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Synthesis of Chiral Building Blocks for Oxygenated Terpenoids through a Simultaneous and Stereocontrolled Construction of Contiguous Quaternary Stereocenters by an Ireland−Claisen Rearrangement

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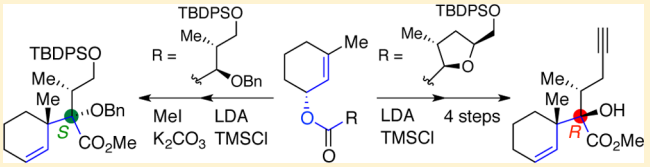
Supporting Information

ABSTRACT: Methods for highly stereocontrolled syntheses of chiral building blocks with a triad of contiguous stereocenters, including two quaternary ones, have been developed. Ireland−Claisen rearrangement of the (*Z*)-silyl ketene acetal generated stereoselectively from the (*R*)-3-methylcyclohex-2-enyl ester derived from an acyclic carboxylic acid proceeded through a chairlike transition state to give the rearranged product with an *S* configuration at the position α to the carboxyl group. Introduction of a cyclic conformational constraint in the acid component completely switched the transition state of the rearrangement to a boatlike one, leading to the predominant formation of a product with an *R* configuration, from which pseudodiastereomeric α-hydroxy esters were obtained in a four-step sequence. The enyne obtained through a base-mediated double eliminative ring-opening reaction was successfully converted into advanced intermediates for the synthesis of 9-oxygenated labdane diterpenoids through a Heck reaction and a regioselective transformation of the resultant diene.



INTRODUCTION

Terpenes with various carbon skeletons undergo oxidation during the biosynthetic process to provide a wide variety of terpenoids. Since the C17 position of triterpenes and the C9 position of diterpenes are prone to oxygenation, C17-oxygenated steroids[1] and C9-oxygenated labdane diterpenoids[2] constitute representative subclasses of this family (Figure 1). Some of these natural products, including the OSWs (**1**) (antitumor),[3] withanone (**2**) (LTB_4 inhibitor),[4] 17,20-dihydroxyvitamin D_2 (**3**) (transcriptional activity stimulator),[5] scillascillosides (**4**) (antitumor),[6] scillasaponins (**5**) (cytotoxic),[7] physagulins (**6**) (trypanocidal),[8] kadcoccilactones (**7**) (cytotoxic),[9] jaborosalactone P (**8**) (antifeedant),[10] marrulibacetal (**9**) (antispasmodic),[11] and isopreleoheterins (**10**) (cytoprotective),[12] have been reported to display remarkable biological activities. An inspection of these structures reveals that motifs **11**α and **11**β, which contain a cyclohexane ring and a triad of contiguous stereocenters, including two quaternary ones, and differ only in the stereochemistry of the oxygen-substituted quaternary stereocenter, are embedded in all of these natural products. In view of the important biological activities and structural complexity of these classes of natural products, compounds including motifs **11**α and **11**β are expected to be valuable building blocks for the synthesis of these natural products and their analogues, whereas all of the reported approaches to these molecules have employed a polycyclic compound having an angular methyl group as the starting material and created an oxygen-substituted quaternary center by either a nucleophilic or an electrophilic addition to an sp^2 carbon in a stereoselective manner.[13]

Because of the ease of substrate preparation, mild reaction conditions, and predictability in the stereochemistry of the products, the Ireland−Claisen rearrangement has been extensively utilized in natural product synthesis.[14] This reaction can be applied for the assembly of contiguous tetrasubstituted carbon atoms,[15] and stereoselective transformations have been realized in some cases.[16] It is well-recognized that the stereoselectivity of the reaction can be controlled by the silyl ketene acetal geometry and the selectivity of the chairlike versus boatlike transition state;[17] however, attempts to synthesize two possible diastereomeric products bearing contiguous quaternary centers in a stereoselective manner have been limited.[18,19] In this article, we describe procedures for the stereodivergent syntheses of chiral building blocks including either motif **11**α or **11**β by an Ireland−Claisen rearrangement.

RESULTS AND DISCUSSION

We envisioned compounds such as **12**α and **12**β as promising building blocks for oxygenated terpenoids with the expectation

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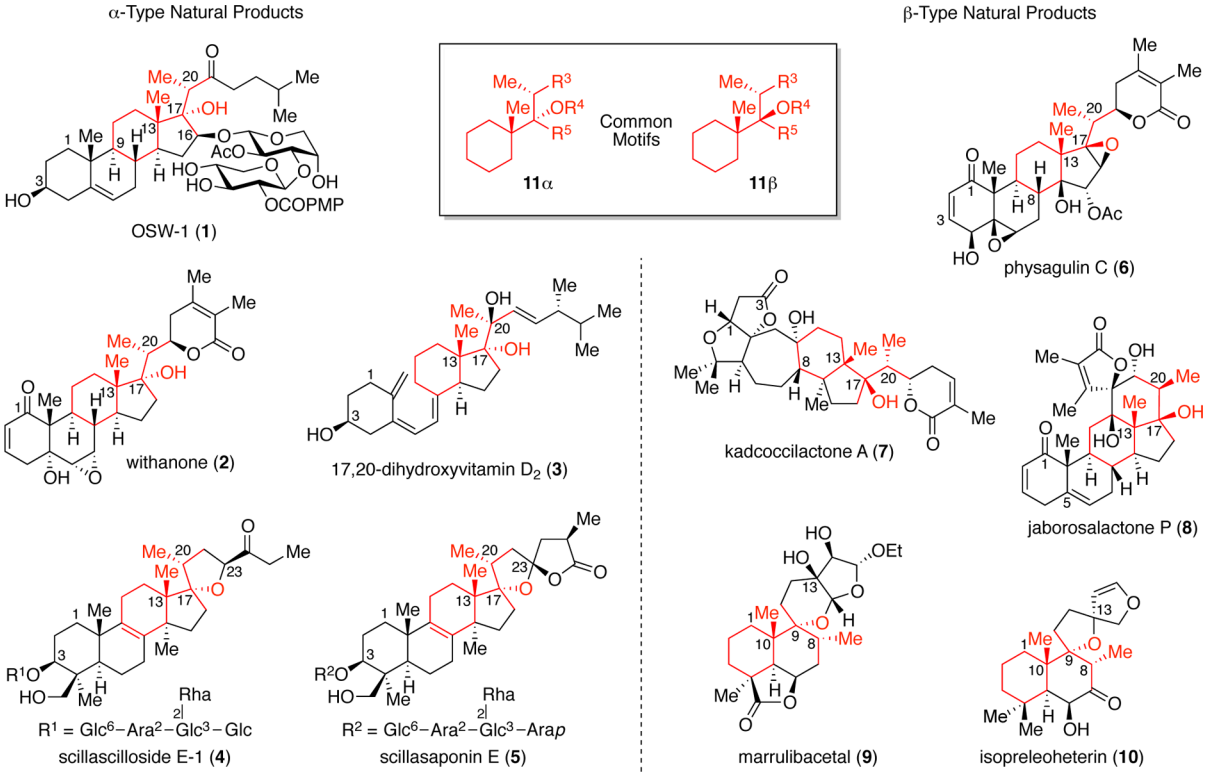
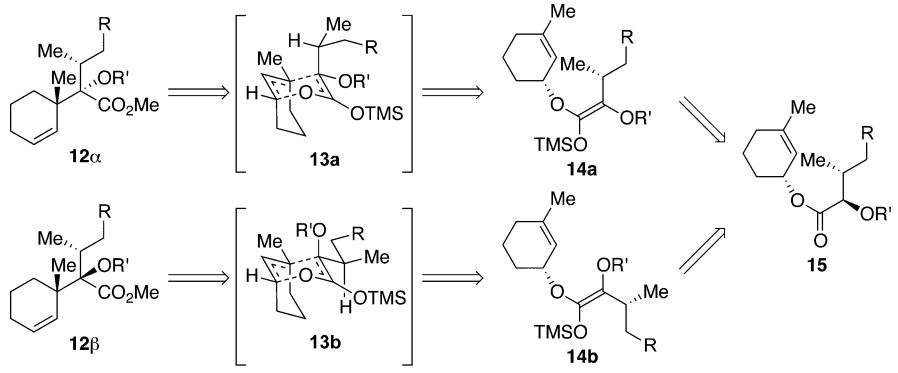


Figure 1. Structures of bioactive C17-oxygenated steroids and C9-oxygenated labdane diterpenoids that contain either **11***α* or **11***β* as a common motif.

Scheme 1. Retrosynthetic Analysis of Building Blocks 12*α* and 12*β*



that an olefin and either an ester or a functional group in the substituent R, which could be varied depending on the target molecule, would serve as handles for the construction of a five- or six-membered ring (Scheme 1). It is known that the Ireland−Claisen rearrangement of silyl ketene acetals derived from glycolates of cyclic alcohols frequently proceeds through a boatlike transition state.[20] In contrast, Zakarian and co-workers have concluded that the rearrangement of *α*,*α*-disubstituted silyl ketene acetals derived from esters of cyclic alcohols shows a preference for a chairlike transition state.[18] Despite the lack of precedent for the reaction of *α*-substituted glycolates of cyclic alcohols, we surmised that compounds **12***α* and **12***β* would be obtained by the rearrangement of *α*,*α*-disubstituted silyl ketene acetals **14a** and **14b** through chairlike transition states **13a** and **13b**, respectively. We also considered that stereoselective formation of silyl ketene acetals **14a** and **14b** from ester **15** could be accomplished by the proper choice of either the protecting group at the hydroxyl group or the reaction conditions.[21]

At the outset of this study, a benzyl group was selected as the protecting group R′ so that (*Z*)-silyl ketene acetal **14a** would be formed predominantly through metal chelate organization. The preparation of substrate **15a** (R = OTBDPS, R′ = Bn) was initiated by regioselective ring opening of known epoxy alcohol **16**[22] (prepared with 95% ee through a Sharpless asymmetric epoxidation[23]) with Me_3Al under Oshima−Nozaki conditions[24] to give 1,2-diol **17** in 86% yield (Scheme 2). The resultant secondary alcohol was selectively protected as its benzyl ether in a two-step sequence involving benzylidene acetal formation with benzaldehyde dimethyl acetal in the presence of a catalytic amount of PPTS (93% yield) and regioselective reductive ring opening with DIBALH (88% yield). The primary alcohol **19** was then converted into carboxylic acid **21** by two successive oxidations (Dess−Martin periodinane;[25] $NaClO_2$[26]), and acid **21** was coupled with chiral alcohol **22**[27,28] in the presence of

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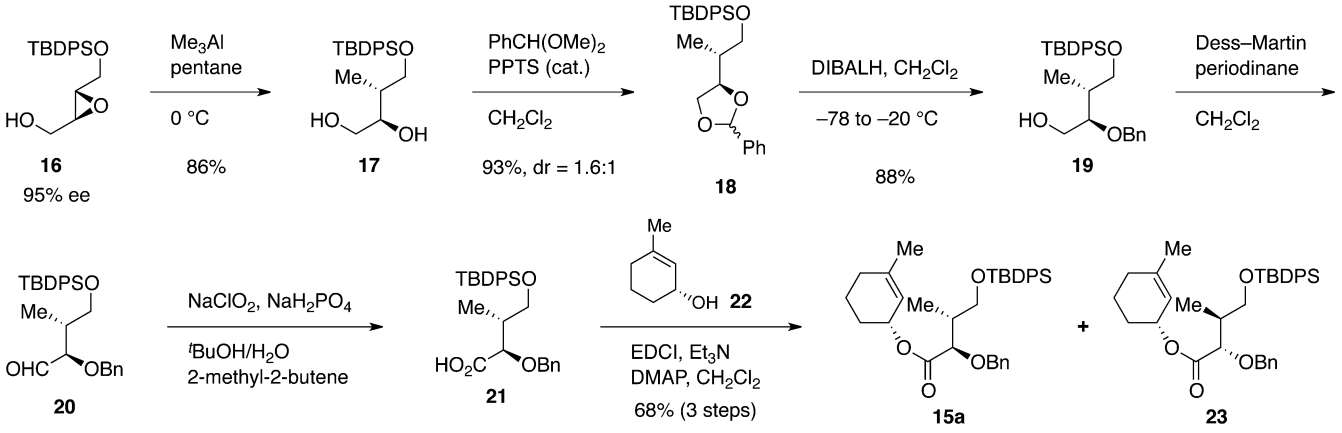
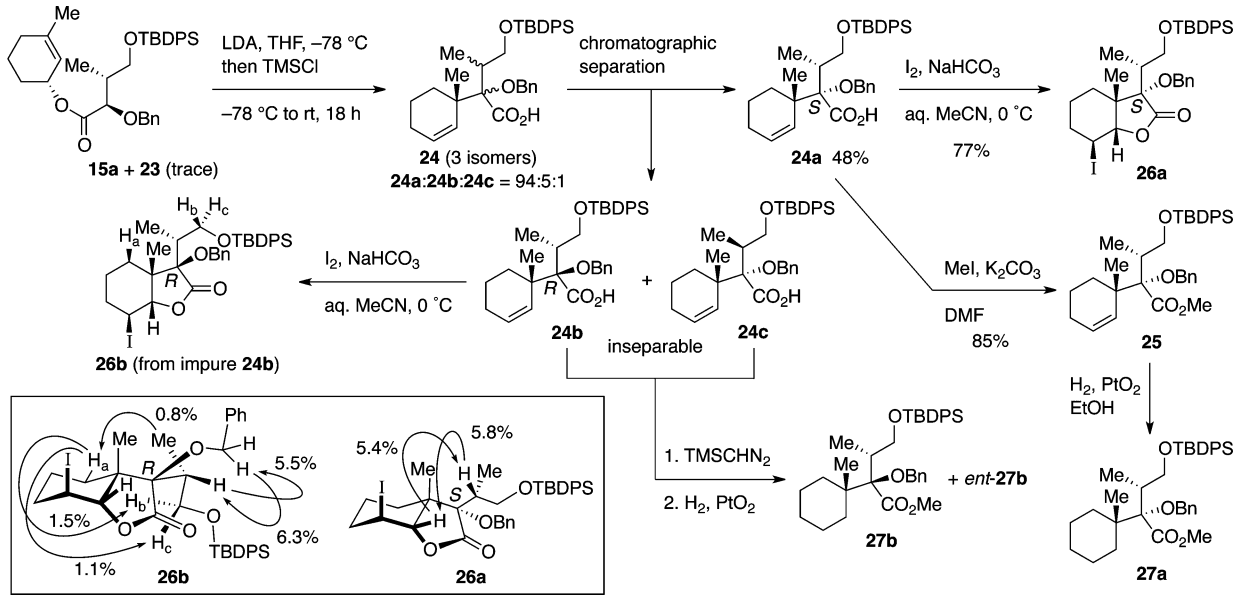
Scheme 2. Preparation of Ester 15a



Scheme 3. Ireland–Claisen Rearrangement of Ester 15a and the Stereochemical Correlation



EDCI, Et_3N, and DMAP in CH_2Cl_2 to yield ester **15a** along with a trace amount of **23** in a combined yield of 68% for the three steps.[29]

With precursor **15a** in hand, we then proceeded to construct the contiguous quaternary stereocenters by an Ireland–Claisen rearrangement (Scheme 3). Treatment of ester **15a**, contaminated with a small amount of isomer **23**, with LDA at −78 °C followed by the addition of TMSCl produced the corresponding silyl ketene acetal, which upon warming to room temperature underwent rearrangement to provide a mixture of three stereoisomers **24** in a 94:5:1 ratio.[30] Esterification of the major isomer **24a**, which could be separated by silica gel column chromatography, with MeI in the presence of K_2CO_3 in DMF gave methyl ester **25** in 41% yield in two steps. The stereochemical assignment of the major isomer **24a** was established by ^{1}H NOE experiments using iodolactone **26a**, obtained from **24a** by the reaction with I_2 and $NaHCO_3$ in aqueous MeCN at 0 °C. On the other hand, the isomers **24b** and **24c** were difficult to separate, but the two isomers were found to possess the opposite configurations at the methyl-bearing and oxygen-substituted stereocenters because of the formation of an enantiomerically enriched racemic mixture upon esterification of the mixture with $TMSCHN_2$ followed by hydrogenation.[31] After considerable experimentation, purification by preparative TLC enabled the isolation of a small amount of slightly impure **24b**, which could be converted to iodolactone **26b** as with **24a**. The equatorial proton H_a adjacent to the quaternary carbon in **26b** exhibited significant ^{1}H NOE interactions with the side-chain protons H_b and H_c, indicating an *R* configuration of the oxygen-substituted stereocenter of **24b**.

In accordance with established precedents,[32] the metal chelate organization in lithium enolate **28** led to the exclusive formation of (*Z*)-silyl ketene acetal **29** from ester **15a** (Scheme 4). Rearrangement of **29** preferentially proceeded through an energetically favorable chairlike transition state to give isomer **24a** as the major product, whereas the formation of the minor isomer **24b** can be attributed to the reaction via a thermodynamically less favored boatlike transition state.

