0, 113.9, 83.9, 73.6, 72.7, 70.3, 60.6, 59.9, 55.4, 49.5, 48.3, 45.6, 39.0, 37.7, 35.0, 29.3, 26.13, 26.12, 23.7, 22.9, 18.5, 18.2, 17.2, –

2.6, –4.4, –5.3, –5.6; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{39}H_{68}O_6Si_2Na$ 711.4452 found 711.4421.

*(1R,5R,6S,7R,8aR)-7-((tert-butyldimethylsilyl)oxy)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-5-(2-hydroxy-1-((4-methoxybenzyl)oxy)propan-2-yl)-1-isopropyl-6,8a-dimethyl-1,2,4,5,6,7,8,8a-octahydroazulen-5-ol (**49**).* To a solution of ketone **47** (0.124 g, 0.179 mmol) in Et_2O (1.8 mL) at –78 °C was added MeMgBr (0.30 mL, 0.90 mmol, 3M in Et_2O). The reaction was stirred at –78 °C for 15 min. The cooling bath was removed, the reaction was allowed to warm to rt and stirring was continued for 45 min. Saturated aqueous NH_4Cl (2 mL) was added. The layers were separated and the aqueous layer was extracted with Et_2O (3 x 2 mL). The combined organic phases were dried with $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography (2–10% EtOAc/hexanes) provided the desired diol **49** (64.6 mg, 51%), the rearranged ketone **48** (15.9 mg, 13%) and recovered **47** (20.1 mg, 16%) as colorless oils. The ratio of products **48** and **49** varied widely in these reaction attempts. Experiments were carried out using the procedure as described above by employing newly purchased bottles of MeLi in place of MeMgBr to yield **49** (40%) and recovered starting material **47** (43%) without formation of ketone **48**. For the characterization of **49**: R_f 0.60 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ –25.8 (*c* 0.75, $CHCl_3$); IR (film) 3506, 2955, 2928, 2856, 1614, 1515, 1471, 1386, 1251, 1083, 1041, 1002 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 50 °C) δ 7.26 (d, *J* = 8.3 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.37 (s, 1H), 4.57 (d, *J* = 11.1 Hz, 1H), 4.39 (d, *J* = 11.1 Hz, 1H), 4.30 (dd, *J* = 9.1, 4.8 Hz, 1H), 3.98 (d, 9.5 Hz, 1H), 3.79–3.73 (m, 2H), 3.81 (s, 3H), 3.66 (s, 1H), 3.55 (s, 1H), 3.50 (d, *J* = 9.3 Hz, 1H), 3.31 (d, *J* = 15.4 Hz, 1H), 2.30 (ddd, *J* = 16.1, 7.9, 2.7 Hz, 1H), 1.95–1.90 (m, 5H), 1.86–1.81 (m, 1H), 1.78–

1.67 (m, 1H), 1.56–1.50 (m, 1H), 1.35 (s, 3H), 1.04 (s, 3H), 1.00 (d, J = 6.8 Hz, 3H), 0.99 (s, 3H), 0.91–0.90 (m, 21H), 0.13 (s, 3H), 0.09 (s, 3H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 159.7, 149.7, 130.0, 129.6, 126.7, 114.2, 83.1, 78.0, 77.8, 73.3, 73.2, 62.5, 60.4, 55.5, 49.5, 48.9, 48.2, 37.1, 36.3, 35.7, 29.91, 29.86, 26.4, 26.2, 22.9, 22.8, 21.0, 18.8, 18.39, 18.37, –3.7, –4.3, –5.18, –5.21; HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $C_{40}H_{72}O_6Si_2Na$ 727.4765 found 727.4785. The rearranged eight-membered ketone **48** was also fully characterized as follows: *(1R,5S,7S,8R,9aR)-8-((tert-butyldimethylsilyl)oxy)-7-(2-((tert-butyldimethylsilyl)oxy)ethyl)-5-hydroxy-1-isopropyl-5-(((4-methoxybenzyl)oxy)methyl)-7,9a-dimethyl-4,5,7,8,9,9a-hexahydro-1H-cyclopenta[8]annulen-6(2H)-one*: R_f 0.72 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ +3.1 (*c* 0.76, $CHCl_3$); IR (film) 3400, 1955, 2928, 2856, 1690, 1612, 1514, 1471, 1380, 1251, 1086, 1039, 1004 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, J = 8.3 Hz, 2H), 6.86 (d, J = 8.3 Hz, 2H), 5.07 (s, 1H), 4.67 (d, J = 7.7 Hz, 1H), 4.54 (d, J = 11.7 Hz, 1H), 4.54 (s, 1H), 4.46 (d, J = 11.8 Hz, 1H), 3.80 (s, 3H), 3.72–3.64 (m, 2H), 3.56 (d, J = 9.8 Hz, 1H), 3.44 (d, J = 9.8 Hz, 1H), 2.98 (ddd, J = 15.9, 10.1, 6.4 Hz, 1H), 2.84 (d, J = 13.9 Hz, 1H), 2.26 (d, J = 13.9 Hz, 1H), 2.19 (ddd, J = 16.5, 8.0, 2.5 Hz, 1H), 1.87 (dt, J = 14.4, 4.1 Hz, 1H), 1.81 (dd, J = 16.5, 8.3 Hz, 1H), 1.71–1.52 (m, 3H), 1.38 (q, 7.9 Hz, 1H), 1.07 (s, 3H), 0.99 (s, 3H), 0.92 (d, J = 6.3 Hz, 3H), 0.88 (s, 9H), 0.86 (s, 9H), 0.79 (d, J = 6.8 Hz, 3H), 0.14 (s, 3H), 0.13 (s, 3H), 0.03 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.4, 159.3, 144.5, 130.6, 129.8 (2C), 113.9, 82.5, 73.2, 73.1, 71.1, 61.0, 58.3, 58.0, 55.4, 49.5, 47.7, 39.0, 34.7, 33.9, 29.1, 26.21, 26.18, 23.3, 21.8, 19.0, 18.7, 18.5, 15.1, –3.1, –4.3, –5.2, –5.3; HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $C_{39}H_{68}O_6Si_2Na$ 711.4452 found 711.4437.

*(1R,3R,3aR,5R,6S,7R,8aS)-5-((tert-butyldimethylsilyl)oxy)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-7-(2-hydroxy-1-((4-methoxybenzyl)oxy)propan-2-yl)-3-isopropyl-3a,6-dimethyldecahydroazulene-1,7,8a-triol (**49a**).* To a solution of **49** (46.6 mg, 0.066 mmol) in ^{t}BuOH (0.7 mL) at 22 °C was added DMAP (16 mg, 0.132 mmol) followed by OsO_4 (0.70 mL, 0.132 mmol, 0.19 M in H_2O). The resulting bright red mixture was heated in a 40 °C oil bath for 18 h, cooled to rt, diluted with $CHCl_3$ (2 mL) and H_2S was bubbled through the reaction mixture for 30 min. The black heterogeneous mixture was filtered through a column of celite, which was flushed with $CHCl_3$ then with water. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic phases were dried with $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography (5–20% EtOAc/hexanes) provided the α-diol of **49** which is described as compound **49a** (39.0 mg, 80%), a colorless oil characterized as follows: R_f 0.73 (hexanes/EtOAc (1:2)); $[\alpha]_D^{20}$ –8.6 (*c* 0.17, $CHCl_3$); IR (film) 3450, 2855, 2910, 2832, 1514, 1471, 1251, 1082, 835, 772 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.24 (s, 1H), 5.60 (s, 1H), 4.50 (d, *J* = 11.6 Hz, 1H), 4.42 (d, *J* = 12.0 Hz, 1H), 4.30 (t, *J* = 5.7 Hz, 1H), 3.81 (s, 3H), 3.81–3.73 (m, 2H), 3.65–3.61 (m, 2H), 3.43 (d, *J* = 9.8 Hz, 1H), 3.35–3.28 (m, 2H), 2.92 (s, 1H), 2.66 (t, *J* = 12.1 Hz, 1H), 2.26 (d, *J* = 15.6 Hz, 1H), 1.87–1.77 (m, 3H), 1.70–1.67 (m, 3H), 1.38 (s, 3H), 1.31–1.27 (m, 1H), 1.09 (s, 3H), 1.02 (s, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.92 (s, 9H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.85 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 130.3, 129.3, 113.9, 82.9, 82.2, 78.6, 75.0, 73.3, 70.2, 68.1, 61.2, 55.4, 53.1, 50.8, 47.3, 46.4, 37.8, 37.2, 34.4, 27.2, 26.1,

26.0, 25.8, 25.2, 24.0, 22.4, 18.5, 18.4, 16.9, –2.5, –4.0, –5.4, –5.7; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{40}H_{74}O_8Si_2Na$ 761.4820 found 761.4838.

