JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

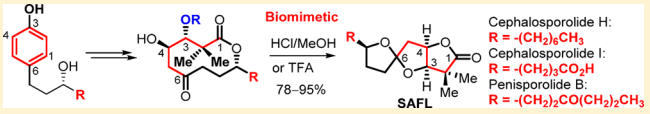
Total Synthesis of Purported Cephalosporolides H and I, Penisporolide B, and Their Stereoisomers

Jian Wang and Rongbiao Tong*

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China

Supporting Information

ABSTRACT: Development of a unified, bioinspired synthetic strategy to access four possible diastereomers of unique 2,2-dimethyl-[5,5]-spiroacetal-cis-fused-γ-lactone (Me_2SAFL) is reported, featuring pyridinium chlorochromate (PCC)-promoted oxidative ring expansion of β-hydroxy cyclic ethers and dehydrative ring-contraction rearrangement of 10-membered lactones. Synthetic utility of this strategy was demonstrated by total syntheses of 12 Me_2SAFLs, corresponding to the purported cephalosporolide H (CesH), cephalosporolide I (CesI), and penisporolide B (PenB) and their possible diastereomers. Comprehensive NMR data analysis suggested that the tricyclic Me_2SAFL core of CesH, CesI, and PenB should be revised to the same relative (3*R**, 4*R**, 6*S**, 9*R**) configuration and that the side chains required an unknown constitutional structure revision.



INTRODUCTION

Since cephalosporolides E and F (CesE and CesF) were first reported in 1985 by Hanson and co-workers[1] with X-ray crystallography substantiating the unprecedented molecular structure of CesE, the unique [5,5]-spiroacetal-cis-fused-γ-lactone (SAFL) of CesE and CesF has been found as the core skeleton in several newly isolated natural products including cephalosporolides H and I (CesH and CesI),[2] penisporolides A and B (PenA and PenB),[3] and ascospiroketal B (AskB)[4] (Figure 1). Although the biological activities of CesE, CesF, and AskB have not been reported and CesH, CesI, PenA, PenB showed no or moderate inhibition against xanthine oxidase (XOD) and 3α-hydroxysteroid dehydrogenase (3α-HSD),[2,3]

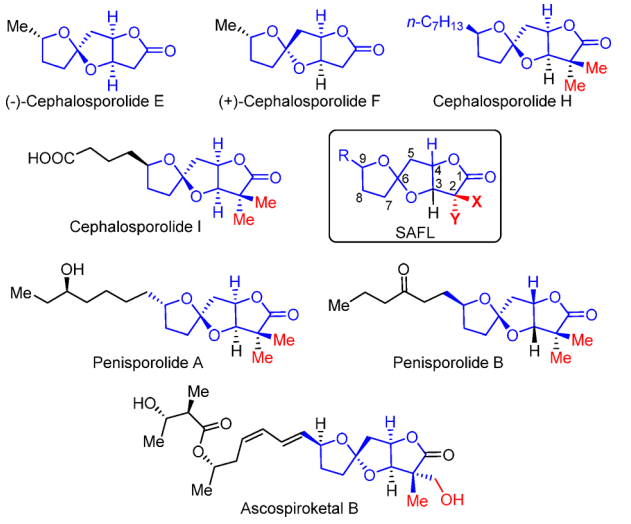


Figure 1. Selected natural products containing [5,5]-spiroacetal-cis-fused-γ-lactone (SAFL) core.

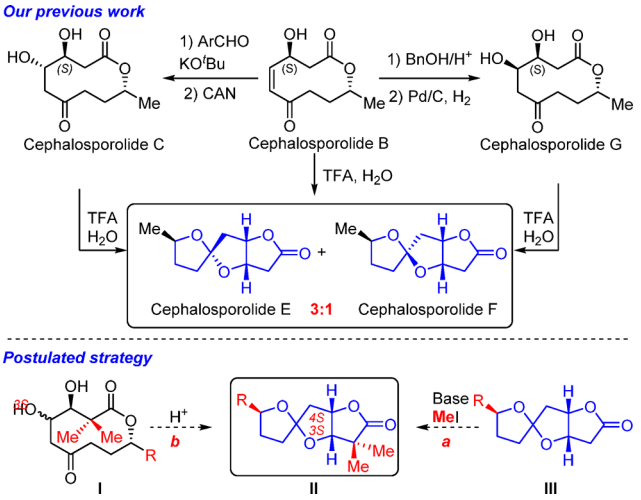
the unprecedented unique tricyclic SAFL structure of this family still aroused intense interest in the community, culminating in eight total syntheses of CesE and CesF achieved by Ramanaet al.,[5a] Chang and Britton,[5b] Tlais and Dudley,[5c] Brimble et al.,[5d] Fernandes and co-workers,[5e,f] Sartillo-Piscil and co-workers,[5g] and Tong and co-workers.[5h] In addition, total synthesis of the proposed structure of CesH containing a 2,2-dimethyl-[5,5]-spiroacetal-cis-fused-γ-lactone (Me_2SAFL) was accomplished independently by Tlais and Dudley,[5c,6a] Fernandes and Halle,[6b] and Du and co-workers.[6c] All these previous synthetic studies revealed that the purported structure for CesH (and CesI)[6d] was incorrect. Notably, Dudley's research group reported the synthesis of four possible stereostructure candidates for CesH, while the groups of both Fernandes and Du synthesized only two of the four diastereomers. Without authentic spectra/samples or X-ray crystallography, the molecular structure and relative configurations of CesH and CesI remain unknown. To shed more light on the structures of this class of molecules and expand our biomimetic strategy[5h] for the synthesis of SAFL-containing natural products, we initiated this project directed to the collective synthesis of four possible stereostructures for CesH, CesI, and PenB, with an expectation that the correct structure for these Me_2SAFL-containing natural products could be identified among these diastereomers.

One obvious structural difference of CesH/I and PenA/B from CesE/F arises from the C2 dimethylation, which poses a synthetic challenge. On the basis of our previous synthetic studies of CesE and CesF,[5h] two approaches to C2 dimethylation of SAFLs were postulated (Scheme 1). The first approach involved a late-stage C2 dimethylation of the parent SAFLs (**III**; method a in Scheme 1), and the second was

Received: April 10, 2016
Published: May 3, 2016

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

Scheme 1. Postulated Unified Strategies to Cephalosporolides H and I and Penisporolide B

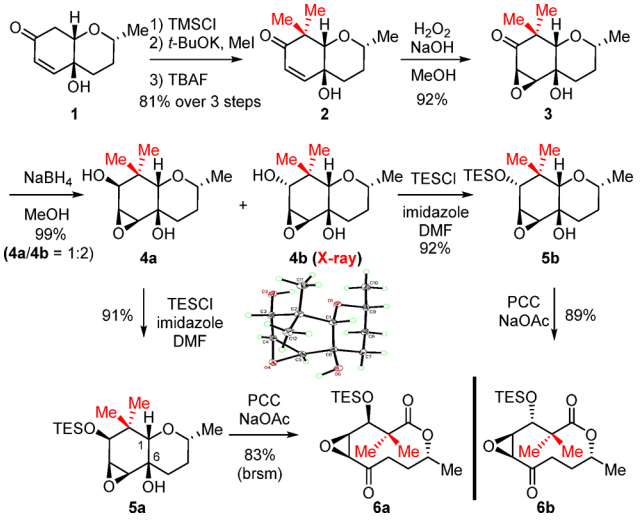


to explore ring contraction rearrangement of the corresponding 2,2-dimethyl decanolide **I** to 2,2-dimethyl SAFL **II** (method b in Scheme 1). Preliminary experimental studies revealed that gem-dimethylation of CesE and CesF (method a) resulted in significant decomposition under various conditions (e.g., KHMDS/MeI,[7] KO^{t}Bu/MeI, LDA/MeI,[8] etc.), possibly due to retro-oxa-Michael addition and subsequent unknown reactions. Therefore, our efforts were concentrated on method b by exploring the key ring contraction rearrangement (RCR) of 2,2-dimethyl decanolides (**I**) to Me$_2$SAFLs of type-**II**.

RESULTS AND DISCUSSION

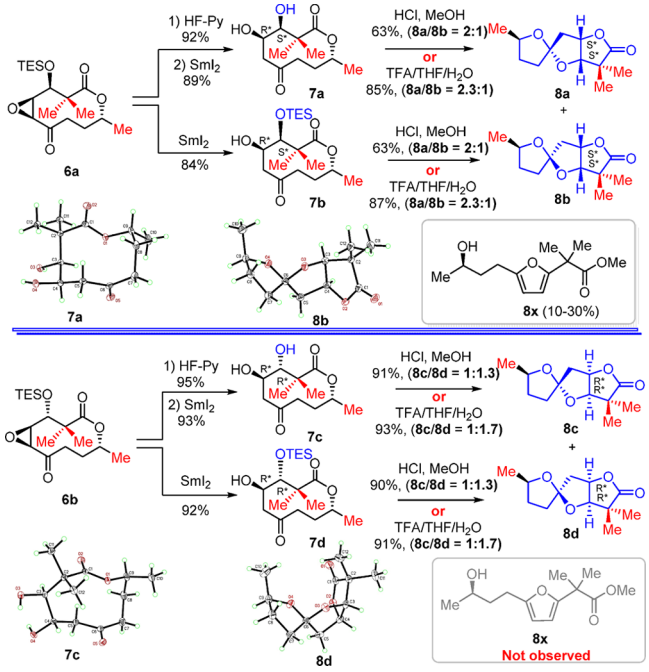
Model Studies. To verify the viability of ring contraction rearrangement (RCR) of 2,2-dimethyl decanolide substrate **I**, a model study was carried out with **6a** and **6b** (Scheme 2) as the

Scheme 2. Synthesis of Epoxydecanolides 6a and 6b



precursor of decanolide **I**, where R was a methyl group. Specifically, our synthesis began with installation of a dimethyl group at C2 on the bicyclic ether **1**,[5h] which was readily prepared from phenol oxidative dearomatization[9] and intramolecular oxa-Michael addition.[10] It was noted that temporary protection of the tertiary alcohol as a silyl ether could substantially improve the yield of C2 dimethylation, which proceeded smoothly with *t*-BuOK/MeI[11] but failed with LDA (monomethylation)[12] or LiHMDS (or KHMDS) (monomethylation and dimethylation)[13] as the base. Epoxidation of **2** with NaOH/H$_2$O$_2$[14] gave 92% yield of epoxy ketone **3**, which was reduced by NaBH$_4$/MeOH to epoxy alcohols **4a** and **4b** as a 1:2 diastereomeric mixture in 99% yield. No attempt was made to improve the diastereomeric ratio because we were interested in synthesis of all possible diastereomers of SAFLs. Facile separation of **4a** from **4b** by column chromatography on silica gel offered us a great opportunity to assign the relative configuration of each sample with the assistance of X-ray diffraction analysis of **4b**. It was noteworthy that the stereochemical information at C3 would not only be retentively transferred to the Me$_2$SAFL product but also control the relative stereochemistry of C4 in the course of the ring contraction rearrangement (Scheme 3). Individual subjection of

