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An Approach to *seco*-Prezizaane Sesquiterpenoids: Enantioselective Total Synthesis of (+)-1*S*-Minwanenone

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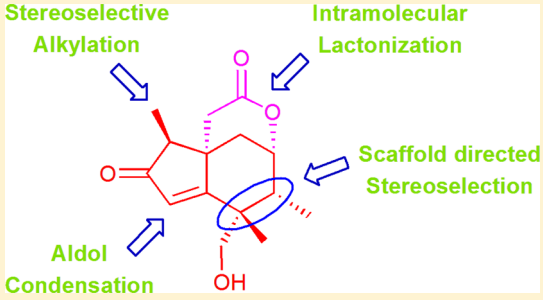
Supporting Information

ABSTRACT: A strategy of general applicability toward *seco*-prezizaane sesquiterpenes, from a chiral, tricyclic synthon, readily available via an enzymatic resolution step from the Diels–Alder adduct of cyclopentadiene and *p*-benzoquinone, has been devised. Our approach enables harnessing of the stereochemical proclivities of the norbornyl system to install the desired stereochemistry at the key stereogenic centers. Recourse to an interesting stratagem to realign a stereochemical divergence into stereoreconvergence forms the cornerstone of our successful approach. The first total synthesis of (+)-1*S*-minwanenone, a prototypical member of *seco*-prezizaane subclass, has been accomplished.



INTRODUCTION

seco-Prezizaane-type sesquiterpenoids constitute a biosynthetically fascinating, architecturally variegated, and rapidly growing class of natural products that are found widely distributed among the exotic *Illicium* species.[1,2] From a structural perspective, *seco*-prezizaanes are compact, caged, polycyclic constructs that are adorned with an array of dense and diverse oxygen functionalities with attendant stereochemical intricacies. A few representative examples (**1**–**4**) of *seco*-prezizaane-type sesquiterpenoids are displayed in Figure 1. Owing to their many uncommon structural features and rich functionalization patterns, *seco*-prezizaanes harbor attributes of being promising new scaffolds for exploring their therapeutical potential. Indeed, several members of this family exhibit wide-ranging bioactivity profiles. However, it is the specific and encouraging role of *seco*-prezizaanes as promoters of neurite growth and as effective inhibitors of GABA action[3e,f] in the central nervous system (CNS) that has captured a great deal of attention.[2,3] This is particularly so because neurodegeneration and attendant disorders are emerging as a major public health challenge in the 21st century in view of the advancing age profile of the world population.

It is hardly surprising therefore that total synthesis endeavors toward *seco*-prezizaane natural products has emerged as an arena of contemporary interest and holds considerable synthetic challenge, not only for developing and validating new methodologies and strategies for total synthesis but also for amplifying Nature's repertoire through diverted total synthesis and make available new natural product inspired entities for therapeutic profiling, particularly as neurotrophic agents. A spate of publications[4] in the recent past, from various research groups spread across continents and our own efforts[5] in the area, bear testimony to the emergent interest of the synthesis community in *seco*-prezizaane natural products. In this regard, pioneering contributions of Danishefsky and more recently of

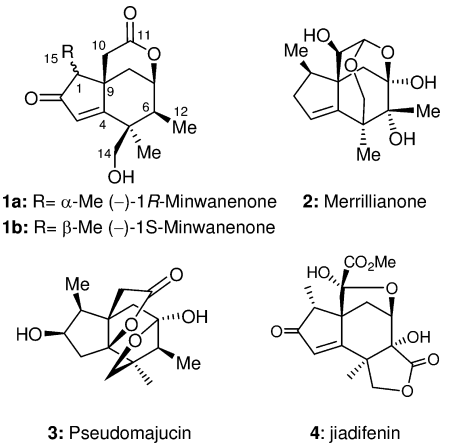


Figure 1. Representative *seco*-prezizaane sesquiterpenoids.

Theodorakis and Fukuyama groups among others are notable.[4] In our laboratory, there are ongoing efforts directed toward developing general protocols to access diverse members of *seco*-prezizaanes and related natural products, particularly those that are neurotrophically active.[5] As an offering from such endeavors, we describe in detail the first total synthesis of (+)-1*S*-minwanenone **5**, an enantiomer of natural product (−)-1*R*-minwanenone **1a** and a prototypical member of the *seco*-prezizaane family.[5c,6] En route our successful journey toward (+)-1*S*-minwanenone **5**, we have witnessed the formation of the tetracyclic core present in the natural product merrillianone **2**, which in turn underlines the inbuilt flexibility of our synthetic approach for adaptation toward the other members of this complex natural product family.[4,5]

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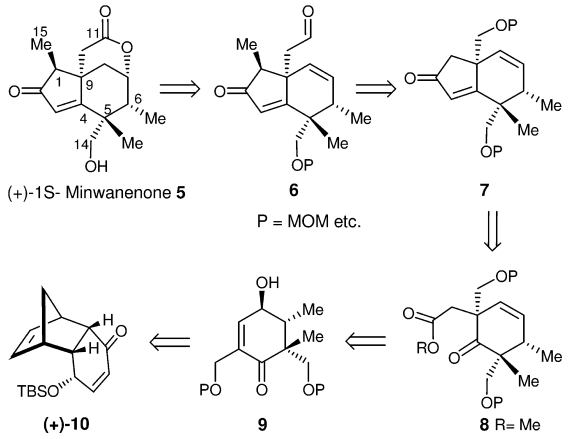


Figure 2. Retrosynthetic analysis of target natural product **5**.

The Fukuyama group's extensive and pioneering search for biologically active substances from the *Illicium* species led to the isolation of (−)-1*R*-minwanenone **1a** and its epimer (−)-1*S*-minwanenone **1b** along with several other *seco*-prezizaane type sesquiterpenoids from the methanol extract of the pericarps of *Illicium minwanense* in 2003.[1] The stereostructures of minwanenones **1a** and **1b** were established through incisive NMR studies, and their biosynthetic kinship with other co-occurring sibling natural products was employed to deduce their absolute configuration.[1] The bioactivity profile of **1a,b** has not yet been reported. However from a truly synthetic perspective, the tricyclic skeleton of minwanenones **1a,b** embodying five stereocenters (two of which are quaternary) and with an array of functional groups such as a bridged lactone, enone, and a primary hydroxyl group, accounting for four oxygens, poses considerable total synthesis challenge. While conceptualizing our synthetic strategy toward minwanenones, we also factored in the possibility of generalizing it toward the other members of the *seco*-prezizaanes family.[2]

Retrosynthetically, it was envisaged that the bridged lactone segment of tricyclic (+)-1*S*-minwanenone **5** could be installed at the end on an appropriately functionalized bicyclic enone **6**, which in turn could be obtained via stereoselective methylation, one carbon homologation, and functional group adjustment in the protected derivative **7**. Access to enone **7** was contemplated from keto-ester **8** through an intramolecular Horner−Wadsworth−Emmons reaction.

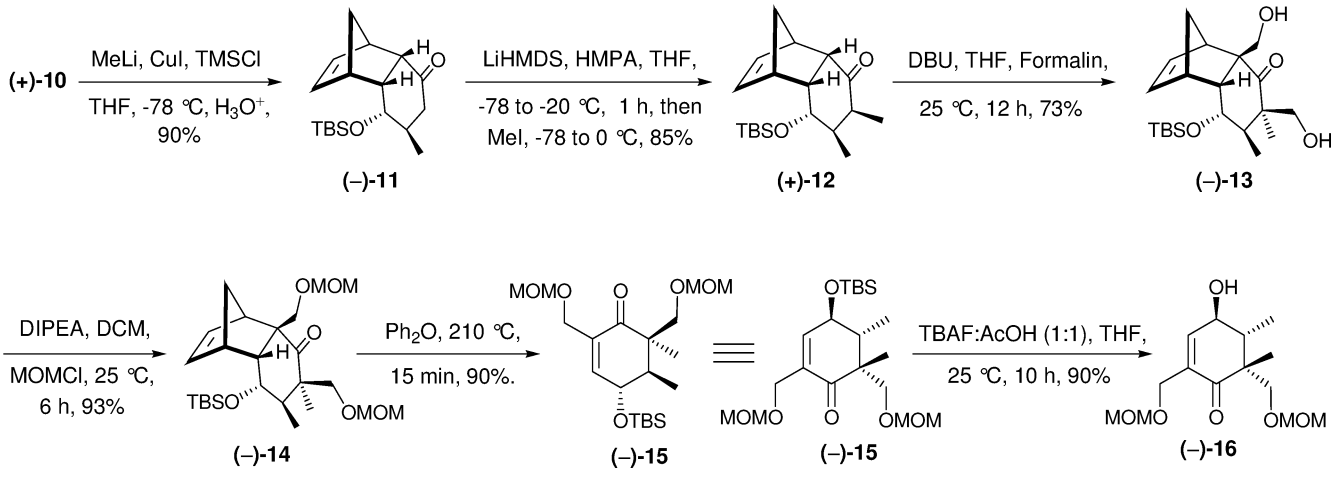
The Johnson orthoester rearrangement in γ-hydroxycyclohexenone **9** was expected to stereoselectively set up the C_9 quaternary center in **8**. The cyclohexenone **9** was to be obtained through elaboration of the previously reported[7] *endo*-tricyclo-[6.2.1.$0^{2,7}$]-undeca-4,9-dien-3-one (+)-**10**. The choice of the chiral *endo*-tricyclic synthon (+)-**10**, as the launching platform, was a key tactic as it harnessed the well established propensity of the *endo*-norbornyl-fused systems toward *exo*-face selectivity due to inherent topological bias. This was expected to facilitate the stereoselective installation of critical C_5,C_6 stereogenic centers during the early stages of the synthesis.

RESULTS AND DISCUSSION

In order to pursue the retrosynthetic theme outlined in Figure 2, starting chiral synthon (+)-**10** was accessed in enantiomerically pure (>99% ee) form and in multigram quantity from the readily available Diels−Alder adduct of cyclopentadiene and *p*-benzoquinone, following a reported procedure and involving enzymatic resolution as the key step.[7] The choice of (+)-**10** rather than its enantiomer (−)-**10** was dictated by the more convenient (relatively speaking) access to it. Michael addition of methyl-cuprate on enone (+)-**10** proceeded smoothly in the presence of TMSCl as an additive and after acidic workup delivered (−)-**11** as a single diastereomer.[8] Methylation of (−)-**11** under kinetically controlled conditions was once again stereoselective (>90%) and afforded the dimethylated product (+)-**12** (see Scheme 1). The C_5 quaternary center with requisite relative disposition with respect to the C_6 stereocenter was now set through stereoselective α-hydroxymethylation in (+)-**12** from the *exo*-face to deliver the diol (−)-**13** as a single diastereomer. Both hydroxyl groups in (−)-**13** were now protected as MOM derivative (−)-**14** prior to the removal of the norbornyl scaffold. Thermal activation in (−)-**14** disengaged the norbornyl scaffold through a facile retro-Diels−Alder process to afford cyclohexenone (−)-**15**. Deprotection of the TBS protecting group in (−)-**15** provided the γ-hydroxycyclohexenone (−)-**16** (see Scheme 1), the precursor for the projected [3,3] sigmatropic rearrangement (see Figure 2).

The Johnson-orthoester rearrangement[9] in (−)-**16** could be implemented under standard protocol and was expectedly stereoselective and furnished the keto-ester (+)-**18** along with the simple dehydrated (under thermal activation) 1,3-diene product (−)-**17** in 2.6:1 ratio (based on isolated yields), respectively (see Scheme 2).

Scheme 1. Synthesis of γ-Hydroxycyclohexenone (−)-16



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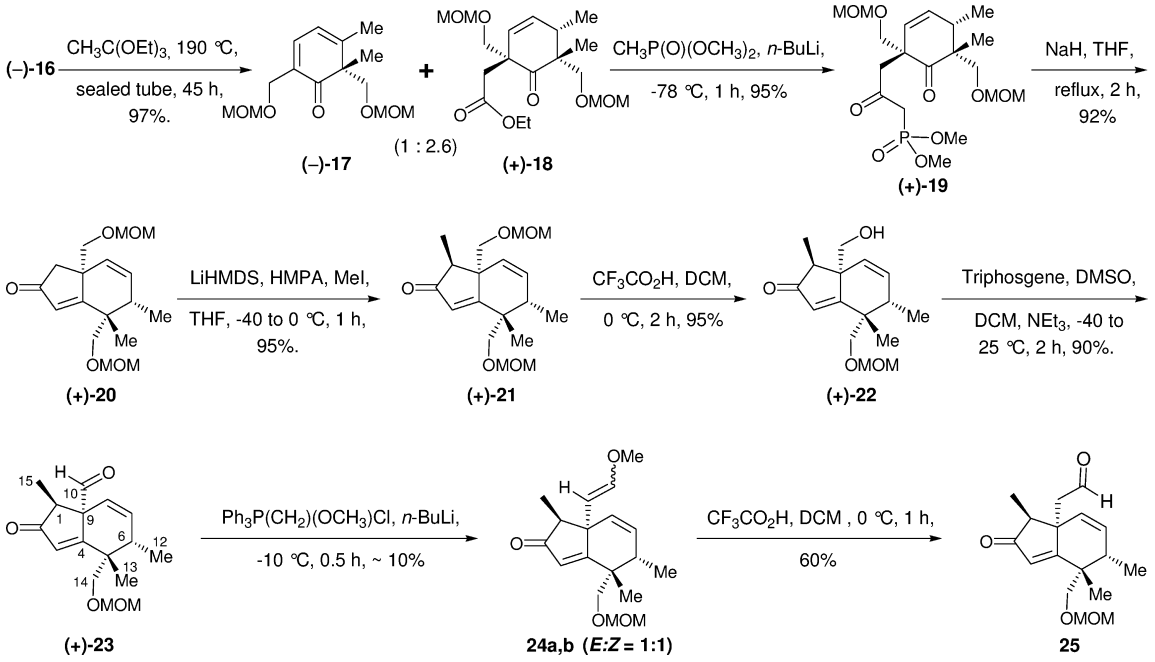
Scheme 2. Preparation of Bicyclic Aldehyde 25



Chemoselective addition of lithiated dimethyl methylphosphonate on keto-ester (+)-**18** proceeded smoothly and delivered the *β*-ketophosphonate (+)-**19** quite conveniently. Subsequent exposure of (+)-**19** to NaH in refluxing THF executed the desired HWE cyclization and provided the bicyclic enone (+)-**20** in excellent yield.[10] Kinetically controlled methylation in (+)-**20** was again stereoselective with addition from the face opposite to the bridgehead substituent and furnished the (+)-**21** as a single diastereomer. At this stage it was considered essential to confirm the stereochemical integrity of (+)-**21**, and therefore a detailed NMR analysis based on ^{1}H–^{1}H COSY and NOESY was carried out to secure its formulation (see Supporting Information). After the successful installation of the four out of five stereocenters present in (+)-1*S*-minwanenone **5** in a stereoselective manner, the next objective was to transform the primary-hydroxyl functionality at the bridgehead position in (+)-**21** to the precursor aldehyde **25** to implement one carbon homologation reaction. After considerable efforts, conditions could be devised for the regioselective deprotection of the MOM group in (+)-**21**, using CF_3CO_2H at 0 °C, to afford the bicyclic alcohol (+)-**22**. It was expected that the C_{10}-MOM group in (+)-**21** would undergo deprotection in preference to the C_{13}-MOM group due to the relatively less steric congestion in its vicinity. In the event, the primary hydroxyl group in (+)-**22** was oxidized to aldehyde (+)-**23** using triphosgene and DMSO (see Scheme 2).[11] The stereostructure of (+)-**23** was secured from the results of ^{1}H–^{1}H COSY and ^{1}H–^{1}H NOESY experiments. In the NOESY experiments, H-1 showed cross peak to H-10 (aldehyde proton), whereas CH_3 at C-12 showed cross peak to CH_2 at C-14 and H-6 (see Supporting Information).

Exposure of (+)-**23** to triphenylphosphonium methoxymethylene-chloride and *n*-BuLi furnished the 1:1 mixture of *E*- and *Z*- methylenolethers **24a,b** (as indicated by ^{1}H NMR analysis) but in dismal yield (~5–10%). Acid-catalyzed hydrolysis of **24a,b** led to the formation of aldehyde **25** (see Scheme 2). While the key precursor **25** was realized, its meager quantities precluded further pursuit of the end game. Several attempts[12] to augment access to **25** through change in reaction conditions and base, solvent, and temperature or recourse to Peterson olefination[12b] or Wittig–Horner reaction[12a] with (alkoxymethyl)-phosphonate ester failed to deliver the desired aldehyde **25** in acceptable yield. It is reasonable to speculate that steric congestion engendered by the neopentyl nature of the aldehyde functionality in (+)-**23** is the causative factor for the poor outcome of the homologation reaction. In addition, formation of undesired dehydration product (–)-**17** during the [3,3]-sigmatropic rearrangement of (–)-**16** was also a significant liability. Overall, access to functionally garnished and stereochemically secured bicycle (+)-**23** in a concise manner was a satisfying outcome; however, our repeated failures to obtain key aldehyde **25** in preparatively viable amounts warranted some reflection and underscored the need to rework our synthetic strategy at this juncture. Grudgingly, it was decided to revert back to the chiral synthon (+)-**10** and craft a *de novo* strategy as depicted in Figure 3.