*(3aS,4R,5aR,6R,8aS,9aR)-4-((tert-butyldimethylsilyl)oxy)-8a-hydroxy-9a-(2-hydroxy-1-((4- methoxybenzyl)oxy)propan-2-yl)-6-isopropyl-3a,5a-dimethyloctahydroazuleno[5,6-b]furan-2,8(3H,8aH)-dione (**44**).* A solution of TBAF:AcOH was prepared from TBAF (0.25 mL, 1M in THF) and glacial AcOH (14.5 μL). To a solution of the triol compound **49a** (4.0 mg, 0.0054 mmol) in THF (0.2 mL) at 22 °C was added the mixture of 1:1 TBAF:AcOH (25 μL, 0.025 mmol). The reaction was stirred at rt for 15 min, quenched with saturated aqueous $NaHCO_3$ and diluted with CH_2Cl_2. The layers were separated and the aqueous layer was re-extracted with CH_2Cl_2 (3 x 2 mL). The combined organic phases were dried with $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography (25% then 50% EtOAc/hexanes) provided a crude polyol characterized as compound **49b** (3.0 mg, 90%); a colorless oil characterized as follows: R_f 0.53 (hexanes/EtOAc (1:2)); $[\alpha]_D^{20}$ –22.1 (*c* 0.16, $CHCl_3$); IR (film) 3402, 2954, 2916, 2864, 1613, 1513, 1463, 1250, 1058, 835, 772 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 50 °C) δ 7.24 (J = 8.3 Hz, 2H), 6.90 (d, *J* = 8.3 Hz, 2H), 5.34 (s, 1H), 4.52 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 11.5 Hz, 1H), 4.39 (d, *J* = 9.8 Hz, 1H), 4.04 (br s, 1H), 3.82 (s, 3H), 3.76 (d, *J* = 9.3 Hz, 1H), 3.70–3.68 (m, 2H), 3.39 (d, *J* = 8.8 Hz, 1H), 3.32–3.27 (m, 1H), 3.22 (s, 1H), 3.12 (d, *J* = 9.8 Hz, 1H), 2.44 (dt, *J* = 15.9, 8.2 Hz, 1H), 2.01 (d, *J* = 15.6 Hz, 1H), 1.94 (d, *J* = 15.6 Hz, 1H), 1.85–1.80 (m, 2H), 1.75–1.63 (m, 3H), 1.42 (s, 3H), 1.35–1.28 (m, 2H), 1.14 (s, 3H), 1.01 (s, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.87 (s, 9H), 0.14 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 159.8, 130.0, 129.5, 114.3, 83.6, 82.1, 81.7, 78.7, 74.1, 73.7, 69.6, 59.6,

55.5, 53.6, 51.0, 47.5, 47.0, 38.5, 38.1, 34.3, 27.1, 26.2, 25.3, 24.0, 22.3, 19.3, 18.5, 16.8, –2.9, –4.0; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{34}H_{60}O_8SiNa$ 647.3955 found 647.3943. This intermediate polyol was submitted for oxidation as described below.

To a solution of compound **49b** (10 mg g, 0.016 mmol) in a 2:1 mixture of CH_2Cl_2 and water (0.45 mL) at 0 0C was added KBr (1.9 mg, 0.016 mmol) and TEMPO (0.5 mg, 0.004 mmol). Separately, a solution was prepared from saturated aqueous $NaHCO_3$ (2 mL) and NaOCl (8.25% in H_2O, 1 mL). This buffered NaOCl solution (0.15 mL, 0.064 mmol) was introduced by dropwise addition over 10 min into the rapidly stirring biphasic mixture. After 20 min, the reaction was quenched with the addition of saturated aqueous $Na_2S_2O_3$ (1 mL) and allowed to warm to room temperature. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL) and the combined organic phases were dried with $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography (30% EtOAc/hexanes) provided lactone **44** (8.3 mg, 84%) as a colorless oil: R_f 0.56 (hexanes/EtOAc (1:1)); $[\alpha]_D^{20}$ +11.7 (*c* 0.21, $CHCl_3$); IR (film) 3469, 2957, 2934, 2839, 1755, 1750, 1612, 1514, 1463, 1251, 1174, 1084, 1042, 836 cm−1; ^{1}H NMR (500 MHz, $CDCl_3$, 50 °C) δ 7.22 (d, *J* = 8.3 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 4.49 (s, 2H), 4.33 (d, *J* = 8.8 Hz, 1H), 3.82 (s, 3H), 3.69 (d, *J* = 9.3 Hz, 1H), 3.35 (d, *J* = 9.3 Hz, 1H), 3.08 (s, 1H), 2.85 (d, *J* = 18.1 Hz, 1H), 2.67 (d, *J* = 18.1 Hz, 1H), 2.61 (s, 1H), 2.39 (dd, *J* = 19.9, 8.5 Hz, 1H), 2.07 (dd, *J* = 15.3, 8.6 Hz, 1H), 2.02–1.87 (m, 3H), 1.80 (d, *J* = 15.6 Hz, 1H), 1.75–1.65 (m, 1H), 1.39 (s, 3H), 1.38 (s, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 1.03 (s, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), 0.15 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$, 50 °C) δ 218.8, 175.3, 159.9, 129.7, 129.5, 114.3, 93.3, 84.3, 80.3, 74.0, 73.8, 69.2, 55.5, 53.8, 50.9, 46.4, 42.5, 38.6, 31.5, 30.5, 29.9, 26.2, 24.5, 23.3, 22.8,

18.4, 16.0, 13.9, –3.1, –4.8; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{34}H_{54}O_8SiNa$ 641.3486 found 641.3462.

*(3aS,4R,5aR,6R,9aR)-9a-(benzyloxymethyl)-6-isopropyl-3a,5a-dimethyl-2,8-dioxo-2,3,3a,4,5,5a,6,7,8,9a-decahydroazuleno[5,6-b]furan-4-yl acetate (**50**).* To a solution of the β-diol **34** (7.6 mg, 0.016 mmol) in CH_2Cl_2 (1 mL) at 0 °C was added H_2O (0.5 mL), KBr (1 mg, 8.4 μmol), TEMPO (1 mg, 6.4 μmol), and aqueous sodium hypochlorite (40 μl, 3% in H_2O, 0.019 mmol). The aqueous sodium hypochlorite solution was prepared from aqueous sodium hypochlorite (1 mL, 10% in H_2O) and saturated aqueous $NaHCO_3$ (2 mL). After stirring for 35 min, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (1 mL) and allowed to warm to rt. The aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL), and the combined organic phases were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude oil was routinely utilized in the next reaction. Purification by flash column chromatography (Hexanes/EtOAc 2:1)) provided a sample of the corresponding ketol, *(3aS,4R,5aR,6R,8aR,9aR)-9a-(benzyloxymethyl)-8a-hydroxy-6-isopropyl-3a,5a-dimethyl- 2,8-dioxododecahydroazuleno[5,6-b]furan-4-yl acetate* (6.8 mg, 90%) which was fully characterized as a clear colorless oil; R_f 0.28 (Hexanes/EtOAc (2:1)); $[\alpha]_D^{20}$ –17.1 (*c* 0.27, $CHCl_3$); IR(film) 3400, 2961,2930, 1775, 1747, 1475, 1379, 1239, 1098, 1019 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39–7.26 (m, 5H), 4.98 (dd, *J* = 11.0, 1.9 Hz, 1H), 4.60 (d, *J* = 11.5 Hz, 1H), 4.56 (d, *J* = 11.0 Hz, 1H), 4.29 (s, 1H), 3.70 (d, *J* = 9.3 Hz, 1H), 3.40 (d, *J* = 9.2 Hz, 1H), 2.70 (d, *J* = 16.2 Hz,1H), 2.67 (d, *J* = 19.2Hz, 1H), 2.61 (d, *J* = 18.5 Hz, 1H), 2.49 (d, *J* = 18.5 Hz, 1H), 2.30 (dd, *J* = 13.6, 11.1 Hz, 1H), 2.07 (s, 3H), 2.06 (d, *J* = 16.3 Hz, 1H), 2.03 (dd, *J* = 18.6, 9.5 Hz, 1H)), 1.92 (dd, *J* = 13.6, 2.0 Hz, 1H), 1.85 (dd, *J*

= 19.2, 9.6 Hz, 1H), 1.68–1.65 (m, 1H), 1.45 (s, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.94 (s, 3H), 0.90 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 211.7, 173.6, 169.8, 135.4, 128.8, 128.7, 128.4, 88.0, 80.1, 74.5, 74.1, 70.9, 49.5, 47.4, 45.7, 41.1, 38.7, 36.1, 34.7, 30.0, 23.3, 23.1, 21.3, 16.5, 14.8; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{27}H_{36}O_7Na$ 495.2359; found, 495.2341. In practice, this α-hydroxy ketone was taken forward for elimination as described below.