Scheme 3. Model Studies on Ring Contraction Rearrangement of 2,2-Dimethyl Decanolides

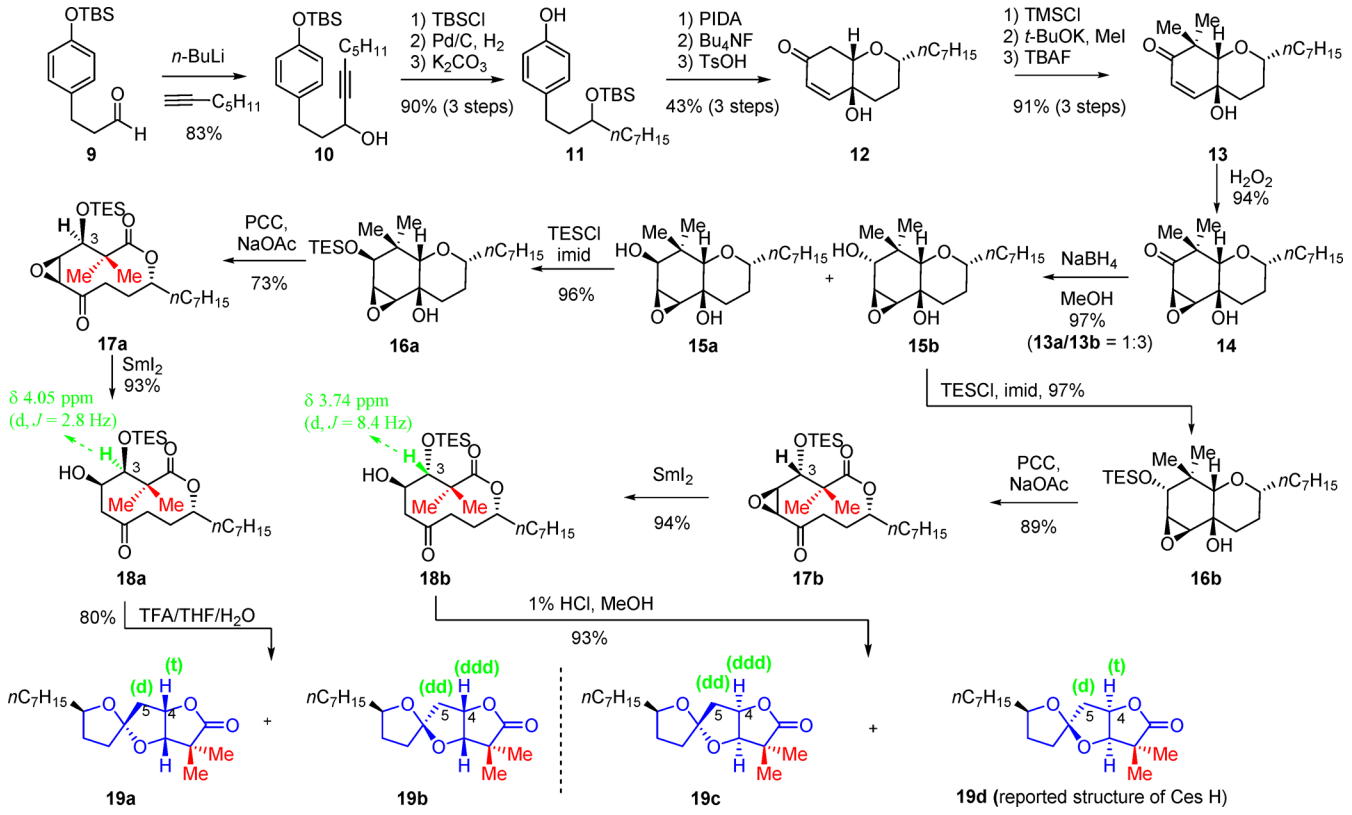


4a and **4b** to O-silylation and pyridinium chlorochromate (PCC)-mediated oxidative ring expansion[15] provided 2,2-dimethylepoxydecanolides **6a** and **6b**, respectively. It was noteworthy that oxidative ring expansion of **5a** proceeded much more slowly than that of **5b**, with maximal 66% conversion regardless of excess PCC (10 equiv) or extended reaction time (1 week). This lower reactivity might arise from unfavorable 1,3-diaxial steric interaction (siloxyl−H) that led to poor accessibility of C6 alcohol and C1 hydrogen to PCC.

Epoxydecanolide **6a** was elaborated to two decanolides **7a** and **7b**, substrates for the key biomimetic RCR reaction, through SmI$_2$-promoted reductive epoxide opening[16] with/without desilylation (HF−pyridine) (Scheme 3). X-ray crystallography of **7a** confirmed its relative configuration, which indirectly supported the relative configuration assigned to **7b**. Analogously, epoxydecanolide **6b** was converted into **7c** and **7d** under identical reaction conditions with comparable overall yield. At this stage, four different decanolides (**7a**−**7d**)

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

Scheme 4. Total Syntheses of Purported Cephalosporolide H and Stereoisomers



were obtained to examine the viability, efficiency, and stereochemical outcomes of the RCR reaction. Gratifyingly, treatment of **7a** with 1% HCl in methanol at room temperature promoted the RCR reaction and afforded the desired Me_2SAFL products **8a** and **8b** in 63% combined yield as a 2:1 spiroisomeric mixture. X-ray diffraction analysis of single-crystal **8b** substantiated the relative configuration of **8b** and provided a basis for stereochemical assignment of the spiroisomeric **8a**. Subsequently, desilylation was found to be unnecessary because the RCR reaction of **7b** under identical conditions would give essentially the same yield and diastereomeric ratio of **8a** and **8b**. The moderate yield (63%) could be attributed to generation of a significant amount of side product **8x**[17] (~30% yield). Fortunately, under our previously reported conditions (TFA/THF/H_2O),[5h] the RCR reaction of **7a** and **7b** gave a considerably better combined yield of Me_2SAFLs **8a** and **8b** (85–87% yield) with a similar spiroisomeric ratio (**8a**/**8b** = 2.3:1), although the formation of **8x** (<10% yield) could not be completely suppressed by additional variations of reaction temperature and/or concentration. In contrast, the RCR reaction of **7c** and **7d** upon treatment of either 1% HCl in MeOH or TFA/THF/H_2O occurred more rapidly to provide over 90% isolated yield of desired separable Me_2SAFLs **8c** and **8d** without detection of **8x**. The spiroisomeric ratio under these two conditions varied slightly from 1:1.3 to 1:1.7. X-ray diffraction analysis of single-crystal **8d** confirmed our structural assignments.

Total Syntheses of Purported Cephalosporolide H and Stereoisomers. The promising results from model studies encouraged us to pursue the total synthesis of Me_2SAFL-containing natural products and their possible diastereomers using the RCR reaction as the key step (Scheme 4). Our first Me_2SAFL-containing target was CesH and its three diastereomers because the heptyl group of CesH might cause the least uncertainty in the key RCR reaction as compared to the methyl group at C9 in our model studies. As depicted in Scheme 4, the synthesis commenced with nucleophilic addition of lithiated 1-octyne to aldehyde **9**, providing the propargylic alcohol **10** in 83% yield. Protection of alcohol **10** as a *tert*-butyldimethylsilyl (TBS) ether, followed by Pd/C-catalyzed hydrogenation and chemoselective desilylation with K_2CO_3 in methanol, produced phenol **11** in 90% yield over three steps. (Diacetoxyiodo)benzene (PIDA) promoted phenol oxidative dearomatization of **11**, and subsequent desilylation and oxa-Michael cyclization delivered the bicylic ether **12** in 43% yield for three steps. Similar to the synthesis of decanolides **7a**–**7d** in Schemes 2 and 3, **12** was smoothly elaborated to two diastereomeric decanolides **18a** and **18b** (**18a**/**18b** = 1:2) in eight steps with 54–67% overall yield. The relative configuration assignments of **18a** and **18b** were based on comparative analysis of ^{1}H NMR spectra of **18a**/**7b** and **18b**/**7d**. The H3 chemical shift of **18a** (*cis*-3-triethylsilyloxy-4-hydroxyl decanolide) was 4.05 ppm with a small coupling constant (doublet, J = 2.8 Hz), which was in a good agreement with that of **7b** (δ_{H3} 4.03 ppm, doublet, J = 2.2 Hz), while H3 of the corresponding trans isomer **18b** resonates at a higher field, 3.74 ppm, with a larger coupling constant (doublet, J = 8.4 Hz), in accord with H3 of trans isomer **7d** (δ_{H3} 3.73 ppm, doublet, J = 6.4 Hz). As previously alluded, the C3 stereochemistry of decanolides **18a** and **18b** was the very important basis for subsequent structural assignments of the Me_2SAFLs. Next, the key RCR reaction of **18a** and **18b** was carried out under optimized conditions (with TFA/THF/H_2O for **18a** and 1% HCl in MeOH for **18b**) at room temperature to afford separable mixtures of spiroisomers **19a**–**19b** in 80% yield (**18a** → **19a** + **19b**) and **19c**–**19d** in 93% yield (**18b** →