Since structural motif **11***α* is involved in the molecule, carboxylic acid **24a** and methyl ester **25** can be employed as building blocks for the synthesis of *α*-type natural products illustrated in Figure 1 through construction of a five-membered ring.[33] Since the 1-oxaspiro[4.4]nonane ring system is a fragment of some *α*-type C17-oxygenated triterpenoids (e.g., **4** and **5** in Figure 1), our attention was next focused on the

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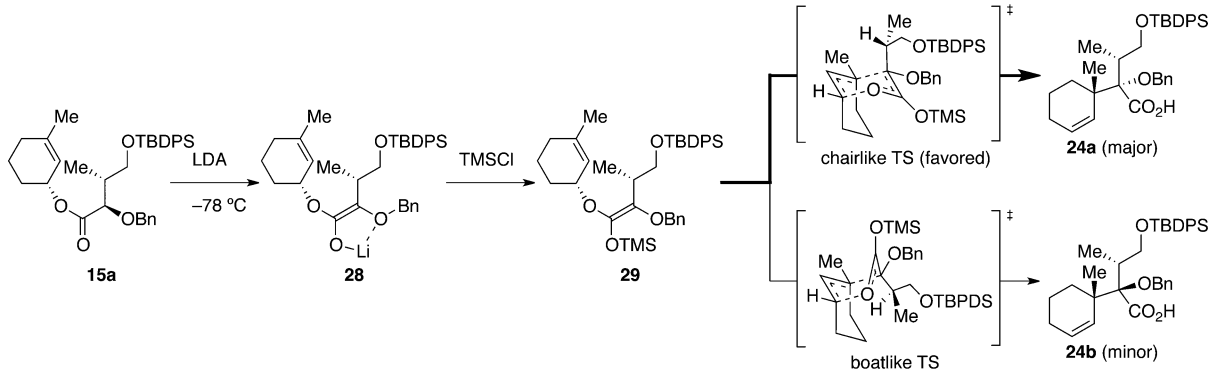
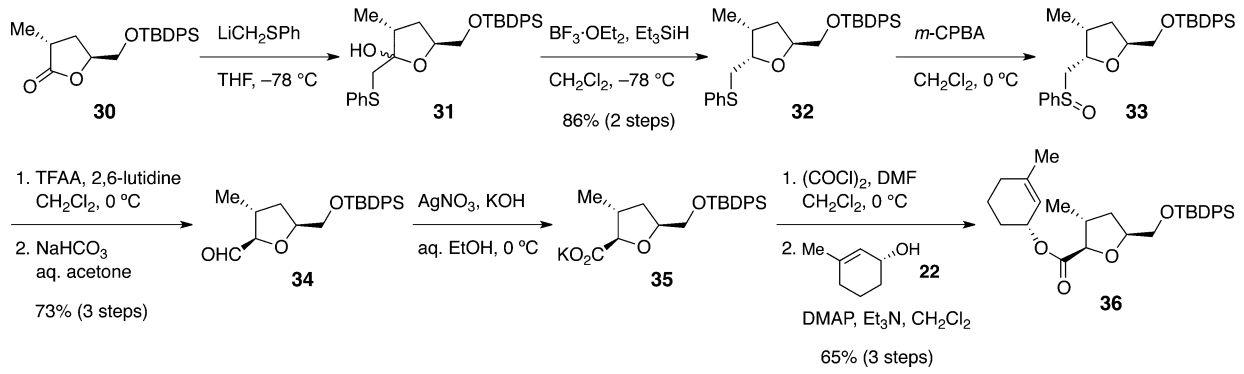
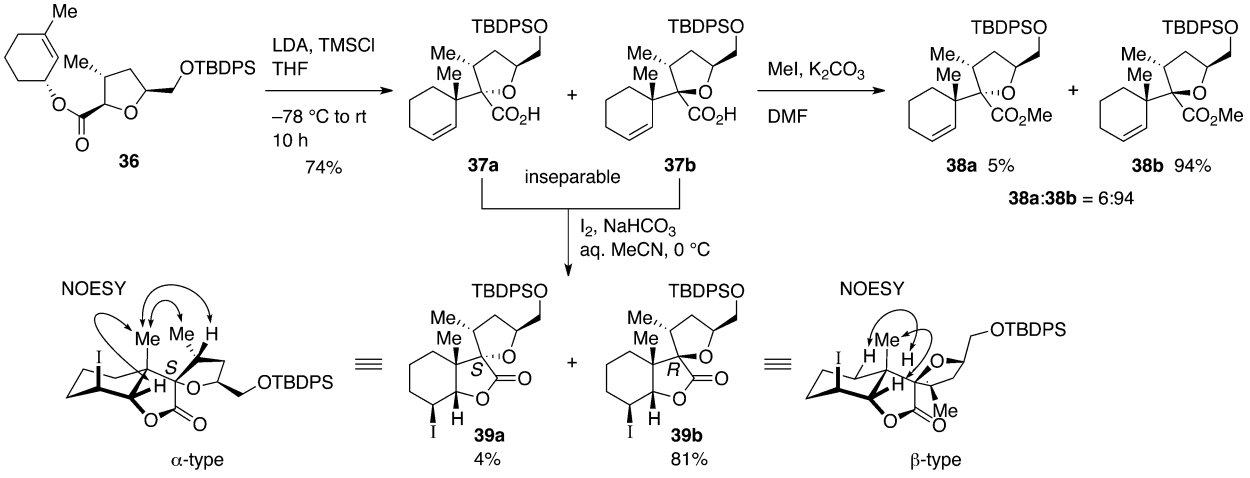
Scheme 4. Plausible Reaction Pathways for the Rearrangement of Ester 15a



Scheme 5. Preparation of Tetrahydrofuran-2-carboxylate 36



Scheme 6. Ireland–Claisen Rearrangement of Tetrahydrofuran-2-carboxylate 36 and the Stereochemical Correlation



Ireland–Claisen rearrangement of tetrahydrofuran-2-carboxylate **36**. The preparation of substrate **36** commenced with the L-glutamic acid-derived lactone **30**[34] and proceeded along the path delineated in Scheme 5. Lithiation of thioanisole under Corey–Seebach conditions[35] followed by addition of lactone **30** furnished hemiacetal **31**, which was subjected to $BF_3{\cdot}OEt_2$-promoted reduction with Et_3SiH[36] to afford 2,5-*trans*-tetrahydrofuran **32** as a single diastereomer in 86% yield in two steps. After oxidation of the sulfide in tetrahydrofuran **32** using *m*-CPBA, treatment of the resultant sulfoxide **33** with TFAA effected a Pummerer rearrangement,[37] providing aldehyde **34** in 73% yield for the three-step sequence after hydrolysis of the corresponding trifluoroacetate intermediate with aqueous $NaHCO_3$ and concomitant epimerization. With regard to the conversion of aldehyde **34** to ester **36**, a two-step sequence involving oxidation to the corresponding carboxylic acid and subsequent esterification with alcohol **22** using a dehydrating agent such as DCC led to irreproducible results, probably because of self-decomposition of the carboxylic acid. Considerable experimentation showed that this problem could be avoided by employing a Tollens oxidation[38] and isolation of the product as the potassium salt **35**, which upon treatment with oxalyl chloride in the presence of a catalytic amount of DMF and subsequent condensation with alcohol **22** reproducibly afforded ester **36** in 65% yield for the three-step sequence on a 23 g scale.

Under the foregoing conditions, the Ireland–Claisen rearrangement of tetrahydrofuran-2-carboxylate **36** furnished

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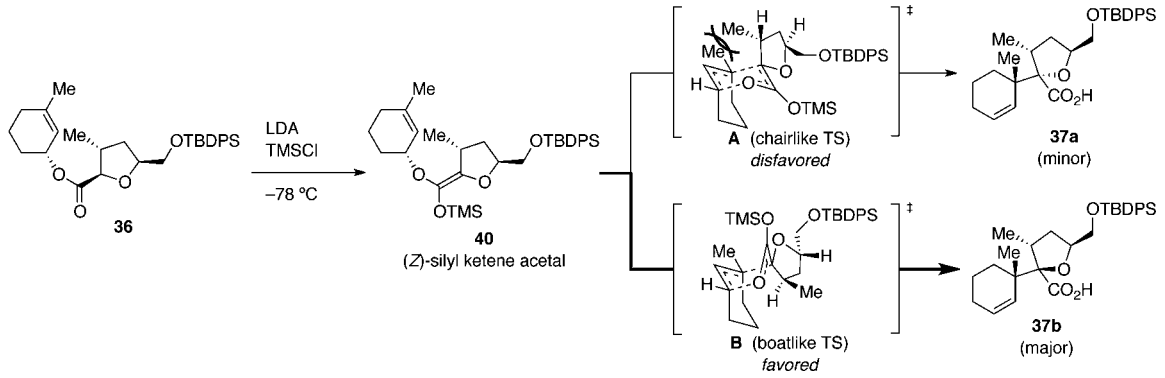
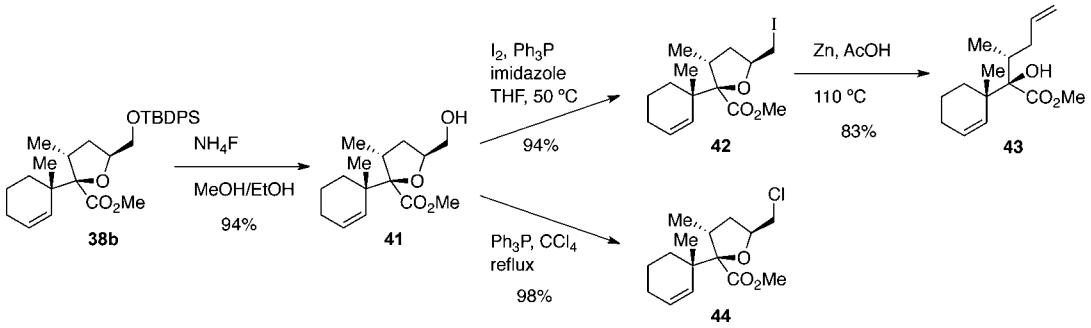
Scheme 7. Plausible Reaction Pathways for the Rearrangement of Tetrahydrofuran-2-carboxylate 36



Scheme 8. Ring Opening of Tetrahydrofuran 38b



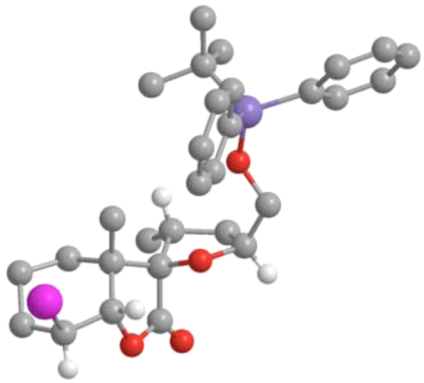


Figure 2. X-ray crystal structure of iodolactone **39b**, rendered in Chem3D. For the purpose of clarity, only protons attached to stereocenters are shown.

an inseparable mixture of rearranged products **37a** and **37b** in 74% yield (Scheme 6). *O*-Alkylation of the mixture with MeI under basic conditions provided a 94:6 mixture of esters,[39] from which esters **38a** and **38b** were isolated in yields of 5% and 94%, respectively, after chromatographic separation. To determine the relative stereochemical relationship between the quaternary stereocenters, the mixture of carboxylic acids **37a** and **37b** was subjected to iodolactonization to give isomers **39a** and **39b** in yields of 4% and 81%, respectively. Surprisingly, a NOESY experiment performed on the major isomer **39b** revealed a diagnostic cross-peak supporting the stereochemical assignment of the *R* configuration at the position α to the carbonyl group, whereas the expected interaction between methyl protons was observed in minor isomer **39a**. Finally, the stereochemistry of the crystalline isomer **39b** was unambiguously established by X-ray crystallography, as shown in Figure 2.

Since (*Z*)-silyl ketene acetal **40** would be exclusively formed from ester **36** via the corresponding chelated enolate,[40,41] the stereochemical outcome of the rearrangement indicates that the reaction of the *Z* isomer **40** did not proceed through chairlike transition state **A**, which suffers from severe steric interaction resulting from the methyl group on the tetrahydrofuran ring (Scheme 7). No such nonbonded destabilization could be observed in boatlike transition state **B**, thus leading to the predominant formation of isomer **37b**. This result suggests that the contiguous quaternary stereocenters should be created prior to construction of the tetrahydrofuran ring in order to apply this method for the synthesis of α-type C17-oxygenated triterpenoids like **4** and **5**.

While the rearrangement of ester **36** provided an unexpected result, we considered that the product **37b** having an *R* configuration at the α position of the carboxyl group is a potential intermediate for the synthesis of β-type natural products. We therefore turned our attention to the ring opening of methyl ester **38b**. In this regard, it is known that both hydroxyalkenes[42] and hydroxyalkynes[43] can be obtained from tetrahydrofuran-2-methanol derivatives by proper choice of the reaction conditions. As a prelude, the TBDPS group was removed with NH_4F[44] to give primary alcohol **41** in 94% yield (Scheme 8). After iodination of primary alcohol **41** with I_2 in the presence of Ph_3P and imidazole in THF at 50 °C, treatment of the resultant iodide **42** with activated zinc in AcOH at 110 °C effected fragmentation to provide alkene **43** in 78% yield in two steps. On the other hand, primary alcohol **41** was converted to chloride **44** by the reaction with PPh_3 in refluxing CCl_4 in preparation for the base-induced double eliminative ring-opening reaction. While LDA proved to be an ineffective base in the reaction of **44**, the desired product **45** could be

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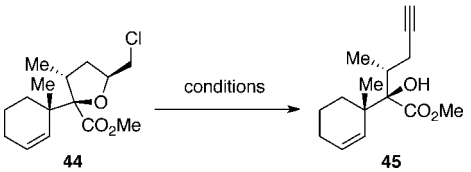
Table 1. Base-Induced Double Eliminative Ring Opening[a]



44 45

entry	base	solvent	temp (°C)	time (h)	yield (%)
1	LDA	THF	−20	1	0
2	LDA	20:1 THF/HMPA	−20	1	15
3	LTMP	20:1 THF/HMPA	−20	1	42
4	BuLi	20:1 THF/HMPA	−78	1	52
5	$NaNH_2$	2:1 NH_3/THF	−40	2	96

[a]The reaction was carried out on a 0.1 mmol scale.

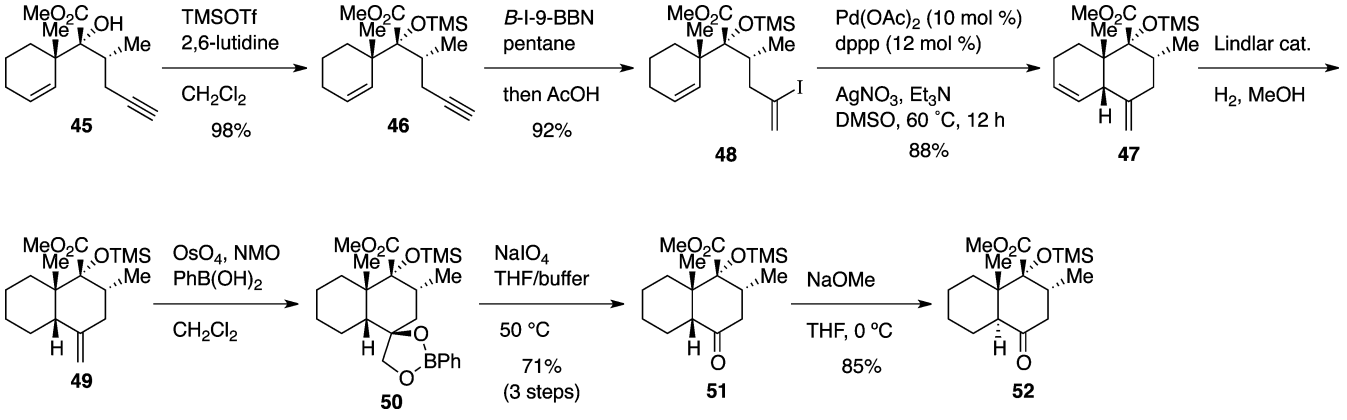
obtained by the use of HMPA as a cosolvent, albeit in low yield (Table 1, entries 1 and 2). Of the lithium amides surveyed, LTMP gave the best result, but the reaction suffered from reproducibility issues and the formation of many byproducts (entry 3). Because of the steric bulk in the vicinity of the carbonyl group, the ester functionality was unaffected upon treatment with 5 equiv of BuLi at −78 °C, and α-hydroxy ester **45** was obtained in 52% yield (entry 4). Finally, we were gratified to find that the use of $NaNH_2$ as the base in liquid NH_3 afforded a significantly improved yield (96%; entry 5).

As stated earlier, motif **11**β can be found in many labdane-type natural products such as marrulibacetal (**9**) and isopreleoheterins (**10**). To demonstrate the potential utility of ring-opening product **45** as a building block, we then addressed the construction of the decaline skeleton from **45** (Scheme 9). While protection of tertiary alcohol **45** as its TMS ether served to set the stage for a cyclization reaction, the attempted $Pd_2(dba)_3$-catalyzed cycloisomerization of enyne **46** according to the procedure of Trost[45] afforded only a trace of the desired diene **47** and led to the formation of a dimerization product. Therefore, enyne **46** was converted to vinyl iodide **48** by iodoboration under Hara–Suzuki conditions[46] in preparation for an intramolecular Heck reaction.[47] With regard to the cyclization reaction, the use of $AgNO_3$ as an additive was found to be effective in providing *cis*-decaline **47** in good yield. At this stage, we were faced with the task of olefin differentiation. After some experimentation, we found that the 1,2-disubstituted (*Z*)-olefin present in the six-membered ring is slightly more reactive and prone to hydrogenation with the aid of Lindlar catalyst than the exocyclic 1,1-disubstituted olefin. Oxidative cleavage of the remaining olefin could be achieved by employing the two-step protocol reported by Narasaka and co-workers[48] (OsO_4-catalyzed dihydroxylation with NMO in the presence of $PhB(OH)_2$ and exposure of the resultant boronate **50** to $NaIO_4$), providing ketone **51** in 71% yield in three steps. Finally, epimerization of *cis*-1-decalone **51** upon brief exposure to NaOMe in THF completed the synthesis of *trans*-1-decalone derivative **52**.[49]

We next considered that the double bond in the ring system could be used for further functionalization if selective cleavage of the exocyclic olefin in diene **47** could be realized. Fortunately, further experimentation with diene **47** led to the discovery that the exocyclic olefin was stereoselectively oxidized, with the internal olefin remaining intact, upon exposure to *m*-CPBA in CH_2Cl_2 at 0 °C to give epoxide **53** in 87% yield (Scheme 10). However, all attempts to convert epoxide **53** to the corresponding diol met with failure due to the propensity of epoxide **53** to undergo desilylative transannular cyclization under either acidic or basic conditions to give alcohol **54**.