A solution of the α-hydroxy ketone derived from **34** (6.8 mg, 0.014 mmol) in pyridine (300 µl) was heated to 50 °C $SOCl_2$ (10 µl, 0.14 mmol) was then added dropwise. After stirring for 30 min, the reaction was cooled to rt and quenched with H_2O. The aqueous layer was extracted with EtOAc (3 x 3 mL), and the combined organic phases were dried over Na_2SO_4, filtered, and concentrated in vacuo. The product was purified by flash column chromatography (Hexanes/EtOAc 3:1)) to provide enone **50** (3.5 mg, 64%) as a light yellow oil; R_f 0.68 (Hexanes/EtOAc (1:1)); $[\alpha]_D^{20}$ +1.8 (*c* 0.28, $CHCl_3$); IR(film) 2961, 2873, 1785, 1735, 1660, 1453, 1374, 1235, 1215, 1078, 1051 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.28 (m, 5H), 6.11 (s, 1H), 4.91 (d, *J* = 7.8 Hz, 1H), 4.61 (d, *J* = 12.5 Hz, 1H), 4.51 (d, *J* = 11.5 Hz, 1H), 3.79 (d, *J* = 11.0 Hz, 1H), 3.64 (d *J* = 11.0 Hz, 1H), 3.05 (d, *J* = 17.8 Hz, 1H), 2.53–2.46 (m, 1H) 2.45 (dd, *J* = 18.7, 7.8 Hz, 1H), 2.31 (d, *J* = 17.8 Hz, 1H), 2.16 (dd, *J* = 18.7, 12.9 Hz, 1H), 1.96 (s, 3H), 1.95 (d, *J* = 16.5 Hz, 1H), 1.81 (dt, *J* = 13.5, 6.7 Hz, 1H), 1.56–1.50 (m, 1H) 1.27 (s, 3H), 1.21 (s, 3H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.8, 175.1, 169.9, 152.6, 136.8, 128.6, 128.1, 127.8, 125.5, 86.2, 76.2 (seen by HMQC), 74.8, 74.1, 50.9, 48.4, 44.1, 43.2, 40.3, 36.5 (seen by HMQC), 28.6, 23.8, 22.2

(2 C), 20.9, 17.9 (seen by HMQC); HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{27}H_{34}O_6Na$ 477.2238; found, 477.2253.

*(3aS,4R,5aR,6R,8aR,10aR)-6-isopropyl-3a,5a-dimethyl-2,8-dioxodecahydro-8a,10a-methanocyclopenta[b]furo[3,2-f]oxocin-4-yl acetate (**51**).* To a solution of diol **35** (5.5 mg, 0.012 mmol) in CH_2Cl_2 (1 mL) at 0 °C was added H_2O (0.5 mL), KBr (1 mg, 8.4 μmol), TEMPO (1 mg, 6.4 μmol), and aqueous sodium hypochlorite (28 μl, 3% in H_2O, 0.014 mmol). The aqueous sodium hypochlorite solution was prepared from aqueous sodium hypochlorite (1 mL, 10% in H_2O) and saturated aqueous $NaHCO_3$ (2 mL). After stirring for 35 min, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (1 mL) and allowed to warm to rt. The aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL), and the combined organic phases were dried over Na_2SO_4, filtered, and concentrated in vacuo. A sample of the crude oil was routinely utilized in the next reaction. The product was purified by flash column chromatography (Hexanes/EtOAc 2:1)) to give corresponding α-hydroxy ketone, *(3aS,4R,5aR,6R,8aS,9aR)-9a-(benzyloxymethyl)-8a-hydroxy-6-isopropyl-3a,5a-dimethyl-2,8-dioxododecahydroazuleno[5,6-b]furan-4-yl* acetate (3.5 mg, 64%) as a clear colorless oil; R_f 0.37 (Hexanes/EtOAc (1:1)); $[\alpha]_D^{20}$ −11.4 (*c* 0.14, $CHCl_3$); IR (film) 2961, 2927, 1773, 1744, 1454, 1370, 1241, 1204, 1106, 1079, 1020 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.26 (m, 5H), 5.47 (d, *J* = 9.2 Hz, 1H), 4.56 (d, *J* = 12.5 Hz, 1H), 4.45 (d, *J* = 11.5 Hz, 1H), 3.55 (d, *J* = 10.4 Hz, 1H), 3.35 (d, *J* = 10.4 Hz, 1H), 2.93 (s, 1H), 2.78 (d, *J* = 18.0 Hz, 1H), 2.45–2.40 (m, 2H), 2.09–2.04 (m, 4H), 2.00–1.94 (m, 1H), 1.88 (d, *J* = 6.7 Hz, 1H), 1.85 (d, *J* = 5.8 Hz, 1H), 1.75 (d, *J* = 15.7 Hz, 1H), 1.72–1.68 (m, 1H), 1.49–1.43 (m, 1H), 1.35 (s, 3H), 1.08 (s, 3H), 1.00 (d, *J* = 6.4 Hz, 3H), 0.92 (d, *J* = 6.5 Hz,

3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 218.1, 174.2, 169.6, 136.9, 128.6, 128.1, 127.8, 88.2, 83.7, 75.9, 74.1, 70.7, 50.4, 48.5, 46.0, 43.5, 42.3, 38.3, 32.5, 30.2, 23.1, 22.6, 21.3, 15.3, 14.7; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{27}H_{36}O_7Na$ 495.2359; found, 495.2352.

A solution of the α-hydroxy ketone from diol **35** (3.3 mg, 7.0 μmol) in pyridine (300 μl) was heated to 50 °C and $SOCl_2$ (10 μl, 0.14 mmol) was then added dropwise. After stirring for 30 min, the reaction was cooled to rt and quenched with H_2O. The aqueous layer was extracted with EtOAc (3 x 3 mL), and the combined organic phases were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was a mixture of **51** and **50** (91:9). The product was purified by flash column chromatography (Hexanes/EtOAc 2:1)) to provide **51** (1.5 mg, 50%) as a light yellow oil, which provided the following characterization data: R_f 0.68 (Hexanes/EtOAc (1:1)); IR (film) 2927, 1772, 1745, 1020 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.18 (d, *J* = 10.7 Hz, 1H), 4.05 (dd, *J* = 9.2, 1.5 Hz, 1H), 3.70 (d, *J* = 9.2 Hz, 1H), 2.72 (d, *J* = 17.6 Hz, 1H), 2.69–2.63 (m, 1H), 2.50 (d, *J* = 13.2 Hz, 1H), 2.43 (d, *J* = 17.6 Hz, 1H), 2.15 (dd, *J* = 13.7, 11.5 Hz, 1H), 2.09 (s, 3H), 2.08–2.03 (m, 1H), 1.97–1.86 (m, 2H), 1.75 (dd, *J* = 13.7, 0.8 Hz, 1H), 1.65–1.57 (m, 1H), 1.28 (s, 3H), 0.98–0.97 (m, 6H), 0.92 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 210.2, 173.1, 170.2, 91.0, 89.9, 74.7, 68.5, 48.2, 46.5, 45.4, 44.0, 39.1, 37.1, 30.7, 30.2, 23.2 (2C), 21.4, 17.1, 14.6; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{20}H_{29}O_6$ 365.1964; found, 365.1956. The desired enone **50** was identical to the substance obtained from diol **34**.