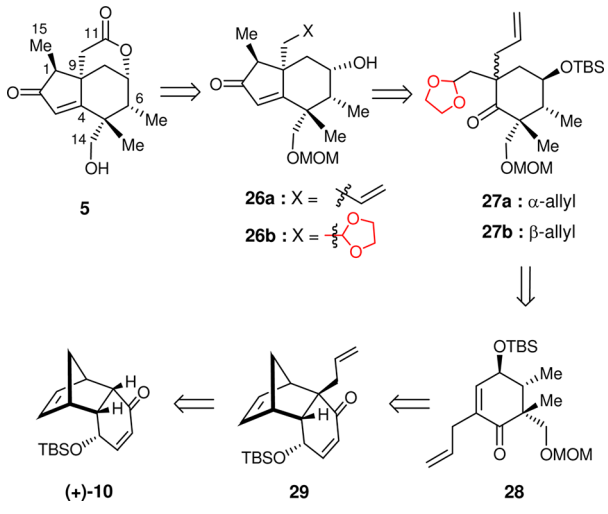


Figure 3. Redefined retrosynthetic strategy toward **5**.

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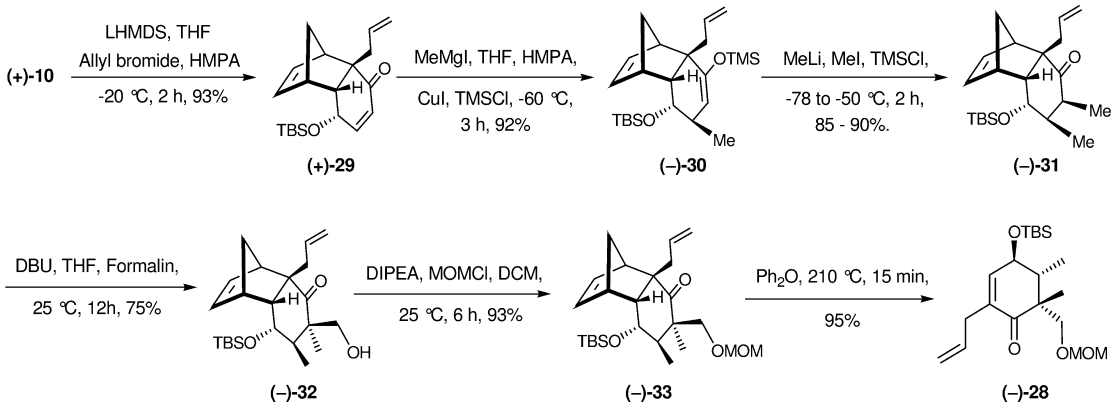
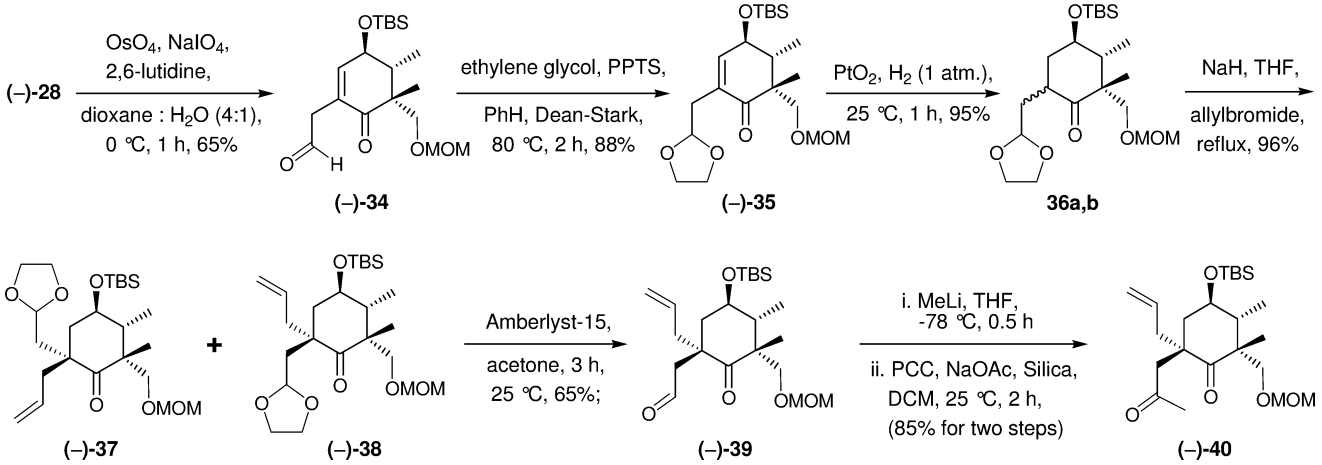
Scheme 3. Synthesis of Cyclohexenone (−)-28



Scheme 4. Synthesis of Aldol Precursor (−)-40



In our redefined strategy toward (+)-1*S*-minwanenone **5**, delineated through the retrosynthetic theme depicted in Figure 3, an appropriately functionalized bicyclic enone **26a** or **26b** was identified as the pivotal precursor, which in turn could be crafted through an intramolecular aldol condensation in a 1,4-dicarbonyl precursor obtainable from either of the diastereomeric allyl group bearing cyclohexanones **27a,b**. Indeed, the allyl group in **27a,b** is strategically placed to function either as a "masked acetaldehyde" or as an "acetone equivalent" to render both the anticipated diastereomers serviceable toward the target structure. Similarly, the acetaldehyde acetal moiety in **27a,b** could either function directly as "protected aldehyde" or elaborated as an acetone equivalent. Access to **27a,b** was contemplated from cyclohexenone **28** through appropriate FGIs and α-allylation. The functionally embellished precursor cyclohexenone **28** was to be obtained from our chiral synthon (+)-**10** via the intermediacy of **29** (see Figure 3). Once again, the choice of the *endo*-tricyclic chiral synthon (+)-**10** (available in both the enantiomeric forms), as the chiral synthon, was crucial for building the requisite C_5,C_6 stereochemistry through exploitation of its inherent topological bias in favor of *exo*-face selectivity.

Our second generation approach to **5** emanated with the smooth and stereoselective allylation of (+)-**10** to furnish *exo*-allylated (+)-**29**. Copper(I) mediated 1,4-addition of MeMgI to (+)-**29** proceeded with expected *exo*-face selectivity and *in situ* capture of the resulting enolate with TMSCl delivered the TMS-enol ether (−)-**30** as a single diastereomer.[13] Metalation of TMS-enol ether (−)-**30** and quenching the resulting lithium enolate with MeI led to the vicinally dimethylated product (−)-**31** (see Scheme 3). In order to establish the C_5 quaternary center with requisite relative stereochemical disposition, (−)-**31** was subjected to α-hydroxymethylation, which occurred preferentially from the *exo*-face to stereoselectively furnish alcohol (−)-**32**. This maneuver, besides establishing the C_5 quaternary center, also secured the relative C_5,C_6 sterochemistry. The newly introduced hydroxyl group in (−)-**32** was protected as MOM derivative (−)-**33** prior to the jettisoning of the norbornyl moiety. A retro Diels−Alder process was executed in (−)-**33** through thermal activation to disengage the norbornyl moiety and liberate functionally enriched cyclohexenone (−)-**28** (Scheme 3). At this stage, chemoselective reduction of the enone double bond in (−)-**28** and subsequent alkylation with 2-bromoacetaldehyde acetal was expected to deliver a diastereomeric mixture of allylated cyclohexenones **27a,b** as envisioned in the retrosynthetic theme depicted in Figure 3. However, attempts toward the chemoselective reduction of the enone double bond in (−)-**28** employing various 1,4-reduction protocols such as LAH/CuI,[14a,b] DIBAL-H/MeCu,[14c] Et_3SiH/Wilkinson's catalyst,[14d] sodium dithionate/aliquot,[14e,f] or Li/liquid ammonia failed to deliver the desired 1,4-reduction product. Since selective reduction of the enone double bond in (−)-**28** proved to be unexpectedly difficult, an alternative strategy was planned that involved the oxidative cleavage of the allyl group

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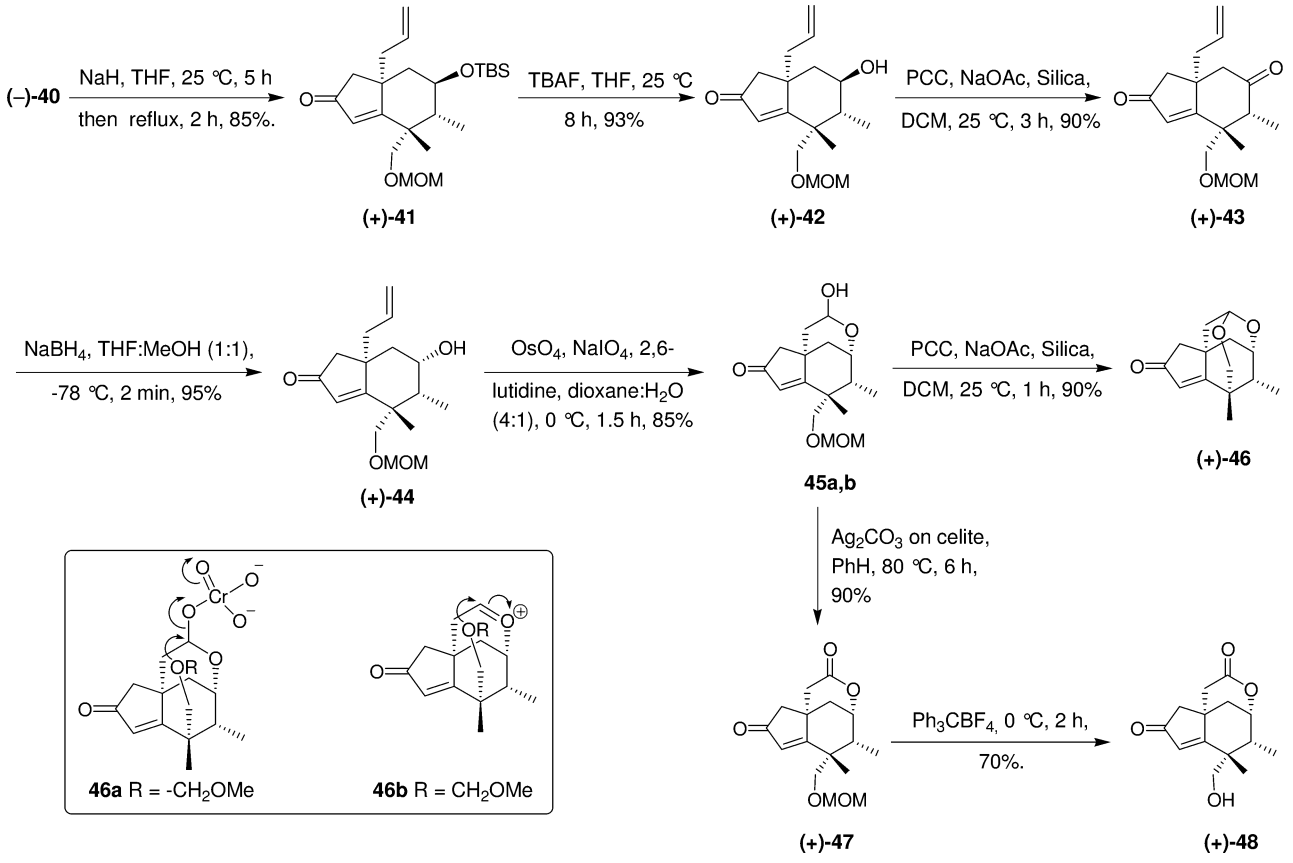
Scheme 5. Synthesis of Desmethyl-minwanenone 48



in (−)-**28** and protection of the resulting aldehyde group prior to the reduction of the enone double bond (see Scheme 4).

Accordingly, a single-pot OsO_4–$NaIO_4$ mediated oxidative cleavage[15] of the allyl group in (−)-**28** furnished the aldehyde (−)-**34**, which was protected as acetal (−)-**35**, Scheme 4. Reduction of the enone double bond in (−)-**35** under catalytic hydrogenation over PtO_2 was now quite uneventful, and the resulting cyclohexanone **36a,b** upon NaH mediated allylation afforded a mixture of diastereomers (−)-**37** and (−)-**38** (40:60 ratio) in excellent yield. The relative stereochemistry at the newly generated C_9 quaternary center in (−)-**37** and (−)-**38** was secured on the basis of ^1H–^1H COSY and ^1H–^1H NOESY experiments (see Supporting Information). The anticipated stereochemical divergence leading to the formation of both (−)-**37** and (−)-**38**, though irksome at first sight, could be fashioned into stereochemical convergence that rendered both the diastereomers serviceable (*vide infra*). Our initial advance toward the natural product target **1** was quite understandably through the major diastereomeric product (−)-**38**, and the intent was to elaborate the protected acetaldehyde arm into a 1,4-dicarbonyl moiety bearing an acetone equivalent for the projected aldol cyclization. Toward this end, acetal moiety in (−)-**38** was carefully deprotected to free aldehyde (−)-**39**. Chemo- and regioselective addition of MeLi to (−)-**39** and PCC oxidation furnished the 1,4-dicarbonyl bearing (−)-**40** (see Scheme 4).

Intramolecular aldol cyclization in (−)-**40** was smoothly effected with NaH in THF to eventuate into bicyclic enone (+)-**41** (see Scheme 5). At this stage, the next key move was to install the required α-hydroxyl stereochemistry at C_7 in (+)-**41**, through inversion of the existing C_7 stereochemistry, for facilitating the intramolecular lactol formation. For this purpose, the TBS group in (+)-**41** was selectively deprotected with TBAF to deliver alcohol (+)-**42**, and further PCC mediated oxidation provided the ketone (+)-**43** in excellent yield. As anticipated, $NaBH_4$ reduction in (+)-**43** was regio- and stereoselective with hydride delivery from the less hindered β-face to afford (+)-**44** having the desired C_7 α-hydroxyl stereochemistry. A one-pot OsO_4/$NaIO_4$ mediated oxidative cleavage of the allyl group[15] in bicyclic enone (+)-**43** proceeded smoothly and furnished diastereomeric lactols **45a,b** in good yield. Attempted oxidation of the resulting lactols **45a,b** to the lactone with PCC led to the formation of the tetracyclic framework of (+)-**46**, most likely through intramolecular displacement of the intermediate chromate ester **46a** by distal but sterically well poised OMOM group or more likely via the oxocarbenium ion intermediate **46b** (see Scheme 5).[19] Formation of the tetracyclic acetal (+)-**46** was a bonus as it represented a conspicuous motif present in cycloparvifloralone type natural products such as merrillianone **2**. However, lactols **45a,b** could be conveniently oxidized using Fetizon oxidation[16] and led to the formation of desired tricyclic lactone (+)-**47** in excellent yield. After several trials, the MOM group in (+)-**47** could be deprotected using triphenylcarbenium tetrafluoroborate in DCM at 0 °C to obtain desmethyl-minwanenone (+)-**48** in moderate yield (see Scheme 5).[17]

Having tested the waters and established a synthetically viable route to access desmethyl-minwanenone (+)-**48** from the advanced bicyclic enone (+)-**40**, attention was immediately turned toward (+)-1*S*-minwanenone **5**. En route to **5**, it was considered prudent to first install the C_1 methyl group in (+)-**41**. Accordingly, (+)-**41** was subjected to methylation under kinetically controlled conditions to furnish (+)-**49** as a single

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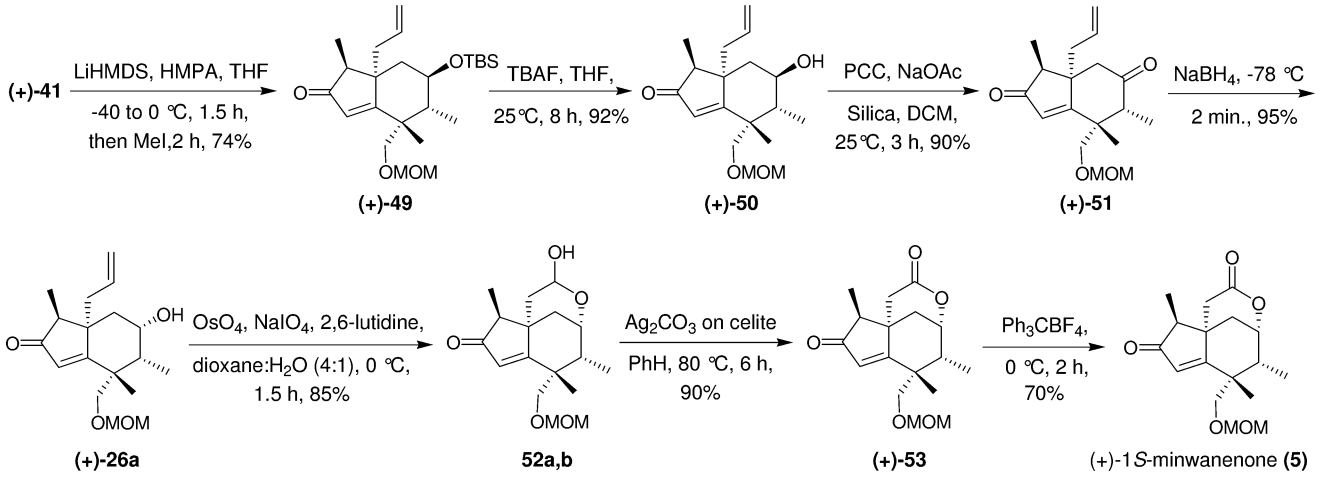
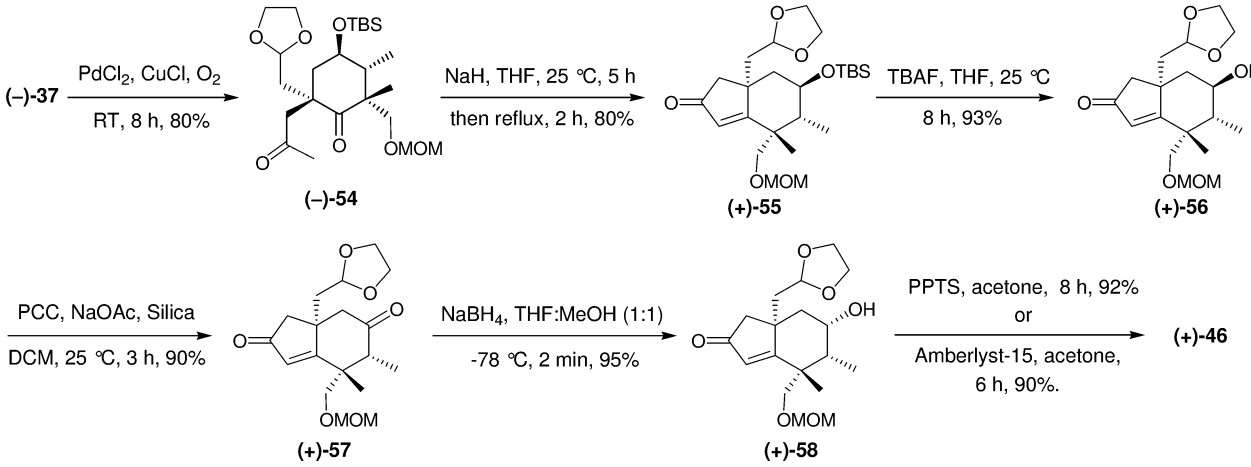
Scheme 6. Completion of Synthesis of (+)-1*S*-Minwanenone 5