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325–4339

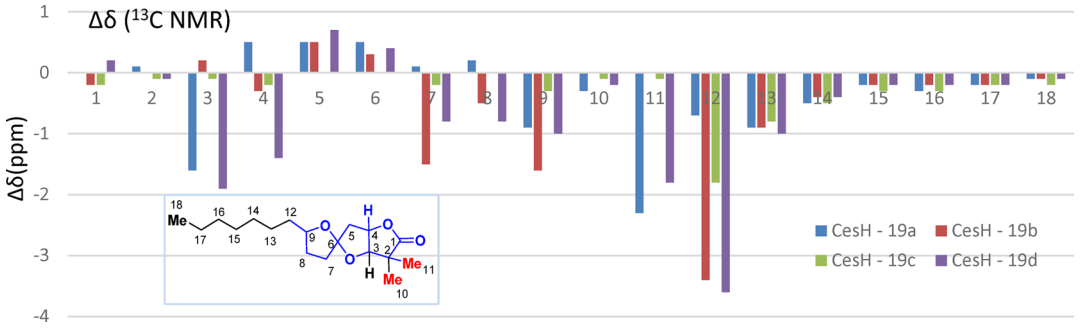
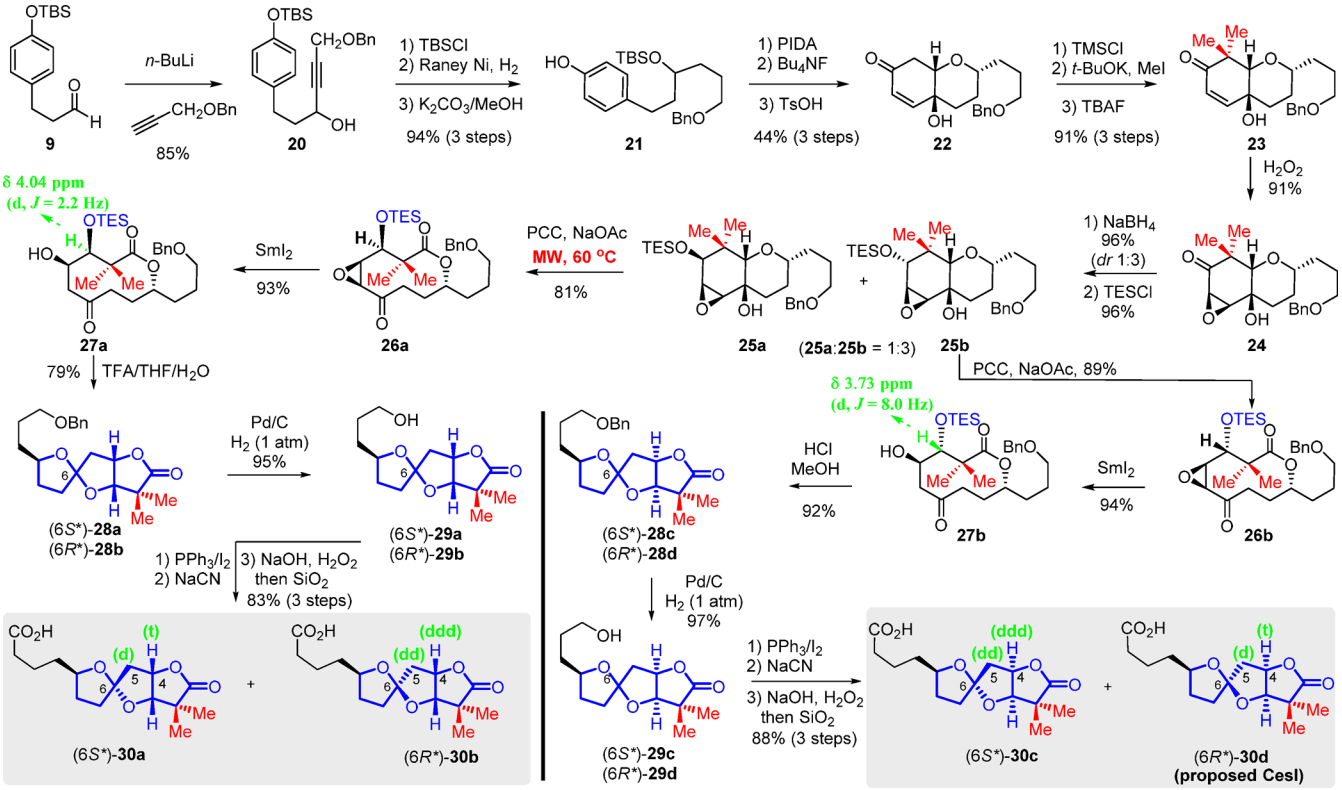


Figure 2. ^{13}C NMR deviations of **19a**−**19d** and CesH.

Scheme 5. Total Syntheses of Purported Cephalosporolide I and Stereoisomers



19c + **19d**). The relative configurations of **19a**−**19d** were proposed on the basis of comprehensive NMR spectral comparison of **19a**−**19d** and **8a**−**8d** (with X-ray confirmation for **8b** and **8d**; see Scheme 3). One of the most distinct differences of **19a** (and **19d**) from the spiroisomer **19b** (and **19c**) in ^{1}H NMR spectra was the spin−spin coupling patterns of the protons at C4 and C5: triplet (t, H4) and doublet (d, H5) (also found in **8a** and **8d**) versus doublet of doublet of doublet (ddd, H4) and doublet of doublet (dd, H5) (also observed in **8b** and **8c**). Related spiroketal isomers were assigned by Brimble et al.[5d] using a similar NMR analysis. Unfortunately, the NMR data derived from these four isomers **19a**−**19d** did not match those reported for the natural CesH (Figure 2). Notably, Me_2SAFL **19c**, a spiroisomer of the proposed CesH, has the smallest deviations ($\Delta\delta \leq 0.2$ ppm) at the Me_2SAFL ring system in the ^{13}C NMR. The obvious difference occurring at C12−C14 ($\Delta\delta > 0.6$ ppm) was very puzzling and precluded us from suggesting any revisions of the proposed structure for CesH (**19d**). However, the NMR data of our synthetic Me_2SAFLs **19a**−**19d** were well consistent with those of the corresponding synthetic SAFLs reported by Dudley and others.[6] These studies clearly revealed that the relative configuration of the tricyclic Me_2SAFL core of the natural CesH should be the same as **19c** and that the side chain was misinterpreted.

Total Syntheses of Purported Cephalosporolide I and Stereoisomers. Next, a divergent synthetic route was devised to access eight Me_2SAFLs corresponding to the structures of CesI and PenB and their possible diastereomers (Scheme 5). Similar to the synthesis of decanolides **18a** and **18b**, aldehyde **9** was elaborated in 13 steps to the bicyclic ethers **25a** and **25b**, which were separated by flash column chromatography and individually subjected to PCC-promoted oxidative ring expansion to provide decanolides **27a** and **27b**, respectively, after SmI_2-mediated reductive epoxide opening. It was noteworthy that the PCC-mediated oxidative ring expansion of **25a** under various conditions resulted in a low yield (<20%) due to oxidation of benzyl group to benzoate, desilylation of TES group followed by oxidation to ketone, and other unknown side reactions. These problems have not been

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

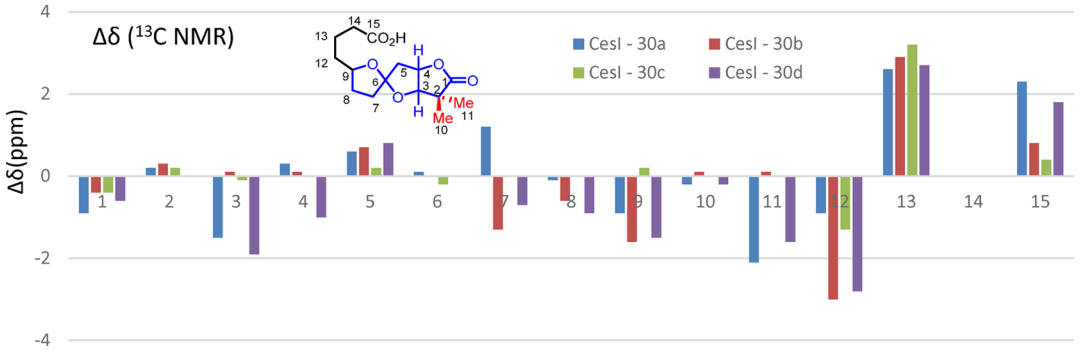
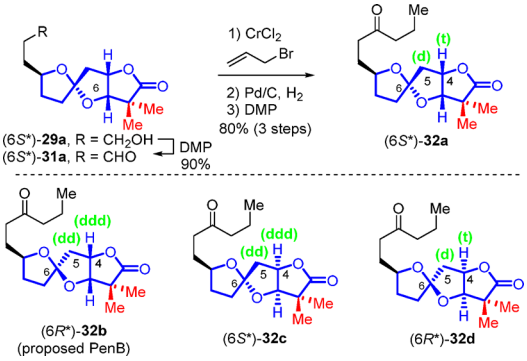


Figure 3. ^{13}C NMR deviations of **30a**−**30d** and CesI.

observed in our previous studies because there were no functional groups on the side chain (methyl or heptyl group). After tremendous efforts on this ring expansion reaction, including replacement of the protecting benzyl group with TBDPS, changing the TES ether to acetyl or MOM ether, and use of different oxidants such as PIDA/I_2,[18] PCC/H_2IO_6[19] and $RuCl_3$/Na_2IO_4,[15a] fortunately, microwave-assisted[20] PCC oxidation of **25a** at 60 °C provided the desired decanolide **27a** in 72% overall yield over two steps after SmI_2-mediated reductive epoxide opening. Subsequent studies found that the microwave could greatly accelerate PCC-mediated oxidative ring expansion for other substrates (**25b**, **16a**, **16b**, etc.) by significantly shortening the reaction time from 12−24 h to 30 min with slightly better yields. The C3 relative configuration of **27a** and **27b** was assigned by using the identical NMR analysis as for **18a**/**18b** and **7b**/**7d**: the chemical shift and coupling constant of H3 derived from **27a** (δ_{H3} 4.04 ppm, d, J = 2.2 Hz) and **27b** (δ_{H3} 3.73 ppm, d, J = 8.0 Hz). These NMR data were well consistent with those of **18a** and **7b** (δ_{H3} 4.03−4.05 ppm, d, J = 2.2−2.8 Hz) and **18b** and **7d** (δ_{H3} 3.73−3.74 ppm, d, J = 6.4−8.4 Hz). This information was very important to determine the relative configurations of C3 and C4 of **30a**−**30d**. Gratifyingly, the key RCR reaction of **27a** and **27b** proceeded smoothly in a parallel manner to provide the four seperable tricyclic Me_2SAFLs **28a**−**28d** (**27a** → **28a** + **28b**; **27b** → **28c** + **28d**) in 79% and 92% yields, respectively. Pd/C-catalyzed debenzylation of **28a**−**28d** (95−97% yields) in a parallel manner and Appel reaction[21] of **29a**−**29d**, followed by S_N2 substitution with NaCN and hydrolysis with $NaOH/H_2O_2$, furnished four diastereomeric Me_2SAFLs, **30a**−**30d**, in excellent overall yield (83−88%). Similar to our previous NMR analysis, the relative configurations for these spiroisomers were assigned on the basis of spin−spin coupling patterns: triplet (t) for H4 and doublet (d) for H5 found in ^{1}H NMR spectra of **30a**/**30d**, and doublet of doublet of doublet (ddd) for H4 and doublet of doublet (dd) for H5 observed in the spectra derived from **30b**/**30c**. Unfortunately, none of these four Me_2SAFL diastereomers (**30a**−**30d**) had identical or similar NMR data with those reported for natural CesI (Figure 3). Nevertheless, when NMR comparison was focused on the tricyclic Me_2SAFL region, **30c** had the smallest deviations from the natural CesI in both ^{1}H and ^{13}C NMR. This might suggest the relative configuration of the tricyclic Me_2SAFL core of CesI should be revised to be that of **30c**, although the side chain apparently required an unknown structural revision.[6c]