(1R,3R,5R,6S,7R,8aR)-5-((benzyloxy)methyl)-3,7-bis((tert-butyldimethylsilyl)oxy)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1-isopropyl-6,8a-

*dimethyl-1,2,3,5,6,7,8,8a-octahydroazulen-5-ol (**52**).* To a solution of **50** (0.167 g, 0.325 mmol) in toluene (6 mL) at –78 °C was added Red-Al (0.49 mL, 1.62 mmol). After stirring at –78 °C for one h, the cooling bath was removed and the reaction was allowed to warm to rt over 30 min. The mixture was then heated in a 65 °C oil bath for 2 h, then cooled to 0 °C, and quenched with 25% Rochelle salt (5 mL). Upon vigorously stirring for two h, the layers were allowed to separate and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). Combined organic phases were dried with $MgSO_4$, filtered and concentrated to provide the crude tetraol as a 9:1 mixture of C_{12} diastereomers. Without further purification, the crude oil was dissolved in CH_2Cl_2 (6 mL) and cooled to 0 °C. To this solution was added 2,6-lutidine (0.40 mL, 3.41 mmol) followed by TBSOTf (0.39 mL, 1.71 mmol). The reaction was stirred at 0 °C for 30 min, and then saturated aqueous $NaHCO_3$ (6 mL) was added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL), dried with $MgSO_4$. Combined organic phases were filtered and concentrated. Purification by silica gel chromatography (1–3% EtOAc/hexanes) provided alcohol **52** (0.203 g, 82% for two steps) as a colorless oil: R_f 0.56 (hexanes/EtOAc (10:1)); $[\alpha]_D^{20}$ –40.1 (*c* 0.29, $CHCl_3$); IR (film) 3583, 2954, 2921, 2856, 1472, 1362, 1254, 1086, 835, 773 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.26 (m, 5H), 5.82 (d, *J* = 2.5 Hz, 1H), 4.58 (dd, *J* = 11.2, 2.9 Hz, 1H), 4.66 (d, *J* = 12.5 Hz, 1H), 4.59 (d, *J* = 12.5 Hz, 1H), 4.35 (ddd, *J* = 9.7, 6.8, 1.9 Hz, 1H), 3.89–3.84 (m, 1H), 3.83 (s, 1H), 3.66 (d, *J* = 8.8 Hz, 1H), 3.63 (ddd, *J* = 10.7, 6.8, 4.4 Hz, 1H), 3.52 (d, *J* = 8.8 Hz, 1H), 2.04–1.94 (m, 3H), 1.71 (dq, *J* = 13.4, 6.6 Hz, 1H), 1.58–1.52 (m, 2H), 1.45–1.38 (m, 1H), 1.36 (s, 3H), 1.15–1.10 (m, 1H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.87 (s, 3H), 0.12 (s, 3H), 0.092 (s,

3H), 0.086 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 138.6, 128.4, 127.7, 127.6, 126.9, 77.3, 75.6, 74.1, 74.0, 69.6, 60.4, 53.4, 46.9, 45.9, 44.6, 38.2, 36.5, 27.6, 26.2, 26.15, 26.14, 24.7, 22.8, 20.0, 19.1, 18.5 (2C), 18.4, –3.2, –4.2, –4.3, –4.4, –5.2, –5.4; HRMS (ESI-TOF) *m*/*z* $[M+K]^+$ calcd for $C_{43}H_{80}O_5Si_3K$ 799.4951; found, 799.4990.

*(1R,3R,5R,6S,7R,8aR)-3,7-bis((tert-butyldimethylsilyl)oxy)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-5-(hydroxymethyl)-1-isopropyl-6,8a-dimethyl-1,2,3,5,6,7,8,8a-octahydroazulen-5-ol (**53**).* A solution of radical anion LiDBB was prepared as follows: To a solution of di-tert-butylbiphenyl (0.5 g, 1.88 mmol) in dry THF (25 mL) at 22 °C was added lithium ribbon (~0.2 g) which was severed into small pieces to directly introduce into the reaction flask. The reaction was stirred for five min at rt, and then cooled to 0 °C with continued stirring for 2 h to provide a dark green solution. To a solution of **52** (0.112 g, 0.147 mmol) in dry THF (1 mL) at 78 °C was added the freshly prepared solution of LiDBB (4 mL) in 1 mL aliquots until a dark green color persisted in the solution. The reaction was quenched by the addition of saturated aqueous NH_4Cl (5 mL), allowed to warm to rt. After dilution with CH_2Cl_2 (10 mL), the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic phases were dried with $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography (0–5% EtOAc/hexanes) provided diol **53** (0.076 g, 77%) as a colorless oil: R_f 0.71 (hexanes/EtOAc (4:1)); $[\alpha]_D^{20}$ –41.6 (*c* 0.39, $CHCl_3$); IR (film) 3410, 3370, 2956, 2856, 1472, 1255, 1078, 1016, 835, 773 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77 (d, *J* = 2.0 Hz, 1H), 4.97 (s, 1H), 4.64 (dd, *J* = 11.2, 2.4 Hz, 1H), 4.33 (ddd, *J* = 10.2, 7.4, 2.5 Hz, 1H), 3.93 (d, *J* = 9.8 Hz, 1H), 3.85 (t, *J* = 10.7 Hz, 1H), 3.64 (dt, *J* = 11.2, 3.7

Hz, 1H), 3.45 (t, *J* = 10.5 Hz, 1H), 2.14 (dd, *J* = 10.5, 1.3 Hz, 1H), 2.02–1.93 (m, 3H), 1.74–1.64 (m, 2H), 1.56 (dd, *J* = 13.1, 11.7 Hz, 1H), 1.45–1.38 (m, 1H), 1.36 (s, 3H), 1.13 (ddd, *J* = 13.2, 6.6, 5.4 Hz, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.85 (s, 9H), 0.82 (s, 3H), 0.12 (s, 3H), 0.11 (br s, 6H), 0.09 (s, 3H), 0.05 (br s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.7, 125.3, 76.2, 73.9, 69.4, 68.1, 60.6, 53.3, 47.3, 45.8, 44.4, 37.0, 36.5, 27.7, 26.14, 26.09, 26.0, 24.7, 22.8, 19.9, 19.6, 18.5, 18.40, 18.36, –3.0, – 4.2, –4.3, –4.5, –5.3, –5.6; HRMS (ESI-TOF) *m/z* $[M+K]^+$ calcd for $C_{36}H_{74}O_5Si_3K$ 709.4481 found 709.4462.

*(1R,3R,6S,7R,8aR)-3,7-bis((tert-butyldimethylsilyl)oxy)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1-isopropyl-6,8a-dimethyl-2,3,6,7,8,8a-hexahydroazulen-5(1H)-one (**54**).* To a solution of **51** (66.9 mg, 0.100 mmol) in CH_2Cl_2 (2 mL) at 0 °C was added anhydrous K_2CO_3 (83 mg, 0.60 mmol), followed by $Pb(OAc)_4$ (89 mg, 0.20 mmol) and the mixture was stirred for 10 min. The crude reaction mixture was then filtered through silica gel (~5 mL) by flushing with CH_2Cl_2 to provide ketone **54** (56.8 mg, 89%). Upon removal of solvent in vacuo, this ketone did not require additional purification; R_f 0.79 (hexanes/EtOAc (4:1)); $[\alpha]_D^{20}$ –44.6 (*c* 0.24, $CHCl_3$); IR (film) 2956, 2930, 2857, 1680, 1472, 1361, 1255, 1087, 1005, 820, 774 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.75 (d, 1.4 Hz, 1H), 4.40 (ddd, *J* = 9.6, 7.4, 1.9 Hz, 1H), 4.00 (dd, *J* = 10.9, 3.2 Hz, 1H), 3.73–3.63 (m, 2H), 2.08–2.03 (m, 2H), 1.94–1.86 (m, 3H), 1.70–1.64 (m, 1H), 1.41 (td, *J* = 12.5, 9.9 Hz, 1H), 1.27–1.21 (m, 1H), 1.13 (s, 3H), 1.01 (d, *J* = 6.6 Hz, 3H), 1.00 (s, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.98 (br s, 16 H), 0.87 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.04 (br s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.1, 163.0, 123.3, 73.4, 70.8, 59.9, 56.8, 52.5, 45.0, 43.9, 38.5, 36.5, 28.0, 26.1, 26.04, 26.02,

24.2, 22.7, 22.2, 18.4, 18.29, 18.27, 18.2, –3.7, –4.3, –4.4, –4.5, –5.1 (2C); HRMS (ESI-TOF) *m*/*z* $[M+H]^+$ calcd for $C_{35}H_{71}O_4Si_3$ 639.4660 found 639.4675.