Given the lability of the tertiary TMS ether under a variety of reaction conditions tested, a decision was made to switch the protecting group to a Boc group with the expectation that the carbonate group could participate in a transannular cyclization. Deprotection of TMS ether **47** with Bu_4NF in THF was followed by protection with $(Boc)_2O$ under basic conditions, producing diene **56** in 95% yield in two steps. Although epoxidation of Boc-protected diene **56** proved less selective (5.4:1 selectivity) even at −20 °C, at which temperature the reaction did not go to completion, the desired epoxide **57** was obtained in 58% yield (66% based on recovered starting material) after one recycle of recovered starting material. As expected, epoxide **57** underwent transannular cyclization when treated with $BF_3{\cdot}OEt_2$ in CH_2Cl_2 at −60 °C[51] to provide cyclic carbonate **59** in 74% yield; upon exposure to NaOMe in MeOH, **59** furnished triol **60** in 93% yield. The superfluous one-carbon unit was successfully removed by oxidative cleavage with $Pb(OAc)_4$ in CH_2Cl_2 at 0 °C. While the ^1H and ^{13}C spectra clearly revealed that product **61** existed exclusively in the hydroxy ketone form, the carbonyl group and tertiary alcohol in **61** could be masked as a lactol TBS ether by the reaction with TBSOTf in the presence of Et_3N in CH_2Cl_2, producing **62** in 94% yield.

Scheme 9. Conversion of Alkyne 45 to *trans*-Decalone 52



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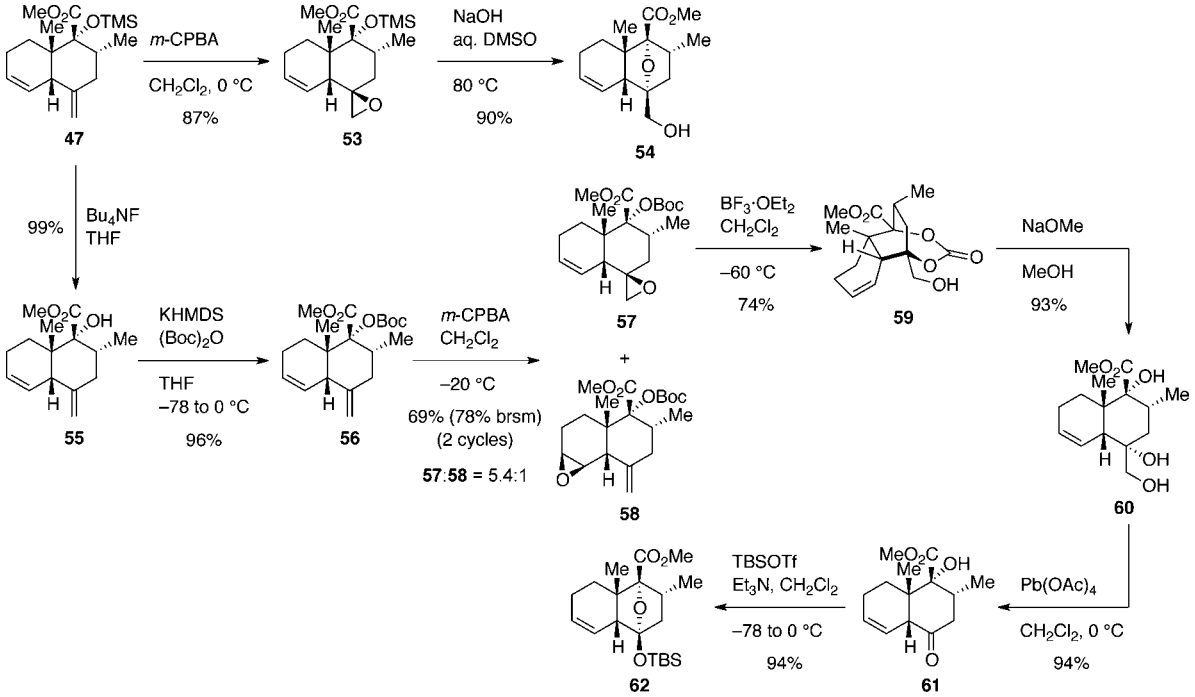
Scheme 10. Conversion of Diene 47 to Tricyclic Compound 62



CONCLUSION

We have developed stereocontrolled methods to access chiral building blocks with a triad of contiguous stereocenters, including two quaternary ones, through an Ireland−Claisen rearrangement. While the use of 2-(benzyloxy)butyrate as a substrate gave the rearranged product resulting from a chairlike transition state in accord with the precedent provided by Zakarian,[18] the introduction of a cyclic conformational constraint in the acid component switched the transition state to a boatlike one because of severe steric repulsion resulting from a methyl group on the ring in the chairlike transition state, leading to the predominant formation of a product with the opposite stereochemistry at the position α to the carboxyl group. Subsequent conversion of the product through a sequence involving base-induced double eliminative ring opening, intramolecular Heck reaction, and olefin differentiation provided bicyclo[4.4.0]decane derivatives having potential for the syntheses of labdane diterpenes. This is the first report of an Ireland−Claisen rearrangement using an α-substituted glycolate derived from a cyclic alcohol wherein both the enolate geometry and the conformation of the transition state have been successfully controlled. Further studies toward the total syntheses of such bioactive natural products are currently underway in our laboratory and will be reported in due course.

EXPERIMENTAL SECTION

(2*R*,3*R*)-4-(*tert*-Butyldiphenylsilyl)oxy-3-methylbutane-1,2-diol (17). Trimethylaluminum in *n*-heptane (2.0 M, 8.15 mL, 16.3 mmol) was added to a solution of epoxy alcohol **16**[22] (1.87 g, 5.44 mmol) in *n*-pentane (60 mL) at 0 °C. After 3 h of stirring, the reaction was quenched with MeOH (2 mL), and 10% aqueous potassium sodium tartrate (100 mL) was added to the solution. The mixture was vigorously stirred at room temperature for 29 h and extracted with AcOEt (3 × 300 mL). The combined organic extracts were washed with brine (100 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (2.19 g), which was purified by flash column chromatography (silica gel 100 g, 10:1 CH_2Cl_2/Et_2O) to give diol **17** (1.67 g, 86%) as a colorless oil. R_f 0.40 (1:1 *n*-hexane/AcOEt); $[\alpha]_D^{17}$ −11.0 (*c* 1.06, $CHCl_3$); IR (neat) 3401, 2960, 2931, 2859, 1472, 1427, 1123, 1113 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.80 (d, *J* = 7.0 Hz, 3H), 1.06 (s, 9H), 1.94 (m, 1H), 2.33 (t, *J* = 5.9 Hz, 1H), 3.60 (m, 1H), 3.66 (dd, *J* = 8.4, 10.3 Hz, 1H), 3.68−3.74 (m, 2H), 3.74 (dd, *J* = 4.0, 10.3 Hz, 1H), 4.00 (d, *J* = 2.5 Hz, 1H), 7.40−7.47 (m, 6H), 7.66−7.69 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 13.1 (CH_3), 19.0 (C), 26.8 (CH_3), 37.0 (CH), 64.9 (CH_2), 68.8 (CH_2), 76.5 (CH), 127.8 (CH), 127.9 (CH), 129.9 (CH), 130.0 (CH), 132.5 (C), 132.6 (C), 135.52 (CH), 135.54 (CH); HRMS (FAB) *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{31}O_3Si$ 359.3043; found 359.3047.

[4*R*,4(1*R*)]-4-[[2-(*tert*-Butyldiphenylsilyl)oxy-1-methyl]ethyl]-2-phenyl-1,3-dioxolane (18). Pyridinium *p*-toluenesulfonate (116 mg, 0.461 mmol) was added to a mixture of diol **17** (1.66 g, 4.63 mmol) and benzaldehyde dimethyl acetal (1.55 mL, 10.4 mmol) in CH_2Cl_2 (46 mL), and the mixture was stirred for 48 h. Triethylamine (1.0 mL) was added to the mixture, and the solvent was removed in vacuo. The residual pale-yellow oil (2.95 g) was purified by flash column chromatography (silica gel 120 g, 30:1 *n*-hexane/AcOEt) to give benzylidene acetal **18** (1.92 g, 93%, dr = 1.6:1) as a colorless oil. R_f 0.42 (10:1 *n*-hexane/AcOEt); $[\alpha]_D^{17}$ −3.6 (*c* 0.95, $CHCl_3$); IR (neat) 2961, 2932, 2859, 1427, 1113 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.01 (d, *J* = 6.9 Hz, 1.2H), 1.03 (d, *J* = 6.9 Hz, 1.8H), 1.06 (s, 3.5H), 1.07 (s, 5.5H), 1.97 (m, 0.38H), 2.03 (m, 0.62H), 3.73 (dd, *J* = 4.3, 10.0 Hz, 0.62H), 3.76 (dd, *J* = 3.8, 9.9 Hz, 0.38H), 3.75−3.82 (m, 1.38H), 3.84 (t, *J* = 7.6 Hz, 0.62H), 4.07 (dd, *J* = 7.1, 7.6 Hz, 0.62H), 4.20−4.27 (m, 1.38H), 5.78 (s, 0.62H), 5.86 (s, 0.38H), 7.32−7.47 (m, 11H), 7.66−7.70 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 12.6 (CH_3), 12.7 (CH_3), 19.31 (C), 19.32 (C), 26.8 (CH_3), 26.9 (CH_3), 38.89 (CH), 38.94 (CH), 65.6 (CH_2), 65.7 (CH_2), 68.0 (CH_2), 69.1 (CH_2), 77.4 (CH), 78.4 (CH), 103.4 (CH), 103.6 (CH), 126.3 (CH), 126.56 (CH), 127.57 (CH), 127.59 (CH), 127.61 (CH), 127.62 (CH), 128.25 (CH), 128.26 (CH), 128.9 (CH), 129.1 (CH), 129.52 (CH), 129.55 (CH), 129.57 (CH), 129.58 (CH), 133.59 (C), 133.65 (C), 133.67 (C), 133.71 (C), 135.59 (CH), 135.60 (CH), 137.8 (C), 138.6 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{28}H_{34}O_3SiNa$ 469.2175; found 469.2152.

(2*R*,3*R*)-2-Benzyloxy-4-(*tert*-butyldiphenylsilyl)oxy-3-methylbutan-1-ol (19). DIBALH in *n*-hexane (1.0 M, 15.0 mL, 15.0

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mmol) was added to a solution of benzylidene acetal **18** (1.92 g, 4.30 mmol) in CH_2Cl_2 (43 mL) at −78 °C. After 9 h of stirring at −20 °C, the reaction was quenched with MeOH (2 mL), and 20% aqueous potassium sodium tartrate (50 mL) was added to the solution. The mixture was vigorously stirred for 16 h and extracted with AcOEt (2 × 200 mL). The combined organic extracts were washed with brine (50 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (2.20 g), which was purified by flash column chromatography (silica gel 60 g, 5:1 *n*-hexane/AcOEt) to give alcohol **19** (1.70 g, 88%) as a colorless oil. R_f 0.42 (3:1 *n*-hexane/AcOEt); $[\alpha]_D^{17}$ −2.4 (*c* 1.05, $CHCl_3$); IR (neat) 3435, 2959, 2857, 1427, 1113 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.96 (d, *J* = 6.9 Hz, 3H), 1.07 (s, 9H), 2.06 (m, 1H), 2.16 (t, *J* = 5.3 Hz, 1H), 3.61−3.66 (m, 2H), 3.68−3.74 (m, 2H), 3.80 (m, 1H), 4.54 (d, *J* = 11.6 Hz, 1H), 4.57 (d, *J* = 11.6 Hz, 1H), 7.27−7.43 (m, 11H), 7.65−7.67 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 13.2 (CH_3), 19.3 (CH), 26.9 (CH_3), 37.1 (CH), 61.6 (CH_2), 65.5 (CH_2), 72.1 (CH_2), 80.9 (CH), 127.65 (CH), 127.66 (CH), 127.70 (CH), 128.4 (CH), 129.6 (CH), 129.7 (CH), 133.4 (C), 133.5 (C), 135.6 (CH), 135.7 (CH), 138.4 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{28}H_{36}O_3SiNa$ 471.2331; found 471.2311.

(2*R*,3*R*)-2-Benzyloxy-4-(*tert*-butyldiphenylsilyl)oxy-3-methyl-1-butanal (20). Dess−Martin periodinane (136 mg, 0.321 mmol) was added to a solution of alcohol **19** (120 mg, 0.267 mmol) in CH_2Cl_2 (2.7 mL) at 0 °C. After 1 h of stirring at room temperature, the reaction was quenched with a mixture of 1 M aqueous $Na_2S_2O_3$ (1 mL) and saturated aqueous $NaHCO_3$ (1 mL), and the resulting mixture was vigorously stirred for 30 min. The mixture was partitioned between AcOEt (30 mL) and H_2O (5 mL), and the aqueous layer was extracted with AcOEt (30 mL). The combined organic extracts were washed with brine (10 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (245 mg), which was purified by column chromatography (silica gel 15 g, 10:1 *n*-hexane/AcOEt) to give aldehyde **20** (112 mg, 94%) as a colorless oil. R_f 0.57 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{15}$ +33.3 (*c* 0.99, $CHCl_3$); IR (neat) 3071, 2961, 2930, 2856, 1732, 1472, 1427, 1389, 1113, 1074 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.93 (d, *J* = 7.0 Hz, 3H), 1.02 (s, 9H), 2.30 (dddq, *J* = 4.3, 4.9, 8.4, 7.0 Hz, 1H), 3.54 (dd, *J* = 4.9, 10.0 Hz, 1H), 3.73 (dd, *J* = 8.4, 10.0 Hz, 1H), 3.78 (dd, *J* = 2.2, 4.3 Hz, 1H), 4.54 (d, *J* = 11.6 Hz, 1H), 4.75 (d, *J* = 11.6 Hz, 1H), 7.32−7.42 (m, 11H), 7.62−7.67 (m, 4H), 9.83 (d, *J* = 2.2 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 13.4 (CH_3), 19.1 (CH), 26.7 (CH_3), 39.2 (CH), 64.3 (CH_2), 73.2 (CH), 85.5 (CH_2), 127.6 (CH), 127.7 (CH), 127.88 (CH), 127.92 (CH), 128.4 (CH), 129.6 (CH), 129.7 (CH), 133.3 (C), 135.59 (CH), 135.60 (CH), 137.58 (C), 204.5 (CH); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{28}H_{34}O_3SiNa$ 469.2174; found 469.2160.

(*R*)-3-Methylcyclohex-2-en-1-ol (22). A mixture of racemic 3-methylcyclohex-2-en-1-ol (50.0 g, 444 mmol), vinyl butyrate (112 mL, 881 mmol), and Novozym 435 (1.11 g, 2.2 wt %) in *n*-heptane (450 mL) was stirred for 3 h. The resulting yellow suspension was filtered, and the filtrate was concentrated in vacuo. The residual oil (127 g) was passed through silica gel (800 g, CH_2Cl_2) to give a mixture of the butyrate of **22** and vinyl butyrate (34.7 g) along with *ent*-**22** (26.7 g). The mixture of the butyrate and vinyl butyrate was dissolved in MeOH (300 mL), and 4 M aqueous NaOH (110 mL, 440 mmol) was added at 0 °C. After 1 h of stirring at room temperature, the mixture was partitioned between CH_2Cl_2 (200 mL) and H_2O (250 mL), and the aqueous layer was extracted with CH_2Cl_2 (175 and 150 mL). The combined organic extracts were washed with brine (200 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (22.9 g), which was used without further purification.

This sequence was repeated, employing vinyl butyrate (52.0 mL, 409 mmol), Novozym 435 (504 mg, 2.2 wt %), *n*-heptane (200 mL), 4 M aqueous NaOH (83 mL, 332 mmol), and MeOH (230 mL). The crude product (17.5 g) was purified by column chromatography (silica gel 200 g, CH_2Cl_2) to give (*R*)-alcohol **22** (17.3 g, 76%, >99% ee) as a colorless oil. R_f 0.49 (2:1 *n*-hexane/AcOEt); $[\alpha]_D^{22}$ +95.1 (*c* 2.88, $CHCl_3$) {lit.[52] $[\alpha]_D$ +96.0 (*c* 0.423, $CHCl_3$)}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.37 (d, *J* = 6.5 Hz, 1H), 1.54−1.61 (m, 2H), 1.69 (s, 3H), 1.69−1.81 (m, 2H), 1.85−1.96 (m, 2H), 4.17 (m, 1H), 5.49 (m, 1H).