Total Synthesis of Purported Penisporolide B and Stereoisomers. Finally, we turned our attention to the synthesis of PenB and its stereoisomers (Scheme 6). Dess−

Scheme 6. Total Synthesis of Purported Penisporolide B and Its Stereoisomers



Martin periodinane (DMP) oxidation[22] of **29a** provided aldehyde **31a** (90% yield), which underwent sequential Nozaki−Hiyama−Kishi (NHK) allylation,[23] Pd-catalyzed hydrogenation, and DMP oxidation to furnished the Me_2SAFL **32a** in 80% overall yield (three steps). It should be noted that nucleophilic addition of related Grignard reagents to the resulting aldehyde from DMP oxidation led to a complex mixture, while allyl zinc[24] and allyl silanes in the presence of BF_3−Et_2O[25] underwent efficient nucleophilic addition with comparable yield (76−93%). The better reproducibility of the NHK reaction on a large or small scale made it our choice. Diastereomeric **32b**−**32d** were prepared from the corresponding **29b**−**29d** with comparable efficiency. Differentiation of the spiroisomers **32a**/**32b** (and **32c**/**32d**) was made on the basis of our previous NMR analysis: triplet (t) for H4 and doublet (d) for H5 suggested the spectrum was derived from the spiroisomer **32a** (**32d**); while doublet of doublet of doublet (ddd) for H4 and doublet of doublet (dd) for H5 was consistent with the spectrum of **32b** (**32c**). Unfortunately, NMR data analysis of **32a**−**32d** and the natural PenB revealed significant inconsistency. Considerable differences ($\Delta\delta$ > 2.0 ppm) of the ^{13}C NMR data between our synthetic Me_2SAFLs and PenB were observed at C12−C15, indicating the structure of the side chain was incorrect (Figure 4). Meticulous ^{13}C NMR comparison of the Me_2SAFL region (C1−C9) between **32a**−**32d** and PenB suggested that the tricyclic Me_2SAFL core of the natural PenB was more likely to be that of **32c** [$\Delta\delta$(^{13}C) 0.0−0.4 ppm], instead of the proposed **32b** [$\Delta\delta$(^{13}C) 0.0−1.5 ppm]. Since all possible diastereomers (**32a**−**32d**) have been synthesized and none of them matched the natural product, we concluded that both relative stereochemistry and constitutional structure assigned to PenB were incorrect in the original paper, which discouraged us from making further efforts on the

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

Figure 4. ^{13}C NMR deviations of **32a−32d** and PenB.

synthesis of related penisporolide A, which included an additional stereochemistry at C16. In particular, our attempt to obtain authentic samples/spectra for these natural products was unsuccessful.

CONCLUSION

In conclusion, we have developed a convergent bioinspired strategy for synthesis of the unique tricyclic 2,2-dimethyl-[5,5]-spiroacetal-cis-fused-γ-lactone (Me_2SAFL). The utility of this strategy was demontrated in the total syntheses of 12 Me_2SAFLs, corresponding to the purported structures of cephalosporolide H (CesH), cephalosporolide I (CesI), penisporolide B (PenB), and their possible diastereomers. Comprehensive and meticulous NMR data analysis of the 12 synthetic Me_2SAFLs and the natural products allowed us to conclude that the tricyclic SAFL cores of CesH, CesI and PenB should be revised to be those of **19c**, **30c**, and **32c**, respectively, with the same relative (3*R**, 4*R**, 6*S**, 9*R**) configuration, and that the side chains required an unknown constitutional structure revision. In addition, a reliable NMR method has been established for stereochemical assignments of the spiroisomers of Me_2SAFLs (e.g., **8a/8b**, **8c/8d**, **19a/19b**, **19c/19d**, **30a/30b**, **30c/30d**, **32a/32b**, and **32c/32d**), which would be very useful in studies of synthetic/natural Me_2SAFL-containing molecules. Most importantly, our synthetic studies provided chemical evidence to support a possible uniform biosynthesis of all SAFL-containing natural products through a ring contraction rearrangement of 10-membered lactones to the characteristic tricyclic SAFLs.

EXPERIMENTAL SECTION

NMR spectra were recorded on a 400 MHz spectrometer (400 MHz for ^1H, 100 MHz for ^{13}C). Chemical shifts are reported in parts per million (ppm) as values relative to the internal chloroform (7.26 ppm for ^1H and 77.00 ppm for ^{13}C). Infrared (IR) spectra were recorded as neat samples (liquid films on KBr plates). High-resolution mass spectra (HRMS) were recorded with a time-of-flight (TOF) detector. Reactions were carried out in oven or flame-dried glassware under a nitrogen atmosphere, unless otherwise noted. Tetrahydrofuran (THF) was freshly distilled before use from sodium, with benzophenone as indicator. Dichloromethane (CH_2Cl_2) was freshly distilled before use from calcium hydride (CaH_2). All other anhydrous solvents were dried over 3 or 4 Å molecular sieves. Standard workup and purification were performed as follows: the reaction was quenched with aqueous saturated $NaHCO_3$ or NH_4Cl; the organic layer was extracted with organic solvent (CH_2Cl_2 or EtOAc) three times; the conbined organic fractions were washed with brine, dried over $MgSO_4$, and concentrated in vacuo; and the resulting residue was purified by flash column chromatography (hexane and ethyl acetate as eluents) on silica gel. Compounds **1** and **9** are known compounds and were prepared according to literature procedures.[5h,26]

General Procedure A: PCC-Mediated Oxidative Ring Expansion. To a solution of β-hydroxy cyclic ether (0.32 mmol) in CH_2Cl_2 (16 mL) were added sodium acetate (637 mg, 7.8 mmol) and pyridinium chlorochromate (PCC; 600 mg, 3.23 mmol) portionwise over 10 min. The resulting dark mixture was stirred at room temperature (rt) for 2 h and filtered through a pad of Florisil. The filtrate was washed with aqueous saturated $CuSO_4$ (3 × 30 mL) and brine, dried over anhydrous Na_2SO_4,and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to give the 10-membered lactone.

General Procedure B: Microwave-Assisted PCC-Mediated Oxidative Ring Expansion. To a solution of β-hydroxy cyclic ether (0.42 mmol) in CH_2Cl_2 (21 mL) were added sodium acetate (0.821 g, 10.08 mmol) and pyridinium chlorochromate (PCC; 1.45 g, 6.72 mmol) portionwise over 10 min. The resulting dark mixture was heated with a microwave (glass vial G30, 60 °C, 600 rpm, 2−5 bar, 3−6 W) for 2 h and filtered through a pad of Florisil. Workup and purification were performed as in General Procedure A to give the desired product.

General Procedure C: Ring Contraction Rearrangement, Method A. To a solution of 10-membered lactone (0.09 mmol) in MeOH (1.0 mL) at 0 °C was added concentrated HCl (50 uL) in a dropwise fashion with vigorous stirring. The resulting mixture was warmed to rt and stirred until thin-layer chromatographic (TLC) analysis indicated complete consumption of the starting material (~5 h). The resulting mixture was cooled with an ice bath and carefully quenched by addition of aqueous saturated $NaHCO_3$ (3 mL) and then $NaHCO_3$ powder. Standard workup (extraction with 5 mL of EtOAc) and purification gave the SAFL product.

General Procedure D: Ring Contraction Rearrangement, Method B. To a solution of trifluoroacetic acid (TFA, 0.9 mL) and water (0.3 mL) at 0 °C was added a solution of 10-membered lactone (0.09 mmol) in THF (0.3 mL) in a dropwise fashion with vigorous stirring. The resulting mixture was warmed to rt and stirred until TLC analysis indicated complete consumption of the starting material (~2 h). The resulting mixture was cooled with an ice bath and carefully quenched by addition of aqueous saturated NaOH (5 mL) and then $NaHCO_3$ powder. Standard workup (extraction with 10 mL of EtOAc) and purification gave the SAFL product.

Details of Syntheses and Characterization Data. *Preparation of 2.* To a solution of **1** (250 mg, 1.37 mmol) in dry CH_2Cl_2 (7 mL) was added imidazole (187 mg, 2.75 mmol). The resulting solution was cooled to 0 °C with an ice−water bath, and then trimethylsilyl chloride (TMSCl, 0.26 mL, 2.06 mmol) dissolved in CH_2Cl_2 (1 mL) was added dropwise. After the addition was complete, the reaction mixture was allowed to warm to rt and stirred overnight. Standard workup (quenching with 10 mL of NH_4Cl; extraction with 10 mL of CH_2Cl_2) and purification (hexane/ethyl acetate = 5:1) gave **A** (295 mg, 85%

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

yield) as a colorless oil. IR (neat, cm^{-1}) 3029, 2967, 2938, 2867, 1693, 1443, 1252, 1104, 1081, 753. ^1H NMR (400 MHz, $CDCl_3$) δ 6.51 (dt, J = 10.1, 1.6 Hz, 1H), 6.01 (d, J = 9.9 Hz, 1H), 3.75−3.74 (m, 1H), 3.57−3.42 (m, 1H), 2.94 (dd, J = 16.8, 2.9 Hz, 1H), 2.40 (dd, J = 16.8, 3.0 Hz, 1H), 2.01 (dt, J = 12.8, 3.5 Hz, 1H), 1.81 (td, J = 13.4, 4.2 Hz, 1H), 1.70−1.55 (m, 1H), 1.28−1.19 (m, 1H), 1.07 (dd, J = 6.2, 1.1 Hz, 3H), 0.17−0.01 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 149.0, 130.9, 79.5, 73.2, 68.1, 40.0, 37.9, 30.9, 21.2, 2.5 (3C). HRMS (CI^+) m/z calcd for $C_{13}H_{22}O_3Si$ $[M]^+$ 254.1333, found 254.1341.