*(1R,3R,5S,6S,7R,8aR)-3,7-bis((tert-butyldimethylsilyl)oxy)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1-isopropyl-6,8a-dimethyl-5-(prop-1-en-2-yl)-1,2,3,5,6,7,8,8a-octahydroazulen-5-ol (**55**).* To a solution of 2-bromopropene (73 μL, 0.81 mmol) in Et_2O (1.6 mL) at –78 °C was added ^{t}BuLi (0.43 mL, 1.7 M in pentanes, 0.73 mmol) dropwise. The reaction was stirred for five min and then freshly distilled TMEDA (110 μL, 0.73 mmol) was added followed by continued stirring for five min. A solution of ketone **54** (52 mg, 0.081 mmol) in Et_2O (0.5 mL) was added slowly down the side of the flask follow by the addition of a small amount of Et_2O (0.5 mL syringe rinse). The reaction was stirred at –78 °C for 45 min, and then quenched with saturated aqueous NH_4Cl (2 mL) and subsequent warming to rt. This mixture was diluted with ether, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 5 mL), and the combined organic phases were dried over $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography (1–3% EtOAc/hexanes) provided alcohol **55** (47.6 mg 87%) and a small amount of isomeric ***epi*-55** (2.3 mg, 4%) as colorless oils. For characterization data of alcohol **55**: R_f 0.34 (hexanes/EtOAc (8:1)); $[\alpha]_D^{20}$ –119.4 (*c* 0.11, $CHCl_3$); IR (film) 3350, 2956, 2857, 1471, 1254, 1078, 835, 773 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.65 (d, *J* = 2.5 Hz, 1H), 5.06 (br s, 1H), 4.97 (s, 1H), 4.62 (dd, *J* = 11.4, 3.1 Hz, 1H), 4.34 (ddd, *J* = 10.5, 7.1, 2.3 Hz, 1H), 3.91 (ddd, *J* =10.4, 9.0, 5.7 Hz, 1H), 2.70 (br s, 1H), 3.60 (ddd, 10.6, 6.8, 4.1 Hz, 1H), 1.98–1.92 (m, 2H), 1.89 (s, 3H), 1.74–1.68 (m, 2H), 1.60–1.55 (m, 2H), 1.44–1.37 (m, 1H), 1.36 (s, 3H), 1.16–1.11 (m, 1H), 1.01 (d, *J* = 6.3 Hz, 3H), 0.94 (s, 3H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.90 (s, 9H), 0.88

(s, 9H), 0.87 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H), 0.07 (s, 3H), 0.06 (s, 6H), 0.05 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 152.8, 129.5, 112.8, 80.0, 74.2, 70.7, 60.9, 53.5, 48.1, 45.9, 44.8, 39.6, 36.2, 27.5, 26.3, 26.2, 26.1, 24.8, 22.7, 22.4, 20.2, 20.0, 18.6, 18.5, –2.8, –4.2, –4.3, –4.4, –5.1, –5.3; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{38}H_{76}O_4Si_3Na$ 703.4949 found 703.4937. The minor product is the diastereomer ***epi*-55**; *(1R,3R,5R,6S,7R,8aR)-3,7-bis((tert-butyldimethylsilyl)oxy)-6-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1-isopropyl-6,8a-dimethyl-5-(prop-1-en-2-yl)-1,2,3,5,6,7,8,8a-octahydroazulen-5-ol*, which is characterized as follows: R_f 0.40 (hexanes/EtOAc (8:1)); $[\alpha]_D^{20}$ –13.6 (*c* 0.94, $CHCl_3$); IR (film) 3385, 2956, 2885, 2857, 1476, 1388, 1361, 1255, 1061, 1004, 836, 773, 669 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.35 (s, 1H), 5.21 (s, 1H), 4.92 (s, 1H), 4.45 (s, 1H), 4.42 (dd, *J* = 10.5, 3.1 Hz, 1H), 4.31 (td, *J* = 7.7, 1.7 Hz, 1H), 3.82 (td, *J* = 10.4, 3.3 Hz, 1H), 3.75–3.71 (m, 1H), 2.13–2.01 (m, 3H), 1.90–1.77 (m, 2H), 1.85 (s, 3H), 1.68–1.61 (m, 1H), 1.35 (td, 12.8, 7.8 Hz, 1H), 1.19–1.14 (m, 1H), 1.10 (s, 3H), 1.07 (s, 3H), 0.97 (d, *J* = 6.8 Hz), 0.88–0.87 (m, 30H), 0.09 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H), 0.054 (s, 3H), 0.049 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.5, 148.6, 132.9, 112.6, 79.7, 74.6, 71.8, 61.1, 55.2, 49.6, 45.5, 44.7, 37.9, 37.0, 27.9, 26.0, 25.9, 25.8, 24.2, 22.6, 22.5, 18.2, 18.1, 18.0, 17.6, 14.6, –3.9, –4.1, – 4.2, –4.6, –5.4, –5.6; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{38}H_{76}O_4Si_3Na$ 703.4949 found 703.4937.

*(1R,3R,3aR,5R,6S,7S)-5-((tert-butyldimethylsilyl)oxy)-6-(2-hydroxyethyl)-3-isopropyl-3a,6-dimethyl-7-(prop-1-en-2-yl)-1,2,3,3a,4,5,6,7-octahydroazulene-1,7-diol (**56**).* A stock solution of TBAF:AcOH (2.5:1 molar ratio) was prepared from TBAF (1 mL, 1M in THF) and glacial AcOH (23.2 μL). To a solution of **55** (15 mg, 0.022 mmol)

in THF (0.5 mL) at 22 °C was added an aliquot of the TBAF: AcOH solution (0.05 mL, 0.05 mmol, 2.5:1 molar ratio). The solution was stirred at rt for two h, and was then quenched with saturated aqueous $NaHCO_3$ and diluted with CH_2Cl_2. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 1 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography (20% then 50% EtOAc/hexanes with 1% MeOH) provided triol **56** (8.7 mg, 87%): R_f 0.27 (hexanes/EtOAc (1:2)); $[\alpha]_D^{20}$ –65.9 (*c* 0.44, $CHCl_3$); IR (film) 3284, 2956, 1471, 1255, 1059, 834, 772 cm^{-1}; 1H NMR (500 MHz, $CDCl_3$) δ 5.73 (d, *J* = 1.9 Hz, 1H), 5.13 (s, 1H), 5.01 (s, 1H), 4.69 (dd, *J* = 11.3, 2.9 Hz, 1H), 4.35 (ddd, *J* = 9.6, 7.8, 2.0 Hz, 1H), 3.91 (br s, 1H), 3.85 (ddd, 11.5, 9.6, 4.2 Hz, 1H), 3.62 (dt, *J* = 11.6, 4.9 Hz, 1H), 2.48 (br s, 1H), 2.18 (ddd, *J* = 12.9, 7.7, 5.8 Hz, 1H), 1.97 (dd, *J* = 13.7, 3.0 Hz, 1H), 1.90 (s, 3H), 1.79 (dt, *J* = 14.8, 4.5 Hz, 1H), 1.75–1.67 (m, 1H), 1.63–1.55 (m, 2H), 1.45–1.35 (m, 1H), 1.32 (s, 3H), 1.22–1.17 (m, 1H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.98 (s, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.86 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.8, 152.1, 131.0, 113.4, 80.8, 74.0, 70.6, 60.2, 54.6, 47.9, 45.9, 45.7, 40.0, 36.2, 27.4, 26.3, 24.9, 22.4, 22.2, 20.3, 20.0, 18.6, –2.9, –4.0; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{26}H_{48}O_4SiNa$ 475.3220 found 475.3203.

*(3aS,4R,5aR,6R,9aS)-4-((tert-butyldimethylsilyl)oxy)-6-isopropyl-3a,5a-dimethyl-9a-(prop-1-en-2-yl)-3a,4,5,5a,6,7-hexahydroazuleno[5,6-b]furan-2,8(3H,9aH)-dione (**57**).* To a rt solution of triol **56** (7.0 mg, 0.015 mmol) in CH_2Cl_2 (0.4 mL) was added oven dried 4Å molecular sieves, TPAP (~1 mg) and NMO (10 mg, 0.085 mmol). The reaction was stirred at rt for 1.5 h then was filtered through silica gel (2 mL) flushing with 30% EtOAc/hexanes. The resulting solution was concentrated to provide lactone **57**

(5.5 mg, 80%) which did not require additional purification: R_f 0.81 (hexanes/EtOAc (1:1)); $[\alpha]_D^{20}$ +7.8 (*c* 0.28, $CHCl_3$); IR (film) 3375, 2957, 2929, 2856, 1788, 1731, 1660, 1472, 1386, 1259, 1211, 1057, 1029, 836, 774 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.30 (s, 1H), 5.13 (d, *J* = 1.0 Hz, 5.05 (s, 1H), 3.99 (dd, *J* = 8.3, 2.7 Hz, 1H), 2.66 (d, *J* = 17.5 Hz, 1H), 2.54 (d, *J* = 17.6 Hz, 1H), 2.50 (dd, *J* = 19.0, 7.8 Hz, 1H), 2.25–2.06 (m, 3H), 1.82 (s, 3H), 1.83–1.75 (m, 1H), 1.66 (dt, *J* = 12.4, 8.1 Hz, 1H), 1.20 (s, 3H), 1.15 (s, 3H), 1.10 (d, *J* = 6.6 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.3, 175.6, 151.0, 144.2, 128.2, 114.2, 89.1, 71.0, 52.2, 51.1, 44.8, 42.7, 41.1, 40.8, 29.9, 29.3, 26.0, 23.8, 22.8, 20.8, 20.1, 18.1, –3.1, –4.7; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{26}H_{42}O_4SiNa$ 469.2750 found 469.2755.