(*R*)-3-Methylcyclohex-2-en-1-yl Benzoate. Benzoyl chloride (0.07 mL, 0.57 mmol) was added to a mixture of (*R*)-alcohol **22** (18.2 mg, 0.16 mmol) and DMAP (99.1 mg, 0.81 mmol) in CH_2Cl_2 (1.6 mL) at 0 °C. After 2 h of stirring at room temperature, the mixture was partitioned between CH_2Cl_2 (10 mL) and saturated aqueous $NaHCO_3$ (2 mL), and the aqueous layer was extracted with CH_2Cl_2 (8 mL). The combined organic extracts were washed with brine (4 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (31.0 mg), which was purified by column chromatography (silica gel 15 g, 20:1 *n*-hexane/AcOEt) to give the corresponding benzoate (26.3 mg, 75%) as a colorless oil. The enantiomeric excess was determined to be >99% ee by HPLC analysis (column, Chiralpak IC-3; eluent, 200:1 *n*-hexane/2-propanol; flow rate, 0.5 mL/min; t_R = 26.4 min for the *R* enantiomer, t_R = 29.2 min for the *S* enantiomer). R_f 0.72 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{23}$ +211.8 (*c* 1.09, $CHCl_3$); IR (neat) 3061, 2936, 1713, 1450, 1271 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.70 (m, 1H), 1.84−1.89 (m, 3H), 1.94−2.06 (m, 2H), 1.74 (s, 3H), 5.49 (m, 1H), 5.60 (m, 1H), 7.41−7.44 (m, 2H), 7.54 (m, 1H), 8.05−8.06 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 19.1 (CH_2), 23.8 (CH_3), 28.1 (CH_2), 29.9 (CH_2), 69.3 (CH), 120.0 (CH), 128.2 (CH), 129.5 (CH), 130.9 (C), 132.6 (CH), 141.2 (C), 166.3 (C); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{14}H_{16}O_2$ 216.1150; found 216.1145.

(*R*)-3-Methylcyclohex-2-en-1-yl (2*R*,3*R*)-2-Benzyloxy-4-(*tert*-butyldiphenylsilyl)oxy-3-methylbutanoate (15a). To a mixture of aldehyde **20** (1.67 g, 3.74 mmol) and 2-methyl-2-butene (8.0 mL, 75.5 mmol) in *t*-BuOH/H_2O (4:1, 35 mL) was added NaH_2PO_4 (672 mg, 5.60 mmol) followed by $NaClO_2$ (507 mg, 5.61 mmol). After 3 h of stirring, the mixture was partitioned between AcOEt (100 mL) and 10% aqueous $NaHSO_4$ (40 mL), and the aqueous layer was extracted with AcOEt (3 × 100 mL). The combined organic extracts were washed with brine (40 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product **21** (1.94 g), which was used without further purification.

To an ice-cooled mixture (0 °C) of crude carboxylic acid **21** (1.94 g) and alcohol **22** (461 mg, 4.11 mmol) in CH_2Cl_2 (37 mL) was added 1-ethyl-3-(dimethylamino)propylcarbodiimide (1.00 g, 5.22 mmol) followed by DMAP (639 mg, 5.23 mmol). After 18 h of stirring at room temperature, the reaction was quenched with H_2O (40 mL), and the resulting mixture was extracted with AcOEt (2 × 200 mL). The combined organic extracts were washed with brine (40 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (3.20 g), which was purified by column chromatography (silica gel 200 g, 20:1 *n*-hexane/AcOEt) to give ester **15a** (1.49 g, 72% for two steps) as a colorless oil. R_f 0.61 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{27}$ +79.1 (*c* 1.48, $CHCl_3$); IR (neat) 3069, 2932, 2859, 1738, 1454, 1427, 1255, 1188, 1111 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.93 (d, *J* = 7.0 Hz, 3H), 1.04 (s, 9H), 1.59−1.79 (m, 4H), 1.69 (s, 3H), 1.87−1.99 (m, 2H), 2.17 (dddq, *J* = 4.7, 5.6, 7.1, 7.0 Hz, 1H), 3.68 (dd, *J* = 4.7, 9.9 Hz, 1H), 3.75 (dd, *J* = 5.6, 9.9 Hz, 1H), 3.97 (d, *J* = 7.1 Hz, 1H), 4.39 (d, *J* = 11.6 Hz, 1H), 4.63 (d, *J* = 11.6 Hz, 1H), 5.30 (m, 1H), 5.43 (m, 1H), 7.28−7.42 (m, 11H), 7.63−7.65 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 13.3 (CH_3), 19.0 (CH_2), 19.3 (C), 23.7 (CH_3), 26.8 (CH_3), 28.0 (CH_2), 29.9 (CH_2), 39.1 (CH), 64.7 (CH_2), 69.4 (CH), 72.4 (CH_2), 80.1 (CH), 119.7 (CH), 127.56 (CH), 127.57 (CH), 127.7 (CH), 128.0 (CH), 128.3 (CH), 129.49 (CH), 129.51 (CH), 133.7 (C), 133.8 (C), 135.57 (CH), 135.62 (CH), 137.7 (C), 141.3 (C), 172.0 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{35}H_{44}O_4SiNa$ 579.2907; found 579.2892. Anal. Calcd for $C_{35}H_{44}O_4Si$: C, 75.50; H, 7.97. Found: C, 75.30; H, 8.02.

[2*R*,2(1*S*),3*R*]-2-Benzyloxy-4-(*tert*-butyldiphenylsilyl)oxy-3-methyl-2-(1-methylcyclohex-2-en-1-yl)butanoic acid (24a). To a cooled solution (−78 °C) of ester **15a** (245 mg, 0.440 mmol) in THF (6 mL) was added a solution of LDA [prepared from diisopropylamine (0.10 mL, 0.70 mmol) and BuLi in *n*-hexane (1.56 M, 0.43 mL, 0.67 mmol)] in THF (3 mL) followed by chlorotrimethylsilane (85 μL, 0.67 mmol). After 5 min of stirring at −78 °C, the mixture was allowed to warm to room temperature and

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stirred for 12 h. The reaction was quenched with saturated aqueous NH_4Cl (10 mL), and the resulting mixture was extracted with AcOEt (3 × 40 mL). The combined organic extracts were washed with brine (10 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (297 mg), which was subjected to flash chromatography (silica gel 70 g, 5:1 *n*-hexane/AcOEt with 0.2% TFA) to provide a mixture of rearranged products. Separation by column chromatography (silica gel 30 g, 9:1 *n*-hexane/AcOEt) yielded carboxylic acid **24a** (117 mg, 48%) as a colorless foam along with a mixture of other products (6.0 mg) as a colorless oil. R_f 0.47 (3:1 *n*-hexane/AcOEt); $[\alpha]_D^{29}$ +14.2 (*c* 1.21, $CHCl_3$); IR (neat) 3088, 2932, 2859, 1703, 1427, 1113 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.13 (s, 3H), 1.22 (d, *J* = 6.8 Hz, 3H), 1.54 (m, 1H), 1.57−1.62 (m, 2H), 1.72−1.81 (m, 2H), 1.89 (m, 1H), 2.62 (m, 1H), 3.86−3.87 (m, 2H), 4.71 (s, 2H), 5.54 (m, 1H), 5.78 (d, *J* = 10.5 Hz, 1H), 7.28−7.41 (m, 11H), 7.65−7.67 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 13.3 (CH_3), 19.2 (C), 19.3 (CH_2), 24.3 (CH_2), 25.1 (CH_3), 26.9 (CH_3), 31.3 (CH_2), 40.3 (CH), 42.9 (C), 66.3 (CH_2), 67.7 (CH_2), 88.8 (C), 126.4 (CH), 127.2 (CH), 127.5 (CH), 127.6 (CH), 127.7 (CH), 128.4 (CH), 129.64 (CH), 129.647 (C), 129.653 (CH), 133.2 (CH), 133.4 (C), 135.62 (CH), 135.63 (CH), 138.5 (C), 174.2 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{35}H_{44}O_4SiNa$ 579.2907; found 579.2893.

Methyl [2*S*,2(1*S*),3*R*]-2-Benzyloxy-4-(*tert*-butyldiphenylsilyl)-oxy-3-methyl-2-[1-methylcyclohex-2-en-1-yl]butanoate (25). Potassium carbonate (87.1 mg, 0.63 mmol) was added to an ice-cooled mixture (0 °C) of carboxylic acid **24a** (117 mg, 0.21 mmol) and iodomethane (40 μL, 0.64 mmol) in DMF (2 mL). After 1 h of stirring, H_2O (40 mL) was added to the yellow mixture, and the resulting mixture was extracted with *n*-hexane/AcOEt (3:1, 2 × 50 mL). The combined organic extracts were washed with brine (40 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (143 mg), which was purified by column chromatography (silica gel 15 g, 9:1 *n*-hexane/AcOEt) to give methyl ester **25** (103 mg, 85%) as a colorless oil. R_f 0.64 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{27}$ −12.1 (*c* 1.05, C_6H_6); IR (neat) 3071, 2932, 2856, 1738, 1429, 1219, 1113, 1028 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.14 (s, 3H), 1.22 (d, *J* = 7.0 Hz, 3H), 1.63−1.72 (m, 3H), 1.85 (dt, *J* = 5.1, 12.7 Hz, 1H), 1.92−1.98 (m, 2H), 2.63 (ddq, *J* = 3.1, 9.6, 7.0 Hz, 1H), 3.49 (s, 3H), 3.59 (dd, *J* = 3.1, 9.6 Hz, 1H), 3.69 (t, *J* = 9.6 Hz, 1H), 4.68 (s, 2H), 5.55 (ddd, *J* = 2.9, 4.4, 10.3 Hz, 1H), 5.83 (d, *J* = 10.3 Hz, 1H), 7.22 (m, 1H), 7.28−7.29 (m, 4H), 7.35−7.44 (m, 6H), 7.64−7.66 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 13.0 (CH_3), 19.2 (C), 19.3 (CH_2), 24.6 (CH_2), 25.5 (CH_3), 26.9 (CH_3), 31.4 (CH_2), 42.0 (CH), 43.1 (C), 51.0 (CH_3), 67.5 (CH_2), 67.9 (CH_2), 89.0 (C), 125.3 (CH), 126.8 (CH), 127.58 (CH), 127.62 (CH), 128.0 (CH), 129.5 (CH), 129.6 (CH), 133.6 (C), 133.8 (C), 134.7 (CH), 135.58 (CH), 135.60 (CH), 139.9 (C), 173.5 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{36}H_{46}O_4SiNa$ 593.3063; found 593.3050.

[1*S*,5*S*,6*S*,9*S*,9(1*R*)]-9-Benzyloxy-9-[2-(*tert*-butyldiphenylsilyl)oxy-1-methyl]ethyl-5-iodo-1-methyl-7-oxabicyclo[4.3.0]nonan-8-one (26a). Iodine (14.3 mg, 0.056 mmol) was added to an ice-cooled solution (0 °C) of carboxylic acid **24a** (26.1 mg, 0.047 mmol) in MeCN/saturated aqueous $NaHCO_3$ (1:1, 1 mL). After 1 h of stirring at 0 °C, the reaction was quenched with 1 M aqueous $Na_2S_2O_3$ (4 mL), and the mixture was extracted with AcOEt (2 × 30 mL). The combined organic extracts were washed with brine (4 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (41.1 mg), which was purified by flash column chromatography (silica gel 10 g, 15:1 *n*-hexane/AcOEt) to give iodolactone **26a** (24.7 mg, 77%) as a colorless oil. R_f 0.52 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{17}$ +15.2 (*c* 1.24, $CHCl_3$); IR (neat) 3069, 2932, 2857, 1778, 1472, 1458, 1427, 1113, 613 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 1.03 (s, 3H), 1.14 (d, *J* = 7.0 Hz, 3H), 1.21 (s, 9H), 1.13−1.63 (m, 6H), 2.31 (ddq, *J* = 5.1, 6.7, 7.0 Hz, 1H), 3.79 (dd, *J* = 6.7, 10.3 Hz, 1H), 4.03 (dd, *J* = 5.1, 10.3 Hz, 1H), 4.15 (d, *J* = 5.1 Hz, 1H), 4.24 (dd, *J* = 5.1, 10.0 Hz, 1H), 4.57 (d, *J* = 11.2 Hz, 1H), 5.17 (d, *J* = 11.2 Hz, 1H), 7.08 (m, 1H), 7.14−7.20 (m, 4H), 7.23−7.26 (m, 6H), 7.79−7.82 (m, 4H); ^{13}C NMR (125.7 MHz, C_6D_6) δ 13.0 (CH_3), 19.1 (C), 19.8 (CH_2), 21.9 (CH_2), 25.9 (CH_3), 26.7 (CH_3), 30.5 (CH_2), 32.4 (CH_2), 38.1 (CH), 47.6 (C), 65.3 (CH_2), 67.0 (CH_2), 84.2 (CH), 85.6 (C), 127.4 (CH), 127.6 (CH), 127.8 (CH), 127.9 (CH), 128.2 (CH), 129.78 (CH), 129.83 (CH), 133.3 (C), 133.4 (C), 135.7 (CH), 135.8 (CH), 138.3 (C), 173.1 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{35}H_{43}IO_4SiNa$ 705.1873; found 705.1858.

Methyl [2*S*,3*R*]-2-Benzyloxy-4-(*tert*-butyldiphenylsilyl)oxy-3-methyl-2-(1-methylcyclohexyl)butanoate (27a). Platinum(IV) oxide (3.0 mg, 0.013 mmol) was added to a solution of ester **25** (27.7 mg, 0.049 mmol) in EtOH (1.5 mL), and the mixture was vigorously stirred under hydrogen (1 atm) for 29 h. The catalyst was filtered through a Celite pad, and the filtrate was evaporated in vacuo. Purification of the crude product (42.2 mg) by preparative thin-layer chromatography (200 mm × 200 mm × 0.25 mm preparative silica gel plate and elution with 20:1 *n*-hexane/AcOEt twice) gave hydrogenated compound **27a** (21.2 mg, 77%) as a colorless oil. R_f 0.59 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{26}$ −10.3 (*c* 1.02, $CHCl_3$); IR (neat) 2930, 2859, 1736, 1427, 1240, 1217, 1113, 1028 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.14 (s, 3H), 1.25−1.31 (m, 2H), 1.28 (d, *J* = 6.7 Hz, 3H), 1.40−1.61 (m, 6H), 1.68 (m, 1H), 1.78 (dt, *J* = 4.3, 13.1 Hz, 1H), 2.61 (m, 1H), 3.47 (s, 3H), 3.56 (dd, *J* = 2.1, 9.4 Hz, 1H), 3.70 (t, *J* = 9.4 Hz, 1H), 4.64 (s, 2H), 7.22 (m, 1H), 7.28−7.29 (m, 4H), 7.37−7.42 (m, 6H), 7.64−7.66 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 14.0 (CH_3), 18.8 (CH_3), 19.3 (C), 22.1 (CH_2), 22.4 (CH_2), 25.8 (CH_2), 26.8 (CH_3), 32.6 (CH_2), 33.8 (CH_2), 41.8 (CH), 42.6 (C), 50.8 (CH_3), 67.9 (CH_2), 68.3 (CH_2), 89.7 (CH_2), 126.8 (CH), 127.58 (CH), 127.64 (CH), 128.0 (CH), 129.5 (CH), 129.6 (CH), 133.6 (C), 133.8 (C), 135.59 (CH), 135.61 (CH), 140.0 (C), 173.9 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{36}H_{48}O_4SiNa$ 595.3220; found 595.3231.

Methyl (2*R,3*R**)-2-Benzyloxy-4-(*tert*-butyldiphenylsilyl)-oxy-3-methyl-2-(1-methylcyclohexyl)butanoate (27b).** Trimethylsilyldiazomethane in *n*-hexane (1.7 M, 35 μL, 0.06 mmol) was added to a 1.6:1 mixture of the minor isomers **24b** and **24c** (15.1 mg) in benzene/MeOH (1:1, 1.5 mL) at 0 °C. After 5 min of stirring, the mixture was concentrated in vacuo, and the residual pale-yellow oil (16.0 mg) was used without further purification.

Platinum(IV) oxide (3.0 mg, 0.013 mmol) was added to a solution of the crude ester (16.0 mg) in EtOH (1.5 mL), and the mixture was vigorously stirred under hydrogen (1 atm) for 26 h. The catalyst was filtered through a Celite pad, and the filtrate was evaporated in vacuo. Purification of the crude product (15.5 mg) by preparative thin-layer chromatography (200 mm × 100 mm × 0.25 mm preparative silica gel plate and elution with 20:1 *n*-hexane/AcOEt twice) gave hydrogenated compound **27b** (4.8 mg) as a colorless oil. R_f 0.59 (5:1 *n*-hexane/AcOEt); ^1H NMR (500 MHz, $CDCl_3$) δ 0.97 (s, 3H), 1.05 (s, 9H), 1.13 (m, 1H), 1.20 (d, *J* = 7.0 Hz, 3H), 1.25−1.43 (m, 6H), 1.50−1.64 (m, 3H), 2.55 (m, 1H), 3.58 (t, *J* = 9.9 Hz, 1H), 3.71 (s, 3H), 4.13 (dd, *J* = 3.9, 9.9 Hz, 1H), 4.79 (d, *J* = 11.3 Hz, 1H), 4.83 (d, *J* = 11.3 Hz, 1H), 7.24 (m, 1H), 7.29−7.30 (m, 4H), 7.35−7.42 (m, 6H), 7.65−7.69 (m, 4H); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{36}H_{48}O_4SiNa$ 595.3220; found 595.3195.