To a solution of **A** (295 mg, 1.17 mmol) in THF (5 mL) cooled in a dry ice/acetone bath was added potassium *t*-butoxide (1.0 M in THF, 3.51 mL, 3.51 mmol) dropwise. The resulting solution was stirred at −78 °C for 30 min before addition of MeI (0.36 mL, 5.85 mmol). The resulting solution was slowly warmed up to rt and stirred for 6 h. Standard workup (quenching by 5 mL of NH_4Cl, extraction with 15 mL of EtOAc) and purification (hexane/ethyl acetate = 5:1) gave **B** (342 mg, 98% yield) as a colorless oil. IR (neat, cm^{-1}) 3000, 2968, 2932, 2850, 1689, 1384, 1253, 1103, 840. ^1H NMR (400 MHz, $CDCl_3$) δ 6.38 (dd, J = 10.1, 2.7 Hz, 1H), 5.94 (d, J = 10.1 Hz, 1H), 3.43−3.39 (m, 1H), 3.36 (d, J = 2.6 Hz, 1H), 2.01 (dt, J = 12.8, 3.5 Hz, 1H), 1.90−1.80 (m, 1H), 1.66−1.58 (m, 1H), 1.27 (s, 3H), 1.25−1.12 (m, 4H), 1.06 (d, J = 6.1 Hz, 3H), 0.15 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.2, 147.1, 129.2, 86.3, 73.3, 69.9, 46.8, 39.4, 31.1, 26.1, 22.2, 21.2, 2.8 (3C). HRMS (CI^+) m/z calcd for $C_{15}H_{26}O_3Si$ $[M]^+$ 282.1646, found 282.1659.

To a solution of **B** (342 mg, 1.22 mmol) in THF (6 mL) at 0 °C was added tetrabutylammonium fluoride (TBAF; 1.0 M in THF, 1.46 mL, 1.46 mmol). The reaction mixture was allowed to warm to rt and stirred for 1 h. Standard workup (quenching with 10 mL of NH_4Cl, extraction with 10 mL of EtOAc) and purification (hexane/ethyl acetate = 1:1) gave **2** (247 mg, 97% yield). IR (neat, cm^{-1}) 3421, 2998, 2973, 2933, 2851, 1678, 1388, 1095. ^1H NMR (400 MHz, $CDCl_3$) δ 6.34 (dd, J = 10.1, 2.7 Hz, 1H), 5.93 (d, J = 10.0 Hz, 1H), 3.42−3.36 (m, 2H), 1.97 (dt, J = 13.0, 3.4 Hz, 1H), 1.79 (td, J = 13.5, 4.3 Hz, 1H), 1.63−1.53 (m, 1H), 1.29 (s, 3H), 1.28−1.11 (m, 4H), 1.04 (d, J = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.3, 146.8, 129.2, 85.7, 73.3, 67.2, 46.8, 39.5, 31.1, 25.8, 21.9, 21.1. HRMS (CI^+) m/z calcd. for $C_{12}H_{19}O_3$ $[M + H]^+$ 211.1329, found 211.1330.

Preparation of ***3***. To a solution of **2** (244 mg, 1.17 mmol) in MeOH (6 mL) at 0 °C were added H_2O_2 (30% in water, 0.88 mL, 7.5 mmol) and NaOH (69 mg 1.72 mmol). The reaction mixture was stirred for 48 h. Standard workup (quenching with 10 mL of Na_2SO_3, extraction with 10 mL of EtOAc) and purification (hexane/ethyl acetate = 1:1) gave **3** (239 mg, 92% yield). IR (neat, cm^{-1}) 3479, 2974, 2933, 2859, 1715, 1445, 1094, 1031, 895. ^1H NMR (400 MHz, $CDCl_3$) δ 3.45 (d, J = 3.6 Hz, 1H), 3.40 (dd, J = 3.6, 2.4 Hz, 1H), 3.38−3.30 (m, 1H), 3.14 (d, J = 2.3 Hz, 1H), 2.59 (s, 1H), 2.10−2.05 (m, 1H), 1.91−1.83 (m, 1H), 1.76−1.69 (m, 1H), 1.35 (s, 3H), 1.33−1.20 (m, 1H), 1.12 (s, 3H), 1.08 (d, J = 6.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.3, 88.7, 73.4, 67.0, 62.5, 56.9, 47.0, 36.7, 31.0, 23.7, 23.2, 21.0. HRMS (CI^+) m/z calcd for $C_{12}H_{18}O_4$ $[M]^+$ 226.1200, found 226.1200.

Preparation of ***4a*** *and* ***4b***. To a solution of ketone **3** (226 mg, 1.0 mmol) in MeOH (5 mL) at 0 °C was added sodium borohydride (78 mg, 2.0 mmol) portionwise. The reaction mixture was stirred for an additional 1.5 h. After TLC analysis indicated complete conversion, the volatiles (mostly MeOH) were evaporated under reduced pressure. To the resulting residue dissolved in EtOAc (10 mL) were sequentially added water (10 mL) and 10% HCl (55 mL). Standard workup (extraction with 10 mL of ethyl acetate) and purification (hexane/ethyl acetate = 1:2) gave the diol products **4a** (74 mg, 33% yield) and **4b** (154 mg, 66% yield) as a colorless solid.

Data for **4a**: IR (neat, cm^{-1}) 3465, 2969, 2929, 2861, 1449, 1096, 1051, 1025. ^1H NMR (400 MHz, $CDCl_3$) δ 3.96 (d, J = 2.4 Hz, 1H), 3.56 (dd, J = 4.1, 2.4 Hz, 1H), 3.35−3.24 (m, 1H), 3.19 (dd, J = 4.1, 2.1 Hz, 1H), 2.94 (d, J = 2.1 Hz, 1H), 2.00−1.93 (m, 1H), 1.84−1.78 (m, 1H), 1.71−1.63 (m, 1H), 1.28−1.17 (m, 1H), 1.17−1.05 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 86.8, 73.0, 71.3, 66.7, 60.7, 60.1, 37.9, 36.8, 31.3, 26.1, 21.2, 20.9. HRMS (CI^+) m/z calcd for $C_{12}H_{21}O_4$ $[M + H]^+$ 229.1434, found 229.1430.

Data for **4b**: mp = 120−121 °C. IR (neat, cm^{-1}) 3496, 2966, 2931, 2862, 1641, 1448, 1143, 1051, 1025. ^1H NMR (400 MHz, $CDCl_3$) δ 3.67−3.50 (m, 2H), 3.35−3.25 (m, 2H), 3.06 (dd, J = 3.7, 1.6 Hz, 1H), 3.03−2.95 (m, 1H), 2.42 (s, 1H), 1.99 (dt, J = 13.5, 3.5 Hz, 1H), 1.85−1.76 (m, 1H), 1.70−1.63 (m, 1H), 1.33−1.25 (m, 1H), 1.11 (d, J = 6.1 Hz, 6H), 1.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 85.5, 73.6, 70.5, 66.6, 59.1, 56.3, 36.9, 36.0, 31.1, 25.2, 24.7, 21.3. HRMS (CI^+) m/z calcd. for $C_{12}H_{20}O_4$ $[M]^+$ 228.1356, found 228.1356. Single crystals of **4b** (CCDC 1469936) suitable for X-ray diffraction analysis were obtained from slow evaporation of solvents (CH_2Cl_2/hexane).

Preparation of ***5a***. To a solution of **4a** (100 mg, 0.44 mmol) in dry *N*,*N*-dimethylformamide (DMF, 2.0 mL) was added imidazole (45 mg, 0.6 mmol). The resulting solution was cooled to 0 °C, and triethylsilyl chloride (TESCl, 0.09 mL, 0.5 mmol) was added dropwise. After the addition was complete, the reaction mixture was allowed to warm to rt and stirred overnight. Standard workup (quenching with 5 mL of NH_4Cl, extraction with 10 mL of Et_2O) and purification (hexane/ethyl acetate = 7:1) gave **5a** (107 mg, 91% yield) as a colorless oil. IR (neat, cm^{-1}) 3492, 2957, 2935, 2913, 2876, 1381, 1093, 726. ^1H NMR (400 MHz, $CDCl_3$) δ 4.04 (d, J = 2.3 Hz, 1H), 3.40 (dd, J = 4.0, 2.4 Hz, 1H), 3.31−3.27 (m, 1H), 3.12 (dd, J = 4.0, 2.0 Hz, 1H), 2.93 (d, J = 2.0 Hz, 1H), 2.48 (s, 1H), 1.96 (dt, J = 13.4, 3.5 Hz, 1H), 1.80 (td, J = 13.8, 4.5 Hz, 1H), 1.70−1.63 (m, 1H), 1.30−1.20 (m, 1H), 1.12 (d, J = 6.1 Hz, 3H), 1.07 (s, 3H), 1.05−0.98 (m, 12H), 0.74−0.59 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 87.2, 73.0, 71.8, 66.7, 60.2, 60.0, 38.5, 36.7, 31.4, 26.6, 21.5, 21.3, 6.9 (3C), 5.1 (3C). HRMS (CI^+) m/z calcd for $C_{18}H_{35}O_4Si$ $[M + H]^+$ 343.2299, found 343.2296.

Preparation of ***5b***. Following the procedure for synthesis of **5a**, **4b** (100 mg, 0.44 mmol) underwent silylation in the presence of dry DMF (4.0 mL), imidazole (45 mg, 0.6 mmol), and TESCl (0.09 mL, 0.5 mmol) at rt to give **5b** (108 mg, 92% yield) as a colorless oil. IR (neat, cm^{-1}) 3509, 2959, 2934, 2877, 1461, 1381, 1098, 1057, 1008, 855. ^1H NMR (400 MHz, $CDCl_3$) δ 3.59 (d, J = 1.5 Hz, 1H), 3.58−3.49 (m, 1H), 3.35 (d, J = 3.7 Hz, 1H), 3.12 (d, J = 3.7 Hz, 1H), 2.95 (s, 1H), 2.29 (s, 1H), 1.96−1.71 (m, 3H), 1.33 (ddd, J = 12.7, 10.1, 7.0 Hz, 1H), 1.11 (d, J = 6.1 Hz, 3H), 1.04−0.93 (m, 15H), 0.64 (q, J = 7.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 85.8, 72.9, 70.0, 67.3, 61.8, 58.7, 39.5, 33.4, 29.6, 25.8, 21.8, 20.1, 6.8 (3C), 4.9 (3C). HRMS (CI^+) m/z calcd for $C_{18}H_{35}O_4Si$ $[M + H]^+$ 343.2299, found 343.2311.