*(3aS,4R,5aR,9aS)-4-((tert-butyldimethylsilyl)oxy)-6-isopropyl-3a,5a-dimethyl-9a-(prop-1-en-2-yl)-3a,4,5,5a-tetrahydroazuleno[5,6-b]furan-2,8(3H,9aH)-dione (**58**)*. To a solution of **57** (5.0 mg, 0.011 mmol) in dioxane (0.25 mL) at 22 °C was added SeO_2 (5.0 mg, 0.045 mmol). The mixture was heated in a 50 °C oil bath for 16 h, then warmed to 60 °C for 3 h, cooled to rt, diluted with CH_2Cl_2 and quenched with saturated aqueous $NaHCO_3$ (1 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated. Purification by a gradient elution using silica gel chromatography (5% to 50% EtOAc/hexanes provided enone **58** (1.0 mg, 20%), the aldehyde **59a** (X = O) (1.1 mg, 22%), and small amounts of the corresponding allylic alcohol **59a** as colorless oils. For characterization data of **58**: R_f 0.75 (hexanes/EtOAc (1:1)); IR (film) 2958, 2929, 2865, 1789, 1709, 1670, 1471, 1255, 1205, 1093, 836 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.24 (s, 1H), 6.13 (s, 1H), 5.17 (s, 1H), 5.13 (s, 1H), 4.10 (d, *J* = 10.5 Hz, 1H), 2.66 (d,

J = 17.1 Hz, 1H), 2.59–2.53 (m, 1H), 2.57 (d, *J* = 17.1 Hz, 1H), 2.24–2.16 (m, 1H), 2.01–1.97 (m, 1H), 1.90 (s, 3H), 1.40 (s, 3H), 1.26 (d, *J* = 6.7, 3H), 1.20 (s, *J* = 6.8, Hz, 3H), 1.12 (s, 3H), 0.91 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 126.36, 125.4, 114.9, 71.3, 47.0, 41.3, 37.9, 29.9, 27.5, 26.0, 24.7, 23.8, 23.7, 21.2, 14.6, –3.2, –4.6; HRMS (ESI-TOF) *m/z* $[M+H]^+$ calcd for $C_{26}H_{41}O_4Si$ 445.2774 found 445.2783. Compound **58** contains eight substituted carbons (without hydrogen substitution), which gave very weak signals in the ^{13}C NMR spectrum. These signals cannot be identified in the baseline noise. The use of micro-NMR techniques and prolonged acquisition times did not lead to improvement. The ^{13}C NMR spectrum for **58** is included in Supporting Information.

The aldehyde **59** (X = O) is identified as *2-((3aS,4R,5aR,9aR)-4-((tert-butyldimethylsilyl)oxy)-6-isopropyl-3a,5a-dimethyl-2,8-dioxo-2,3,3a,4,5,5a,8,9a-octahydroazuleno[5,6-b]furan-9a-yl)acrylaldehyde* and was characterized as follows: R_f 0.52 (hexanes/EtOAc (1:1)); IR (film) 2956, 2929, 2856, 1792, 1743, 1708, 1666, 1471, 1379, 1255, 1063, 835, 773 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.63 (d, *J* = 1.0 Hz, 1H), 6.55 (s, 1H), 6.38 (s, 1H), 6.14 (s, 1H), 6.09 (s, 1H), 4.15 (dd, 9.1, 3.4 Hz, 1H), 2.74 (d, *J* = 17.3 Hz, 1H), 2.60–2.55 (m, 1H), 2.35 (d, *J* = 17.3 Hz, 1H), 2.00 (br s, 2H), 1.40 (s, 3H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.21 (d, *J* = 6.8 Hz, 3H), 1.01 (s, 3H), 0.92 (s, 9H), 0.18 (s, 3H), 0.16 (s, 3H); HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{26}H_{38}O_5SiNa$ 481.2386 found 481.2417. Carbon NMR data could not be obtained due to insufficient quantities of sample. The corresponding allylic alcohol was characterized as *(3aS,4R,5aR,9aS)-4-((tert-butyldimethylsilyl)oxy)-9a-(3-hydroxyprop-1-en-2-yl)-6-isopropyl-3a,5a-dimethyl-3a,4,5,5a-tetrahydroazuleno[5,6-b]furan-2,8(3H,9aH)-dione* (**59a**) R_f 0.34

(hexanes/EtOAc (1:1)); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.25 (s, 1H), 6.14 (s, 1H), 5.65 (s, 1H), 5.38 (s, 1H), 4.16 (br s, 2H), 4.10 (d, *J* = 10.9 Hz, 1H), 2.68 (d, *J* = 17.1 Hz, 1H), 2.60–2.54 (m, 1H), 2.54 (d, *J* = 17.2 Hz, 1H), 2.01 (d, *J* = 13.9, 1H), 1.88 (dd, *J* = 13.8, 10.6 Hz, 1H), 1.40 (s, 3H), 1.26 (d, *J* = 6.7 Hz, 3H), 1.20 (d, *J* = 6.7 Hz, 3H), 1.10 (s, 3H), 0.91 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H); HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{26}H_{40}O_5SiNa$ 483.2543 found 483.2556. Carbon NMR data could not be obtained due to insufficient quantities of sample.

*(1R,3R,5S,6S,7R,8aR)-3,7-bis((tert-butyldimethylsilyl)oxy)-6-(2-hydroxyethyl)-1-isopropyl-6,8a-dimethyl-5-(prop-1-en-2-yl)-1,2,3,5,6,7,8,8a-octahydroazulen-5-ol (**60**).* A stock solution of TBAF:AcOH (1:1 molar ratio) was prepared from TBAF (0.25 mL, 1M in THF) and glacial AcOH (14.5 μL). To a solution of **55** (43 mg, 0.065 mmol) in THF (1.3 mL) at 22 °C was added an aliquot of the TBAF:AcOH solution (0.13 mL, 0.13 mmol). The reaction was stirred at rt for one h, then was quenched with saturated aqueous $NaHCO_3$ and diluted with CH_2Cl_2. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography using a gradient elution (5% then 30% EtOAc/hexanes) provided alcohol **60** (34 mg, 96%): R_f 0.26 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ –105.1 (*c* 0.11, $CHCl_3$); IR (film) 3360, 2955, 1430, 1220, 1130, 835 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.65 (s, 1H), 5.13 (s, 1H), 5.01 (s, 1H), 4.66 (dd, *J* = 11.6, 2.9 Hz), 4.35 (t, *J* = 7.8 Hz, 1H), 3.87 (ddd, *J* = 11.3, 8.7, 5.6 Hz, 1H), 3.58 (dt, *J* = 11.4, 5.4 Hz, 1H), 2.49 (br s, 1H), 2.00–1.95 (m, 2H), 1.89 (s, 3H), 1.81 (dt, *J* = 14.5, 5.3 Hz, 1H), 1.74–1.68 (m, 1H), 1.61–1.56 (m, 1H), 1.45–1.36 (m, 1H), 1.31 (s, 3H), 1.18–1.13 (m, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.95 (s, 3H), 0.92 (d, *J* = 6.8

Hz, 3H), 0.88 (s, 9H), 0.87 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.0, 151.8, 129.2, 113.1, 80.6, 74.2, 70.4, 60.0, 53.6, 47.5, 45.6, 45.0, 40.0, 36.1, 27.4, 26.2, 26.1, 24.8, 22.6, 22.3, 20.2, 20.1, 18.52, 18.48, –3.1, –4.1, –4.2, –4.4; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{32}H_{62}O_4Si_2Na$ 589.4084 found 589.4073.

*(3aS,4R,5aR,6R,8R,9aS)-4-((tert-butyldimethylsilyl)oxy)-8-hydroxy-6-isopropyl-3a,5a-dimethyl-9a-(prop-1-en-2-yl)-3,3a,4,5,5a,6,7,8-octahydroazuleno[5,6-b]furan-2(9aH)-one (**61**).* To a solution of alcohol **60** (33 mg, 0.058 mmol) in CH_2Cl_2 (1 mL) at 22 °C was added oven dried 4Å molecular sieves, TPAP (2.5 mg, 0.007 mmol) and NMO (40 mg, 0.40 mmol). The reaction was stirred at rt for 40 min, and was then filtered through silica gel (3 mL) using a with CH_2Cl_2 elution. The resulting solution was concentrated to provide the expected lactone **60a** (29.6 mg, 90%) as a colorless oil which did not require additional purification. This intermediate compound **60a** was characterized as follows: R_f 0.71 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ –18.5 (*c* 0.11, $CHCl_3$); IR (film) 2927, 1771, 1471, 1254, 1087, 834, 773; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.26 (s, 1H), 5.06 (s, 1H), 5.02 (s, 1H), 4.28 (ddd, *J* = 8.0, 6.5, 1.5 Hz, 1H), 4.02 (d, *J* = 10.3 Hz, 1H), 2.71 (d, *J* = 17.2 Hz, 1H), 2.48 (d, *J* = 17.3 Hz, 1H), 2.19 (dt, *J* = 13.2, 7.6 Hz, 1H), 1.96 (d, *J* = 14.1 Hz, 1H), 1.85–1.80 (m, 1H), 1.82 (s, 3H), 1.74–1.68 (m, 1H), 1.48 (td, *J* = 12.9, 6.5 Hz, 1H), 1.20 (s, 3H), 1.12 (s, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.87 (s, 9H), 0.12 (s, 6H), 0.042 (s, 3H), 0.039 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.5, 160.0, 145.6, 122.1, 113.4, 90.6, 75.5, 70.3, 54.7, 52.0, 45.6, 43.7, 41.6, 37.4, 28.5, 26.1, 26.03, 26.00, 24.1, 22.5, 21.1, 19.8, 18.2, 15.8, –3.2, –4.2, –4.3, –4.7; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{32}H_{58}O_4Si_2Na$ 585.3771 found