(2*S*,3*R*,5*S*)-5-[(*tert*-Butyldiphenylsilyl)oxymethyl]-3-methyl-2-(phenylthiomethyl)tetrahydrofuran (32). BuLi in *n*-hexane (2.2 M, 12.0 mL, 26.4 mmol) was added to an ice-cooled mixture (0 °C) of thioanisole (3.10 mL, 26.5 mmol) and DABCO (2.97 g, 26.5 mmol) in THF (160 mL). After 1 h of stirring, the mixture was cooled to −78 °C, and a solution of lactone **30** (7.50 g, 20.4 mmol) in THF (40 mL) was added dropwise. After 20 min of stirring, the reaction was quenched with saturated aqueous NH_4Cl (170 mL), and the resulting mixture was extracted with AcOEt (350 and 250 mL). The combined organic extracts were washed with brine (200 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (12.1 g), which was chromatographed (silica gel 250 g, 4:1 *n*-hexane/AcOEt) to give a mixture containing hemiketal **31** (8.70 g) as a colorless oil.

To a cooled solution (−78 °C) of hemiketal **31** (8.70 g) in CH_2Cl_2 (180 mL) was added triethylsilane (4.2 mL, 26.5 mmol) followed by $BF_3{\cdot}OEt_2$ (3.3 mL, 26.5 mmol). After 1 h of stirring, the reaction was

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quenched with saturated aqueous $NaHCO_3$ (120 mL), and the resulting mixture was extracted with AcOEt (300 and 200 mL). The combined organic extracts were washed with brine (80 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (9.20 g), which was purified by column chromatography (silica gel 250 g, 19:1 *n*-hexane/AcOEt) to give sulfide **32** (7.28 g, 86% for two steps) as a colorless oil. R_f 0.36 (10:1 *n*-hexane/AcOEt); $[\alpha]_D^{26}$ −21.3 (*c* 1.36, $CHCl_3$); IR (neat) 3071, 3049, 2959, 2930, 2857, 1427, 1113 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (d, *J* = 4.2 Hz, 3H), 1.06 (s, 9H), 1.64 (dt, *J* = 11.7, 7.0 Hz, 1H), 2.07−2.16 (m, 2H), 3.05 (dd, *J* = 6.4, 13.3 Hz, 1H), 3.08 (dd, *J* = 5.1, 13.3 Hz, 1H), 3.62−3.66 (m, 3H), 4.13 (dt, *J* = 12.3, 4.7 Hz, 1H), 7.15 (m, 1H), 7.23−7.25 (m, 2H), 7.33−7.43 (m, 8H), 7.66−7.70 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 17.6 (CH_3), 19.3 (C), 26.9 (CH_3), 36.3 (CH_2), 37.9 (CH), 38.1 (CH_2), 66.3 (CH_2), 78.6 (CH), 84.7 (CH), 125.7 (CH), 127.64 (CH), 127.65 (CH), 128.8 (CH), 128.9 (CH), 129.59 (CH), 129.62 (CH), 133.6 (C), 135.64 (CH), 135.65 (CH), 136.9 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{29}H_{36}O_2SSiNa$ 499.2103; found 499.2087. Anal. Calcd for $C_{29}H_{36}O_2SSi$: C, 73.06; H, 7.61. Found: C, 72.89; H, 7.68.

(2*R*,3*R*,5*S*)-5-[(*tert*-Butyldiphenylsilyl)oxymethyl]-3-methyltetrahydrofuran-2-carbaldehyde (34). *m*-CPBA (ca. 70%, 21.1 g, ca. 85.6 mmol) was added to an ice-cooled (0 °C) solution of sulfide **32** (40.0 g, 83.9 mmol) in CH_2Cl_2 (420 mL). After 1 h of stirring, the reaction mixture was quenched with solid $Na_2S_2O_3{\cdot}5H_2O$ (20.0 g), and saturated aqueous $NaHCO_3$ (500 mL) was added. The resulting mixture was extracted with AcOEt (3 × 500 mL), and the combined organic extracts were washed with brine (400 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product **33** (43.8 g), which was used without further purification.

TFAA (35.0 mL, 249 mmol) was added to an ice-cooled mixture (0 °C) of crude sulfoxide **33** (43.8 g) and 2,6-lutidine (29 mL, 249 mmol) in CH_2Cl_2 (400 mL). After 1 h of stirring, the reaction was quenched with saturated aqueous $NaHCO_3$ (400 mL), and the resulting mixture was extracted with AcOEt (3 × 600 mL). The combined organic extracts were successively washed with saturated aqueous $NaHCO_3$ (400 mL) and brine (400 mL) and then dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (69.1 g), which was used without further purification.

$NaHCO_3$ (70.5 g, 839 mmol) was added to a solution of the crude trifluoroacetate (69.1 g) in acetone/H_2O (1:1, 400 mL). After 24 h of stirring, the mixture was diluted with AcOEt (200 mL), and acetone was removed in vacuo. The residue was passed through a Celite pad, and the filtrate was partitioned between AcOEt (600 mL) and H_2O (200 mL). The aqueous layer was extracted with AcOEt (3 × 600 mL), and the combined organic extracts were washed with brine (200 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (65.2 g), which was purified by column chromatography (silica gel 500 g, 5:1 *n*-hexane/AcOEt) to give aldehyde **34** (26.3 g, 82% for three steps) as a colorless oil. R_f 0.45 (3:1 *n*-hexane/AcOEt); $[\alpha]_D^{16}$ +39.4 (*c* 1.03, $CHCl_3$); IR (neat) 3071, 2961, 2930, 2859, 1734, 1472, 1460, 1427, 1112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.06 (s, 9H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.70 (dt, *J* = 12.4, 7.8 Hz, 1H), 2.12 (ddd, *J* = 5.0, 7.8, 12.4 Hz, 1H), 2.40 (dtq, *J* = 7.3, 7.8, 6.8 Hz, 1H), 3.67 (dd, *J* = 4.2, 10.9 Hz, 1H), 3.74 (dd, *J* = 4.7, 10.9 Hz, 1H), 3.76 (dd, *J* = 2.5, 7.3 Hz, 1H), 4.32 (dddd, *J* = 4.2, 4.7, 5.0, 7.8 Hz, 1H), 7.38−7.45 (m, 6H), 7.67−7.71 (m, 4H), 9.63 (d, *J* = 2.5 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 17.2 (CH_3), 19.2 (C), 26.8 (CH_3), 35.9 (CH_2), 36.0 (CH), 66.1 (CH_2), 80.5 (CH), 89.6 (CH), 127.70 (CH), 127.72 (CH), 129.7 (CH), 129.8 (CH), 133.26 (C), 133.28 (C), 135.58 (CH), 135.61 (CH), 203.0 (CH); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{30}O_3SiNa$ 405.1862; found 405.1871.

(*R*)-3-Methylcyclohex-2-en-1-yl (2*R*,3*R*,5*S*)-5-[(*tert*-Butyldiphenylsilyl)oxymethyl]-3-methyltetrahydrofuran-2-carboxylate (36). To an ice-cooled solution (0 °C) of aldehyde **34** (3.00 g, 7.84 mmol) in EtOH (10 mL) was added a solution of $AgNO_3$ (5.30 g, 31.2 mmol) in H_2O (5 mL) followed by a solution of KOH (3.50 g, 62.4 mmol) in H_2O (5 mL). After 1 h of stirring, the resulting black suspension was diluted with H_2O (40 mL) and passed through a Celite pad. The yellow filtrate was extracted with AcOEt (4 × 120 mL), and the combined organic extracts were washed with brine (40 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (3.19 g), which was chromatographed (silica gel 100 g, 3:1 CH_2Cl_2/MeOH) to give potassium carboxylate **35** (3.19 g) as a pale-yellow solid.

To an ice-cooled solution (0 °C) of crude potassium carboxylate **35** (3.19 g) in CH_2Cl_2 (40 mL) was added oxalyl chloride (1.0 mL, 11.8 mmol) followed by DMF (60 μL, 0.77 mmol). After 1 h of stirring at room temperature, the mixture was concentrated in vacuo, and the residue was dissolved in CH_2Cl_2 (40 mL). A mixture of alcohol **22** (1.06 g, 9.45 mmol), Et_3N (5.5 mL, 39.5 mmol), and DMAP (87.0 mg, 0.712 mmol) in CH_2Cl_2 (10 mL) was added to the solution of crude acyl chloride at 0 °C. After 2 h of stirring, the reaction mixture was partitioned between AcOEt (200 mL) and H_2O (40 mL), and the aqueous layer was extracted with AcOEt (200 mL). The combined organic extracts were washed with brine (40 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (4.15 g), which was purified by column chromatography (silica gel 200 g, 20:1 *n*-hexane/AcOEt) to give ester **36** (2.52 g, 65% for three steps) as a colorless oil. R_f 0.52 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{27}$ +77.0 (*c* 1.49, $CHCl_3$); IR (neat) 3071, 3049, 2932, 2859, 1748, 1458, 1427, 1275, 1198, 1113 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.16 (d, *J* = 6.8 Hz, 3H), 1.56−1.76 (m, 5H), 1.67 (s, 3H), 1.84−1.96 (m, 2H), 2.07 (m, 1H), 2.35 (m, 1H), 3.64 (dd, *J* = 6.8, 10.3 Hz, 1H), 3.83 (dd, *J* = 4.9, 10.3 Hz, 1H), 3.96 (d, *J* = 6.6 Hz, 1H), 4.25 (m, 1H), 5.24 (m, 1H), 5.41 (m, 1H), 7.35−7.43 (m, 6H), 7.66−7.69 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.2 (CH_3), 19.0 (CH_2), 19.2 (C), 23.7 (CH_3), 26.8 (CH_2), 27.9 (CH_2), 29.9 (CH_3), 36.3 (CH), 38.0 (CH_2), 66.1 (CH_2), 69.3 (CH), 80.1 (CH), 84.1 (CH), 119.8 (CH), 127.617 (CH), 127.625 (CH), 129.57 (CH), 129.58 (CH), 133.61 (C), 133.64 (C), 135.61 (CH), 135.63 (CH), 141.1 (C), 172.4 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{30}H_{40}O_4SiNa$ 515.2594; found 515.2593. Anal. Calcd for $C_{30}H_{40}O_4Si$: C, 73.13; H, 8.18. Found: C, 73.10; H, 8.02.

Methyl (2*R*,2(1*S*),3*R*,5*S*)-5-[(*tert*-Butyldiphenylsilyl)oxymethyl]-3-methyl-2-[1-methylcyclohex-2-en-1-yl]tetrahydrofuran-2-carboxylate (38b). To a cooled solution (−78 °C) of ester **36** (1.25 g, 2.54 mmol) in THF (40 mL) was added a solution of LDA [prepared from diisopropylamine (0.55 mL, 3.92 mmol) and BuLi in *n*-hexane (1.56 M, 2.50 mL, 3.90 mmol)] in THF (10 mL) followed by chlorotrimethylsilane (0.48 mL, 0.38 mmol). After 5 min of stirring at −78 °C, the mixture was allowed to warm to room temperature and stirred for 10 h. The reaction was quenched with saturated aqueous NH_4Cl (40 mL), and the resulting mixture was extracted with AcOEt (3 × 100 mL). The combined organic extracts were washed with brine (40 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (1.75 g), which was chromatographed (silica gel 150 g, 7:1 *n*-hexane/AcOEt) to give an inseparable mixture of carboxylic acids **37a** and **37b** (921 mg, 74%) as a colorless oil.

Potassium carbonate (775 mg, 5.61 mmol) was added to an ice-cooled mixture (0 °C) of carboxylic acids **37a** and **37b** (921 mg, 1.87 mmol) and iodomethane (0.35 mL, 5.62 mmol) in DMF (19 mL). After 4 h of stirring, the resulting yellow mixture was partitioned between *n*-hexane/AcOEt (3:1, 50 mL) and H_2O (40 mL), and the aqueous layer was extracted with *n*-hexane/AcOEt (3:1, 2 × 50 mL). The combined organic extracts were washed with brine (40 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (1.41 g), which was subjected to flash chromatography (silica gel 30 g, 9:1 *n*-hexane/AcOEt) to give a mixture of methyl esters **38a** and **38b** (938 mg, 99%) as a colorless oil. The diastereomeric ratio (**38a**:**38b**) was determined to be 6:94 by HPLC analysis (column, Zorbax Sil, 4.6 mm × 250 mm; eluent, 50:1 *n*-hexane/THF; flow rate, 1.5 mL/min; detection, 254 nm; t_R = 10.0 min for the major isomer **38b**, t_R = 11.4 min for the minor isomer **38a**). Separation of diastereomers **38a** and **38b** by flash column chromatography (silica gel 100 g, 50:1 *n*-hexane/AcOEt) yielded isomer **38a** (61.0 mg, 5%) and isomer **38b** (877 mg, 94%) as colorless

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oils. Data for **38b**: R_f 0.31 (10:1 *n*-hexane/AcOEt); $[\alpha]_D^{26}$ +7.1 (*c* 1.08, $CHCl_3$); IR (neat) 3071, 2932, 2859, 1732, 1456, 1427, 1227, 1113 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.04 (d, *J* = 7.1 Hz, 3H), 1.05 (s, 9H), 1.08 (s, 3H), 1.49−1.62 (m, 4H), 1.80−1.89 (m, 3H), 2.16 (ddd, *J* = 5.0, 8.6, 13.5 Hz, 1H), 2.46 (m, 1H), 3.66 (dd, *J* = 4.3, 10.6 Hz, 1H), 3.69 (dd, *J* = 5.2, 10.6 Hz, 1H), 3.71 (s, 3H), 4.29 (m, 1H), 5.65 (m, 1H), 5.95 (m, 1H), 7.36−7.43 (m, 6H), 7.67 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.0 (CH_3), 19.49 (C), 19.51 (CH_2), 23.6 (CH_3), 25.1 (CH_2), 27.1 (CH_3), 30.8 (CH_2), 36.9 (CH), 37.3 (CH_2), 42.1 (C), 51.4 (CH_3), 66.0 (CH_2), 78.3 (CH), 94.2 (C), 127.3 (CH), 127.87 (CH), 127.89 (CH), 129.8 (CH), 129.9 (CH), 133.0 (CH), 133.7 (C), 133.9 (C), 135.85 (CH), 135.90 (CH), 173.9 (C); HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{42}O_4SiNa$ 529.2750; found 529.2769.

Data for the [2*S*,2(1*S*),3*R*,5*S*] isomer **38a**: R_f 0.28 (10:1 *n*-hexane/AcOEt); $[\alpha]_D^{26}$ −14.2 (*c* 0.16, $CHCl_3$); IR (neat) 3028, 2932, 2856, 1732, 1460, 1427, 1227, 1113 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.056 (s, 9H), 1.063 (d, *J* = 6.7 Hz, 3H), 1.10 (s, 3H), 1.51−1.66 (m, 3H), 1.72 (dt, *J* = 3.4, 13.1 Hz, 1H), 1.86 (m, 1H), 1.90−1.93 (m, 2H), 2.20 (ddd, *J* = 7.0, 9.1, 12.2 Hz, 1H), 2.48 (m, 1H), 3.69 (dd, *J* = 3.8, 10.7 Hz, 1H), 3.71 (s, 3H), 3.80 (dd, *J* = 4.9, 10.7 Hz, 1H), 4.29 (m, 1H), 5.68 (dt, *J* = 10.0, 3.3 Hz, 1H), 5.76 (dd, *J* = 1.6, 10.0 Hz, 1H), 7.36−7.43 (m, 6H), 7.66−7.70 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.6 (CH_3), 19.1 (CH_2), 19.3 (CH), 23.3 (CH_3), 24.9 (CH_2), 26.8 (CH_3), 31.3 (CH_2), 36.8 (C), 37.4 (CH_2), 42.5 (C), 51.2 (CH_3), 65.2 (CH_2), 78.4 (CH), 94.8 (C), 127.63 (CH), 127.65 (CH), 129.56 (CH), 129.61 (CH), 132.6 (CH), 133.5 (C), 133.6 (C), 135.6 (CH), 135.7 (CH), 173.4 (C); HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{42}O_4SiNa$ 529.2750, found 529.2730.

(1*S*,3*S*,5*R*,3a′*S*,4′*S*,7a′*S*)-3-[(*tert*-Butyldiphenylsilyl)-oxymethyl]-4′-iodo-5,7a′-dimethyl-2,3′-dioxaspiro-[cyclopentane-1,1′-hexahydroindan]-2′-one (39b). Iodine (453 mg, 1.78 mmol) was added to a solution of carboxylic acids **37a** and **37b** (797 mg, 1.62 mmol) in MeCN/saturated aqueous $NaHCO_3$ (1:1, 20 mL) at 0 °C. After 90 min of stirring, the reaction was quenched with 1 M aqueous $Na_2S_2O_3$ (30 mL), and the resulting mixture was extracted with AcOEt (2 × 100 mL). The combined organic extracts were washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (977 mg), which was purified by flash column chromatography (silica gel 70 g, 20:1 *n*-hexane/AcOEt) to give isomer **39b** (802 mg, 81%) as a white solid along with isomer **39a** (35.5 mg, 4%) as a colorless oil. Data for **39b**: R_f 0.54 (5:1 *n*-hexane/AcOEt); mp 139−140 °C (colorless prisms from *n*-hexane); $[\alpha]_D^{25}$ +53.7 (*c* 1.08, $CHCl_3$); IR (KBr) 3071, 2934, 2857, 1780, 1460, 1233, 1113, 970, 702 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 0.79 (m, 1H), 0.95−1.04 (m, 2H), 1.14 (d, *J* = 6.7 Hz, 3H), 1.16 (s, 9H), 1.28 (s, 3H), 1.33 (m, 1H), 1.48−1.60 (m, 2H), 1.83 (m, 1H), 1.93 (m, 1H), 2.10 (m, 1H), 3.51 (dd, *J* = 4.8, 10.7 Hz, 1H), 3.58 (dd, *J* = 4.7, 10.7 Hz, 1H), 4.19 (m, 1H), 4.28 (m, 1H), 4.72 (s, 1H), 7.25−7.26 (m, 6H), 7.75−7.79 (m, 4H); ^{13}C NMR (125.7 MHz, C_6D_6) δ 15.9 (CH_3), 17.4 (CH_2), 17.8 (CH_3), 19.4 (C), 23.5 (CH), 27.0 (CH_3), 29.3 (CH_2), 30.6 (CH_2), 32.8 (CH), 36.7 (CH_2), 43.9 (C), 66.0 (CH_2), 77.7 (CH), 83.7 (CH), 91.4 (C), 128.11 (CH), 128.14 (CH), 128.3 (CH), 130.06 (CH), 130.10 (CH), 133.8 (C), 133.9 (C), 136.0 (CH), 172.0 (C); HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{39}IO_4SiNa$ 641.1560; found 641.1549. Anal. Calcd for $C_{30}H_{39}IO_4Si$: C, 58.25; H, 6.35. Found: C, 58.17; H, 6.35.