Preparation of ***6a***. Following General Procedure A, **5a** (110 mg, 0.32 mmol) in CH_2Cl_2 (16 mL) underwent PCC-mediated oxidative ring expansion in the presence of sodium acetate (637 mg, 7.8 mmol) and PCC (600 mg, 3.23 mmol) at rt to give **6a** [60 mg, 83% based on recovered starting material (brsm); recovered **5a** (38 mg)] as a colorless oil. IR (neat, cm^{-1}) 2956, 2877, 1741, 1715, 1464, 1265, 1098. ^1H NMR (400 MHz, $CDCl_3$) δ 4.85 (ddd, J = 11.8, 6.1, 2.9 Hz, 1H), 4.03 (d, J = 5.1 Hz, 1H), 3.42 (d, J = 4.3 Hz, 1H), 3.13 (t, J = 4.8 Hz, 1H), 2.90−2.74 (m, 1H), 2.25−2.03 (m, 2H), 1.83 (ddd, J = 14.4, 7.5, 2.3 Hz, 1H), 1.27 (s, 3H), 1.15 (d, J = 6.2 Hz, 3H), 1.10 (s, 3H), 0.98 (t, J = 7.9 Hz, 9H), 0.69 (q, J = 7.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.5, 175.2, 71.2, 68.9, 61.8, 60.6, 46.8, 37.3, 32.7, 24.7, 19.8, 16.6, 6.8 (3C), 4.7 (3C). HRMS (CI^+) m/z calcd for $C_{18}H_{33}O_5Si$ $[M + H]^+$ 357.2092, found 357.2083.

Preparation of ***6b***. Following General Procedure A, **5b** (110 mg, 0.32 mmol) in CH_2Cl_2 (16 mL) underwent PCC-mediated oxidative ring expansion in the presence of sodium acetate (637 mg, 7.8 mmol) and PCC (600 mg, 3.23 mmol) at rt to give **6b** (106 mg, 89% yield) as a colorless oil. IR (neat, cm^{-1}) 2954, 2913, 2877, 1728, 1462, 1382, 1266, 1091. ^1H NMR (400 MHz, $CDCl_3$) δ 4.94−4.72 (m, 1H), 3.86 (d, J = 4.7 Hz, 1H), 3.53 (dd, J = 8.2, 2.6 Hz, 1H), 3.32 (ddd, J = 7.8, 4.6, 2.9 Hz, 1H), 2.76 (ddd, J = 15.3, 7.1, 2.9 Hz, 1H), 2.41 (ddd, J = 15.2, 11.6, 3.6 Hz, 1H), 2.20−2.10 (m, 1H), 2.10−1.99 (m, 1H), 1.27 (dd, J = 6.5, 2.6 Hz, 3H), 1.21 (d, J = 2.5 Hz, 3H), 1.12 (d, J = 2.8 Hz, 3H), 0.96 (td, J = 8.0, 2.5 Hz, 9H), 0.80−0.60 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6, 174.0, 71.9, 71.1, 60.9, 57.8, 46.8, 40.6, 31.2, 23.3, 19.9, 18.0, 6.8 (3C), 4.9 (3C). HRMS (CI^+) m/z calcd for $C_{18}H_{33}O_5Si$ $[M + H]^+$ 357.2092, found 357.2086.

Preparation of ***7a***. To a solution of **6a** (50 mg, 0.15 mmol) in THF (2 mL) at 0 °C was added hydrogen fluoride pyridine (70% HF, 0.4 mL). The reaction mixture was allowed to warm to rt and stirred for 8

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

h. Standard workup (quenching with 2 mL of NaOH, extraction with 10 mL of EtOAc) and purification (hexane/ethyl acetate = 1:1) gave crude compound **C** (30 mg, 92% yield) as a colorless oil, which was used directly for next step without further purification. A flame-dried Schlenk tube under nitrogen atmosphere was charged with **C** (23 mg, 0.10 mmol), THF (3.0 mL), and MeOH (1.5 mL). The solution was cooled to −78 °C and samarium diiodide (1.9 mL, 0.1 M in THF, 0.19 mmol) was added dropwise. The reaction mixture was warmed to −20 °C over 1 h. Standard workup (quenching with 5 mL of $NaHCO_3$, extraction with 10 mL of ethyl acetate and purification (hexane/ethyl acetate =1:2) gave **7a** (20 mg, 89% yield) as a white solid, mp = 122−125 °C. IR (neat, cm^{-1}) 3500, 2956, 2910, 1779, 1729, 1463, 1262, 1122, 1065, 840, 742. ^1H NMR (400 MHz, $CDCl_3$) δ 5.22−5.12 (m, 1H), 4.54 (d, J = 10.3 Hz, 1H), 3.79 (d, J = 2.0 Hz, 1H), 2.96−2.90 (m, 1H), 2.50−2.40 (m, 2H), 2.31−2.25 (m, 1H), 2.15−2.04 (m, 1H), 2.04−1.98 (m, 1H), 1.31 (s, 3H), 1.22 (d, J = 6.3 Hz, 3H), 1.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.9, 176.3, 71.9 (2C), 68.8, 46.0, 44.6, 40.1, 33.6, 29.7, 19.5, 14.1. HRMS (CI^+) m/z calcd for $C_{12}H_{20}O_5$ $[M]^+$ 244.1305, found 244.1300. Single crystals of **7a** (CCDC 1469937) suitable for X-ray diffraction analysis were obtained from slow evaporation of solvents (Et_2O/hexane).

Preparation of ***7b***. Following the procedure for synthesis of **7a**, **6a** (50 mg, 0.15 mmol) in THF/MeOH (3.0 mL/1.5 mL) underwent SmI_2-mediated reductive epoxide ring opening to give **7b** (43 mg, 84% yield) as a colorless oil. IR (neat, cm^{-1}) 3500, 2957, 2914, 2878, 1779, 1729, 1463, 1262, 1122, 1065, 840, 742. ^1H NMR (400 MHz, $CDCl_3$) δ 5.22−5.16 (m, 1H), 4.52−4.34 (m, 1H), 4.03 (d, J = 2.2 Hz, 1H), 2.66 (t, J = 8.8 Hz, 2H), 2.41 (ddd, J = 12.5, 8.1, 6.0 Hz, 1H), 2.33−2.22 (m, 1H), 2.10−1.97 (m, 2H), 1.23 (s, 3H), 1.20 (d, J = 6.3 Hz, 3H), 1.14 (s, 3H), 1.01 (t, J = 7.9 Hz, 9H), 0.70 (qd, J = 7.8, 2.3 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.3, 176.3, 71.7, 71.3 (2C), 45.6, 45.5, 40.3, 33.6, 27.5, 19.3, 18.7, 6.9 (3C), 5.0 (3C). HRMS (CI^+) m/z calcd for $C_{18}H_{35}O_5Si$ $[M + H]^+$ 359.2248, found 359.2241.

Preparation of ***7c***. Following the procedure for synthesis of **C**, **6b** (50 mg, 0.15 mmol) in THF (2 mL) underwent desilylation to give **D** (31 mg, 95% yield) as a colorless oil, which was used directly for the next step without further purification. Following the procedure for synthesis of **7a**, **D** (23 mg, 0.10 mmol) underwent SmI_2-mediated reductive epoxide ring opening to give **7c** (21 mg, 93% yield) as a a white solid, mp =79−80 °C. IR (neat, cm^{-1}) 3500, 2956, 2910, 1779, 1729, 1463, 1262, 1122, 1065, 840, 742. ^1H NMR (400 MHz, $CDCl_3$) δ 4.96−4.85 (m, 1H), 4.16−4.05 (m, 1H), 3.61 (d, J = 8.7 Hz, 1H), 2.79 (dd, J = 18.0, 7.5 Hz, 1H), 2.58 (dd, J = 18.1, 1.7 Hz, 1H), 2.39 (dd, J = 7.7, 4.7 Hz, 2H), 2.25−1.95 (m, 1H), 2.03−1.93 (m, 1H), 1.29 (d, J = 6.5 Hz, 3H), 1.26 (s, 3H), 1.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.8, 176.2, 78.6, 72.9, 68.4, 46.6, 45.4, 40.4, 32.0, 25.7, 19.5, 16.4. HRMS (CI^+) m/z calcd for $C_{12}H_{20}O_5$ $[M]^+$ 244.1305, found 244.1300. Single crystals of **7c** (CCDC 1469938) suitable for X-ray diffraction analysis were obtained from slow solvent evaporation (Et_2O/hexane).

Preparation of ***7d***. Following the procedure for synthesis of **7a**, **6b** (50 mg, 0.15 mmol) underwent SmI_2-mediated reductive epoxide ring opening to give **7d** (30 mg, 92% yield) as a colorless oil. IR (neat, cm^{-1}) 3511, 2954, 2877, 1717, 1465, 1361, 1267, 1105, 1006, 738. ^1H NMR (400 MHz, $CDCl_3$) δ 4.94−4.86 (m, 1H), 4.15 (td, J = 6.6, 4.3 Hz, 1H), 3.73 (d, J = 6.4 Hz, 1H), 2.73−2.60 (m, 2H), 2.57−2.50 (m, 1H), 2.35−2.29 (m, 1H), 2.21−2.13 (m, 1H), 2.05−1.98 (m, 1H), 1.28 (d, J = 6.4 Hz, 3H), 1.19 (s, 3H), 1.08−0.96 (m, 12H), 0.74−0.69 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.2, 176.0, 79.3, 71.9, 68.2, 48.4, 46.7, 38.8, 31.8, 26.1, 19.1, 17.2, 6.9 (3C), 5.4 (3C). HRMS (CI^+) m/z calcd for $C_{18}H_{35}O_5Si$ $[M + H]^+$ 359.2248, found 359.2240.

Preparation of [5,5]-Spiroacetal-cis-fused-γ-lactones ***8a*** *and* ***8b***. Following General Procedure C, **7a** (22 mg, 0.09 mmol) in MeOH (1.0 mL) rearranged upon treatment with 37% HCl (50 μL) to **8a** (8.1 mg, 44% yield, colorless oil) and **8b** (4.0 mg, 22% yield, colorless solid). Following General Procedure D, **7a** (22 mg, 0.09 mmol) rearranged upon treatment with a solution of TFA/H_2O/THF (0.9 mL/0.3 mL/0.3 mL) to **8a** (12.5 mg, 57% yield) and **8b** (5.5 mg, 25% yield). Following General Procedure C, **7b** (16 mg, 0.045 mmol) rearranged to give **8a** (4.2 mg, 42% yield) and **8b** (2.1 mg, 21% yield). Following General Procedure D, **7b** (16 mg, 0.045 mmol) underwent dehydrative ring contraction rearrangement to give **8a** (6.1 mg, 61% yield) and **8b** (2.6 mg, 26% yield).