Scheme 7. Formation of Merrillianone Framework (+)-46



isomer in a stereoselective manner (see Scheme 6). Deprotection of the TBS group in (+)-**49** proceeded smoothly to furnish alcohol (+)-**50**, which upon PCC oxidation provided the bicyclic keto-enone (+)-**51**. Regio- and stereoselective reduction of the cyclohexanone functionality in (+)-**51** furnished (+)-**26a** with the desired C_7 α-hydroxyl stereochemistry. Oxidative cleavage of the allyl group in (+)-**26a** was achieved following a one-pot oxidation protocol with OsO_4/$NaIO_4$ to furnish a mixture of lactols **52a,b**.[15] Fetizon oxidation[16] of lactols **52a,b** led to tricyclic lactone (+)-**53**. Lastly, the MOM protecting group in (+)-**53** could be removed employing triphenylcarbenium-tetrafluoroborate[17] to provide (+)-1*S*-minwanenone **5**, which was found to be spectroscopically (^{1}H and ^{13}C NMR spectrum) identical to the natural product (−)-1*R*-minwanenone **1** (see Scheme 6).[1] However, the specific rotation, $[\alpha]_D$ +23.3°, of our synthetic (+)-1*S*-minwanenone **5** was found to be opposite in sign to that reported, $[\alpha]_D$ −17.9°, for the natural (−)-1*R*-minwanenone **1**.[1] Since our synthesis emanated from the *endo*-tricyclic chiral synthon (+)-**10** of well established absolute stereochemistry, the present effort independently validated the previously inferred[1] absolute configuration of the natural product.

Having completed an enantioselective total synthesis of (+)-**5** from a functionally adorned and stereochemically well-defined cyclohexanone (−)-**38**, it was considered useful to explore and demonstrate the serviceability of its diastereomeric sibling (−)-**37** (see Scheme 4). The intent was to showcase an interesting feature of our strategy that enabled stereochemical convergence in the face of stereodivergence, when a seemingly unwanted diastereomer was encountered along a reaction path. Thus, the objective was to realign the diastereomer (−)-**37** into the main pathway leading to minwanenone and its sibling *seco*-prezizaane natural products. Wacker oxidation[18] of the allyl group in (−)-**37** generated the 1,4-dicarbonyl bearing moiety (−)-**54**, which underwent aldol cyclization on exposure to NaH in THF to furnish functionally embellished bicyclic enone (+)-**55** (see Scheme 7). Deprotection of the TBS group in (+)-**55** to (+)-**56** and PCC oxidation led to the enedione (+)-**57** and set the stage for the inversion of the C_7 hydroxyl group stereochemistry. Controlled chemo- and stereoselective reduction of (+)-**57** with $NaBH_4$ furnished (+)-**58** having the desired stereochemistry at the C_7-hydroxyl group. At this stage, deprotection of the acetal moiety in (+)-**58** was expected to reveal the aldehyde group and engage the C_7-hydroxyl to lactols **45a,b** (Scheme 5), which on further oxidation was expected to deliver the tricyclic skeleton of minwanenone. However, attempts to deprotect the acetal group in (+)-**58** under a range of acidic conditions drew a blank and led instead to the generation of a tetracyclic framework (+)-**46**, obtained previously (*vide supra*) from the major diastereomer (+)-**38**. Thus, both of the diastereomers (−)-**37** and (+)-**38** have been

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shown to converge to the same tetracyclic *seco*-prezizaane framework (+)-**46** present in natural products such as merrillianone **2** (see Scheme 7). Interestingly, facile formation of (+)-**46** reveals the interactive proclivities of scattered but well directed functionalities on this framework and augurs well for extending the applicability of the present approach to access other *seco*-prezizaane natural products.[1,2]

SUMMARY

In summary, the first total synthesis of (+)-1*S*-minwanenone, a prototypical *seco*-prezizaane, has been accomplished from a readily available chiral building block in 21 steps and in 2.5% overall yield. The strategy unfolded here harnesses the topological preferences of a norbornyl fused system to build the requisite stereochemistry. Our synthesis of (+)-1*S*-minwanenone is regio- and stereoselective, and in one case of significant deviation in stereoselectivity a strategic concept of realigning stereochemical divergence to achieve overall convergence is demonstrated. Access to several functionally embellished derivatives bearing the bicyclo[4.3.0]nonane core present in *seco*-prezizaanes, through an adaptable strategy, opens opportunities to target other members of this exotic family.

EXPERIMENTAL SECTION

General Experimental Methods. All moisture- and air-sensitive reactions were performed under argon atmosphere with dry, freshly distilled solvents under anhydrous conditions using standard syringe-septum technique. Low temperatures were maintained using liquid nitrogen in combination with appropriate solvent. Hexane refers to the petroleum ether fraction boiling between 60 and 80 °C. Dry solvents such as THF, ether, 1,4-dioxane, DME, benzene, and toluene were prepared by distilling them from sodium benzophenone radical anion. Dry DCM, $CHCl_3$, pyridine, DMSO, TEA, DIPA, HMDS, and HMPA were distilled freshly from calcium hydride. Acetone was distilled over preactiviated K_2CO_3. Methanol was distilled from its alkoxide (formed by the reaction with activated magnesium) and stored over 4 Å molecular sieves. Reactions were monitored by thin layer chromatography (TLC), which was performed either on (10 × 5 cm) glass plates or on microscopic slides coated with silica gel G or GF_{254} (250 mmol), containing 13% calcium sulfate as a binder. Visualization of the spots on TLC plates was achieved either by exposure to iodine vapor or by using UV light or by spraying with either ethanolic vanillin or 30% methanol/sulfuric acid solution and heating the plates at ∼120 °C. Commercial silica gel (100−200 mesh particle size) was used for column chromatography. All yields reported are of isolated products used for characterization and wherever applicable are based on recovered starting material. ^{1}H and ^{13}C NMR samples were generally made in $CDCl_3$,and chemical shifts are expressed in parts per million (δ) scale using tetramethylsilane (Me_4Si) as the internal standard. The standard abbreviations s, d, t, q, and m refer to singlet, doublet, triplet, quartet, and multiplet, respectively. Coupling constant (J), whenever discernible, have been reported in Hz. High resolution mass spectra (HRMS) were recorded on Q-TOF Micromass mass spectrometer.

(2*S*,5*R*,6*S*,7*R*)-6-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-5-methyltricyclo[6.2.1.0^{2,7}]undec-9-en-3-one (11). To a cooled (0 °C) THF (20 mL) solution of CuI (1.1 g, 6.2 mmol) was added methyl lithium (8.3 mL, 1.5 M ethereal solution), and the resulting clear solution was cooled to −78 °C prior to the sequential addition of enone-TBS (+)-**10** (1.5 g, 5.17 mmol, in 10 mL THF) and TMSCl (0.72 mL, 5.7 mmol). The reaction mixture was allowed to warm to −50 °C over a period of 2 h and then quenched carefully with dropwise addition of water. The aqueous phase was extracted with ether (2 × 60 mL). The combined organic extracts were washed successively with 10% HCl (20 mL × 3), water, and brine and dried over Na_2SO_4. After the evaporation of solvent, the crude residue was purified through a silica gel column chromatography (eluent: 5% ethyl acetate in hexane) to afford a ketone (−)-**11** (1.4 g, 90%) as a colorless oil: $[\alpha]^{22}_D$ −36.0 (c 1.0, $CHCl_3$); IR (Neat) 2956, 2931, 2858, 1701, 1253 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.19−6.16 (m, 1H), 6.05−6.02 (m, 1H), 3.80−3.75 (m, 1H), 3.33 (s, 1H), 3.15 (s, 1H), 2.86−2.77 (m, 2H), 2.22−2.11 (m, 1H), 1.90−1.82 (m, 2H), 1.36 (d(1/2ABq), J = 8.4 Hz, 1H), 1.25 (d(1/2ABq), J = 8.4 Hz, 1H), 0.96 (s, 9H), 0.86 (d, J = 5.7 Hz, 3H), 0.14 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.4, 137.0, 135.8, 75.6, 52.3, 49.4, 47.5, 47.1, 46.0, 44.9, 31.9, 25.9, 19.0, 18.1, −4.0, −4.9; HRMS(ES) m/z calcd for $C_{18}H_{30}NaO_2Si$ (M + Na) 329.1913, found 329.1912.

(2*S*,4*S*,5*R*,6*R*,7*R*)-6-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-4,5-dimethyltricyclo[6.2.1.0^{2,7}]undec-9-en-3-one (12). To a stirred solution of LiHMDS in dry THF (12 mL, 0.5 M, freshly prepared from equimolar amount of HMDS and *n*-BuLi, at 0 °C) and kept at −78 °C, was added a solution of ketone (−)-**11** (1.4 g, 4.6 mmol) in dry THF (10 mL) over a period of 15 min. The resulting solution was stirred at −20 °C for 1 h and then recooled to −78 °C prior to the sequential addition of HMPA (1 mL, 6.0 mmol) and MeI (0.37 mL, 6.0 mmol). The reaction mixture was allowed to warm to 0 °C, stirred for 1 h, and then quenched with satd NH_4Cl solution. The aqueous layer was extracted with ether (2 × 50 mL), and the combined organic extracts were washed water and brine and dried over Na_2SO_4. After the evaporation of solvent, the resulting crude material was purified by silica gel column chromatography (eluent: 5% ethyl acetate in hexane) to afford the dimethylated ketone (+)-**12** (1.24 g, 85%) as a colorless oil: $[\alpha]^{24}_D$ +76.7 (c 1.5, $CHCl_3$); IR (Neat) 2958, 2937, 2857, 1703, 1461, 1251, 1080 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.22 (dd, J = 5.4 and 3.0 Hz, 1H), 5.94 (dd, J = 5.4 and 3.0 Hz, 1H), 4.08−4.01 (m, 1H), 3.29 (bs, 1H), 3.04 (bs, 1H), 2.88−2.80 (m, 2H), 2.29 (dq, J = 7.2 and 3.9 Hz, 1H), 1.85−1.75 (m, 1H), 1.37−1.25 (m, 2H), 0.97 (d, J = 7.2 Hz, 3H), 0.93 (s, 9H), 0.85 (d, J = 6.9 Hz, 3H), 0.14 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 216.1, 137.9, 133.3, 71.5, 50.9, 49.3, 47.2, 46.4, 45.6, 44.4, 39.2, 26.0(3C), 18.1, 13.7, 11.32, −4.18, −5.00; HRMS(ES) m/z calcd for $C_{19}H_{32}NaO_2Si$ (M + Na) 343.2069, found 343.2073.

(2*S*,4*R*,5*R*,6*R*,7*R*)-6-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-2,4-di(hydroxymethyl)-4,5-dimethyltricyclo[6.2.1.0^{2,7}]undec-9-en-3-one (13). To an ice-cooled solution of a dimethylated ketone (+)-**12** (1.0 g, 3.14 mmol) in 10 mL of distilled THF were added DBU (0.88 mL, 6.3 mmol) and formalin (2 mL of 35% of aqueous solution, 22 mmol) successively. The reaction was continued at 25 °C for 12 h and then diluted with water (25 mL). The aqueous phase was extracted with ethyl acetate (2 × 50 mL), and the combined organic phases were washed with water and brine and dried over Na_2SO_4. After the evaporation of the solvent, the crude residue was purified by silica gel column chromatography (eluent: EA/ hexane = 1:20 to 1:5) to afford a starting material (+)-**12** (0.2 g, 20%) and a diol (−)-**13** (0.836 g, 73%, 88% borsm): $[\alpha]^{24}_D$ −25.0 (c 0.8, $CHCl_3$); IR (Neat) 3350, 2956, 2929, 1687, 1471, 1253 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.32 (dd, J = 5.4 and 3.0 Hz, 1H), 5.91 (dd, J = 5.4 and 3.0 Hz, 1H), 4.50 (dd, J = 11.4 and 6.9 Hz, 1H), 4.28 (d, J = 9.6 Hz, 1H), 3.62 (s, 2H), 3.52 (d, J = 9.6 Hz, 1H), 3.24 (s, 1H), 2.88 (s, 1H), 2.73−2.67 (bs, 1H), 2.65 (dd, J = 6.9 and 3.0 Hz, 1H), 1.75−1.69 (m, 1H), 1.47−1.23 (m, 3H), 0.97 (s, 9H), 0.96 (d, J = 6.9 Hz, 3H), 0.85 (s, 3H), 0.15 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 224.0, 138.6, 134.7, 73.0, 72.3, 69.6, 61.3, 53.2, 52.0, 50.0, 48.6, 45.9, 40.3, 26.0(3C), 19.9, 18.2, 12.5, −3.9, −4.8; HRMS(ES) m/z calcd for $C_{21}H_{36}NaO_4Si$ (M + Na) 403.2281, found 403.2278.

(2*S*,4*R*,5*R*,6*R*,7*R*)-6-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-2,4-di[(methoxymethoxy)methyl]-4,5-dimethyltricyclo[6.2.1.0^{2,7}]-undec-9-en-3-one (14). To the stirred ice-cooled solution of compound (−)-**13** (0.7 g, 1.84 mmol) in 7 mL of dry DCM were added DIPEA (1.9 mL, 11.04 mmol), DMAP (0.18 mmol) and MOMCl (0.56 mL, 7.36 mmol) successively. The resulting solution was stirred at 25 °C for 6 h and then quenched with satd $NaHCO_3$. The aqueous layer was extracted with DCM (2 × 50 mL), and the combined organic layers were washed with water and brine and dried over Na_2SO_4. After the removal of solvent, the crude material was purified by passing through a silica gel column (eluent: EA/hexane = 1:9) to obtain

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compound (−)-**14** (800 mg, 93%): $[\alpha]^{24}_{D}$ −48.9 (*c* 0.9, $CHCl_3$); IR (Neat) 2951, 2930, 2883, 1687, 1471, 1061 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.29 (dd, *J* = 5.4 and 3.0 Hz, 1H), 5.95 (dd, *J* = 5.4 and 3.0 Hz, 1H), 4.56 (s, 2H), 4.46 (s, 2H), 4.26 (dd, *J* = 11.4 and 7.2 Hz, 1H), 3.85 (d, *J* = 9.3 Hz, 1H), 3.55−3.51 (m, 2H), 3.38 (d, *J* = 9.3 Hz, 1H), 3.34 (s, 3H), 3.30 (s, 3H), 3.16 (s, 1H), 2.93 (s, 1H), 2.65 (dd, *J* = 6.6 and 3.0 Hz, 1H), 1.76−1.58 (m, 3H), 1.60−1.58 (m, 1H), 1.34−1.23 (m, 3H), 0.96 (s, 9H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.12 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.8, 138.4, 135.9, 96.7, 96.6, 75.5, 71.6, 71.2, 59.7, 55.3, 55.2, 52.6, 51.6, 49.2, 48.7, 45.6, 39.9, 26.0, 19.7, 18.2, 12.7, −3.9, −4.8; HRMS(ES) *m*/*z* calcd for $C_{25}H_{44}NaO_6Si$ (M + Na) 491.2805, found 491.2785.