Data for the (1*R*,3*S*,5*R*,3a′*S*,4′*S*,7a′*S*) isomer **39a**: R_f 0.52 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{27}$ +2.5 (*c* 1.19, $CHCl_3$); IR (neat) 3071, 2932, 2859, 1782, 1456, 1236, 1113, 970, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.06 (s, 9H), 1.10 (d, *J* = 7.1 Hz, 3H), 1.36 (s, 3H), 1.55−1.63 (m, 3H), 1.75 (m, 1H), 1.88−2.00 (m, 3H), 2.15 (ddd, *J* = 4.7, 8.1, 12.5 Hz, 1H), 2.50 (m, 1H), 3.60 (dd, *J* = 4.0, 10.9 Hz, 1H), 3.70 (dd, *J* = 4.4, 10.9 Hz, 1H), 4.43 (m, 1H), 4.50 (d, *J* = 3.1 Hz, 1H), 4.62 (dt, *J* = 3.1, 3.3 Hz, 1H), 7.37−7.45 (m, 6H), 7.65−7.69 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 15.7 (CH_3), 18.1 (CH_2), 19.2 (C), 20.1 (CH_3), 24.3 (CH), 26.8 (CH_3), 30.0 (CH_2), 31.2 (CH_2), 35.3 (CH_2), 35.5 (CH), 43.2 (C), 65.7 (CH_2), 78.1 (CH), 83.5 (CH), 93.2 (C), 127.68 (CH), 127.72 (CH), 129.67 (CH), 129.74 (CH), 133.2 (C), 133.4 (C), 135.5 (CH), 135.6 (CH), 175.9 (C); HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{39}IO_4SiNa$ 641.1560; found 641.1568.

Methyl [2*R*,2(1*S*),3*R*,5*S*]-5-(Hydroxymethyl)-3-methyl-2-(1-methylcyclohex-2-en-1-yl)tetrahydrofuran-2-carboxylate (41). NH_4F (249 mg, 6.72 mmol) was added to a solution of TBDPS ether **38b** (341 mg, 0.673 mmol) in MeOH/EtOH (5:2, 7 mL). After 24 h of stirring, the mixture was partitioned between AcOEt (70 mL) and H_2O (15 mL), and the aqueous layer was extracted with AcOEt (70 mL). The combined organic extracts were washed with brine (20 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (391 mg), which was purified by column chromatography (silica gel 10 g, 2:1 *n*-hexane/AcOEt) to give alcohol **41** (170 mg, 94%) as a colorless oil. R_f 0.31 (3:1 *n*-hexane/AcOEt); $[\alpha]_D^{22}$ +19.5 (*c* 1.17, $CHCl_3$); IR (neat) 3442, 2937, 1732, 1456, 1227, 1101, 1051 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.06 (d, *J* = 7.0 Hz, 3H), 1.20 (s, 3H), 1.52−1.71 (m, 4H), 1.81 (dt, *J* = 3.3, 12.5 Hz, 1H), 1.92−1.94 (m, 2H), 2.04 (ddd, *J* = 5.6, 9.0, 12.5 Hz, 1H), 2.55 (m, 1H), 3.47 (dd, *J* = 5.1, 11.6 Hz, 1H), 3.73 (s, 3H), 3.74 (dd, *J* = 3.4, 11.6 Hz, 1H), 4.32 (m, 1H), 5.75 (m, 1H), 5.84 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.0 (CH_3), 19.2 (CH_2), 23.2 (CH_3), 24.8 (CH_2), 31.1 (CH_2), 36.5 (CH_2), 37.0 (CH), 42.0 (C), 51.3 (CH_3), 65.0 (CH_2), 78.0 (CH), 94.1 (C), 127.8 (CH), 132.4 (CH), 173.2 (C); HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{24}O_4Na$ 291.1572; found 291.1555.

Methyl [2*R*,2(1*S*),3*R*,5*S*]-5-(Iodomethyl)-3-methyl-2-(1-methylcyclohex-2-en-1-yl)tetrahydrofuran-2-carboxylate (42). Iodine (103 mg, 0.405 mmol) was added to a mixture of alcohol **41** (72.4 mg, 0.270 mmol), triphenylphosphine (106 mg, 0.405 mmol), and imidazole (55.1 mg, 0.809 mmol) in toluene (2.7 mL). After 1 h of stirring at 50 °C, the reaction was quenched with 1 M aqueous $Na_2S_2O_3$ (5 mL), and the resulting mixture was extracted with AcOEt (2 × 30 mL). The combined organic extracts were washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (247 mg), which was purified by column chromatography (silica gel 10 g, 20:1 *n*-hexane/AcOEt) to give iodide **42** (96.3 mg, 94%) as a colorless oil. R_f 0.42 (10:1 *n*-hexane/AcOEt); $[\alpha]_D^{20}$ −15.5 (*c* 1.20, $CHCl_3$); IR (neat) 2936, 2876, 1732, 1454, 1433, 1229, 1061 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.04 (d, *J* = 6.7 Hz, 3H), 1.11 (s, 3H), 1.57−1.62 (m, 2H), 1.67 (m, 1H), 1.76 (ddd, *J* = 8.0, 8.8, 12.9 Hz, 1H), 1.82 (dt, *J* = 3.2, 12.5 Hz, 1H), 1.90−1.94 (m, 2H), 2.02 (ddd, *J* = 4.8, 8.7, 12.9 Hz, 1H), 2.52 (ddq, *J* = 8.7, 8.8, 6.7 Hz, 1H), 3.12 (dd, *J* = 8.4, 9.7 Hz, 1H), 3.29 (dd, *J* = 4.4, 9.7 Hz, 1H), 3.72 (s, 3H), 4.35 (dddd, *J* = 4.4, 4.8, 8.0, 8.4 Hz, 1H), 5.59 (m, 1H), 5.91 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 9.8 (CH_2), 17.6 (CH_3), 19.3 (CH_2), 23.4 (CH_3), 24.9 (CH_2), 30.8 (CH_2), 36.2 (CH_2), 40.6 (CH), 41.8 (C), 51.3 (CH_3), 77.5 (CH), 95.2 (C), 127.5 (CH), 132.3 (CH), 173.0 (C); HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{23}IO_3Na$ 401.0590; found 401.0587.

Methyl [2*R*,2(1*S*),3*R*]-2-(1-Methylcyclohex-2-en-1-yl)-3-methyl-2-hydroxyhex-5-enoate (43). Activated zinc powder (80.0 mg, 1.22 mmol) was added to a solution of iodide **42** (92.6 mg, 0.245 mmol) in AcOH (1.2 mL). After 1 h of stirring at 110 °C, the suspension was filtered through a Celite pad, and the filtrate was concentrated in vacuo. The residue was azeotropically dried with toluene (3 × 5 mL) to furnish the crude product (127 mg), which was purified by column chromatography (silica gel 5 g, 20:1 *n*-hexane/AcOEt) to give diene **43** (51.3 mg, 83%) as a colorless oil. R_f 0.42 (10:1 *n*-hexane/AcOEt); $[\alpha]_D^{23}$ +27.4 (*c* 1.06, $CHCl_3$); IR (neat) 3510, 2938, 1720, 1639, 1437, 1229, 1153 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.77 (d, *J* = 6.7 Hz, 3H), 1.09 (s, 3H), 1.51−1.71 (m, 3H), 1.91−2.01 (m, 4H), 2.19 (m, 1H), 2.57 (m, 1H), 3.36 (s, 1H), 3.77 (s, 3H), 4.96−5.03 (m, 2H), 5.67 (m, 1H), 5.70−5.79 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 14.8 (CH_3), 19.4 (CH_2), 24.0 (CH_3), 24.5 (CH_2), 30.7 (CH_2), 35.8 (CH_2), 37.8 (CH), 41.9 (C), 52.4 (CH_3), 83.9 (C), 115.9 (CH_2), 126.5 (CH), 133.0 (CH), 137.5 (CH), 177.4 (C); HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{24}O_3Na$ 275.1623; found 275.1642.

Methyl [2*R*,2(1*S*),3*R*,5*S*]-5-(Chloromethyl)-3-methyl-2-(1-methylcyclohex-2-en-1-yl)tetrahydrofuran-2-carboxylate (44). A mixture of alcohol **41** (170 mg, 0.632 mmol) and triphenylphos-

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phine (829 mg, 3.16 mmol) in CCl_4 (6 mL) was heated at reflux for 12 h. After cooling, the resulting brown suspension was concentrated in vacuo. Purification of the residue (1.12 g) by column chromatography (silica gel 50 g, 20:1 *n*-hexane/AcOEt) gave chloride **44** (177 mg, 98%) as a colorless oil. R_f 0.47 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{23}$ −5.2 (*c* 1.03, $CHCl_3$); IR (neat) 2940, 2876, 1732, 1458, 1229, 1076, 739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (d, *J* = 6.9 Hz, 3H), 1.11 (s, 3H), 1.54 (m, 1H), 1.60 (m, 1H), 1.67 (m, 1H), 1.71 (ddd, *J* = 8.4, 9.1, 13.0 Hz, 1H), 1.83 (dt, *J* = 13.3, 3.9 Hz, 1H), 1.90−1.93 (m, 2H), 2.08 (ddd, *J* = 4.5, 8.6, 13.0 Hz, 1H), 2.50 (ddq, *J* = 8.4, 8.6, 6.9 Hz, 1H), 3.46 (dd, *J* = 7.0, 11.0 Hz, 1H), 3.57 (dd, *J* = 4.4, 11.0 Hz, 1H), 3.72 (s, 3H), 4.42 (dddd, *J* = 4.4, 4.5, 7.0, 9.1 Hz, 1H), 5.69 (m, 1H), 5.91 (dd, *J* = 1.5, 10.6 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 17.5 (CH_3), 19.3 (CH_2), 23.2 (CH_3), 24.8 (CH_2), 30.5 (CH_2), 36.3 (CH), 38.2 (CH_2), 41.8 (C), 46.7 (CH_2), 51.3 (CH_3), 77.1 (CH), 94.5 (C), 127.4 (CH), 132.3 (CH), 173.1 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{23}ClO_3Na$ 309.1233; found 309.1238.

Methyl [2*R*,2(1*S*),3*R*]-2-Hydroxy-2-(1-methylcyclohex-2-en-1-yl)-3-methylhex-5-ynoate (45). Sodium (167 mg, 7.26 mmol) was added to a yellow solution of $Fe(NO_3)_3{\cdot}9H_2O$ (10.0 mg, 0.025 mmol) in liquid ammonia (10 mL) at −40 °C. After 30 min of stirring, chloride **44** (139 mg, 0.485 mmol) in THF (5 mL) was added to the brown-colored suspension, and the reaction mixture was stirred for 2 h. The reaction was quenched with solid NH_4Cl (1.0 g), and ammonia was evaporated at room temperature. The residue was partitioned between AcOEt (40 mL) and H_2O (15 mL), and the aqueous layer was extracted with AcOEt (40 mL). The combined organic extracts were washed with brine (15 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (150 mg), which was purified by column chromatography (silica gel 10 g, 20:1 *n*-hexane/AcOEt) to give alkyne **45** (116 mg, 96%) as a colorless oil. R_f 0.44 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{23}$ +45.8 (*c* 1.03, $CHCl_3$); IR (neat) 3505, 3306, 2934, 2116, 1719, 1458, 1437, 1381, 1369, 1242, 1098, 629 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.97 (d, *J* = 6.7 Hz, 3H), 1.06 (s, 3H), 1.51 (m, 1H), 1.60 (m, 1H), 1.69 (m, 1H), 1.87−1.95 (m, 3H), 1.97 (t, *J* = 2.6 Hz, 1H), 2.18 (ddd, *J* = 2.6, 10.5, 16.3 Hz, 1H), 2.35 (ddq, *J* = 3.6, 10.5, 6.7 Hz, 1H), 2.64 (ddd, *J* = 2.6, 3.6, 16.3 Hz, 1H), 3.38 (s, 1H), 3.77 (s, 3H), 5.66−5.72 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 15.4 (CH_3), 19.4 (CH_2), 21.2 (CH_2), 23.9 (CH_3), 24.5 (CH_2), 30.7 (CH_2), 37.3 (CH), 41.9 (C), 52.5 (CH_3), 69.4 (CH), 83.2 (C), 83.5 (C), 126.9 (CH), 132.6 (CH), 176.8 (C); HRMS (DART) *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{23}O_3$ 251.1647; found 251.1658.

Methyl [2*R*,2(1*S*),3*R*]-3-Methyl-2-(1-methylcyclohex-2-en-1-yl)-2-(trimethylsilyl)oxyhex-5-ynoate (46). TMSOTf (1.50 mL, 8.29 mmol) was added to a mixture of alcohol **45** (1.01 g, 4.03 mmol) and 2,6-lutidine (1.40 mL, 12.0 mmol) in CH_2Cl_2 (40 mL) at 0 °C. After 14 h of stirring at room temperature, the reaction was quenched with saturated aqueous $NaHCO_3$ (40 mL), and the resulting mixture was extracted with AcOEt (2 × 200 mL). The combined organic extracts were washed with brine (40 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (2.91 g), which was purified by column chromatography (silica gel 100 g, 40:1 *n*-hexane/AcOEt) to give TMS ether **46** (1.28 g, 98%) as a colorless oil. R_f 0.47 (20:1 *n*-hexane/AcOEt); $[\alpha]_D^{23}$ +36.9 (*c* 1.00, $CHCl_3$); IR (neat) 3312, 2949, 2118, 1746, 1458, 1435, 1248, 1173 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.17 (s, 9H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.99 (s, 3H), 1.38 (m, 1H), 1.60 (m, 1H), 1.68 (m, 1H), 1.84−1.93 (m, 3H), 1.94 (t, *J* = 2.6 Hz, 1H), 2.06 (ddd, *J* = 2.6, 11.0, 16.2 Hz, 1H), 2.36 (ddq, *J* = 3.7, 11.0, 6.6 Hz, 1H), 2.62 (ddd, *J* = 2.6, 3.7, 16.2 Hz, 1H), 3.70 (s, 3H), 5.65 (m, 1H), 5.73 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 2.8 (CH_3), 16.2 (CH_3), 19.9 (CH_2), 20.9 (CH_2), 24.5 (CH_2), 24.6 (CH_3), 31.1 (CH_2), 38.4 (CH), 42.4 (C), 51.4 (CH_3), 69.1 (CH), 83.8 (C), 88.0 (C), 126.2 (CH), 133.1 (CH), 175.0 (C); HRMS (DART) *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{31}O_3Si$ 323.2043; found 323.2037.

Methyl [2*R*,2(1*S*),3*R*]-5-Iodo-3-methyl-2-(1-methylcyclohex-2-en-1-yl)-2-(trimethylsilyl)oxyhex-5-enoate (48). *B*-Iodo-9-BBN in hexanes (1.0 M, 2.0 mL, 2.0 mmol) was added to a solution of alkyne **46** (435 mg, 1.35 mmol) in *n*-pentane (14 mL) at 0 °C. After 1 h of stirring at room temperature in the dark, AcOH (230 μL, 4.0 mmol) was added at 0 °C. After 10 min, a mixture of 1 M aqueous $Na_2S_2O_3$ (15 mL) and saturated aqueous $NaHCO_3$ (15 mL) was added, and the resulting mixture was extracted with AcOEt (2 × 60 mL). The combined organic extracts were washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (652 mg), which was purified by column chromatography (silica gel 20 g, 40:1 *n*-hexane/Et_2O) to give vinyl iodide **48** (568 mg, 93%) as a colorless oil. R_f 0.76 (20:1 *n*-hexane/Et_2O); $[\alpha]_D^{26}$ +31.7 (*c* 1.17, $CHCl_3$); IR (neat) 3028, 2972, 2949, 2835, 1746, 1616, 1456, 1435, 1248, 1173 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.19 (s, 9H), 0.67 (d, *J* = 6.7 Hz, 3H), 1.04 (s, 3H), 1.44 (m, 1H), 1.62 (m, 1H), 1.71 (m, 1H), 1.88−2.00 (m, 3H), 2.05 (dd, *J* = 11.3, 13.5 Hz, 1H), 2.44 (ddq, *J* = 3.4, 11.3, 6.7 Hz, 1H), 2.87 (dd, *J* = 3.4, 13.5 Hz, 1H), 3.79 (s, 3H), 5.69 (m, 1H), 5.74 (s, 1H), 5.76 (m, 1H), 6.04 (s, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 2.8 (CH_3), 15.1 (CH_3), 19.9 (CH_2), 24.5 (CH_2), 24.6 (CH_3), 31.1 (CH_2), 38.0 (CH), 42.6 (C), 46.5 (CH_2), 51.5 (CH_3), 88.4 (C), 111.9 (C), 126.3 (CH), 126.8 (CH_2), 133.1 (CH), 175.2 (C); HRMS (DART) *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{32}IO_3Si$ 451.1165; found 451.1150.