Data for **8a**: IR (neat, cm^{-1}) 2968, 2929, 2870, 1774, 1460, 1346, 1124, 1093, 1056. ^1H NMR (400 MHz, $CDCl_3$) δ 5.10 (t, J = 5.2 Hz, 1H), 4.34 (d, J = 5.0 Hz, 1H), 4.22−4.14 (m, 1H), 2.46 (d, J = 14.1 Hz, 1H), 2.20−2.06 (m, 4H), 1.44 (ddd, J = 11.8, 7.0, 2.1 Hz, 1H), 1.24 (s, 3H), 1.21 (s, 3H), 1.18 (d, J = 6.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.9, 115.1, 86.7, 80.0, 75.5, 44.3, 41.8, 34.7, 31.4, 25.3, 20.8, 18.4. HRMS (CI^+) m/z calcd for $C_{12}H_{19}O_4$ $[M + H]^+$ 227.1278, found 227.1272.

Data for **8b**: mp =110−112 °C. IR (neat, cm^{-1}) 2968, 2929, 2870, 1774, 1460, 1346, 1124, 1093, 1056. ^1H NMR (400 MHz, $CDCl_3$) δ 5.08−4.97 (ddd, J = 6.2, 3.7, 1.5 Hz, 1H), 4.33 (d, J = 3.7 Hz, 1H), 4.24−4.13 (m, 1H), 2.49 (dd, J = 15.0, 6.2 Hz, 1H), 2.34 (dd, J = 15.0, 1.5 Hz, 1H), 2.13−2.02 (m, 2H), 1.96 (td, J = 12.7, 11.9, 8.0 Hz, 1H), 1.79−1.68 (m, 1H), 1.28 (d, J = 6.2 Hz, 3H), 1.26 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.0, 115.5, 85.1, 80.4, 68.0, 44.5, 42.0, 37.5, 32.4, 23.1, 22.7, 18.1. HRMS (CI^+) m/z calcd for $C_{12}H_{19}O_4$ $[M + H]^+$ 227.1278, found 227.1275. Single crystals of **8b** (CCDC 1469945) suitable for X-ray diffraction analysis were obtained from slow evaporation of solvents (CH_2Cl_2/hexane).

Preparation of [5,5]-Spiroacetal-cis-fused-γ-lactones ***8c*** *and* ***8d***. Following General Procedure C, **8c** (7.3 mg, 39% yield, colorless oil) and **8d** (9.6 mg, 52% yield, colorless solid) were obtained from **7c** (22 mg, 0.09 mmol). Following General Procedure D, **8c** (7.1 mg, 34% yield, colorless oil) and **8d** (12.4 mg, 59% yield, colorless solid) were obtained from **7c** (22 mg, 0.09 mmol). Following General Procedure C, **8c** (3.9 mg, 39% yield) and **8d** (5.1 mg, 51% yield) were obtained from **7d** (16 mg, 0.045 mmol). Following General Procedure D, **8c** (3.4 mg, 34% yield) and **8d** (5.9 mg, 59% yield) were obtained from **7d** (16 mg, 0.045 mmol).

Data for **8c**: IR (neat, cm^{-1}) 2955, 2925, 2855, 1779, 1461, 1142, 1053. ^1H NMR (400 MHz, $CDCl_3$) δ 5.02 (ddd, J = 6.2, 3.6, 1.5 Hz, 1H), 4.28 (d, J = 3.7 Hz, 1H), 4.22−4.17 (m, 1H), 2.52 (dd, J = 15.0, 6.4 Hz, 1H), 2.36 (d, J = 15.1 Hz, 1H), 2.16−2.01 (m, 3H), 1.46 (ddd, J = 9.2, 6.8, 3.8 Hz, 1H), 1.26 (d, J = 1.0 Hz, 3H), 1.21 (d, J = 6.3 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.9, 115.6, 85.2, 80.5, 74.9, 44.4, 42.5, 35.9, 31.9, 23.1, 20.9, 18.1. HRMS (CI^+) m/z calcd for $C_{12}H_{19}O_4$ $[M + H]^+$ 227.1278, found 227.1278.

Data for **8d**: mp =70−71 °C. IR (neat, cm^{-1}) 2955, 2925, 2855, 1779, 1461, 1142, 1053. ^1H NMR (400 MHz, $CDCl_3$) δ 5.08 (t, J = 4.9 Hz, 1H), 4.30 (d, J = 4.7 Hz, 1H), 4.21−4.08 (m, 1H), 2.44 (d, J = 14.1 Hz, 1H), 2.12 (dd, J = 14.3, 5.4 Hz, 2H), 2.08−1.95 (m, 2H), 1.69 (ddd, J = 12.2, 10.0, 8.1 Hz, 1H), 1.31 (s, 3H), 1.26 (d, J = 6.2 Hz, 3H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.7, 115.3, 87.0, 79.9, 77.7, 44.5, 41.7, 36.6, 32.4, 24.8, 22.3, 18.3. HRMS (CI^+) m/z calcd for $C_{12}H_{19}O_4$ $[M + H]^+$ 227.1278, found 227.1284. Single crystals of **8d** (CCDC 1469944) suitable for X-ray diffraction analysis were obtained from slow evaporation of solvents (CH_2Cl_2/hexane).

Preparation of ***10***. To a solution of 1-heptyne (2.50 g, 26.0 mmol) in THF (100 mL) at −78 °C was added dropwise *n*-BuLi (2.0 M in THF, 12.0 mL, 24.0 mmol) with vigorous stirring. The resulting mixture was stirred for 45 min before addition of aldehyde **9** (5.29 g, 20 mmol). The resulting mixture was stirred until TLC analysis indicated complete consumption of **9** (∼2 h). Standard workup (quenching with 100 mL of NH_4Cl, extraction with 100 mL of EtOAc) and purification (hexane/ethyl acetate = 5:1) gave **10** (6.48 g, 90% yield) as a colorless oil. IR (neat, cm^{-1}) 3351, 3029, 2955, 2931, 2858, 1610, 1580, 1510, 1256, 917, 839, 780. ^1H NMR (400 MHz, $CDCl_3$) δ 7.06 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 8.4 Hz, 2H), 4.39−4.30 (m, 1H), 2.72 (t, J = 7.8 Hz, 2H), 2.24−2.20 (m, 2H), 2.02−1.94 (m, 3H), 1.56−1.50 (m, 1H), 1.41−1.32 (m, 4H), 0.99 (s, 9H), 0.91 (t, J = 4.4 Hz, 3H), 0.19 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 134.1, 129.2 (2C), 119.8 (2C), 85.8, 81.0, 62.0, 39.8, 31.0, 30.6, 28.3, 25.6 (3C), 22.1, 18.6, 18.1, 13.9, −4.5 (2C). HRMS (CI^+) m/z calcd for $C_{22}H_{36}O_2Si$ $[M]^+$ 360.2485, found 360.2481.

Preparation of ***11***. Following the procedure for synthesis of **5a**, **10** (6.29 g, 17.4 mmol) underwent silylation to give **E** (7.80 g, 94% yield)

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

as a colorless oil, which was used directly for the next step without further purification.

To a solution of **E** (7.83 g, 16.5 mmol) in EtOAc (83 mL) was added palladium on carbon (5%, 850 mg, 0.83 mmol). The flask was charged with hydrogen (1 atm, balloon), and the resulting mixture was stirred overnight at rt. The reaction mixture was filtered through Celite and concentrated under reduced pressure to give **F** (7.81 g, 99% yield) as a colorless oil, which was used directly for next step without further purification. Data for **F**: IR (neat, cm^{-1}) 3056, 3028, 2929, 2857, 1610, 1510, 1467, 1254, 1073, 917, 837. ^1H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, J = 7.9 Hz, 2H), 6.80−6.69 (m, 2H), 3.67 (t, J = 5.7 Hz, 1H), 2.68−2.46 (m, 2H), 1.80−1.62 (m, 2H), 1.46 (q, J = 7.1 Hz, 2H), 1.38−1.24 (m, 10H), 0.98 (d, J = 1.7 Hz, 9H), 0.95−0.84 (m, 12H), 0.18 (s, 6H), 0.04 (d, J = 3.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 135.4, 129.1 (2C), 119.8 (2C), 71.9, 39.1, 37.1, 31.8, 30.9, 29.8, 29.3, 25.9 (3C), 25.7 (3C), 25.3, 22.7, 18.2, 14.1, −4.3 (2C), −4.4 (2C). HRMS (CI^+) m/z calcd for $C_{28}H_{55}O_2Si_2$ $[M + H]^+$ 479.3735, found 479.3731.

To a solution of **F** (7.81 g, 16.3 mmol) in MeOH (83 mL) at 0 °C was added K_2CO_3 (2.73 g, 19.8 mmol). The reaction mixture was allowed to warm to rt and stirred for 5 h. Standard workup (quenching with 100 mL of NH_4Cl, extraction with 100 mL of EtOAc) and purification (hexane/ethyl acetate = 1:1) gave **11** (5.8 g, 97% yield) as a colorless oil. IR (neat, cm^{-1}) 3321, 3021, 2928, 2856, 1613, 1513, 1463, 1252, 1073, 834. ^1H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, J = 8.2 Hz, 2H), 6.75 (d, J = 8.5 Hz, 2H), 3.72−3.64 (m, 1H), 3.49 (s, 1H), 2.69−2.57 (m, 1H), 2.57−2.46 (m, 1H), 1.72−1.68 (m, 1H), 1.47 (s, 1H), 1.26 (d, J = 5.3 Hz, 12H), 0.89 (d, J = 9.0 Hz, 12H), 0.05 (d, J = 2.7 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.4, 135.1, 129.3 (2C), 115.1 (2C), 71.9, 39.2, 37.1, 31.8, 30.8, 29.8, 29.3, 25.9 (3C), 25.3, 22.7, 18.2, 14.1, −4.3, −4.4. HRMS (CI^+) m/z calcd for $C_{22}H_{40}O_2Si$ $[M]^+$ 364.2798, found 364.2793.