(4*R*,5*R*,6*S*)-4-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-2,6-di-[(methoxymethoxy)methyl]-5,6-dimethyl-2-cyclohexen-1-one (15). To compound (−)-**14** (0.8 g, 1.7 mmol) placed in a 50 mL RB flask, fitted with an air condenser, was added 15 mL of diphenyl ether. The reaction mixture was stirred at 210 °C (oil bath temperature) for about 15 min. The reaction mixture was allowed to cool to 25 °C and then directly charged on a silica gel column. Eluting the column with 2% ethyl acetate in hexane removed the solvent (diphenyl ether) and further elution with 15% ethyl acetate in hexane furnished the cyclohexenone (−)-**15** (0.62 g, 90%): $[\alpha]^{24}_{D}$ −62.0 (*c* 1.0, $CHCl_3$); IR (Neat) 2931, 1668, 1471, 1151, 1043 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.77 (s, 1H), 4.66 (s, 2H), 4.53−4.44 (m, 3H), 4.21 (s, 2H), 3.65 (d(1/2AB$_q$), *J* = 9.6 Hz, 1H), 3.49 (d(1/2AB$_q$), *J* = 9.6 Hz, 1H), 3.37 (s, 3H), 3.27 (s, 3H), 2.04−1.94 (m, 1H), 1.13 (s, 3H), 1.13 (d, *J* = 6.6 Hz, 3H), 0.93 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.5, 148.3, 134.1, 96.5, 96.3, 71.5, 70.7, 64.3, 55.3, 49.7, 46.3, 25.8(3C), 19.8, 18.0, 12.4, −4.1, −4.7; HRMS(ES) *m*/*z* calcd for $C_{20}H_{38}NaO_6Si$ (M + Na) 425.2335, found 425.2333.

(4*R*,5*R*,6*S*)-4-Hydroxy-2,6-di[(methoxymethoxy)methyl]-5,6-dimethyl-2-cyclohexen-1-one (16). To a solution of compound (−)-**15** (600 mg, 1.49 mmol) in 2 mL of dry THF was added freshly prepared equimolar solution of TBAF (785 mg, 3.0 mmol) and AcOH (0.017 mL, 3.0 mmol) in 1 mL of THF, and the reaction was stirred for 10 h at 25 °C. After the completion of reaction (as indicated by TLC analysis), the solvent was removed under reduced pressure. The crude residue was directly loaded on a silica gel column and eluted with 50% ethyl acetate in hexane to obtain the γ-hydroxy-cyclohexenone (−)-**16** (387 mg, 90%) as a colorless oil: $[\alpha]^{24}_{D}$ −21.0 (*c* 1.0, $CHCl_3$); IR (Neat) 3440, 2927, 2886, 1670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.91 (d, *J* = 1.5 Hz, 1H), 4.68 (s, 2H), 4.52 (bs, 1H), 4.46 (ABq, *J* = 6.6 Hz, 2H), 4.23 (bs, 1H), 3.65 (d, *J* = 9.6 Hz, 1H), 3.49 (d, *J* = 9.6 Hz, 1H), 3.38 (s, 3H), 3.26(s, 3H), 2.04−1.90 (m, 1H), 1.74 (bs, 1H), 1.24 (d, *J* = 7.2 Hz, 3H), 1.14 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.4, 147.4, 134.8, 96.4, 96.3, 71.4, 70.3, 64.1, 55.3, 49.7, 46.7, 19.5, 11.9; HRMS(ES) *m*/*z* calcd for $C_{14}H_{24}NaO_6$ (M + Na) 311.1471, found 311.1472.

Ethyl 2-(1*S*,4*S*,5*S*)-1,5-Di[(methoxymethoxy)methyl]-4,5-dimethyl-6-oxo-2-cyclohexenylacetate (18) and (6*S*)-2,6-Di-[(methoxymethoxy)methyl]-5,6-dimethyl-2,4-cyclohexadien-1-one (17). To a γ-hydroxy-cyclohexenone (−)-**16** (185 mg, 0.64 mmol), placed in a sealed tube, were added freshly distilled triethylorthoacetate (3.0 mL) and catalytic amount of propionic acid (0.05 mL). The sealed tube was flushed with nitrogen and placed in an oil bath kept at 190 °C. Reaction was monitored by TLC. After completion of the reaction (40−45 h, as indicated by TLC analysis), the reaction mixture was diluted with ethyl acetate (30 mL) and washed successively with 5% HCl, water, and brine. The organic phase was dried over Na_2SO_4 prior to the evaporation of solvent, and the crude residue was purified through a silica gel column (eluent: EA/hexane = 1:9 to 1:2) to obtain the dienone (−)-**17** (59 mg, 27%) and the keto-ester (+)-**18** (150 mg, 70%) respectively. Data for **17**: $[\alpha]^{22}_{D}$ −47.5 (*c* 0.8, $CHCl_3$); IR (neat) 2933, 2855, 2823, 1662, 1641, 1592 cm^{-1} ; ^1H NMR (300 MHz, $CDCl_3$) δ 7.05 (d, *J* = 6.3 Hz, 1H), 6.16 (d, *J* = 6.3 Hz, 1H), 4.69 (s, 2H), 4.51 (d, *J* = 6.6 Hz, 1H), 4.47 (d, *J* = 6.6 Hz, 1H), 4.37 (d(1/2ABq), *J* = 13.5 Hz, 1H), 4.26 (d(1/2ABq), *J* = 13.5 Hz, 1H), 4.04 (d, *J* = 9.0 Hz, 1H), 3.67 (d, *J* = 9.0 Hz, 1H), 3.38 (s, 3H), 3.27 (s, 3H), 2.02 (s, 3H), 1.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.4, 153.7, 138.9, 130.1, 119.5, 96.6, 96.2, 72.6, 64.0, 55.3, 54.8, 21.9, 19.2, 19.2; HRMS(ES) *m*/*z* calcd for $C_{14}H_{22}O_5$ (M + Na) 293.1365, found 293.1369. Data for **18**: $[\alpha]^{24}_{D}$ = +25.0° (*c* 0.8, $CHCl_3$); IR (Neat) 2935, 2885, 1735, 1710, 1047 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.80−5.70(m, 2H), 4.55(s, 2H), 4.54(s, 2H), 4.05(dq, *J* = 7.2 and 1.8 Hz, 2H), 3.77(d, *J* = 9.6 Hz, 1H), 3.62(d, *J* = 9.6 Hz, 1H), 3.52(d, *J* = 9.6 Hz, 1H), 3.45(d, *J* = 9.6 Hz, 1H), 3.33(s, 3H), 3.31(s, 3H), 2.99(d(1/2ABq), *J* = 15.6 Hz, 1H), 2.78−2.70(m, 1H), 2.56(d(1/2ABq), *J* = 15.6 Hz, 1H), 1.30(s, 3H), 1.21(t, *J* = 7.5 Hz, 3H), 1.06(d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 212.5, 170.9, 133.8, 127.2, 96.9, 96.6, 72.0, 69.8, 60.4, 55.5, 55.2, 51.4, 50.1, 40.8, 38.3, 19.6, 15.8, 14.1; HRMS(ES) *m*/*z* calcd for $C_{18}H_{30}NaO_7$ (M + Na) 381.1889, found 381.1875.

Dimethyl (3-(1*S*,4*S*,5*S*)-1,5-Di[(methoxymethoxy)methyl]-4,5-dimethyl-6-oxo-2-cyclohexenyl-2-oxopropyl)phosphonate (19). To a cooled (−78 °C) solution of dimethyl methylphosphonate (0.18 mL, 1.68 mmol) in 2 mL of dry THF was added *n*-BuLi (1.0 mL, 1.6M) over a period of 5 min, and the resulting cloudy mixture was stirred at the same temperature for 30 min. To this mixture was added a solution of ester (+)-**18** (100 mg, 0.28 mmol) in 1 mL of dry THF, and the reaction was continued at −78 °C for a further 1 h. The reaction was quenched carefully by addition of water (5 mL), and the aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with water and brine and dried over Na_2SO_4. The solvent was removed under vacuum, and the crude residue was filtered through a short pad of silica gel (eluent: EA/hexane = 1:2 to 1:0) to afford β-keto phosphonate (+)-**19** (115 mg, 95%) as a colorless oil: $[\alpha]^{24}_{D}$ +20.0 (*c* 0.7, $CHCl_3$); IR (Neat) 2933, 2884, 2823, 1712, 1587, 1261 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.69 (bs, 2H), 4.55 (s, 2H), 4.53 (s, 2H), 3.80−3.72 (m, 6H), 3.55−3.34 (m, 4H), 3.33 (s, 3H), 3.32 (s, 3H), 3.12−2.88 (m, 4H), 1.28 (s, 3H), 1.09 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.3, 198.8, 133.7, 126.8, 96.8, 96.6, 72.2, 69.9, 55.5, 55.3, 53.1(d, *J* = 9.0 Hz), 51.6, 50.8, 49.6, 42.4, 40.7, 38.5, 19.0, 15.5; HRMS(ES) *m*/*z* calcd for $C_{19}H_{33}NaO_9P$ (M + Na) 459.1760, found 459.1757.

(4*S*,5*S*,7a*R*)-4,7a-Di[(methoxymethoxy)methyl]-4,5-dimethyl-2-methylene-2,4,5,7a-tetrahydro-1*H*-indene (20). To a solution of phosphonate (+)-**19** (100 mg, 0.22 mmol) in 5 mL of dry THF was added NaH (27 mg, 1.14 mmol) at 25 °C. The reaction mixture was refluxed for 2 h, then cooled to 0 °C, and quenched with water. The organic phase was diluted with ether (20 mL), washed with water (5 mL × 2) and brine, and dried over Na_2SO_4. After the evaporation of solvent the crude material was purified on a silica gel column (eluent: 40% ethyl acetate in hexane) to furnish the bicyclic enone (+)-**20** (65 mg, 92%) as a colorless oil: $[\alpha]^{24}_{D}$ +58.7 (*c* 0.8, $CHCl_3$); IR (Neat) 2931, 2883, 1712, 1695, 1604, 1043 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.09 (s, 1H), 5.79(dd, *J* = 9.9 and 3.0 Hz, 1H), 5.46 (d, *J* = 9.9 Hz, 1H), 4.58 (s, 4H), 3.79 (d, *J* = 9.6 Hz, 1H), 3.66 (d, *J* = 9.6 Hz, 1H), 3.51 (d, *J* = 9.6 Hz, 1H), 3.37 (d, *J* = 9.6 Hz, 1H), 3.36 (s, 3H), 3.34 (s, 3H), 2.78 (d(1/2ABq), *J* = 17.1 Hz, 1H), 2.29−2.26 (m, 1H), 2.22 (d(1/2ABq), *J* = 17.1 Hz, 1H), 1.39 (s, 3H), 1.08 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.1, 185.0, 131.8, 130.8, 128.4, 96.9, 96.6, 73.3, 70.2, 55.7, 55.5, 49.8, 49.3, 42.9, 42.8, 22.0, 15.3; HRMS(ES) *m*/*z* calcd for $C_{17}H_{26}NaO_5$ (M + Na) 333.1678, found 333.1678.

(1*R*,4*S*,5*S*,7a*S*)-4,7a-Di[(methoxymethoxy)methyl]-1,4,5-trimethyl-2-methylene-2,4,5,7a-tetrahydro-1*H*-indene (21). To a cooled (−40 °C) solution of LiHMDS (1 mL, 0.5 M, freshly prepared from equimolar amount of HMDS and *n*-BuLi, at 0 °C) in dry THF was added dropwise a solution of bicyclic enone (+)-**20** (50 mg, 0.16 mmol) in 1 mL of dry THF. The resulting solution was stirred at −20 °C for 1 h and then cooled to −78 °C prior to the sequential addition of HMPA (0.1 mL, 0.56 mmol) and MeI (0.035 mL, 0.56 mmol). The reaction mixture was allowed to warm to 0 °C, stirred for 1 h, and then quenched with water. The aqueous phase was extracted with ether (2 × 15 mL), and the combined organic layers were washed with water (5 mL) and brine and dried over Na_2SO_4. After the evaporation of solvent, the resulting crude material was purified through a silica gel column chromatography (eluent: 40% ethyl acetate in hexane) to obtain the methylated enone (+)-**21** (49.4 mg, 95%) as a colorless oil: $[\alpha]^{23}_{D}$ +55.7 (*c* 0.7, $CHCl_3$); IR (Neat) 2967, 2929, 2883, 1707,

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1604, 1047 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.01 (s, 1H), 5.68(dd, J = 9.9 and 3.0 Hz, 1H), 5.57 (dd, J = 9.9 and 1.8 Hz, 1H), 4.57 (s, 2H), 4.56 (s, 2H), 3.80 (d, J = 9.6 Hz, 1H), 3.66 (d, J = 9.0 Hz, 1H), 3.50 (d, J = 9.6 Hz, 1H), 3.35 (s, 3H), 3.33 (s, 3H), 3.28 (d, J = 9.0 Hz, 1H), 2.67 (q, J = 7.8 Hz, 1H), 2.25−2.23 (m, 1H), 1.38 (s, 3H), 1.08 (d, J = 7.8 Hz, 3H), 0.97 (d, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.0, 183.7, 133.4, 128.4, 126.3, 96.9, 96.6, 74.3, 70.2, 55.6, 55.4, 53.4, 51.5, 42.9, 42.1, 21.8, 15.7, 15.3; HRMS(ES) m/z calcd for $C_{18}H_{28}NaO_5$ (M + Na) 347.1834, found 347.1822

(1*R*,4*S*,5*S*,7a*S*)-4-[(Methoxymethoxy)methyl]-1,4,5-trimethyl-2-methylene-2,4,5,7a-tetrahydro-1*H*-7-indenylmethanol (22). To an ice-cooled solution of methylated enone (+)-**21** (25 mg, 0.077 mmol) in 2 mL of distilled DCM was added CF_3CO_2H (0.1 mL). The resulting solution was stirred at 0 °C for 2 h and then kept in refrigerator for about 6−8 h. The reaction was quenched with triethylamine (0.1 mL) and diluted with DCM (15 mL). The organic phase was washed with water (2 × 5 mL) and brine and dried over Na_2SO_4. After the evaporation of solvent, the resulting oily residue was purified by silica gel column chromatography (eluent: 60% ethyl acetate in hexane) to furnish the alcohol (+)-**22** (17 mg, 80%) as a colorless oil: $[\alpha]^{23}_D$ +65.0 (c 0.7, $CHCl_3$); IR (Neat) 3436, 1705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.09 (s, 1H), 5.62−5.48 (m, 2H), 4.57 (ABq, J = 6.6 Hz, 2H), 3.89 (d, J = 9.3 Hz, 1H), 3.61−3.50 (m, 2H), 3.46 (d, J = 9.3 Hz, 1H), 3.36 (s, 3H), 2.49 (q, J = 7.8 Hz, 1H), 2.29 (q, J = 7.8 Hz, 1H), 2.16 (dd, J = 11.1 and 4.2 Hz, 1H), 1.38 (s, 3H), 1.05 (d, J = 7.5 Hz, 3H), 0.98 (d, J = 7.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.3, 180.4, 133.7, 129.9, 125.8, 97.2, 71.2, 68.1, 55.9, 55.6, 51.8, 42.6, 42.0, 22.3, 14.9; HRMS(ES) m/z calcd for $C_{16}H_{24}NaO_4$ (M + Na) 303.1572, found 303.1570.

(1*R*,4*S*,5*S*,7a*S*)-4-[(Methoxymethoxy)methyl]-1,4,5-trimethyl-2-methylene-2,4,5,7a-tetrahydro-1*H*-7a-indenecarbaldehyde (23). To a stirred solution of bis(trichloromethyl)carbonate (triphosgene) (60 mg, 0.2 mmol) in 2 mL of dry DCM at −45 °C was added dry DMSO (0.087 mL, 1.23 mmol), and the reaction mixture was stirred at the same temperature for 15 min. Then a solution of alcohol (+)-**22** (23 mg, 0.08 mmol) in 1 mL of dry DCM was slowly added at the same temperature. After 15 min of stirring, triethyl amine (0.3 mL) was added dropwise, maintaining the temperature below −40 °C. The resulting suspension was allowed to come to 25 °C over a period of 2 h. The reaction was monitored by TLC. The reaction mixture was diluted with DCM (20 mL), washed with water (2 × 5 mL) and brine, and dried over Na_2SO_4. After the evaporation of solvent the crude material was purified through a silica gel column (eluent: 40% ethyl acetate in hexane) to furnish aldehyde (+)-**23** (20 mg, 90%): $[\alpha]^{23}_D$ +10.0 (c 0.4, $CHCl_3$); IR (Neat) 2969, 2929, 2850, 1709, 1608, 1043 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.97 (s, 1H), 6.23 (s, 1H), 5.77 (m, 2H), 4.43 (d(1/2ABq), J = 6.6 Hz, 1H), 4.35 (d(1/2ABq), J = 6.6 Hz, 1H), 3.47 (d(1/2ABq), J = 9.0 Hz, 1H), 3.40 (d(1/2ABq), J = 9.0 Hz, 1H), 3.30 (s, 3H), 2.57 (q, J = 7.5 Hz, 1H), 2.29 (q, J = 7.5 Hz, 1H), 1.41 (s, 3H), 1.07 (d, J = 7.5 Hz, 3H), 1.06 (d, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.4, 197.1, 181.6, 135.7, 129.3, 122.4, 96.5, 68.5, 63.8, 55.6, 47.6, 43.4, 41.9, 21.0, 14.8, 14.0; HRMS(ES) m/z calcd for $C_{16}H_{22}NaO_4$ (M + Na) 301.1416, found 301.1423.