Methyl (1*S*,2*R*,3*R*,6*S*)-1,3-Dimethyl-5-methylene-2-(trimethylsilyl)oxybicyclo[4.4.0]dec-7-ene-2-carboxylate (47). A yellow mixture of vinyl iodide **48** (92.5 mg, 0.205 mmol), palladium acetate (4.6 mg, 0.021 mmol), 1,3-bis(diphenylphosphino)propane (10.1 mg, 0.025 mmol), $AgNO_3$ (69.6 mg, 0.410 mmol), and triethylamine (0.11 mL, 0.787 mmol) in DMSO (21 mL) was degassed by bubbling a stream of argon for 5 min, and the mixture was heated at 60 °C for 12 h. After cooling, the resulting black suspension was filtered through a Celite pad, and the filtrate was partitioned between *n*-hexane/AcOEt (5:1, 150 mL) and H_2O (40 mL). The aqueous layer was extracted with *n*-hexane/AcOEt (5:1, 2 × 100 mL), and the combined organic extracts were washed with brine (50 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (72.3 mg), which was purified by flash column chromatography (silica gel 40 g, 40:1 *n*-hexane/Et_2O) to give diene **47** (58.3 mg, 88%) as a colorless oil. R_f 0.64 (20:1 *n*-hexane/Et_2O); $[\alpha]_D^{27}$ −126.2 (*c* 1.06, $CHCl_3$); IR (neat) 3022, 2953, 2843, 1735, 1437 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.09 (s, 9H), 0.86 (s, 3H), 0.95 (d, *J* = 6.7 Hz, 3H), 1.31 (m, 1H), 1.60 (dt, *J* = 6.0, 12.9 Hz, 1H), 1.91 (m, 1H), 1.96 (dd, *J* = 8.5, 15.0 Hz, 1H), 2.03 (dt, *J* = 18.3, 6.0 Hz, 1H), 2.32 (ddq, *J* = 8.3, 15.0, 6.7 Hz, 1H), 2.54 (m, 1H), 2.57 (m, 1H), 3.71 (s, 3H), 4.63 (dd, *J* = 1.9, 4.0 Hz, 1H), 4.76 (m, 1H), 5.52 (dddd, *J* = 1.5, 2.6, 4.6, 10.0 Hz, 1H), 5.77 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 1.9 (CH_3), 16.9 (CH_3), 21.3 (CH_2), 23.1 (CH_2), 24.5 (CH_3), 33.8 (CH_2), 38.5 (CH), 42.2 (C), 46.5 (CH), 51.0 (CH_3), 85.9 (C), 109.5 (CH_2), 127.11 (CH), 127.14 (CH), 147.6 (C), 174.0 (C); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{18}H_{30}O_3Si$ 322.1964; found 322.1966.

Methyl (1*R*,4*R*,5*R*,6*S*)-4,6-Dimethyl-2-oxo-5-(trimethylsilyl)-oxybicyclo[4.4.0]decane-5-carboxylate (51). Lindlar catalyst (51.3 mg, 100 wt %) was added to a solution of diene **47** (51.3 mg, 0.159 mmol) in MeOH (3 mL), and the mixture was vigorously stirred for 6 h under hydrogen (1 atm). The catalyst was filtered through a Celite pad, and the filtrate was evaporated in vacuo. The crude product **49** (49.2 mg) was used without further purification.

To a solution of crude alkene **49** (49.2 mg) and phenylboronic acid (58.2 mg, 0.477 mmol) in CH_2Cl_2 (3 mL) was added a 0.16 M solution of OsO_4 in THF (0.15 mL, 0.024 mmol) followed by NMO (55.9 mg, 0.477 mmol). After 72 h of stirring, the reaction was quenched with 1 M aqueous $Na_2S_2O_3$ (5 mL), and the resulting mixture was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product **50** (190 mg), which was used without further purification.

$NaIO_4$ (170 mg, 0.795 mmol) was added to a solution of crude phenylboronate **50** (190 mg) in THF/pH 7 phosphate buffer (1:1, 3 mL). After 3 h of stirring at 50 °C, the reaction was quenched with 1 M aqueous $Na_2S_2O_3$ (15 mL), and the resulting mixture was extracted with AcOEt (2 × 40 mL). The combined organic extracts were washed

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with brine (15 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (133 mg), which was purified by flash column chromatography (silica gel 10 g, 10:1 *n*-hexane/AcOEt) to give ketone **51** (36.9 mg, 71% for three steps) as a pale-yellow oil. R_f 0.33 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{27}$ −65.3 (*c* 0.95, $CHCl_3$); IR (neat) 2951, 1737, 1714, 1462, 1437, 1250 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.11 (s, 9H), 0.87 (d, *J* = 6.7 Hz, 3H), 0.94 (s, 3H), 1.07 (ddd, *J* = 3.9, 7.7, 13.9 Hz, 1H), 1.28−1.36 (m, 2H), 1.41 (m, 1H), 1.53 (m, 1H), 1.67 (m, 1H), 1.75 (ddd, *J* = 3.9, 8.7, 13.9 Hz, 1H), 1.94 (m, 1H), 2.17 (dd, *J* = 5.5, 15.7 Hz, 1H), 2.17 (m, 1H), 2.26 (dd, *J* = 11.1, 15.7 Hz, 1H), 2.62 (ddq, *J* = 5.5, 11.1, 6.7 Hz, 1H), 3.68 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 2.6 (CH_3), 17.7 (CH_3), 21.7 (CH_2), 23.1 (CH_2), 24.5 (CH_2), 26.3 (CH_3), 32.2 (CH_2), 35.2 (CH), 43.1 (CH_2), 43.4 (C), 51.5 (CH_3), 55.4 (CH), 86.5 (C), 173.5 (C), 213.3 (C); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{17}H_{30}O_4Si$ 326.1913; found 326.1909.

Methyl (1*S*,4*R*,5*R*,6*S*)-4,6-Dimethyl-2-oxo-5-(trimethylsilyl)-oxybicyclo[4.4.0]decane-5-carboxylate (52). A 2.0 M solution of NaOMe in MeOH (0.01 mL, 0.02 mmol) was added to a solution of *cis*-decalone **51** (30.1 mg, 92.2 μmol) in THF (1.9 mL) at 0 °C. After 30 min of stirring, the reaction was quenched with saturated aqueous NH_4Cl (5 mL), and the resulting mixture was extracted with AcOEt (2 × 30 mL). The combined organic extracts were washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (34.8 mg), which was purified by column chromatography (silica gel 10 g, 10:1 *n*-hexane/AcOEt) to give *trans*-decalone **52** (25.4 mg, 85%) as a pale-yellow solid. R_f 0.42 (5:1 *n*-hexane/AcOEt); mp 88−89 °C (colorless prisms from MeOH); $[\alpha]_D^{27}$ −25.2 (*c* 1.15, $CHCl_3$); IR (neat) 2951, 1738, 1713, 1462, 1252 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.22 (s, 9H), 0.85 (d, *J* = 6.5 Hz, 3H), 0.90 (s, 3H), 0.98 (m, 1H), 1.08 (tq, *J* = 4.0, 13.3 Hz, 1H), 1.31 (tq, *J* = 3.9, 13.5 Hz, 1H), 1.40 (dq, *J* = 3.7, 13.5 Hz, 1H), 1.53 (m, 1H), 1.67 (m, 1H), 1.72−1.78 (m, 2H), 2.15 (dd, *J* = 5.3, 14.0 Hz, 1H), 2.21 (dd, *J* = 12.6, 14.0 Hz, 1H), 2.72 (ddq, *J* = 5.3, 12.6, 6.5 Hz, 1H), 2.76 (dd, *J* = 3.7, 12.6 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 2.7 (CH_3), 15.6 (CH_3), 17.7 (CH_3), 20.3 (CH_2), 21.2 (CH_2), 24.8 (CH_2), 32.4 (CH_2), 35.9 (CH), 45.2 (CH_2), 46.6 (C), 50.0 (CH), 51.6 (CH_3), 86.0 (C), 173.0 (C), 211.8 (C); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{17}H_{30}O_4Si$ 326.1913; found 326.1919.

Methyl (1*R*,2*R*,4*R*,5*R*,6*S*)-4,6-Dimethyl-5-(trimethylsilyl)-oxyspiro[bicyclo[4.4.0]dec-9-en-2,2′-oxirane]-5-carboxylate (53). *m*-CPBA (ca. 70%, 7.6 mg, ca. 31.0 μmol) was added to a solution of 1,4-diene **47** (10.0 mg, 31.0 μmol) in CH_2Cl_2 (1.0 mL) at 0 °C. After 3 h of stirring, the reaction was quenched with a mixture of 1 M aqueous $Na_2S_2O_3$ (3 mL) and saturated aqueous $NaHCO_3$ (3 mL), and the resulting mixture was extracted with AcOEt (2 × 30 mL). The combined organic extracts were washed with brine (6 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (12.7 mg), which was purified by column chromatography (silica gel 5 g, 20:1 *n*-hexane/AcOEt) to give epoxide **53** (9.1 mg, 87%) as a white amorphous solid. R_f 0.38 (10:1 *n*-hexane/AcOEt); $[\alpha]_D^{27}$ −119.6 (*c* 1.34, $CHCl_3$); IR (neat) 3021, 2953, 2884, 2843, 1738, 1647, 1458, 1435, 1248 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.11 (s, 9H), 0.89 (s, 3H), 0.95 (d, *J* = 6.6 Hz, 3H), 1.29 (dd, *J* = 9.7, 13.6 Hz, 1H), 1.34 (m, 1H), 1.72 (dt, *J* = 5.6, 12.0 Hz, 1H), 1.90 (m, 1H), 2.06 (dd, *J* = 7.6, 13.6 Hz, 1H), 2.09 (m, 1H), 2.26 (m, 1H), 2.46 (ddq, *J* = 7.6, 9.7, 6.6 Hz, 1H), 2.48 (d, *J* = 5.1 Hz, 1H), 2.80 (d, *J* = 5.1 Hz, 1H), 3.73 (s, 3H), 5.42 (dddd, *J* = 1.3, 2.6, 4.2, 10.1 Hz, 1H), 5.77 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 2.2 (CH_3), 17.4 (CH_3), 22.6 (CH_2), 23.0 (CH_3), 25.6 (CH_2), 32.4 (CH), 37.1 (CH_2), 41.9 (C), 43.7 (CH), 51.1 (CH_3), 54.0 (CH_2), 58.6 (C), 86.1 (C), 124.4 (CH), 128.8 (CH), 173.4 (C); HRMS (EI) *m*/*z* $[M]^+$ calcd for $C_{18}H_{30}O_4Si$ 338.1913; found 338.1910.

Methyl (1*R*,2*S*,7*R*,8*S*,10*R*)-8-(Hydroxymethyl)-2,10-dimethyl-11-oxatricyclo[6.2.1.0^{2,7}]undec-5-ene-1-carboxylate (54). A solution of epoxide **53** (14.1 mg, 41.9 μmol) in DMSO/4 M aqueous NaOH (5:2, 0.7 mL) was heated at 80 °C for 2 h. After cooling, the reaction mixture was partitioned between AcOEt (20 mL) and H_2O (20 mL), and the aqueous layer was extracted with AcOEt (20 mL). The combined organic extracts were washed with brine (20 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (15.1 mg), which was purified by column chromatography (silica gel 10 g, 2:3 *n*-hexane/AcOEt) to give alcohol **54** (10.0 mg, 90%) as a colorless oil. R_f 0.50 (1:1 *n*-hexane/AcOEt); $[\alpha]_D^{24}$ −54.9 (*c* 0.48, $CHCl_3$); IR (neat) 3493, 3024, 2955, 2878, 1755, 1732, 1458, 1437, 1339, 1321, 1290, 1248, 1109, 1090, 1057 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.94 (d, *J* = 7.0 Hz, 3H), 1.20 (m, 1H), 1.25 (s, 3H), 1.57 (dd, *J* = 4.3, 11.7 Hz, 1H), 1.64 (dt, *J* = 5.3, 11.8 Hz, 1H), 1.78 (br, 1H), 1.84 (dd, *J* = 8.4, 11.7 Hz, 1H), 1.87 (m, 1H), 1.89−1.99 (m, 2H), 2.73 (ddq, *J* = 4.3, 8.4, 7.0 Hz, 1H), 3.72 (d, *J* = 12.2 Hz, 1H), 3.78 (s, 3H), 3.95 (d, *J* = 12.2 Hz, 1H), 5.56 (d, *J* = 10.0 Hz, 1H), 5.90 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.7 (CH_3), 20.58 (CH_3), 20.60 (CH_2), 28.9 (CH_2), 34.8 (CH), 41.9 (CH_2), 46.8 (C), 51.5 (CH_3), 52.0 (CH), 62.4 (CH_2), 87.8 (C), 94.0 (C), 123.9 (CH), 129.2 (CH), 170.6 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{22}O_4Na$ 289.1416; found 289.1434.

Methyl (1*S*,2*R*,3*R*,6*S*)-2-Hydroxy-1,3-dimethyl-5-methylenebicyclo[4.4.0]dec-7-ene-2-carboxylate (55). Bu_4NF in THF (1.0 M, 0.15 mL, 0.15 mmol) was added to a solution of TMS ether **47** (22.8 mg, 0.071 mmol) in THF (1 mL) at 0 °C. After 2 h of stirring, the mixture was partitioned between AcOEt (30 mL) and H_2O (5 mL), and the aqueous layer was extracted with AcOEt (30 mL). The combined organic extracts were washed with brine (5 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (23.9 mg), which was purified by column chromatography (silica gel 5 g, 10:1 *n*-hexane/AcOEt) to give tertiary alcohol **55** (17.7 mg, 99%) as a colorless oil. R_f 0.41 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{23}$ −164.7 (*c* 0.53, $CHCl_3$); IR (neat) 3536, 2936, 1721, 1458, 1375, 1252, 1234 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (d, *J* = 6.3 Hz, 3H), 0.95 (s, 3H), 1.36 (dt, *J* = 6.8, 13.6 Hz, 1H), 1.79 (dt, *J* = 6.4, 13.6 Hz, 1H), 2.02 (m, 1H), 2.11 (m, 1H), 2.27−2.36 (m, 3H), 2.63 (m, 1H), 3.15 (s, 1H), 3.79 (s, 3H), 4.73 (s, 1H), 4.85 (s, 1H), 5.35 (m, 1H), 5.83 (ddd, *J* = 3.2, 6.3, 9.8 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 15.9 (CH_3), 24.2 (CH_2), 25.0 (CH_3), 28.2 (CH_2), 34.3 (CH), 36.7 (CH_2), 39.8 (C), 48.8 (CH), 52.0 (CH_3), 83.3 (C), 110.1 (CH_2), 128.1 (CH), 128.8 (CH), 148.2 (C), 175.6 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{22}O_3Na$ 273.1467; found 273.1452.

Methyl (1*S*,2*R*,3*R*,6*S*)-2-(*tert*-Butoxycarbonyl)oxy-1,3-dimethyl-5-methylenebicyclo[4.4.0]dec-7-ene-2-carboxylate (56). KHMDS in toluene (0.5 M, 1.10 mL, 0.55 mmol) was added to a solution of tertiary alcohol **55** (70.9 mg, 0.283 mmol) in THF (2 mL) at −78 °C. After 30 min of stirring, di-*tert*-butyl dicarbonate (185 mg, 0.85 mmol) in THF (1 mL) was added, and the mixture was stirred at 0 °C for 30 min. The reaction was quenched with saturated aqueous NH_4Cl (15 mL), and the resulting mixture was extracted with AcOEt (2 × 50 mL). The combined organic extracts were washed with brine (15 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (291 mg), which was purified by column chromatography (silica gel 30 g, 15:1 *n*-hexane/AcOEt) to give carbonate **56** (95.5 mg, 96%) as a colorless oil. R_f 0.40 (10:1 *n*-hexane/AcOEt); $[\alpha]_D^{28}$ −98.8 (*c* 1.13, $CHCl_3$); IR (neat) 2978, 1740, 1458, 1369, 1290, 1257, 1163 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.92 (s, 3H), 0.99 (d, *J* = 7.2 Hz, 3H), 1.47 (s, 9H), 1.66−1.75 (m, 2H), 1.94−2.03 (m, 2H), 2.08 (dd, *J* = 4.1, 13.8 Hz, 1H), 2.69 (d, *J* = 4.0 Hz, 1H), 3.02 (ddq, *J* = 4.1, 5.2, 7.2 Hz, 1H), 3.11 (dd, *J* = 5.2, 13.8 Hz, 1H), 3.72 (s, 3H), 4.77 (s, 1H), 4.89 (s, 1H), 5.56 (m, 1H), 5.74 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 17.1 (CH_3), 20.6 (CH_3), 23.6 (CH_2), 24.4 (CH_2), 27.7 (CH_3), 34.1(CH), 39.2 (CH_2), 41.9 (C), 46.3 (CH), 51.4 (CH_3), 81.6 (C), 88.4 (C), 112.3 (CH_2), 126.8 (CH), 127.0 (CH), 146.3 (C), 152.4 (C), 171.9 (C); HRMS (ESI) *m*/*z* $[M + K]^+$ calcd for $C_{20}H_{30}O_5K$ 389.1730; found 389.1748.