585.3755. This intermediate lactone **60a** was carried forward for deprotection as described below.

A stock solution of TBAF:AcOH (2.5:1) was prepared from TBAF (1 mL, 1M in THF) and glacial AcOH (23.2 μL). To a solution of **60a** (30 mg, 0.053 mmol) in THF (1 mL) at 22 °C was added an aliquot of the TBAF: AcOH (0.10 mL, 0.10 mmol). The reaction was stirred at rt for three h, and then was quenched with saturated aqueous $NaHCO_3$ and diluted with CH_2Cl_2. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography using a gradient elution (10% then 40% EtOAc/hexanes) provided lactone **61** (21 mg, 88%) as a colorless oil: R_f 0.21 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ –6.8 (*c* 0.47, $CHCl_3$); IR (film) 3427, 2956, 2857, 1782, 1471, 1254, 1089, 1053, 1004, 836, 774 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.42 (s, 1H), 5.08 (s,1H), 5.02 (s, 1H), 4.35 (t, *J* = 7.2 Hz, 1H), 4.02 (d, *J* = 10.1 Hz, 1H), 2.71 (d, *J* = 17.3 Hz, 1H), 2.50 (d, *J* = 17.3 Hz, 1H), 1.97 (d, *J* = 14.3 Hz, 1H), 1.83 (s, 3H), 1.77–1.70 (m, 1H), 1.67 (br s, 1H), 1.53 (ddd, *J* = 13.6, 12.4, 6.2 Hz, 1H), 1.87–1.27 (m, 1H), 1.24 (s, 3H), 1.14 (s, 3H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 161.3, 145.3, 123.2, 113.6, 90.2, 75.5, 70.2, 55.2, 52.1, 45.8, 43.6, 41.4, 36.1, 28.6, 26.0, 24.0, 22.4, 21.1, 19.9, 18.1, 15.8, –3.2, –4.8; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{26}H_{44}O_4SiNa$ 471.2906 found 471.2919.

*(3aS,4R,5aR,6R,8R,9aS)-4-((tert-butyldimethylsilyl)oxy)-8-hydroxy-9a-(3-hydroxyprop-1-en-2-yl)-6-isopropyl-3a,5a-dimethyl-3,3a,4,5,5a,6,7,8-octahydroazuleno[5,6-b]furan-2(9aH)-one (**62**).* To a solution of **61** (21 mg, 0.047

mmol) in dioxane (1 mL) at 22 °C was added SeO_2 (30 mg, 0.27 mmol). The mixture was heated in a 65 °C oil bath for 10 h, cooled to rt, diluted with MeOH (1 mL) with the addition of $CeCl_3 \bullet 7H_2O$ (25 mg, 0.067 mmol). The resulting suspension stirred at rt for five min and $NaBH_4$ (2.5 mg, 0.066 mmol) was then added. After 10 min, the reduction was quenched with saturated aqueous NH_4Cl (5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography using a gradient elution (10% to 50% EtOAc/hexanes then 50% EtOAc/hexanes with 2% MeOH) provided diol **62** (13.2 mg, 60%) and recovered starting material **60** (7 mg, 33%) as colorless oils. For characterization data of **62**: R_f 0.21 (hexanes/EtOAc (1:2)); $[\alpha]_D^{20}$ –10.4 (*c* 0.08, $CHCl_3$); IR (film) 3389, 2930, 2857, 1781, 1481, 1387, 1454, 1185, 1089, 1052, 929, 860, 837, 774 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.54 (s, 1H), 5.50 (d, *J* = 1.4 Hz, 1H), 5.30 (s, 1H), 4.35 (ddd, *J* = 8.1, 6.4, 1.4 Hz, 1H), 4.16 (d, *J* = 13.0 Hz, 1H), 4.09 (d, *J* = 14.0 Hz, 1H), 4.02 (d, *J* = 9.8 Hz, 1H), 2.74 (d, *J* = 17.1 Hz, 1H), 2.46 (d, *J* = 17.1 Hz, 1H), 2.32 (ddd, *J* = 13.5, 8.3, 7.3 Hz, 1H), 1.98 (d, *J* = 14.4 Hz, 1H), 1.84 (dd, *J* = 14.4, 10.2 Hz, 1H), 1.77–1.69 (m, 1H), 1.56–1.49 (m, 2H), 1.31–1.22 (m, 1H), 1.25 (s, 3H), 1.09 (s, 3H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.90 (s, 9H), 0.133 (s, 3H), 0.126 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.9, 162.4, 150.8, 122.4, 114.8, 89.7, 75.4, 70.3, 63.1, 55.1, 51.9, 45.8, 43.4, 41.5, 36.1, 28.5, 26.0, 24.0, 22.4, 20.0, 18.1, 15.3, –3.2, –4.7; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{26}H_{44}O_5SiNa$ 487.2856 found 487.2836. A small amount of the corresponding aldehyde of **62** (X = O) was also fully characterized from experiments which did not employ the borohydride quench. This compound, *2-((3aS,4R,5aR,6R,8R,9aR)-4-((tert-*

*butyldimethylsilyl)oxy)-8-hydroxy-6-isopropyl-3a,5a- dimethyl-2-oxo-2,3,3a,4,5,5a,6,7,8,9a-decahydroazuleno[5,6-b]furan-9a-yl)acrylaldehyde (**62** X = O)* is characterized by the following data: R_f 0.64 (hexanes/EtOAc (1:2)); $[\alpha]_D^{20}$ –29.3 (*c* 0.13, $CHCl_3$); IR (film) 3583, 3445, 2957, 2857, 1782, 1702, 1486, 1386, 1256, 1214, 1090, 1033 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.61 (s, 1H), 6.43 (s, 1H), 6.28 (s, 1H), 5.31 (s, 1H), 4.35 (ddd, *J* = 8.2, 6.6, 1.5 Hz, 1H), 4.05 (dd, *J* = 9.2, 2.3 Hz, 1H), 2.78 (d, *J* = 17.5 Hz, 1H), 2.33 (dt, *J* = 13.7, 7.8 Hz, 1H), 2.28 (d, *J* = 17.6 Hz, 1H), 1.99–1.92 (m, 2H), 1.77–1.70 (m, 1H), 1.56–1.49 (m, 1H), 1.41–1.36 (m, 1H), 1.25 (s, 3H), 1.02 (s, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.7, 175.6, 160.8, 151.5, 134.8, 122.1, 87.8, 75.3, 70.1, 54.6, 52.1, 45.7, 43.1, 41.1, 36.1, 28.4, 26.0, 24.1, 22.3, 20.0, 18.1, 15.9, –3.2, –4.7; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{26}H_{42}O_5SiNa$ 485.2699 found 485.2693.