(1*S*,4*S*,5*S*,7a*S*)-7a-[(*E*)-2-Methoxy-1-ethenyl]-4-[(methoxymethoxy)-methyl]-1,4,5-trimethyl-2,4,5,7a-tetrahydro-1*H*-2-indenone and (1*S*,4*S*,5*S*,7a*S*)-7a-[(*Z*)-2-Methoxy-1-ethenyl]-4-[(methoxymethoxy)methyl]-1,4,5-trimethyl-2,4,5,7a-tetrahydro-1*H*-2-indenone (24a,b). To cooled (−20 °C) solution of predried methoxymethyltriphenyl-phosphonium chloride (72 mg, 0.21 mmol) in 2 mL of dry THF was added *n*-BuLi (0.1 mL, 1.6 M solution in dry hexane). The resulting suspension was stirred at 0 °C for a period of 30 min and then allowed to stand for 10 min. The supernatant blood red ylide (about 1.0 mL) was added to a cooled (−20 °C) solution of the aldehyde **23** (10 mg, 0.036 mmol) in dry THF (1 mL), and the reaction mixture was stirred further for 1 h at the same temperature. The reaction mixture was quenched with water (2 mL) and diluted with ether (10 mL). The organic layer separated, and the aqueous layer was extracted with ether (1 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated *in vaccuo*. The residue obtained was chromatographed over silica gel by eluting first with hexane to remove traces of triphenyl phosphine, followed by elution with 40% ethyl acetate/hexane to obtain methoxy Wittig product **24a,b** (∼1 mg) in about 10% yield: IR (Neat) 2929, 1705, 1651, 1045 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.30 (s, 1H), 6.26 (s, 1H), 6.02−5.92 (m, 4H), 5.71−5.56 (m, 4H), 4.73−4.04 (m, 4H), 3.84−3.68 (m, 4H), 3.58 (s, 3H), 3.44 (s, 3H), 3.35 (s, 3H), 3.32 (s, 3H), 2.65 (q, J = 6.9 Hz, 1H), 2.39 (q, J = 7.5 Hz, 1H), 2.25−2.17 (m, 2H), 1.36 (s, 6H), 1.08−0.98 (m, 12H); HRMS(ES) m/z calcd for $C_{18}H_{26}NaO_4$ (M + Na) 329.1729, found 329.1726

2-(1*S*,4*S*,5*S*,7a*R*)-4-[(Methoxymethoxy)methyl]-1,4,5-trimethyl-2-oxo-2,4,5,7a-tetrahydro-1*H*-7-indenylacetaldehyde (25). To an ice-cooled solution of Wittig product **24a,b** (1 mg, 0.0032 mmol) in 1 mL of distilled DCM was added 10 μL of CF_3CO_2H, and the resulting reaction mixture was stirred at ice-bath temperature for 1 h. Then, the reaction mixture was diluted with satd $NaHCO_3$ (1 mL), and the aqueous phase was extracted with DCM (2 × 5 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated in *vaccuo*. The organic residue was filtered through a short pad of silica gel column (eluent: 50% EA in hexane) to obtain aldehyde **25** (0.5 mg, 60%): IR (Neat) 2927, 1705, 1604, 1014 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.66 (s, 1H), 6.04 (s, 1H), 5.77 (dd, J = 9.9 and 2.4 Hz, 1H), 5.51 (d, J = 9.9 Hz, 1H), 4.58−4.53 (m, 2H), 3.85 (d, J = 9.9 Hz, 1H), 3.52 (d, J = 9.1 Hz, 1H), 3.35 (s, 3H), 2.83 (d, J = 17.1 Hz, 1H), 2.59−2.50 (m, 2H), 2.24−2.20 (m, 1H), 1.41 (s, 3H), 1.07 (d, J = 6.9 Hz, 3H), 1.05 (d, J = 6.3 Hz, 3H); HRMS(ES) m/z calcd for $C_{17}H_{24}NaO_4$ (M + Na) 315.1572, found 315.1570.

(2*S*,6*S*,7*R*)-2-Allyl-6-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxytricyclo-[6.2.1.0^{2,7}]undeca-4,9-dien-3-one (29). To the stirred solution of LiHMDS (41.2 mL, 0.5 M, freshly prepared from equimolar amount of HMDS and *n*-BuLi, at 0 °C) in dry THF at −20 °C, was added dropwise a solution of enone (+)-**10** (2.0 g, 6.9 mmol) in 10 mL of dry THF. The resulting solution was stirred at −20 °C for 1 h and then cooled to −40 °C prior to the sequential addition of HMPA (3.6 mL, 20.7 mmol) and allyl bromide (1.8 mL, 20.7 mmol). The reaction mixture was allowed to warm to −20 °C, stirred for 2 h, and then quenched with water. The aqueous phase was extracted with ether (2 × 150 mL). The combined organic layers were washed with water and brine and dried over Na_2SO_4. After evaporation of solvent, the resulting crude material was purified through a silica gel column chromatography (eluent: 5% ethyl acetate in hexane) to afford the allylated enone (+)-**29** (2.1 g, 93%) as a colorless oil: $[\alpha]^{24}_D$ +113.3 (c 1.5, $CHCl_3$); IR (Neat) 2956, 2931, 2858, 1666, 1253 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.33 (dd, J = 10.5 and 0.9 Hz, 1H), 6.11−6.09 (m, 1H), 5.81−5.56 (m, 3H), 5.12−4.98 (m, 2H), 4.62 (d, J = 9.3 Hz, 1H), 3.13 (s, 1H), 3.06 (dd, J = 12.9 and 5.7 Hz, 1H), 2.92 (s, 1H), 2.64−2.61 (m, 1H), 2.06 (dd, J = 12.9 and 8.7 Hz, 1H), 1.53 (d(1/2ABq), J = 8.7 Hz, 1H), 1.38 (d(1/2ABq), 8.7 Hz, 1H), 0.95 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.1, 151.1, 137.1, 135.1, 135.0, 130.0, 117.1, 66.8, 55.9, 55.7, 48.3, 46.6, 44.8, 25.8, 18.1, −4.9, −5.0; HRMS(ES) m/z calcd for $C_{20}H_{30}NaO_2Si$ (M + Na) 353.1913, found 353.1918.

[(2*R*,3*S*,4*R*,7*S*)-7-Allyl-6-(*tert*-butoxy)-4-methyltricyclo-[6.2.1.0^{2,7}]undeca-5,9-dien-3-yl]oxy(*tert*-butyl)dimethylsilane (30). To a cooled (−78 °C) THF (20 mL) solution of $CuBr.Me_2S$ (154 mg, 0.75 mmol) was added freshly prepared ethereal solution of methylmagnesiumiodide (prepared from 15 mmol of MeI and 15 mmol of magnesium in 15 mL of dry ether) and HMPA (2.35 mL, 13.5 mmol). To this mixture were added sequentially TMSCl (1.7 mL, 13.5 mmol) and allylated enone (+)-**29** (2.0 g, 6.1 mmol, in 10 mL THF) over a period of 30 min, and the resulting suspension was stirred at −60 °C for 3 h. The reaction was quenched with triethylamine (5 mL) and water and diluted with hexane (200 mL). The aqueous layer was extracted with hexane (200 mL), and the combined extracts were washed with water (50 mL) and brine and dried over Na_2SO_4. After the evaporation of solvent, the crude residue was purified through a short pad of silica gel column (eluent: 1% ethyl acetate in hexane) to afford enol-TMS ether (−)-**30** (2.33 g, 92%): $[\alpha]^{23}_D$ −82.0 (c 1.5, $CHCl_3$); IR (Neat) 2929, 1658, 1253, 1076 cm^{-1};

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^{1}H NMR (300 MHz, $CDCl_3$) δ 6.10−6.07(m, 1H), 5.98−5.95 (m, 1H), 5.77−5.63 (m, 1H), 5.06−4.99 (m, 2H), 4.18 (d, J = 1.5 Hz, 1H), 3.33 (dd, J = 9.3 and 7.2 Hz, 1H), 3.03 (s, 1H), 2.81 (dd, J = 12.9 and 5.4 Hz, 1H), 2.53 (s, 1H), 2.10 (dd, J = 6.6 and 3.0 Hz, 1H), 1.88−1.77 (m, 2H), 1.50 (d(1/2ABq), J = 8.7 Hz, 1H), 1.43 (d(1/2ABq), 8.7 Hz, 1H), 0.93 (s, 9H), 0.88 (d, J = 6.9 Hz, 3H), 0.20 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.7, 136.1, 135.2, 134.7, 115.0, 106.2, 75.5, 51.7, 51.4, 49.7, 47.6, 45.2, 42.7, 34.5, 25.6, 19.9, 17.8, 0.0, −4.3, −5.1; HRMS(ES) m/z calcd for $C_{24}H_{42}NaO_2Si_2$ (M + Na) 441.2621, found 441.2621.

(2*S*,4*S*,5*R*,6*S*,7*R*)-2-Allyl-6-[1-(*tert*-butyl)-1,1-dimethylsilyl]-oxy-4,5-dimethyltricyclo[6.2.1.0^{2,7}]undec-9-en-3-one (31). To an ice-cooled solution of enol-TMS ether (−)-**30** (2.33 g, 5.57 mmol) in dry THF (20 mL) were added *n*-BuLi (4.2 mL, 1.6M) and HMPA (1.2 mL, 6.7 mmol) successively, and the resulting solution was stirred for a further 0.5 h at 0 °C. The reaction mixture was cooled to −40 °C prior to the addition of MeI and allowed to warm to 0 °C over a period of 1 h. The reaction was quenched with water and diluted with ether (300 mL), and the organic layer was washed with water (50 mL) and brine and dried over Na_2SO_4. After the evaporation of the solvent, the crude residue was charged on a silica gel column (eluent: 5% ethyl acetate in hexane) to furnish the dimethylated ketone (−)-**31** (1.72 g, 85%) as a colorless oil: $[\alpha]^{24}_D$ −98.0 (c 1.0, $CHCl_3$); IR (Neat) 3074, 2958, 1693, 1639, 1083 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.26−6.24 (m, 1H), 5.98−5.96 (m, 1H), 5.79−5.65 (m, 1H), 5.07−5.01 (m, 2H), 3.92 (dd, J = 11.4 and 6.9 Hz, 1H), 3.11 (s, 1H), 2.93 (s, 1H), 2.67 (dd, J = 13.2 and 7.2 Hz, 1H), 2.40 (dd, J = 7.2 and 3.3 Hz, 1H), 2.26−1.92 (m, 3H), 1.51 (d(1/2ABq), J = 8.7 Hz, 1H), 1.37 (d(1/2ABq), 8.7 Hz, 1H), 0.95 (s, 9H), 0.93 (d, J = 6.0 Hz, 3H), 0.79 (d, J = 7.2 Hz, 3H), 0.11 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.9, 137.9, 135.9, 134.8, 117.4, 71.0, 59.6, 53.5, 51.5, 48.4, 47.8, 46.7, 45.9, 33.3, 25.9, 18.2, 15.1, 12.2, −4.0, −4.8; HRMS(ES) m/z calcd for $C_{22}H_{36}NaO_2Si$ (M + Na) 383.2382, found 383.2381

(2*S*,4*R*,5*R*,6*S*,7*R*)-2-Allyl-6-[1-(*tert*-butyl)-1,1-dimethylsilyl]-oxy-4-(hydroxymethyl)-4,5-dimethyltricyclo[6.2.1.0^{2,7}]undec-9-en-3-one (32). The reaction was performed using (−)-**31** (1.7 g, 4.74 mmol) under exactly the identical experimental conditions as reported earlier for preparation of substrate **13**. The crude residue was purified by silica gel column chromatography (eluent: EA/hexane = 1:20 to 1:8) to afford starting ketone (−)-**31** (0.25 g, 15%) and primary alcohol (−)-**32** (1.39 g, 75%, 90% borsm), respectively: $[\alpha]^{24}_D$ −16.9 (c 1.6, $CHCl_3$); IR (Neat) 3488, 2956, 1685, 1471 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.33−6.30 (m, 1H), 5.96−5.93 (m, 1H), 5.85−5.71 (m, 1H), 5.13−5.05 (m, 2H), 4.03 (dd, J = 11.7 and 6.6 Hz, 1H), 3.52−3.44 (m, 2H), 3.18 (bs, 1H), 2.93−2.86 (m, 2H), 2.46 (dd, J = 6.6 and 3.3 Hz, 1H), 2.16 (dd, J = 13.2 and 7.5 Hz, 1H), 1.88 (dd, J = 7.5 and 4.2 Hz, 1H), 1.82−1.74 (m, 1H), 1.55 (d(1/2ABq), J = 9.0 Hz, 1H), 1.43 (d(1/2ABq), J = 9.0 Hz, 1H), 0.97 (s, 3H), 0.95 (s, 9H), 0.85 (d, J = 6.9 Hz, 3H), 0.12 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 221.8, 138.3, 135.0, 117.8, 71.7, 64.1, 59.3, 55.5, 52.1, 50.9, 49.1, 46.8, 46.0, 39.8, 25.99, 25.96, 19.4, 18.2, 12.4, −3.9, −4.7; HRMS(ES) m/z calcd for $C_{23}H_{38}NaO_3Si$ (M + Na) 413.2488, found 413.2483.

(2*S*,4*R*,5*R*,6*S*,7*R*)-2-Allyl-6-[1-(*tert*-butyl)-1,1-dimethylsilyl]-oxy-4-[(methoxymethoxy)methyl]-4,5-dimethyltricyclo-[6.2.1.0^{2,7}]undec-9-en-3-one (33). Reaction was performed using (−)-**32** (1.39 g, 3.54 mmol) under exactly the identical experimental conditions as reported earlier for preparation of substrate **14**. The crude oily material was purified through a silica gel column (eluent: EA/hexane = 1:9) to yield the methoxymethyl (MOM) derivative (−)-**33** (1.44 g, 93%) as a colorless oil: $[\alpha]^{24}_D$ −70.0 (c 2.2, $CHCl_3$); IR (Neat) 2929, 2856, 1687, 1471 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.28−6.26 (m, 1H), 5.95−5.82 (m, 2H), 5.02−4.97 (m, 2H), 4.47 (ABq, J = 6.6 Hz, 2H), 4.27 (dd, J = 11.7 and 6.6 Hz, 1H), 3.46 (d(1/2ABq), J = 9.0 Hz, 1H), 3.36 (d(1/2ABq), J = 9.0 Hz, 1H), 3.31 (s, 3H), 3.11(s, 1H), 2.88(s, 1H), 2.72 (dd, J = 14.1 and 7.2 Hz, 1H), 2.41 (dd, J = 6.0 and 3.0 Hz, 1H), 2.31 (dd, J = 13.5 and 8.4 Hz, 1H), 1.74−1.64 (m, 1H), 1.54 (d(1/2ABq), J = 9.0 Hz, 1H), 1.37 (d(1/2ABq), 9.0 Hz, 1H), 0.95 (s, 9H), 0.90 (d, J = 6.9 Hz, 3H), 0.87 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 220.3, 138.2, 135.9, 116.4, 96.8, 74.0, 71.7, 58.9, 55.8, 54.1, 51.6, 51.0, 49.0, 45.6, 40.2, 26.1, 20.5, 18.3, 12.6, −3.8, −4.6; HRMS(ES) m/z calcd for $C_{25}H_{42}NaO_4Si$ (M + Na) 457.2741, found 457.2741.

((1*R*,5*S*,6*R*)-3-Allyl-5-[(methoxymethoxy)methyl]-5,6-dimethyl-4-methylene-2-cyclohexenyloxy)(*tert*-butyl)dimethylsilane (28). Reaction was performed using (−)-**33** (1.44 g, 3.29 mmol) under exactly the identical experimental conditions as reported earlier for preparation of substrate **15**. Column chromatographic purification (Mobile phase -2% ethyl acetate in hexane to 15% ethyl acetate in hexane) afforded the cyclohexenone (−)-**28** (1.15 g, 95%) as a colorless oil: $[\alpha]^{27}_D$ = −79.0° (c 2.2, $CHCl_3$); IR (Neat) 3079, 1670, 1641, 1471 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.48 (s, 1H), 5.86−5.73 (m, 1H), 5.09−5.03 (m, 2H), 4.54−4.40 (m, 3H), 3.64 (d(1/2ABq), J = 9.6 Hz, 1H), 3.49 (d(1/2ABq), J = 9.6 Hz, 1H), 3.28 (s, 3H), 2.95 (d, J = 7.2 Hz, 2H), 2.92−2.04 (m, 1H), 1.13 (s, 3H), 1.12 (d, J = 7.8 Hz, 3H), 0.93 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.8, 147.7, 136.0, 135.3, 116.5, 96.5, 71.5, 70.9, 55.3, 49.5, 46.4, 33.6, 25.8, 20.0, 18.0, 12.4, −4.1, −4.7; HRMS(ES) m/z calcd for $C_{20}H_{36}NaO_4Si$ (M + Na) 391.2281, found 391.2278.

2-(3*R*,4*R*,5*S*)-3-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-5-[(methoxymethoxy)-methyl]-4,5-dimethyl-6-methylene-1 Cyclohexenylacetaldehyde (34). To a cooled (0 °C) solution of compound (−)-**28** (200 mg, 0.54 mmol) in 1,4-dioxane/water (3:1, 8 mL) were added 2,6-lutidine (0.1 mL, 0.81 mmol), $NaIO_4$ (347 mg, 1.62 mmol), and OsO_4 (0.054 mmol). The reaction mixture was stirred for a further 1.5−2 h at 0 °C. After the reaction was complete (as indicated by TLC analysis), water (5 mL), and ethyl acetate (30 mL) were added. The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (20 mL × 2). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the resulting oily residue was purified by silica gel column chromatography (eluent: 15% ethyl acetate in hexane) to afford 1,4-keto-aldehyde (−)-**34** (130 mg, 65%): $[\alpha]^{24}_D$ −78.0 (c 1.0, $CHCl_3$); IR (Neat) 2929, 1728, 1670, 1043 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.62 (s, 1H), 6.63 (s, 1H), 4.54−4.45 (m, 3H), 3.66 (d(1/2ABq), J = 9.3 Hz, 1H), 3.49 (d(1/2ABq), J = 9.3 Hz, 1H), 3.34− 3.16 (m, 2H), 3.27 (s, 3H), 2.08−1.98 (m, 1H), 1.14 (s, 3H), 1.13 (d, J = 6.3 Hz, 3H), 0.92 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.7, 198.7, 151.6, 130.5, 96.6, 71.6, 70.6, 55.3, 49.3, 46.4, 44.7, 25.8, 19.9, 18.0, 12.3, −4.2, −4.8; HRMS(ES) m/z calcd for $C_{19}H_{34}NaO_5Si$ (M + Na) 393.2073, found 393.2076.