Methyl (1*R*,2*R*,4*R*,5*R*,6*S*)-5-(*tert*-Butoxycarbonyl)oxy-4,6-dimethylspiro[bicyclo[4.4.0]dec-9-en-2,2′-oxirane]-5-carboxylate (57). *m*-CPBA (ca. 70%, 60.0 mg, ca. 0.243 mmol) was added to a solution of 1,4-diene **56** (84.6 mg, 0.241 mmol) in CH_2Cl_2 (12 mL) at −40 °C. After 40 h of stirring at −20 °C, the reaction was quenched with a mixture of 1 M aqueous $Na_2S_2O_3$ (10 mL) and saturated aqueous $NaHCO_3$ (10 mL), and the resulting mixture was extracted

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with AcOEt (2 × 50 mL). The combined organic extracts were washed with brine (20 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (120 mg), which was purified by column chromatography (silica gel 15 g, 20:1 → 10:1 → 5:1 *n*-hexane/AcOEt) to give a mixture of epoxides **57** and **58** (44.4 mg, 50%, **57**:**58** = 5.4:1) as a colorless oil along with recovered diene **56** (27.1 mg, 32%, colorless oil) and bis-epoxide (11.1 mg, 12%, white solid).

This sequence was repeated, employing recovered **56** (27.1 mg, 77.3 μmol), *m*-CPBA (ca. 70%, 19.1 mg, ca. 77.5 μmol), and CH_2Cl_2 (4 mL). The crude product (35.6 mg) was purified by column chromatography (silica gel 5 g, 20:1 → 10:1 → 5:1 *n*-hexane/AcOEt) to give a mixture of epoxides **57** and **58** (16.5 mg, 58%, **57**:**58** = 5.4:1) as a colorless oil along with recovered diene **56** (9.7 mg, 32%, colorless oil) and bis-epoxide (2.5 mg, 9%, white solid). Separation of epoxides **57** and **58** by flash column chromatography (silica gel 120 g, $CHCl_3$) yielded the desired epoxide **57** (51.3 mg, 58%) as a colorless oil and **58** (9.4 mg, 11%) as a white solid. Data for **57**: R_f 0.44 (5:1 *n*-hexane/AcOEt), 0.24 ($CHCl_3$); $[\alpha]_D^{25}$ −143.6 (*c* 1.36, $CHCl_3$); IR (neat) 2978, 2949, 1748, 1458, 1292, 1258, 1161 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.96 (s, 3H), 1.16 (d, *J* = 7.0 Hz, 3H), 1.46 (s, 9H), 1.47 (br, 1H), 1.67 (m, 1H), 1.99−2.00 (m, 2H), 2.19−2.32 (br, 3H), 2.59 (d, *J* = 5.0 Hz, 1H), 2.87 (d, *J* = 5.0 Hz, 1H), 2.97 (m, 1H), 3.75 (s, 3H), 5.45 (m, 1H), 5.77 (d, *J* = 10.0 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.2 (CH_3), 23.6 (CH_2), 27.7 (CH_3), 33.4 (CH), 36.5 (C), 51.4 (CH_3), 52.7 (C), 81.7 (C), 88.2 (C), 124.4 (CH), 129.2 (CH), 152.4 (C), 170.5 (C), other peaks too broad to detect; HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{30}O_6Na$ 389.1940; found 389.1938.

Data for methyl (1*S*,2*R*,3*R*,6*S*,7*S*,8*R*)-2-(*tert*-butoxycarbonyl)oxy-7,8-epoxy-1,3-dimethyl-5-methylenebicyclo[4.4.0]decane-2-carboxylate (**58**): R_f 0.44 (5:1 *n*-hexane/AcOEt), 0.34 ($CHCl_3$); $[\alpha]_D^{25}$ −60.8 (*c* 0.38, $CHCl_3$); IR (neat) 2982, 2955, 1748, 1456, 1283, 1258, 1140 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.80 (s, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 1.15 (dt, *J* = 6.8, 14.2 Hz, 1H), 1.45 (s, 9H), 1.89 (m, 2H), 2.12 (dd, *J* = 3.9, 13.9 Hz, 1H), 2.18−2.25 (m, 2H), 2.27 (s, 1H), 2.45 (m, 1H), 2.99 (d, *J* = 4.0 Hz, 1H), 3.26 (m, 1H), 3.76 (s, 3H), 4.88 (s, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.9 (CH_3), 23.1 (CH_2), 26.0 (CH_3), 27.7 (CH_3), 30.8 (CH_2), 36.0 (CH), 37.0 (CH_2), 38.2 (C), 51.5 (CH_3), 52.6 (CH), 54.7 (CH), 56.8 (CH), 81.8 (C), 88.8 (C), 111.8 (CH_2), 145.6 (C), 151.6 (C), 168.9 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{30}O_6Na$ 389.1940; found 389.1940.

Data for methyl (1*S*,2*R*,4*R*,5*R*,6*S*,9*R*,10*S*)-5-(*tert*-butoxycarbonyl)-oxy-9,10-epoxy-4,6-dimethylspiro[bicyclo[4.4.0]decan-2,2′-oxirane]-5-carboxylate (bis-epoxide): R_f 0.18 (5:1 *n*-hexane/AcOEt); mp 140−141 °C (colorless prisms from *n*-hexane); $[\alpha]_D^{25}$ −77.9 (*c* 0.80, $CHCl_3$); IR (neat) 2982, 2955, 1746, 1458, 1285, 1261, 1144 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.00 (s, 3H), 1.04 (d, *J* = 6.7 Hz, 3H), 1.09 (dq, *J* = 14.5, 1.5 Hz, 1H), 1.14 (m, 1H), 1.33 (m, 1H), 1.46 (s, 9H), 1.84 (m, 1H), 1.89 (m, 1H), 2.10 (t, *J* = 14.5 Hz, 1H), 2.23 (m, 1H), 2.69 (d, *J* = 4.5 Hz, 1H), 2.78 (m, 1H), 2.82 (d, *J* = 4.5 Hz, 1H), 3.09 (d, *J* = 4.2 Hz, 1H), 3.28 (m, 1H), 3.78 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.8 (CH_3), 22.7 (CH_2), 26.2 (CH_3), 27.7 (CH_3), 30.7 (CH_2), 33.0 (CH), 35.0 (CH_2), 38.4 (C), 50.3 (CH), 50.6 (CH_2), 51.6 (CH_3), 54.3 (CH), 54.5 (CH), 58.5 (C), 81.9 (C), 88.6 (C), 151.5 (C), 168.6 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{30}O_7Na$ 405.1889; found 405.1873.

Methyl (1*R*,2*S*,7*R*,8*S*,12*R*)-8-(Hydroxymethyl)-2,12-dimethyl-10-oxo-9,11-dioxatricyclo[6.3.2.0^{2,7}]tridec-5-ene-1-carboxylate (59). A 0.2 M solution of $BF_3{\cdot}OEt_2$ in CH_2Cl_2 (0.20 mL, 40.0 μmol) was added to a solution of epoxide **57** (11.9 mg, 32.5 μmol) in CH_2Cl_2 (0.7 mL) at −78 °C. After 30 min of stirring at −60 °C, the reaction was quenched with Et_3N (10 μL), and the resulting mixture was partitioned between AcOEt (40 mL) and saturated aqueous $NaHCO_3$ (15 mL). The aqueous layer was extracted with AcOEt (40 mL), and the combined organic extracts were washed with brine (15 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (12.1 mg), which was purified by column chromatography (silica gel 5 g, 1:1 *n*-hexane/AcOEt) to give cyclic carbonate **59** (7.5 mg, 74%) as a white solid. R_f 0.45 (1:2 *n*-hexane/AcOEt); mp 124−125 °C (colorless prisms from 3:1 *n*-hexane/$CHCl_3$); $[\alpha]_D^{24}$ −66.0 (*c* 1.20, $CHCl_3$); IR (neat) 3462, 2926, 1738, 1458, 1250, 1113, 1090, 1049 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.06 (s, 3H), 1.14 (d, *J* = 6.7 Hz, 3H), 1.62 (m, 1H), 1.69 (ddd, *J* = 5.4, 10.2, 13.8 Hz, 1H), 1.80 (dd, *J* = 8.1, 15.8 Hz, 1H), 1.98−2.04 (m, 2H), 2.15 (m, 1H), 2.23 (m, 1H), 2.43 (dd, *J* = 9.8, 15.8 Hz, 1H), 2.70 (ddq, *J* = 8.1, 9.8, 6.7 Hz, 1H), 3.61 (dd, *J* = 7.0, 11.1 Hz, 1H), 3.73 (dd, *J* = 3.6, 11.1 Hz, 1H), 3.81 (s, 3H), 5.59 (m, 1H), 6.02 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 16.9 (CH_3), 21.5 (CH_2), 24.5 (CH_3), 26.7 (CH_2), 30.5 (CH), 37.5 (CH_2), 39.9 (C), 44.2 (CH), 52.5 (CH_3), 66.4 (CH_2), 84.9 (C), 92.8 (C), 121.3 (CH), 130.8 (CH), 149.5 (C), 168.3 (C); HRMS (EI) *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{22}O_6Na$ 333.1314; found 333.1328.

Methyl (1*S*,2*R*,3*R*,5*S*,6*R*)-2,5-Dihydroxy-5-(hydroxymethyl)-1,3-dimethylbicyclo[4.4.0]dec-7-ene-2-carboxylate (60). A 0.9 M solution of NaOMe in MeOH (0.76 mL, 0.69 mmol) was added to a solution of cyclic carbonate **59** (43.0 mg, 139 μmol) in MeOH (1.4 mL) at 0 °C. After 5 h of stirring at room temperature, the reaction was quenched with saturated aqueous NH_4Cl (10 mL), and the resulting mixture was extracted with AcOEt (2 × 40 mL). The combined organic extracts were washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (39.0 mg), which was purified by column chromatography (silica gel 15 g, 1:2 *n*-hexane/AcOEt) to give triol **60** (36.9 mg, 93%) as a white solid. R_f 0.42 (1:2 *n*-hexane/AcOEt); mp 139−140 °C (colorless needles from 3:1 *n*-hexane/$CHCl_3$); $[\alpha]_D^{27}$ −185.8 (*c* 0.96, $CHCl_3$); IR (neat) 3397, 3024, 2930, 1719, 1437, 1250, 1026 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.90 (s, 3H), 0.96 (d, *J* = 6.4 Hz, 3H), 1.28 (dd, *J* = 5.0, 12.4 Hz, 1H), 1.47 (dd, *J* = 10.5, 15.0 Hz, 1H), 1.84 (m, 1H), 1.93−1.98 (m, 2H), 2.06 (dt, *J* = 12.4, 5.3 Hz, 1H), 2.13 (dd, *J* = 8.6, 15.0 Hz, 1H), 2.15 (m, 1H), 2.25 (ddq, *J* = 8.6, 10.5, 6.4 Hz, 1H), 3.47 (dd, *J* = 4.4, 10.5 Hz, 1H), 3.60 (d, *J* = 10.5 Hz, 1H), 3.80 (s, 3H), 3.88 (s, 1H), 4.45 (s, 1H), 5.65 (m, 1H), 5.91 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 16.3 (CH_3), 21.9 (CH_2), 23.9 (CH_3), 25.3 (CH_2), 29.6 (CH), 39.8 (C), 40.6 (CH_2), 45.5 (CH), 52.2 (CH_3), 69.3 (CH_2), 73.1 (C), 82.5 (C), 124.3 (CH), 128.8 (CH), 175.1 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{24}O_5Na$ 307.1521; found 307.1507.

Methyl (1*S*,2*R*,5*R*,6*R*)-2-Hydroxy-1,3-dimethyl-5-oxobicyclo-[4.4.0]dec-7-ene-2-carboxylate (61). $Pb(OAc)_4$ (14.8 mg, 33.4 μmol) was added to a solution of triol **60** (7.9 mg, 27.8 μmol) in CH_2Cl_2 (0.6 mL) at 0 °C. After 5 min of stirring, the reaction was quenched with saturated aqueous $NaHCO_3$ (10 mL), and the resulting mixture was extracted with AcOEt (2 × 30 mL). The combined organic extracts were washed with brine (10 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (11.6 mg), which was purified by column chromatography (Wako gel 5 g, 3:1 *n*-hexane/AcOEt) to give ketone **61** (6.6 mg, 94%) as a white solid. R_f 0.41 (2:1 *n*-hexane/AcOEt); mp 144−146 °C (colorless needles from 20:1 *n*-hexane/$CHCl_3$); $[\alpha]_D^{25}$ −268.7 (*c* 0.87, $CHCl_3$); IR (neat) 3391, 2930, 2855, 1717, 1433, 1265, 1163, 1045 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.00 (d, *J* = 6.5 Hz, 3H), 1.11 (s, 3H), 1.25 (ddd, *J* = 3.1, 5.0, 12.8 Hz, 1H), 1.75 (ddd, *J* = 5.4, 11.5, 12.8 Hz, 1H), 1.97 (m, 1H), 2.14 (m, 1H), 2.22 (dd, *J* = 10.8, 17.4 Hz, 1H), 2.45 (dd, *J* = 7.3, 17.4 Hz, 1H), 2.78 (m, 1H), 2.83 (ddq, *J* = 7.3, 10.8, 6.5 Hz, 1H), 3.09 (s, 1H), 3.83 (s, 3H), 5.64 (m, 1H), 5.94 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 15.7 (CH_3), 22.1 (CH_2), 24.0 (CH_3), 26.0 (CH_2), 32.2 (CH), 43.6 (C), 43.7 (CH_2), 52.3 (CH_3), 53.9 (CH), 81.4 (C), 122.6 (CH), 128.8 (CH), 174.8 (C), 210.7 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{20}O_4Na$ 275.1259; found 275.1265.

Methyl (1*R*,2*S*,7*R*,8*R*,10*R*)-8-(*tert*-Butyldimethylsilyl)oxy-2,10-dimethyl-11-oxatricyclo[6.2.1.0^{2,7}]undec-5-ene-1-carboxylate (62). To a cooled solution (−78 °C) of hydroxy ketone **61** (3.4 mg, 13.5 μmol) in CH_2Cl_2 (1 mL) was added Et_3N (10 μL, 72 μmol) followed by a 0.5 M solution of TBSOTf in CH_2Cl_2 (60 μL, 30 μmol). After 15 min of stirring at 0 °C, the reaction was quenched with saturated aqueous $NaHCO_3$ (10 mL), and the resulting mixture was extracted with AcOEt (2 × 30 mL). The combined organic extracts were washed with brine (10 mL) and dried over anhydrous Na_2SO_4. Filtration and evaporation in vacuo furnished the crude product (6.8

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mg), which was purified by flash column chromatography (silica gel 3 g, 30:1 *n*-hexane/AcOEt) to give lactol TBS ether **62** (4.6 mg, 94%) as a colorless oil. R_f 0.50 (5:1 *n*-hexane/AcOEt); $[\alpha]_D^{23}$ −67.7 (*c* 1.07, $CHCl_3$); IR (neat) 3032, 2953, 2930, 2857, 1763, 1732, 1462, 1335, 1298, 1107, 1069, 920, 833 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.17 (s, 3H), 0.18 (s, 3H), 0.91 (s, 9H), 0.95 (d, *J* = 6.9 Hz, 3H), 1.18 (m, 1H), 1.21 (s, 3H), 1.28 (dd, *J* = 4.4, 11.7 Hz, 1H), 1.59 (m, 1H), 1.81−1.88 (m, 2H), 1.94 (m, 1H), 2.08 (dd, *J* = 8.3, 11.7 Hz, 1H), 2.61 (ddq, *J* = 4.4, 8.3, 6.9 Hz, 1H), 3.73 (s, 3H), 5.73 (d, *J* = 10.3 Hz, 1H), 5.90 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ −3.2 (CH_3), −3.0 (CH_3), 18.1 (C), 19.0 (CH_3), 20.6 (CH_2), 21.2 (CH_3), 25.9 (CH_3), 29.6 (CH_2), 34.7 (CH), 46.40 (CH), 46.43 (CH_2), 51.2 (CH_3), 52.9 (C), 88.7 (C), 107.6 (C), 125.7 (CH), 128.0 (CH), 170.6 (C); HRMS (ESI) *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{34}O_4SiNa$ 389.2124; found 389.2117.

■ ASSOCIATED CONTENT

Supporting Information

^1H and ^{13}C NMR spectra for all new compounds and X-ray crystallographic data for iodolactone **39b** (CIF). 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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(28) The Novozym 435-catalyzed optical resolution/hydrolysis cycle was repeated twice to give allyl alcohol **22** in 35% yield with >99% ee.
(29) Although distinct peaks assignable to the minor isomer **23** could not be detected by either ^{1}H or ^{13}C NMR spectroscopy, the formation of isomer **24c** ambiguously suggested contamination of **23**.
(30) The ratio was determined by HPLC analysis (column, Zorbax Sil, 4.6 mm × 250 mm; eluent, 60:1 *n*-hexane/THF; flow rate, 1.5 mL/min; t_R = 6.6 min for major isomer **25**, t_R = 7.4 min for the isomer derived from **24b**, t_R = 7.8 min for the isomer derived from **24c**) after conversion to the corresponding methyl esters. After esterification, the rearranged products were difficult to separate.
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