*(3aS,4R,5aR,6R,8R,9aS)-4-((tert-butyldimethylsilyl)oxy)-9a-(3-((tert-butyldimethylsilyl)oxy)prop-1-en-2-yl)-8-hydroxy-6-isopropyl-3a,5a-dimethyl-3,3a,4,5,5a,6,7,8-octahydroazuleno[5,6-b]furan-2(9aH)-one (**62a**).* To a solution of diol **62** (6.5 mg, 0.014 mmol) in CH_2Cl_2 (0.2 mL) at 22 °C was added Et_3N (0.02 mL, 0.14 mmol) followed by TBSCl (10.5 mg, 0.07 mmol). The mixture was stirred at rt for 18 h and was then quenched with saturated aqueous $NaHCO_3$ (1 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 1 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography using a gradient elution (5% to 15% EtOAc in hexanes provided **62a** (5.0 mg, 62%) and recovered starting material **62** (1.4 mg, 22%) as colorless oils. For characterization data of **62a**: R_f 0.41 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ –6.5 (*c* 0.18, $CHCl_3$);

IR (film) 3435, 2956, 2857, 1783, 1472, 1254, 1090, 1005, 837, 775 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.51 (s, 1H), 5.46 (s, 1H), 5.20 (s, 1H), 4.33 (ddd, *J* = 8.0, 6.1, 4.2 Hz, 1H), 4.10 (d, *J* = 13.0 Hz, 1H), 4.06 (d, *J* = 13.5 Hz, 1H), 4.01 (d, 9.8 Hz, 1H), 2.70 (d, *J* = 17.3 Hz, 1H), 2.49 (d, *J* = 17.4 Hz, 1H), 2.32 (dt, *J* = 13.7, 7.8 Hz, 1H), 1.97 (d, *J* = 14.4 Hz, 1H), 1.85 (dd, *J* = 14.4, 10.0 Hz, 1H), 1.77–1.71 (m, 1H), 1.58 (d, *J* = 4.2, 1H), 1.66–1.49 (m, 1H), 1.30 (dt, *J* = 12.4, 7.2 Hz, 1H), 1.25 (s, 3H), 1.11 (s, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.3 Hz, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H), 0.082 (s, 3H), 0.077 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0, 161.8, 149.7, 122.8, 114.0, 89.6, 75.5, 70.4, 62.8, 55.1, 52.0, 45.7, 43.4, 41.5, 36.1, 28.6, 26.07, 26.03, 23.9, 22.4, 20.1, 18.4, 18.2, 15.5, –3.2, –4.7, –5.2; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{32}H_{58}O_5Si_2Na$ 601.3721 found 601.3702.

*(3aS,4R,5aR,6R,9aS)-4-((tert-butyldimethylsilyl)oxy)-9a-(3-((tert-butyldimethylsilyl)oxy)prop-1-en-2-yl)-6-isopropyl-3a,5a-dimethyl-3a,4,5,5a,6,7-hexahydroazuleno[5,6-b]furan-2,8(3H,9aH)-dione (**63**).* To a solution of **62a** (3.8 mg, 0.0066 mmol) in CH_2Cl_2 (0.2 mL) at 22 °C was added over dried 4Å molecular sieves, TPAP (1 mg, 0.0028 mmol) and NMO (5 mg, 0.043 mmol). The mixture was stirred at rt for 1 h, diluted with CH_2Cl_2, and then filtered through a pipette containing silica gel (1 mL) with CH_2Cl_2 elution. The resulting solution was concentrated to provide **63** (3.5 mg, 92%) which did not require additional purification: R_f 0.55 (hexanes/EtOAc (3:1)); $[\alpha]_D^{20}$ +15.9 (*c* 0.23, $CHCl_3$); IR (film) 2956, 2929, 2857, 1789, 1731, 1656, 1472, 1255, 1211, 1087, 837, 755, 680 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.31 (s, 1H), 5.55 (s, 1H), 5.18 (s, 1H), 4.11 (d, *J* = 13.5 Hz, 1H), 4.05 (d, *J* = 13.0 Hz, 1H), 3.95 (dd, *J* = 8.6, 2.0 Hz, 1H), 2.60 (s, 2H), 2.50 (dd, 19.0, 7.8 Hz, 1H), 2.33–2.09 (m, 3H), 1.84–1.74 (m, 1H),

1.70 (dt, J = 12.3, 8.1 Hz, 1H), 1.20 (s, 3H), 1.13 (s, 3H), 1.09 (d J = 6.8 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H), 0.91 (s, 9H), 0.88 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.2, 175.5, 151.2, 148.8, 128.7, 115.0, 88.7, 72.0, 62.8, 52.0, 51.0, 44.6, 42.2, 41.4, 40.9, 29.4, 26.02, 25.98, 25.9, 23.7, 22.8, 20.4, 18.4, 18.1, –3.1, –4.6, –5.25, –5.32; HRMS (ESI-TOF) m/z $[M+Na]^+$ calcd for $C_{32}H_{56}O_5Si_2Na$ 599.3564 found 599.3531.

*Trichoaurantianolide C (**3**).* To a solution of **63** (4.0 mg, 0.0069 mmol) in DMF (0.2 mL) at 22 °C was added TAS-F (30 mg, 0.12 mmol). The reaction was stirred for six h at rt, diluted with Et_2O and quenched with pH 7 buffer (2 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 x 4 mL). The combined organic layers were washed with water (2 x 5 mL), dried over $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography using a gradient elution (10–30% EtOAc/hexanes) provided trichoaurantianolide C (**3**) (1.8 mg, 75%) as a colorless oil: R_f 0.78 (hexanes/EtOAc (1:2)); $[\alpha]_D^{20}$ +11.6 (c 0.15, CH_2Cl_2); IR (film) 3468, 2958, 1797, 1771, 1743, 1461, 1422, 1383, 1250, 1211, 1075, 1049, 1009 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.14 (td, J = 2.2, 1.1 Hz, 1H), 5.06 (td, J = 2.7, 1.2 Hz, 1H), 4.47 (dt, J = 13.7, 2.5 Hz, 1H), 4.37 (dt, J = 13.6, 2.3 Hz, 1H), 4.17 (d, J = 2.0 Hz, 1H), 3.68 (dd, J = 8.8, 4.9 Hz, 1H), 3.06 (d, J = 18.1 Hz, 1H), 2.65 (dd, J = 14.4, 9.0 Hz, 1H), 2.54 (d, J = 18.1 Hz, 1H), 2.50 (dd, 19.0, 7.8 Hz, 1H), 2.21 (br s, 1H), 2.11 (ddd, J = 18.9, 12.5, 1.3 Hz, 1H), 1.98 (dt, J = 12.3, 8.5 Hz, 1H), 1.87 (d, J = 14.2 Hz, 1H), 1.75–1.68 (m, 1H), 1.49 (d, J = 5.4 Hz, 1H) 1.27 (s, 3H), 1.13 (s, 3H), 1.04 (d, J = 6.3 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.6, 174.4, 146.3, 106.7, 89.5, 83.6, 70.3,

68.5, 57.9, 52.4, 50.2, 45.2, 43.1, 42.5, 39.8, 29.8, 23.2, 22.9, 22.0, 15.8; HRMS (ESI-TOF) *m*/*z* $[M+H]^+$ calcd for $C_{20}H_{29}O_5$ 349.2015 found 349.2004.

Trichoaurantianolide D (4). To a 0 °C solution of **3** (1.0 mg, 0.0029 mmol) in CH_2Cl_2 (0.2 mL) was added Et_3N (24 μL, 0.17 mmol), DMAP (one crystal) and Ac_2O (8 μL, 0.086 mmol). The cooling bath was removed and the reaction was allow to warm to rt, stirred for 10 min, diluted with CH_2Cl_2 (1 mL) and then quenched with saturated aqueous $NaHCO_3$ (1 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 1 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated. Purification by silica gel chromatography using a gradient elution (20% to 25% EtOAc provided 4 (0.9 mg, 80%): R_f 0.52 (hexanes/EtOAc (1:1)); $[\alpha]_D^{20}$ +8.5 (*c* 0.09, CH_2Cl_2); IR (film) 2960, 1797, 1780, 1742, 1461, 1372, 1236, 1051, 1019, 950, 770 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.17 (q, *J* = 1.9 Hz, 1H), 5.06 (td, *J* = 2.6, 1.3 Hz, 1H), 4.83 (d, *J* = 9.2 Hz, 1H), 4.47 (dt, *J* = 13.8, 2.6 Hz, 1H), 4.37 (dt, *J* = 13.8, 2.2 Hz, 1H), 4.20 (d, *J* = 2.0 Hz, 1H), 2.57 (d, *J* = 18.1 Hz, 1H), 2.55 (dd, *J* = 14.5, 9.1 Hz, 1H), 2.50 (d, *J* = 18.1 Hz, 1H), 2.48 (dd, 19.1, 8.0 Hz, 1H), 2.32 (br s, 1H), 2.11 (ddd, *J* = 18.9, 12.5, 1.3 Hz, 1H), 2.09 (s, 3H), 1.98 (dt, *J* = 12.4, 8.4 Hz, 1H), 1.84 (d, *J* = 14.5 Hz, 1H), 1.74–1.67 (m, 1H), 1.36 (s, 3H), 1.20 (s, 3H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.6, 173.3, 169.5, 146.2, 107.1, 89.1, 83.6, 70.9, 70.3, 57.9, 52.6, 49.1, 42.9, 42.3, 41.9, 40.0, 29.6, 23.2, 22.8, 22.0, 21.1, 17.3; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{22}H_{30}O_6Na$ 413.1940 found 413.1941.

ASSOCIATED CONTENT

Supporting Information

Proton and carbon NMR spectra of all new compounds, tabulated comparison data of synthetic and natural trichoaurantianolides C and D, and X-ray crystallographic analysis of compound **32**. 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.

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