***tert*-Butyl((1*R*,5*S*,6*R*)-3-(1,3-dioxolan-2-ylmethyl)-5-[(methoxymethoxy)-methyl]-5,6-dimethyl-4-methylene-2-cyclohexenyloxy) Dimethylsilane (35).** To a solution of aldehyde (−)-**34** (250 mg, 0.67 mmol) in 5 mL of dry benzene were added ethylene glycol (0.11 mL, 2.0 mmol) and PPTS (34 mg, 0.13 mmol). The resulting solution was refluxed for 2 h, and water formed during reaction was removed continuously by azeotropic distillation using Dean−Stark apparatus. After the completion of reaction, satd $NaHCO_3$ (10 mL) and ether (20 mL) were added. The organic layer was separated, and aqueous phase was extracted with ether (20 mL × 2). The combined organic layers were washed with water (15 mL) and brine and dried over Na_2SO_4. The solvent was removed *in vaccuo*, and the product was purified using silica gel column chromatography (eluent: 15% ethyl acetate in hexane) to afford the acetal (−)-**35** (245 mg, 88%): $[\alpha]^{26}_D$ −91.0 (c 1.1, $CHCl_3$); IR (Neat) 2884, 1672, 1471, 1043 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.66 (s, 1H), 4.95 (t, J = 4.8 Hz, 1H), 4.50−4.44 (m, 3H), 3.95−3.92 (m, 2H), 3.84−3.79 (m, 2H), 3.62 (d(1/2ABq), J = 9.3 Hz, 1H), 3.52 (d(1/2ABq), J = 9.3 Hz, 1H), 3.28 (s, 3H), 2.58−2.56 (m, 2H), 2.01−1.95 (m, 1H), 1.14 (s, 3H), 1.11 (d, J = 6.9 Hz, 3H), 0.93 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.8, 149.7, 132.3, 102.8, 96.5, 71.4, 70.8, 64.8, 64.7, 55.2, 49.4, 46.2, 34.1, 25.76, 20.0, 18.0, 12.4, −4.2, −4.7; HRMS(ES) m/z calcd for $C_{21}H_{38}NaO_6Si$ (M + Na) 437.2335, found 437.2328.

(2*S*,3*R*,4*R*,6*S*)-4-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-6-(1,3-dioxolan-2-ylmethyl)-2,3-dimethyl-2-pentylcyclohexan-1-one and (2*S*,3*R*,4*R*,6*R*)-4-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-6-(1,3-dioxolan-2-ylmethyl)-2,3-dimethyl-2-pentylcyclohexan-1-one (36a,b). In a 25 mL RB flask, fitted with three-way stopcock, were

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added 20 mg of PtO_2 and 2 mL of ethyl acetate. The reaction setup was flushed with hydrogen, the mixture was stirred for 5 min prior to the addition of solution of acetal (−)-**35** (245 mg, 0.59 mmol) in 2 mL of ethyl acetate, and once again the system was flushed with hydrogen. The reaction was continued at 25 °C for 1 h under the atmospheric pressure of hydrogen and then filtered through a short pad of a silica gel column (eluent: 10% ethyl acetate in hexane) to afford mixture of reduced products **36a,b** (234 mg, 95%). Data for more polar compound): $[\alpha]^{24}_{D}$ +16.7 (*c* 1.2, $CHCl_3$); IR (Neat) 2953, 2931, 1718, 1470, 1042 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.90 (dd, *J* = 6.0 and 3.9 Hz, 1H), 4.54 (ABq, *J* = 6.9 Hz, 2H), 3.98−3.64 (m, 6H), 3.38 (d, *J* = 8.4 Hz, 1H), 3.32 (s, 3H), 3.01−2.91 (m, 1H), 2.33−2.26 (m, 2H), 1.59−1.33 (m, 3H), 1.15 (s, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.88 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.41, 102.99, 96.74, 71.26, 71.19, 64.66, 64.61, 55.47, 51.91, 49.56, 42.19, 40.55, 33.51, 25.79, 19.28, 17.96, 12.81, −3.98, −4.69; HRMS(ES) *m*/*z* calcd for $C_{21}H_{40}NaO_6Si$ (M + Na) 439.2492, found 439.2492. Data for less polar compound): $[\alpha]^{22}_{D}$ −33.3 (*c* 0.3, $CHCl_3$); IR (Neat) 2929, 1702, 1043 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.92 (t, *J* = 4.8 Hz, 1H), 4.58 (s, 2H), 3.96−3.79 (m, 6H), 3.65 (d, *J* = 9.6 Hz, 1H), 3.43 (d, *J* = 9.6 Hz, 1H), 3.34 (s, 3H), 2.29−2.07 (m, 4H), 1.82−1.72 (m, 1H), 1.40 (s, 3H), 0.93 (s, 9H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.09 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.7, 103.1, 96.9, 72.5, 71.5, 64.8, 64.6, 55.4, 51.2, 45.6, 38.4, 36.85, 32.45, 25.8, 23.21, 18.0, 14.8, −4.8 (2C); HRMS(ES) *m*/*z* calcd for $C_{21}H_{40}NaO_6Si$ (M + Na) 439.2492, found 439.2492.

((1*R*,2*R*,3*S*,5*R*)-5-Allyl-5-(1,3-dioxolan-2-ylmethyl)-3-[(methoxymethoxy)-methyl]-2,3-dimethyl-4-methylenecyclohexyloxy)(*tert*-butyl)dimethylsilane (−)-38 and ((1*R*,2*R*,3*S*,5*S*)-5-Allyl-5-(1,3-dioxolan-2-ylmethyl)-3-[(methoxymethoxy)-methyl]-2,3-dimethyl-4-methylenecyclohexyloxy)(*tert*-butyl)-dimethylsilane (−)-37. To a solution of compounds **36a,b** (210 mg, 0.5 mmol) in 6 mL of dry THF were sequentially added NaH (61 mg, 2.5 mmol) and allyl bromide (0.22 mL, 2.5 mmol) at 25 °C. The reaction mixture was refluxed for 2 h and then quenched at 0 °C with water. The aqueous phase was extracted with ether (2 × 25 mL), and the combined organic layers were washed with water (10 mL) and brine and dried over Na_2SO_4. After the evaporation of solvent, the crude material was purified on a silica gel column (eluent: 8% ethyl acetate in hexane) to afford allylated cyclohexenones (−)-**38** (135 mg, 58%) and (−)-**37** (90 mg, 38%) respectively. Data for **38**: $[\alpha]^{22}_{D}$ −25.0 (*c* 1.0, $CHCl_3$); IR (Neat) 3077, 2930, 2857, 1695, 1638 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.74−5.55 (m, 1H), 5.11−5.01 (m, 2H), 4.80 (dd, *J* = 5.1 and 3.9 Hz, 1H), 4.53 (d(1/2ABq), *J* = 6.9 Hz, 1H), 4.47 (d(1/2ABq), *J* = 6.9 Hz, 1H), 4.13 (dt, *J* = 9.9 and 4.2 Hz, 1H), 3.97−3.70 (m, 4H), 3.48 (ABq, *J* = 9.1 Hz, 2H), 3.32 (s, 3H), 2.59 (dd, *J* = 13.5 and 6.6 Hz, 1H), 2.24 (dd, *J* = 13.5 and 5.4 Hz, 1H), 2.07−1.66 (m, 5H), 1.05 (d, *J* = 6.9 Hz, 3H), 1.02 (s, 3H), 0.91 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.91, 134.15, 118.82, 102.27, 96.74, 73.76, 69.10, 64.65, 64.23, 55.58, 51.88, 49.81, 47.08, 43.01, 41.57, 40.58, 25.91, 22.35, 18.08, 12.53, −4.18, −4.72; HRMS(ES) *m*/*z* calcd for $C_{24}H_{44}SiO_6$ (M + Na) 479.2805, found 479.2805. Data for **37**: $[\alpha]^{27}_{D}$ −55.0 (*c* 1.0, $CHCl_3$); IR (Neat) 2954, 2929, 1695, 1471 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.76−5.63 (m, 1H), 5.14−5.08 (m, 2H), 4.80 (t, *J* = 5.1 Hz, 1H), 4.50 (ABq, *J* = 6.6 Hz, 2H), 4.12 (dt, *J* = 9.9 and 3.9 Hz, 1H), 3.82−3.67 (m, 3H), 3.99−3.80 (m, 1H), 3.47 (s, 2H), 3.31 (s, 3H), 2.46 (dd, *J* = 14.1 and 7.8 Hz, 1H), 2.29−2.18 (m, 2H), 2.04−1.81 (m, 3H), 1.69 (dd, *J* = 14.1 and 4.8 Hz, 1H), 1.06 (d, *J* = 6.6 Hz, 3H), 1.06 (s, 3H), 0.91 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.5, 133.8, 118.7, 102.4, 96.7, 74.2, 68.7, 64.8, 64.0, 55.6, 51.9, 49.2, 47.0, 41.9, 40.9, 40.4, 25.9, 22.8, 18.1, 12.3, −4.0, −4.6; HRMS(ES) *m*/*z* calcd for $C_{24}H_{44}NaO_6Si$ (M + Na) 479.2805, found 479.2813.

2-(1*R*,3*S*,4*R*,5*R*)-1-Allyl-5-[1-(*tert*-butyl)-1,1-dimethylsilyl]-oxy-3-[(methoxymethoxy)methyl]-3,4-dimethyl-2-methylene-cyclohexylacetaldehyde (39). To a solution of compound (−)-**38** (150 mg, 0.33 mmol) in 3 mL of acetone was added Amberlyst-15 (50 mg), and the resulting reaction mixture was stirred at 25 °C for 3 h and then filtered through a short pad of Celite. The solvent was removed *in vaccuo*, and the crude oily residue was charged on a silica gel column (eluent: 10% ethyl acetate in hexane) to afford the aldehyde (−)-**39** (88 mg, 65%) as a colorless oil: $[\alpha]^{23}_{D}$ −52.7 (*c* 1.5, $CHCl_3$); IR (Neat) 3077, 2931, 1725, 1694, 1638, 1065 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.58 (s, 1H), 5.74−5.60 (m, 1H), 5.17−5.07 (m, 2H), 4.50 (ABq, *J* = 6.6 Hz, 2H), 4.17 (dt, *J* = 9.9 and 3.9 Hz, 1H), 3.54 (d(1/2ABq), *J* = 9.0 Hz, 1H), 3.40 (d(1/2ABq), *J* = 9.0 Hz, 1H), 3.31 (s, 3H), 3.17 (d, *J* = 18.6 Hz, 1H), 2.47 (d, *J* = 18.6 Hz, 1H), 2.24 (dd, *J* = 14.4 and 6.6 Hz, 1H), 2.07−1.98 (m, 1H), 1.85−1.78 (m, 2H), 1.63 (d, *J* = 3.9 Hz, 1H), 1.18 (s, 3H), 1.08(d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.0, 199.8, 133.2, 119.3, 96.7, 74.3, 68.2, 55.7, 53.3, 52.3, 47.8, 46.6, 41.1, 40.6, 25.92, 25.86, 22.7, 18.0, 12.1, −4.1, −4.6; HRMS(ES) *m*/*z* calcd for $C_{22}H_{40}NaO_5Si$ (M + Na) 435.2543, found 435.2541.

1-(1*R*,3*S*,4*R*,5*R*)-1-Allyl-5-[1-(*tert*-butyl)-1,1-dimethylsilyl]-oxy-3-[(methoxymethoxy)methyl]-3,4-dimethyl-2-methylene-cyclohexylacetone (40). To a cooled (−78 °C) THF (5 mL) solution of aldehyde (−)-**39** (88 mg, 0.21 mmol) was added methyl lithium (0.5 mL, 1.5 M ethereal solution), and the resulting solution was stirred for 30 min at the same temperature. Reaction was quenched with satd NH_4Cl, and the aqueous layer was extracted with ether (2 × 20 mL). The combined extracts were washed with water and brine and dried over Na_2SO_4. After the evaporation of the solvent, the crude residue was purified by passing through a short silica gel column (eluent: 10% ethyl acetate in hexane) to afford the mixture of alcohols. To a solution of the above obtained mixture of alcohols (90 mg) in 3 mL of dry DCM, kept at 0 °C, was added NaOAc (51 mg, 0.63 mmol), PCC (135 mg, 0.63 mmol) and silica gel (135 mg, 100−200 mesh) successively. The resulting orange colored suspension was stirred at 25 °C for 5−6 h and then directly charged on a silica gel column (eluent: 50% ethyl acetate in hexane) to afford the 1,4-diketone (−)-**40** (77 mg, 85% for 2 steps) as a colorless oil: $[\alpha]^{24}_{D}$ −58.3 (*c* 1.2, $CHCl_3$); IR (Neat) 3077, 1717, 1694 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.74−5.60 (m, 1H), 5.15−5.05 (m, 2H), 4.52 (d(1/2ABq), *J* = 6.6 Hz, 1H), 4.47 (d(1/2ABq), *J* = 6.6 Hz, 1H), 4.17 (dt, *J* = 10.5 and 4.5 Hz, 1H), 3.51 (d, *J* = 9.3 Hz, 1H), 3.38 (d, *J* = 9.3 Hz, 1H), 3.31 (s, 3H), 3.21 (d, *J* = 18.6 Hz, 1H), 2.47−2.41 (m, 2H), 2.20−2.07 (m, 1H), 2.06 (s, 3H), 1.85−1.65 (m, 3H), 1.18 (s, 3H), 1.07 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.8, 206.3, 133.7, 118.9, 96.7, 74.5, 68.2, 55.7, 53.3, 52.3, 48.1, 46.3, 40.8, 40.7, 29.8, 25.9, 22.6, 18.0, 12.1, −4.1, −4.6; HRMS(ES) *m*/*z* calcd for $C_{23}H_{42}NaO_5Si$ (M + Na) 449.2699, found 449.2697.

(4*S*,5*R*,6*R*,7a*R*)-7a-Allyl-6-[1-(*tert*-butyl)-1,1-dimethylsilyl]-oxy-4-[(methoxymethoxy)methyl]-4,5-dimethyl-2,4,5,6,7,7a-hexahydro-1*H*-2-indenone (41). To a solution of compound (−)-**40** (75 mg, 0.18 mmol) in 12 mL of dry THF was added NaH (22 mg, 0.9 mmol) at 25 °C. The reaction mixture was refluxed for 2 h and then quenched at 0 °C with water. The aqueous phase was extracted with ether (2 × 15 mL). The combined organic phases were washed with water (5 mL × 2), brine and dried over Na_2SO_4. After the evaporation of solvent, the crude material was purified on a silica gel column (eluent: 30% ethyl acetate in hexane) to furnish the bicyclic enone (+)-**41** (61 mg, 85%) as a colorless oil: $[\alpha]^{24}_{D}$ +48.0 (*c* 1.0, $CHCl_3$); IR (Neat) 3077, 2930, 1698, 1043 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.02 (s, 1H), 5.77−5.63 (m, 1H), 5.13−5.07 (m, 2H), 4.56 (s, 2H), 3.85−3.75 (m, 2H), 3.49 (d(1/2ABq), *J* = 9.6 Hz, 1H), 3.34 (s, 3H), 2.51 (d(1/2ABq), *J* = 18.0 Hz, 1H), 2.42 (d, *J* = 6.9 Hz, 2H), 2.24 (dd, *J* = 13.2 and 4.2 Hz, 1H), 2.10 (d(1/2ABq), *J* = 18.0 Hz, 1H), 1.49−1.37 (m, 2H), 1.35 (s, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.2, 187.5, 133.9, 131.6, 119.2, 97.0, 71.2, 68.9, 55.7, 50.8, 49.2, 47.4, 46.8, 43.9, 42.5, 25.8, 24.6, 17.9, 12.0, −4.0, −4.7; HRMS(ES) *m*/*z* calcd for $C_{23}H_{40}NaO_4Si$ (M + Na) 431.2594, found 431.2596.

(4*S*,5*R*,6*R*,7a*R*)-7a-Allyl-6-hydroxy-4-[(methoxymethoxy)-methyl]-4,5-dimethyl-2,4,5,6,7,7a-hexahydro-1*H*-2-indenone (42). To a solution of compound (+)-**41** (28 mg, 0.07 mmol) in 1 mL of dry THF was added TBAF (37 mg, 0.14 mmol) at 25 °C, and reaction was continued for a further 8 h. Solvent was removed under reduced pressure, and the crude residue was directly loaded on a silica gel column (eluent: 80% ethyl acetate in hexane) to afford the alcohol

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(+)-**42** (19 mg, 93%) as a colorless oil: $[\alpha]^{24}_{D}$ = +95.0° (*c* 0.8, $CHCl_3$); IR (Neat) 3427, 2931, 1689, 1597, 1043 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.03 (s, 1H), 5.75−5.62 (m, 1H), 5.11−5.05 (m, 2H), 4.54 (s, 2H), 3.85 (dt, *J* = 10.8 and 3.9 Hz, 1H), 3.74 (d(1/2ABq), *J* = 9.6 Hz, 1H), 3.50 (d(1/2ABq), *J* = 9.6 Hz, 1H), 3.32 (s, 3H), 2.52 (d(1/2ABq), *J* = 18.0 Hz, 1H), 2.43−2.34 (m, 3H), 2.10 (d(1/2ABq), *J* = 18.0 Hz, 1H), 1.75 (bs, 1H), 1.44−1.38 (m, 2H), 1. 36 (s, 3H), 1.15 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.0, 187.9, 133.7, 131.8, 119.2, 97.0, 71.0, 68.3, 55.7, 50.7, 49.1, 47.3, 46.6, 43.9, 42.4, 24.4, 11.5; HRMS(ES): *m*/*z* calcd for $C_{17}H_{26}NaO_4$ (M + Na) 317.1729, found 317.1737.

(4*S*,5*R*,7a*S*)-7a-Allyl-4-[(methoxymethoxy)methyl]-4,5-dimethyl-2,4,5,6,7,7a-hexahydro-1*H*-2,6-indenedione (43). To a solution of compound (+)-**42** (19 mg, 0.065 mmol) in 2 mL of dry DCM, kept at 0 °C, were sequentially added NaOAc (16 mg, 0.2 mmol), PCC (43 mg, 0.2 mmol), and silica gel (43 mg, 100−200 mesh). The resulting orange colored suspension was stirred at 25 °C for 3 h and then filtered through a short pad of a silica gel column (eluent: 50% ethyl acetate in hexane) to obtain the compound (+)-**43** (17 mg, 90%) as a colorless oil: $[\alpha]^{24}_{D}$ +121.2 (*c* 0.8, $CHCl_3$); IR (Neat) 3077, 2929, 1712, 1698, 1602, 1044 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.20 (s, 1H), 5.71−5. 57 (m, 1H), 5.12−5.06 (m, 2H), 4.50 (s, 2H), 3.53 (d(1/2ABq), *J* = 9.9 Hz, 1H), 3.44 (d(1/2ABq), *J* = 9.9 Hz, 1H), 3.31 (s, 3H), 2.78 (d(1/2ABq), *J* = 12.6 Hz, 1H), 2.65−2.50 (m, 3H), 2.40 (dd, *J* = 15.9 and 5.4 Hz, 1H), 2.30−2.21 (m, 2H), 1.49 (s, 3H), 1.10 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.2, 205.8, 183.6, 132.7, 132.6, 120.2, 96.9, 70.7, 55.8, 52.6, 52.4, 50.2, 49.9, 47.1, 42.8, 24.5, 8.2; HRMS(ES) *m*/*z* calcd for $C_{17}H_{24}NaO_4$ (M + Na) 315.1572, found 315.1581.

(4*S*,5*R*,6*S*,7a*R*)-7a-Allyl-6-hydroxy-4-[(methoxymethoxy)-methyl]-4,5-dimethyl-2,4,5,6,7,7a-hexahydro-1*H*-2-indenone (44). To a cooled (−78 °C) solution of ketone (+)-**43** (17 mg, 0.06 mmol) in 1.5 mL of THF/MeOH (1:1) was added $NaBH_4$ (3.5 mg, 0.09 mmol). The resulting white suspension was stirred for 2 min and then quenched with satd NH_4Cl. The aqueous phase was extracted with ethyl acetate (2 × 15 mL), and the combined extracts were washed with water (5 mL) and brine and dried over Na_2SO_4 prior to the evaporation of solvent. The crude oily residue was filtered through a short pad of silica gel column (eluent: 70% ethyl acetate in hexane) to afford the alcohol (+)-**44** (16 mg, 95%) as a colorless oil: $[\alpha]^{24}_{D}$ +146.7 (*c* 0.6, $CHCl_3$); IR (Neat) 3446, 3074, 1683, 1593, 1044 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.05 (s, 1H), 5.82−5.69 (m, 1H), 5.09−5.04 (m, 2H), 4.56 (s, 2H), 4.32 (d, *J* = 9.6 Hz, 1H), 3.96−3.95 (m, 1H), 3.53 (d, *J* = 9.3 Hz, 1H), 3.33 (s, 3H), 2.73 (d, *J* = 7.5 Hz, 2H), 2.55 (d, *J* = 18.3 Hz, 1H), 2.42−2.36 (m, 1H), 2.10 (bs, 1H), 2.04 (d, *J* = 18.3 Hz, 1H), 1.62−1.56 (m, 2H), 1.36 (s, 3H), 1.16 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.5, 189.2, 134.9, 131.6, 118.5, 96.8, 71.7, 71.2, 55.5, 52.0, 46.5, 45.4, 44.2, 43.8, 43.7, 24.6, 12.6; HRMS(ES) *m*/*z* calcd for $C_{17}H_{26}NaO_4$ (M + Na) 317.1729, found 317.1730.

(1*R*,6*S*,7*R*,8*S*)-6-[(Methoxymethoxy)methyl]-6,7-dimethyl-9-oxatricyclo[6.3.1.0^{1,5}]dodec-4-ene-3,10-dione (47). To a cooled (0 °C) solution of compound (+)-**44** (16 mg, 0.054 mmol) in 1,4-dioxane/water (3:1, 4 mL) were added 2,6-lutidine (0.018 mL, 0.15 mmol), $NaIO_4$ (63 mg, 0.3 mmol), and OsO_4 (0.1 equiv). The resulting suspension was stirred at 0 °C for a further 1.5− 2 h. After the completion of reaction (as indicated by TLC analysis), reaction mixture was filtered through a short pad of silica gel and eluted with ethyl acetate. The organic solvent was removed under vacuum, and the crude material was purified through a silica gel column (eluent: 80% ethyl acetate in hexane) to afford the lactol **45a,b** (13.4 mg, 85%). To a solution of the above lactol **45a,b** (13 mg) in 5 mL of dry benzene was added Ag_2CO_3 on Celite (100 mg). The reaction mixture was refluxed for about 10 h and then filtered through a short pad of silica gel column (eluent: 90% ethyl acetate in hexane) to obtain the bridge lactone (+)-**47** (11 mg, 90%) as a colorless oil: $[\alpha]^{24}_{D}$ +106.7 (*c* 0.3, $CHCl_3$); IR (Neat) 2932, 1731, 1699, 1604, 1045 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.08 (s, 1H), 4.64−4.60 (m, 1H), 4.52 (s, 2H), 3.60 (d, *J* = 9.9 Hz, 1H), 3.37 (d, *J* = 9.9 Hz, 1H), 3.32 (s, 3H), 2.83 (dd, *J* = 18.6 and 2.4 Hz, 1H), 2.72 (d, *J* = 18.6 Hz, 1H), 2.52 (d, *J* = 18.6 Hz, 1H), 2.39 (dd, *J* = 13.8 and 4.2 Hz, 1H), 2.32 (d, *J* = 18.6 Hz, 1H), 1.88−1.78 (m, 2H), 1.34 (s, 3H), 1.25 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.0, 186.5, 169.6, 131.0, 96.4, 78.7, 71.6, 55.7, 50.8, 45.1, 42.3, 42.1, 41.7, 37.9, 25.7, 12.2; HRMS(ES) *m*/*z* calcd for $C_{16}H_{22}NaO_5$ (M + Na) 317.1365, found 317.1364.

1*R*,6*S*,7*R*,8*S*)-6-(Hydroxymethyl)-6,7-dimethyl-9-oxatricyclo-[6.3.1.0^{1,5}]dodec-4-ene-3,10-dione (48). To a cooled (0 °C) solution of compound (+)-**47** (5 mg, 0.02 mmol) in 2 mL of dry DCM was added a solution of triphenylcarbenium-tetrafluoroborate (20 mg, 0.06 mmol) in 1 mL of dry DCM. The resulting dark yellow solution was stirred at ice bath temperature for 1 h and then directly loaded on a silica gel column. Elution with 10% ethyl acetate in hexane removed the reagent derived impurities, further elution with 60% ethyl acetate in hexane afforded the starting material (+)-**47** (1 mg), and further elution with neat ethyl acetate afforded the demethylminwanenone (+)-**48** (2.5 mg, 70%): $[\alpha]^{22}_{D}$ +65.0 (*c* 0.2, $CHCl_3$); IR (Neat) 3421, 2929, 1724, 1695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.09 (s, 1H), 4.65−4.60 (m, 1H), 3.72 (d, *J* = 11.1 Hz, 1H), 3.56 (d, *J* = 12.0 Hz, 1H), 2.88 (dd, *J* = 18.6 and 2.7 Hz, 1H), 2.76 (d, *J* = 19.2 Hz, 1H), 2.52 (d, *J* = 18.6 Hz, 1H), 2.40 (dd, *J* = 15.9 and 5.7 Hz, 1H), 2.33 (d, *J* = 18.6 Hz, 1H), 1.90−1.78 (m, 2H), 1.70 (bs, 1H), 1.37 (s, 3H), 1.24 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6, 185.1, 169.7, 131.8, 79.1, 65.1, 50.5, 45.1, 43.6, 41.9, 41.5, 38.1, 24.6, 12.1; HRMS(ES) *m*/*z* calcd for $C_{14}H_{18}NaO_4$ (M + Na) 273.1103, found 273.1100.

(1*S*,4*S*,5*R*,6*R*,7a*R*)-7a-Allyl-6-[1-(*tert*-butyl)-1,1-dimethylsilyl]-oxy-4-[(methoxymethoxy)methyl]-1,4,5-trimethyl-2,4,5,6,7,7a-hexahydro-1*H*-2-indenone (49). To a cooled (−40 °C) solution of LiHMDS (0.7 mL, 0.5 M, freshly prepared from equimolar amount of HMDS and *n*-BuLi in THF, at 0 °C) was added THF (2 mL) solution of enone (+)-**41** (55 mg, 0.13 mmol) over a period of 5 min. The resulting pale yellow colored solution was stirred at 0 °C for 1 h and then cooled to −40 °C prior to the sequential addition of HMPA (0.05 mL, 0.27 mmol) and MeI (0.02 mL, 0.27 mmol). The reaction mixture was allowed to warm to 0 °C, stirred for 1 h, and then quenched with water. The aqueous phase was extracted with ether (2 × 15 mL). The combined organic layers were washed with water and brine and dried over Na_2SO_4. After the evaporation of solvent, the resulting crude residue was purified by silica gel column chromatography to furnish the methylated enone (+)-**49** (42 mg, 74%) as colorless oil: $[\alpha]^{24}_{D}$ = +42.0° (*c* 1.0, $CHCl_3$); IR (Neat) 3078, 2930, 1705, 1601, 1043 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.99 (s, 1H), 5.80−5.66 (m, 1H), 5.14−5.08 (m, 2H), 4.57 (s, 2H), 3.89 (dt, *J* = 10.8 and 3.6 Hz, 1H), 3.78 (d, *J* = 9.6 Hz, 1H), 3.49 (d, *J* = 9.6 Hz, 1H), 3.34 (s, 3H), 2.58−2.48 (m, 1H), 2.43−2.23(m, 2H), 1.96 (dd, *J* = 12.9 and 3.9 Hz, 1H), 1.39−1.32 (m, 2H), 1.35 (s, 3H), 1.06 (d, *J* = 6.0 Hz, 3H), 1.04 (d, *J* = 7.5 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.9, 186.8, 134.1, 129.7, 119.2, 97.0, 71.5, 69.4, 55.7, 50.7, 49.9, 49.4, 44.0, 43.5, 41.0, 25.8, 24.7, 18.0, 12.6, 12.1, −3.9, −4.6; HRMS(ES) *m*/*z* calcd for $C_{24}H_{42}NaO_4Si$ (M + Na) 445.2750, found 445.2744.

(1*S*,4*S*,5*R*,6*R*,7a*R*)-7a-Allyl-6-hydroxy-4-[(methoxymethoxy)-methyl]-1,4,5-trimethyl-2,4,5,6,7,7a-hexahydro-1*H*-2-indenone (50). To a solution of methylated enone (+)-**49** (40 mg, 0.095 mmol) in 1 mL of dry THF was added TBAF (50 mg, 0.019 mmol) at 25 °C, and the reaction was further continued for 8 h. The solvent was removed under reduced pressure, and the crude residue was directly charged on a silica gel column. Eluting the column with 80% ethyl acetate in hexane furnished the alcohol (+)-**50** (27 mg, 92%): $[\alpha]^{24}_{D}$ +95.0 (*c* 0.2, $CHCl_3$); IR (Neat) 3424, 3076, 2931, 1697, 1043 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.02 (s, 1H), 5.76−5.67 (m, 1H), 5.14−5.07 (m, 2H), 4.56 (s, 2H), 3.93 (dt, J = 10.8 and 3.6 Hz, 1H), 3.76 (d, *J* = 9.6 Hz, 1H), 3.51 (d, *J* = 9.6 Hz, 1H), 3.34 (s, 3H), 2.63−2.34 (m, 3H), 2.11 (dd, *J* = 12.3 and 4.2 Hz, 1H), 1.42−1.32 (m, 2H), 1.40 (s, 3H), 1.16 (d, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 7.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.7, 186.3, 133.8, 130.0, 119.2, 97.0, 71.2, 68.9, 55.7, 50.5, 49.8, 49.3, 44.0, 43.3, 40.9, 24.6, 12.5, 11.5; HRMS(ES) *m*/*z* calcd for $C_{18}H_{28}NaO_4$ (M + Na) 331.1885, found 331.1884.

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(1*S*,4*S*,5*R*,7a*R*)-7a-Allyl-4-[(methoxymethoxy)methyl]-1,4,5-trimethyl-2,4,5,6,7,7a-hexahydro-1*H*-2,6-indenedione (51). To the solution of alcohol (+)-**50** (25 mg, 0.08 mmol) in 2 mL of dry DCM, kept at 0 °C, were added NaOAc (20 mg, 0.24 mmol), PCC (51 mg, 0.24 mmol), and silica gel (51 mg, 100−200 mesh) successively. The resulting orange colored suspension was stirred at 25 °C for 3 h and then filtered through a short pad of silica gel column (eluent: 50% ethyl acetate in hexane) to furnish the compound (+)-**51** (22 mg, 90%) as a colorless oil: $[\alpha]^{23}_{D}$ = +91.4° (*c* 0.7, $CHCl_3$); IR (Neat) 3078, 1706, 1604, 1044 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.18 (s, 1H), 5.74−5.61 (m, 1H), 5.15−5.04 (m, 2H), 4.52 (s, 2H), 3.56 (d, *J* = 9.9 Hz, 1H), 3.44 (d, *J* = 9.6 Hz, 1H), 3.32 (s, 3H), 2.56−2.45 (m, 5H), 2.35 (d, *J* = 7.5 Hz, 1H), 1.50 (s, 3H), 1.10 (d, *J* = 7.2 Hz, 3H), 1.06 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.6, 209.4, 182.9, 132.7, 130.8, 120.3, 96.8, 70.8, 55.8, 52.8, 52.5, 49.8, 47.5, 47.2, 43.4, 24.7, 12.7, 8.2; HRMS(ES) *m*/*z* calcd for $C_{18}H_{26}NaO_4$ (M + Na) 329.1729, found 329.17333.

(1*S*,4*S*,5*R*,6*S*,7a*R*)-7a-Allyl-6-hydroxy-4-[(methoxymethoxy)-methyl]-1,4,5-trimethyl-2,4,5,6,7,7a-hexahydro-1*H*-2-indenone (26a). To a solution of compound (+)-**51** (20 mg, 0.065 mmol) in 1.5 mL of THF/MeOH (1:1) was added $NaBH_4$ (4 mg, 0.1 mmol) at −78 °C. The resulting white colored suspension was stirred for 2 min and then quenched with satd NH_4Cl. The aqueous phase was extracted with ethyl acetate (2 × 15 mL), and the combined organic layers were washed with water and brine and dried over Na_2SO_4 prior to evaporation of solvent. The crude material was filtered through a silica gel column (eluent: 70% ethyl acetate in hexane) to afford the alcohol (+)-**26a** (19 mg, 95%) as a colorless oil: $[\alpha]^{24}_{D}$ +170.9 (*c* 0.55, $CHCl_3$); IR (Neat) 3460, 2925, 1689, 1044 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.02 (s, 1H), 5.84−5.73 (m, 1H), 5.11−5.01 (m, 2H), 4.57 (s, 2H), 4.34 (d, *J* = 9.6 Hz, 1H), 4.02 (s, 1H), 3.54 (d, *J* = 9.6 Hz, 1H), 3.34 (s, 3H), 2.93 (dd, *J* = 13.8 and 8.4 Hz, 1H), 2.61 (dd, *J* = 13.8 and 5.7 Hz, 1H), 2.42 (q, *J* = 7.8 Hz, 1H), 2.12 (dd, *J* = 14.7 and 3.0 Hz, 1H), 2.01 (bs, 1H), 1.59−1.46 (m, 2H), 1.36 (s, 3H), 1.16 (d, *J* = 7.2 Hz, 3H), 1.01 (d, *J* = 7.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.1, 188.6, 135.2, 129.7, 118.5, 96.8, 71.9, 71.4, 55.5, 51.7, 48.9, 45.9, 44.7, 44.0, 38.3, 24.9, 12.5, 12.4; HRMS(ES) *m*/*z* calcd for $C_{18}H_{28}NaO_4$ (M + Na) 331.1885, found 331.1887.

(1*S*,2*S*,6*S*,7*R*,8*S*)-6-[(Methoxymethoxy)methyl]-2,6,7-trimethyl-9-oxatricyclo[6.3.1.0^{1,5}]dodec-4-ene-3,10-dione (53). To an ice-cooled solution of compound (+)-**26a** (19 mg, 0.06 mmol) in 1,4-dioxane/water (3:1, 4 mL) were added 2,6-lutidine (0.018 mL, 0.15 mmol), $NaIO_4$ (63 mg, 0.3 mmol), and OsO_4 (0.006 mmol) successively. The resulting suspension was stirred for a further 1.5−2 h at 0 °C. After the completion of reaction (as indicated by TLC analysis) the reaction mixture was filtered through a short pad of silica gel and eluted with ethyl acetate. The organic solvent was removed under reduced pressure, and the crude material was again purified through a silica gel column (eluent: 80% ethyl acetate in hexane) to afford the lactol **52a,b** (15 mg, 80%). To a solution of the above lactol in 5 mL of dry benzene was added Ag_2CO_3 on Celite (100 mg), and the resulting suspension was refluxed for about 10 h and then filtered through a short pad of silica gel column (eluent: 90% ethyl acetate in hexane) to obtain the lactone (+)-**53** (13 mg, 90%) as a colorless oil: $[\alpha]^{24}_{D}$ +56.7 (*c* 0.3, $CHCl_3$); IR (Neat) 1732, 1704, 1605, 1041 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.07 (s, 1H), 4.65−4.63 (m, 1H), 4.55−4.50 (m, 2H), 3.63 (d, *J* = 10.2 Hz, 1H), 3.40 (d, *J* = 10.2 Hz, 1H), 3.32 (s, 3H), 2.80 (dd, *J* = 19.2 and 2.4 Hz, 1H), 2.68 (d, *J* = 19.2 Hz, 1H), 2.22 (dd, *J* = 13.2 and 3.9 Hz, 1H), 2.15 (q, *J* = 7.5 Hz, 1H), 1.78−1.68 (m, 2H), 1.36 (s, 3H), 1.25 (d, *J* = 7.2 Hz, 3H), 1.13 (d, *J* = 7.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.8, 185.2, 169.9, 129.7, 96.5, 78.7, 71.4, 55.7, 52.1, 45.7, 44.9, 42.5, 41.5, 34.7, 25.6, 12.2, 9.9; HRMS(ES) *m*/*z* calcd for $C_{17}H_{24}NaO_5$ (M + Na) 331.1521, found 331.1523.

(1*S*,2*S*,6*S*,7*R*,8*S*)-6-(Hydroxymethyl)-2,6,7-trimethyl-9-oxatricyclo[6.3.1.0^{1,5}]dodec-4-ene-3,10-dione (5). To an ice-cooled solution of tricyclic lactone (+)-**53** (5 mg, 0.02 mmol) in 2 mL of dry DCM was added dropwise a solution of triphenylcarbenium-tetrafluoroborate (20 mg, 0.06 mmol) in 1 mL of dry DCM. The resulting dark yellow colored solution was stirred at ice bath temperature for 1 h and then directly loaded on a silica gel column. Elution with 10% ethyl acetate in hexane removed the reagent derived impurities, further elution with 60% ethyl acetate in hexane afforded starting material (+)-**53** (1 mg), and elution with neat ethyl acetate afforded the desired (+)-1S-minwanenone **5** (2.4 mg, 56% yield, 70% yield borsm): $[\alpha]^{22}_{D}$ +23.3 (*c* 0.3, EtOH); IR (Neat) 3424, 2930, 1729, 1703, 1603 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 6.04 (s, 1H), 4.68 (m, 1H), 3.63 (d, *J* = 11.5 Hz, 1H), 3.49 (d, *J* = 11.5 Hz, 1H), 2.89 (d, *J* = 19.0 Hz, 1H), 2.81 (dd, *J* = 19.0 and 2.0 Hz, 1H), 2.32 (dd, *J* = 13.5 and 4.0 Hz, 1H), 2.18 (q, *J* = 7.5 Hz, 1H), 1.85 (dq, *J* = 7.5 and 3.0 Hz, 1H), 1.80 (ddd, J = 14.0, 2.0, and 2.0 Hz, 1H), 1.36 (s, 3H), 1.19 (d, *J* = 7.0 Hz, 3H), 1.10 (d, *J* = 8.0 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 211.1, 188.2, 173.5, 130.8, 81.3, 65.4, 53.0, 46.8, 46.2, 45.4, 41.7, 35.1, 24.8, 12.1, 10.0; HRMS(ES) *m*/*z* calcd for $C_{15}H_{20}NaO_4$ (M + Na) 287.1259, found 287.1260.

1-(1*R*,3*S*,4*R*,5*R*)-5-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-1-(1,3-dioxolan-2-ylmethyl)-3-[(methoxymethoxy)methyl]-3,4-dimethyl-2-methylene-cyclohexylacetone (54). To a solution of allylated cyclohexenone (−)-**37** (90 mg, 0.2 mmol) in 2 mL of DMF/water (9:1) were sequentially added $PdCl_2$ (9 mg, 0.05 mmol) and CuCl (40 mg, 0.4 mmol). The resulting dark brown colored suspension was stirred under an atmospheric pressure of oxygen for a further 8 h. After the completion of reaction (as indicated by TLC analysis), water (5 mL) and ethyl acetate (20 mL) were added. The organic layer was separated, and aqueous phase was extracted with ethyl acetate (20 mL × 2). The combined organic layers were washed with water (5 mL × 3) and brine and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent: 20% ethyl acetate in hexane) to afford the 1,4-diketone (−)-**54** (75 mg, 80%). as a colorless oil: $[\alpha]^{23}_{D}$ −56.0 (*c* 1.0, $CHCl_3$); IR (Neat) 2929, 2885, 2857, 1716, 1693, 1063 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.77−4.74 (m, 1H), 4.50 (ABq, *J* = 6.6 Hz, 2H), 4.21−4.13 (m, 1H), 3.97−3.72 (m, 5H), 3.53 (d, *J* = 9.6 Hz, 1H), 3.52 (d, *J* = 18.6 Hz, 1H), 3.35 (d, *J* = 2.7 Hz, 1H), 3.32 (s, 3H), 2.62 (d, *J* = 18.6 Hz, 1H), 2.08(s, 3H), 2.04 (s, 1H), 1.94−1.77 (m, 3H), 1.19 (s, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 218.4, 206.5, 102.2, 96.7, 74.6, 68.3, 64.9, 64.1, 55.6, 53.5, 52.4, 46.6, 46.3, 42.5, 39.4, 29.8, 25.9, 22.6, 18.0, 12.1, −4.2, −4.7; HRMS(ES) *m*/*z* calcd for $C_{24}H_{44}NaO_7Si$ (M + Na) 495.2754, found 495.2752.

(4*S*,5*R*,6*R*,7a*R*)-6-[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy-7a-(1,3-dioxolan-2-ylmethyl)-4-[(methoxymethoxy)methyl]-4,5-dimethyl-2,4,5,6,7,7a-hexahydro-1*H*-2-indenone (55). To a solution of diketone (−)-**54** (75 mg, 0.16 mmol) in dry THF (15 mL) was added NaH (19 mg, 0.8 mmol) at 25 °C. The resulting reaction mixture was refluxed for 2 h and then quenched at 0 °C with water. The aqueous phase was extracted with ether (2 × 15 mL), and the combined organic phases were washed with water (10 mL) and brine and dried over Na_2SO_4. After the evaporation of solvent, the crude material was purified through a silica gel column (eluent: 30% ethyl acetate in hexane) to afford the bicyclic enone (+)-**55** (58 mg, 80%) as a colorless oil: $[\alpha]^{24}_{D}$ +51.0 (*c* 1.0, $CHCl_3$); IR (Neat) 2954, 2858, 2857, 1699, 1601, 1044 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.03 (s, 1H), 4.76 (t, *J* = 4.5 Hz, 1H), 4.58 (d, *J* = 6.6 Hz, 2H), 4.52 (d, *J* = 6.6 Hz, 1H), 3.99−3.69 (m, 6H), 3.49 (d, *J* = 9.9 Hz, 1H), 3.34 (s, 3H), 2.81 (d, *J* = 18.3 Hz, 1H), 2.38 (dd, *J* = 12.9 and 4.2 Hz, 1H), 2.17 (d, *J* = 18.3 Hz, 1H), 2.05 (d, *J* = 4.8 Hz, 2H), 1.49−1.36 (m, 2H), 1.35 (s, 3H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.88 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.2, 187.5, 131.7, 102.8, 96.9, 71.0, 69.0, 65.1, 64.0, 55.7, 51.1, 49.4, 47.5, 45.8, 44.0, 41.3, 25.8, 24.7, 18.0, 12.1, −4.1, −4.7; HRMS(ES) *m*/*z* calcd for $C_{24}H_{42}NaO_6Si$ (M + Na) 477.2648, found 477.2648.

(4*S*,5*R*,6*R*,7a*R*)-7a-(1,3-Dioxolan-2-ylmethyl)-6-hydroxy-4-[(methoxy methoxy)methyl]-4,5-dimethyl-2,4,5,6,7,7a-hexahydro-1*H*-2-indenone (56). To a solution of bicyclic enone (+)-**55** (25 mg, 0.055 mmol) in 1 mL of dry THF was added TBAF (29 mg, 0.11 mmol) at rt, and the reaction was continued for a further 10 h. The solvent was removed under reduced pressure, and the crude residue was directly charged on a silica gel column

(eluent: 80% ethyl acetate in hexane) to obtain the alcohol (+)-**56** (17.7 mg, 93%) as a colorless oil: $[\alpha]^{22}_{D}$ +94.0 (*c* 0.5, $CHCl_3$); IR (Neat) 3440, 2929, 1694, 1598, 1041 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.05 (s, 1H), 4.77 (dd, *J* = 5.4 and 3.3 Hz, 1H), 4.58 (d(1/2ABq), *J* = 6.6 Hz, 1H), 4.52 (d(1/2ABq), *J* = 6.6 Hz, 1H), 3.99−3.70 (m, 5H), 3.51 (d(1/2ABq), *J* = 9.9 Hz, 1H), 3.34 (s, 3H), 2.86 (d(1/2ABq), *J* = 18.3 Hz, 1H), 2.48 (dd, *J* = 12.9 and 3.9 Hz, 1H), 2.19 (d(1/2ABq), *J* = 18.3 Hz, 1H), 2.07−2.05 (m, 2H), 1.68−1.64 (m, 3H), 1.42−1.36 (m, 1H), 1.37 (s, 3H), 1.15 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.1, 187.0, 132.0, 102.6, 96.8, 70.8, 68.4, 65.1, 64.1, 55.7, 51.0, 49.1, 47.2, 45.8, 43.9, 41.2, 24.6, 11.5; HRMS(ES) *m*/*z* calcd for $C_{18}H_{28}NaO_6$ (M + Na) 363.1784, found 363.1783.

(4*S*,5*R*,7a*S*)-7a-(1,3-Dioxolan-2-ylmethyl)-4-[(methoxymethoxy)- methyl]-4,5-dimethyl-2,4,5,6,7,7a-hexahydro-1*H*-2,6-indenedione (57). To the solution of compound (+)-**56** (17 mg, 0.05 mmol) in 3 mL of dry DCM, kept at 0 °C, were added NaOAc (12 mg, 0.15 mmol), PCC (32 mg, 0.15 mmol), and silica gel (32 mg, 100−200 mesh) successively. The resulting orange colored suspension was stirred at 25 °C for 3 h and then passed through a short pad of silica gel column (eluent: 50% ethyl acetate in hexane) to afford compound (+)-**57** (15 mg, 90%) as a colorless oil: $[\alpha]^{27}_{D}$ +120.0 (*c* 0.6, $CHCl_3$); IR (Neat) 2887, 1699, 1603, 1043 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.23 (s, 1H), 4.77 (dd, *J* = 6.4 and 2.2 Hz, 1H), 4.54 (d(1/2ABq), *J* = 6.8 Hz, 1H), 4.49 (d(1/2ABq), *J* = 6.8 Hz, 1H), 3.96−3.68 (m, 4H), 3.48 (s, 2H), 3.33 (s, 3H), 3.08 (d(1/2ABq), *J* = 18.0 Hz, 1H), 2.87 (d(1/2ABq), *J* = 12.8 Hz, 1H), 2.54−2.48 (m, 2H), 2.31 (d(1/2ABq), *J* = 12.8 Hz, 1H), 2.07 (dd, *J* = 14.8 and 2.4 Hz, 1H), 1.91 (dd, *J* = 14.4 and 6.6 Hz, 1H), 1.49 (s, 3H), 1.11 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.9, 206.0, 183.4, 132.9, 101.9, 96.7, 70.4, 64.9, 64.1, 55.8, 53.6, 52.4, 50.6, 48.4, 47.1, 41.5, 24.7, 8.2; HRMS(ES) *m*/*z* calcd for $C_{18}H_{26}NaO_6$ (M + Na) 361.1627, found 361.1616.

(4*S*,5*R*,6*S*,7a*R*)-7a-(1,3-Dioxolan-2-ylmethyl)-6-hydroxy-4-[(methoxymethoxy)methyl]-4,5-dimethyl-2,4,5,6,7,7a-hexahydro-1*H*-2-indenone (58). To a solution of the compound (+)-**57** (15 mg, 0.044 mmol) in 1.5 mL of THF-MeOH (1:1) was added $NaBH_4$ (3 mg, 0.07 mmol) at −78 °C. The resulting white suspension was stirred for 2 min and then quenched with satd NH_4Cl. The aqueous phase was extracted with ethyl acetate (2 × 10 mL), and the combined organic extracts were washed with water (4 mL) and brine and dried over Na_2SO_4 prior to evaporation of solvent. The crude material was filtered through a short silica gel column (eluent: 70% ethyl acetate in hexane) to afford the hydroxy compound (+)-**58** (14 mg, 95%) as a colorless oil: $[\alpha]^{27}_{D}$ +120.0 (*c* 0.6, $CHCl_3$); IR (Neat) 3465, 2885, 1687, 1595 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.06 (s, 1H), 4.90 (d, *J* = 7.2 Hz, 1H), 4.56 (ABq, *J* = 6.6 Hz, 2H), 4.46 (d, *J* = 9.9 Hz, 1H), 4.03−3.77 (m, 5H), 3.50 (d(1/2ABq), *J* = 9.3 Hz, 1H), 3.33 (s, 3H), 3.25 (s, 1H), 2.71−2.59 (m, 3H), 2.18 (d(1/2ABq), *J* = 18.3 Hz, 1H), 1.94 (d, *J* = 14.1 Hz, 1H), 1.54−1.49 (m, 2H), 1.37 (s, 3H), 1.17 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.9, 189.8, 131.5, 103.8, 96.8, 71.5, 71.2, 65.1, 64.2, 55.5, 52.5, 45.5, 44.6, 43.8, 42.8, 42.6, 25.1, 12.4; HRMS(ES) *m*/*z* calcd for $C_{18}H_{28}NaO_6$ (M + Na) 363.1784, found 363.1776.

(1*S*,6*R*,8*S*,13*R*)-1,13-Dimethyl-9,11-dioxatetracyclo-[6.4.1.1^{6,10}.0^{2,6}]tetradec-2-en-4-one (46). In 25 mL RB flask, fitted with reflux condenser, were added compound (+)-**58** (8 mg, 0.023 mmol), PPTS (2.5 mg, 0.01 mmol), and 2 mL of acetone. The resulting reaction mixture was heated at reflux for 8 h and then diluted with ethyl acetate (15 mL). The organic layer was washed with water (5 mL × 2) and brine and dried over Na_2SO_4. After the evaporation of solvent, the resulting crude material was purified by passing through a silica gel column (eluent: 40% ethyl acetate in hexane) to furnish the tetracyclic acetal (+)-**46** (5 mg, 92%) as a white solid: mp 131−131.5 °C; $[\alpha]^{27}_{D}$ +122.5 (*c* 0.6, $CHCl_3$); IR (Neat) 2939, 1701, 1682, 1599 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.83 (s, 1H), 5.34 (d, *J* = 5.1 Hz, 1H), 3.96−3.94 (m, 1H), 3.84 (d(1/2ABq), *J* = 12.3 Hz, 1H), 3.54 (d(1/2ABq), *J* = 12.0 Hz, 1H), 2.29−2.18 (m, 4H), 1.83−1.78 (m, 2H), 1.65−1.62 (m, 1H), 1.34 (d, *J* = 7.2 Hz, 3H), 1.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.2, 191.5, 123.6, 94.8, 72.6, 71.5, 49.6, 46.3, 45.0, 41.5, 40.2, 37.4, 21.0, 12.6; HRMS(ES) *m*/*z* calcd for $C_{14}H_{18}NaO_3$ (M + Na) 257.1154, found 257.1156.

■ ASSOCIATED CONTENT

Supporting Information

Scanned copies of ^1H NMR spectra, ^{13}C NMR spectra of all new compounds and $^1H-^1H$ COSY and $^1H-^1H$ NOESY spectra of compounds (+)-**21**, (+)-**23**, (−)-**37** and (−)-**38**. 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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(19) Facile formation of (+)-**46** can be rationalized either through the protonation of the intermediate lactol **59** and displacement by the distant but stereochemically well poised oxygen of MOM protective group or through the direct attack of the C_7-hydroxyl group on the activated acetal **60** to give intermediate **61**, which on displacement by the distal but stereochemically well poised oxygen of the MOM group results in (+)-**46**. As indicated in Scheme 5, formation of **46** can also be reconciled in terms of an oxocarbenium ion intermediate **46b**.