Preparation of ***12***. To a solution of **11** (5.46 g, 15.0 mmol) in acetonitrile (75 mL) and water (20 mL) at 0 °C was added $PhI(OAc)_2$ (PIDA; 5.80 g, 18 mmol) portionwise over 5 min, and the reaction mixture was stirred vigorously for 15 min. Standard workup (quenching with 30 mL of Na_2SO_3 and 50 mL of Et_2O, extraction with 50 mL of EtOAc) and purification gave **G** (2.56 g, 50% yield) as a colorless oil. IR (neat, cm^{-1}) 3386, 3042, 2929, 2856, 1669, 1625, 1465, 1392, 1253, 1055, 861. ^1H NMR (400 MHz, $CDCl_3$) δ 6.91−6.77 (m, 2H), 6.18 (d, J = 9.9 Hz, 2H), 3.71−3.63 (m, 1H), 1.82 (t, J = 8.4 Hz, 2H), 1.55−1.39 (m, 4H), 1.25 (s, 10H), 1.01−0.81 (m, 12H), 0.05 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.5, 151.4, 151.1, 128.2 (2C), 71.8, 69.6, 36.6, 35.2, 31.8, 30.4, 29.7, 29.2, 25.9 (3C), 25.4, 22.6, 18.1, 14.1, −4.4 (2C). HRMS (CI^+) m/z calcd for $C_{22}H_{41}O_3Si$ $[M + H]^+$ 381.2819, found 381.2812.

Following the procedure for synthesis of **2**, **G** (2.54 g, 6.68 mmol) underwent desilylation to give **H** (1.59 g, 95% yield) as a colorless oil, which was used directly for next step without further purification. To crude product **H** (1.59 g, 6.34 mmol) in chloroform (100 mL) at 0 °C was added $TsOH·H_2O$ (1.0 g, 0.76 mmol). The reaction mixture was stirred overnight at rt. Standard workup (quenching with 100 mL of Na_2CO_3, extraction with 100 mL of EtOAc) and purification (hexane/ethyl acetate = 1:1) gave **12** (1.52 g, 90% yield) as a colorless oil. IR (neat, cm^{-1}) 3342, 2920, 2852, 1663, 1466, 1214, 1188, 1098. ^1H NMR (400 MHz, $CDCl_3$) δ 6.49 (dd, J = 10.0, 2.5 Hz, 1H), 6.05 (d, J = 10.1 Hz, 1H), 3.83−3.79 (m, 1H), 3.34−3.29 (m, 1H), 2.96 (dd, J = 16.8, 3.0 Hz, 1H), 2.51 (dd, J = 16.8, 2.9 Hz, 1H), 2.03 (dt, J = 12.7, 3.4 Hz, 1H), 1.78 (td, J = 13.4, 4.2 Hz, 1H), 1.71−1.65 (m, 1H), 1.44−1.37 (m, 1H), 1.37−1.30 (m, 2H), 1.24 (d, J = 6.6 Hz, 9H), 0.86 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.5, 148.3, 131.2, 78.7, 77.4, 66.1, 40.0, 37.5, 35.5, 31.8, 29.5, 29.3, 29.2, 25.5, 22.6, 14.1. HRMS (CI^+) m/z calcd for $C_{16}H_{27}O_3$ $[M + H]^+$ 267.1955, found 267.1968.

Preparation of ***13***. Following the procedure for synthesis of **A**, **12** (1.1 g, 4.4 mmol) underwent silylation to give **I** (1.32 g, 95% yield) as a colorless oil. IR (neat, cm^{-1}) 3029, 2928, 2857, 1693, 1251, 1104, 841. ^1H NMR (400 MHz, $CDCl_3$) δ 6.51 (dd, J = 10.1, 2.5 Hz, 1H), 6.02 (dd, J = 10.0, 1.1 Hz, 1H), 3.74−3.71 (m, 1H), 3.33−3.28 (m, 1H), 2.95 (dd, J = 16.6, 2.9 Hz, 1H), 2.43 (dd, J = 16.8, 3.0 Hz, 1H), 2.03 (dt, J = 12.7, 3.4 Hz, 1H), 1.87−1.76 (m, 1H), 1.69−1.59 (m, 1H), 1.45−1.37 (m, 1H), 1.34−1.28 (m, 2H), 1.27−1.20 (m, 9H), 0.92−0.81 (m, 3H), 0.12 (d, J = 1.2 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 149.1, 131.0, 79.6, 77.2, 68.5, 40.1, 38.0, 35.5, 31.8, 29.5, 29.2, 29.1, 25.5, 22.6, 14.1, 2.6 (3C). HRMS (CI^+) m/z calcd for $C_{19}H_{35}O_3Si$ $[M + H]^+$ 339.2350, found 339.2362.

Following the procedure for synthesis of **B**, **I** (1.65 g, 5.13 mmol) underwent dimethylation to give the pure enone **J** (1.73 g, 97% yield) as a colorless oil. IR (neat, cm^{-1}) 3026, 2999, 2928, 2855, 1689, 1467, 1252, 1101, 840. ^1H NMR (400 MHz, $CDCl_3$) δ 6.37 (dd, J = 10.1, 2.7 Hz, 1H), 5.92 (d, J = 10.1 Hz, 1H), 3.33 (d, J = 2.6 Hz, 1H), 3.27−3.14 (m, 1H), 2.02 (dt, J = 12.8, 3.4 Hz, 1H), 1.84 (td, J = 13.4, 4.3 Hz, 1H), 1.63−1.52 (m, 1H), 1.33 (d, J = 6.7 Hz, 2H), 1.27 (s, 5H), 1.25−1.19 (m, 7H), 1.18 (s, 4H), 0.86 (t, J = 6.8 Hz, 3H), 0.14 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.1, 147.1, 129.2, 86.3, 77.1, 70.1, 47.0, 39.4, 35.6, 31.8, 29.6, 29.4, 29.2, 26.0, 25.6, 22.6, 22.2, 14.1, 2.8 (3C). HRMS (CI^+) m/z calcd for $C_{21}H_{39}O_3Si$ $[M + H]^+$ 367.2663, found 367.2665.

Following the procedure for synthesis of **2**, **J** (2.84 g, 2.11 mmol) underwent desilylation to give **13** (2.40 g, 99% yield). IR (neat, cm^{-1}) 3421, 3027, 2998, 2928, 2855, 1677, 1457, 1389, 1094. ^1H NMR (400 MHz, $CDCl_3$) δ 6.34 (dd, J = 10.1, 2.7 Hz, 1H), 5.97 (d, J = 10.0 Hz, 1H), 3.38 (d, J = 2.7 Hz, 1H), 3.28−3.19 (m, 1H), 2.00 (dt, J = 12.9, 3.4 Hz, 1H), 1.79 (td, J = 13.4, 4.5 Hz, 2H), 1.63−1.58 (m, 1H), 1.32 (s, 7H), 1.26−1.21 (m, 10H), 0.86 (t, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.8, 146.3, 129.6, 86.0, 77.3, 67.7, 46.9, 39.6, 35.5, 31.8, 29.6, 29.4, 29.2, 25.9, 25.6, 22.6, 21.9, 14.1. HRMS (CI^+) m/z calcd for $C_{18}H_{31}O_3$ $[M + H]^+$ 295.2268, found 295.2274.

Preparation of ***14***. Following the procedure for synthesis of **3**, **13** (1.49 g, 5.1 mmol) underwent epoxidation to give **14** (1.49 g, 94% yield). IR (neat, cm^{-1}) 3482, 3000, 2929, 2856, 1717, 1459, 1388, 1091. ^1H NMR (400 MHz, $CDCl_3$) δ 3.47 (d, J = 3.5 Hz, 1H), 3.41 (dd, J = 3.6, 2.3 Hz, 1H), 3.18 (dd, J = 8.0, 2.6 Hz, 1H), 3.14 (d, J = 2.3 Hz, 1H), 2.10 (dt, J = 13.3, 3.4 Hz, 1H), 1.87 (td, J = 13.9, 4.5 Hz, 1H), 1.76−1.66 (m, 1H), 1.37 (s, 3H), 1.35−1.31 (m, 2H), 1.30−1.18 (m, 10H), 1.15 (s, 3H), 0.87 (t, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.3, 88.9, 77.3, 67.3, 62.6, 57.0, 47.2, 36.7, 35.5, 31.8, 29.5, 29.4, 29.2, 25.6, 23.8, 23.3, 22.6, 14.1. HRMS (CI^+) m/z calcd for $C_{18}H_{30}O_4$ $[M]^+$ 310.2139, found 310.2141.

Preparation of ***15a*** *and* ***15b***. Following the procedure for synthesis of **4a** and **4b**, **14** (1.50 g, 5.0 mmol) underwent reduction to give **15a** (360 mg, 24% yield, colorless oil) and **15b** (1.09 g, 73% yield, colorless oil).

Data for **15a**: IR (neat, cm^{-1}) 3416, 2927, 2854, 1457, 1092. ^1H NMR (400 MHz, $CDCl_3$) δ 3.99 (d, J = 2.5 Hz, 1H), 3.57 (t, J = 3.2 Hz, 1H), 3.41 (s, 1H), 3.23−3.10 (m, 2H), 2.94 (d, J = 2.2 Hz, 1H), 2.04−1.92 (m, 1H), 1.88−1.77 (m, 1H), 1.70−1.60 (m, 2H), 1.38 (s, 2H), 1.27 (d, J = 8.4 Hz, 10H), 1.11 (d, J = 6.3 Hz, 6H), 0.88 (t, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 86.9, 76.9, 71.5, 67.0, 60.8, 60.2, 38.2, 36.9, 35.7, 31.8, 29.7, 29.5, 29.2, 26.2, 25.6, 22.6, 20.9, 14.1. HRMS (CI^+) m/z calcd for $C_{18}H_{33}O_4$ $[M + H]^+$ 313.2373, found 313.2373.

Data for **15b**: IR (neat, cm^{-1}) 3511, 2999, 2928, 2856, 1413, 1088, 1028. ^1H NMR (400 MHz, $CDCl_3$) δ 3.67−3.62 (m, 2H), 3.36 (d, J = 11.5 Hz, 1H), 3.22−3.07 (m, 2H), 3.02 (s, 1H), 2.05 (dt, J = 13.6, 3.4 Hz, 1H), 1.84 (td, J = 13.9, 4.3 Hz, 1H), 1.75−1.66 (m, 1H), 1.44−1.38 (m, 2H), 1.27 (d, J = 12.0 Hz, 10H), 1.16 (s, 3H), 1.07 (s, 3H), 0.87 (t, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 85.8, 77.6, 70.6, 67.0, 59.4, 56.5, 37.0, 36.3, 35.8, 31.7, 29.7, 29.4, 29.1, 25.7, 25.3, 24.9, 22.6, 14.0. HRMS (CI^+) m/z calcd for $C_{18}H_{33}O_4$ $[M + H]^+$ 313.2373, found 313.2369.

Preparation of ***16a***. Following the procedure for synthesis of **5a**, **15a** (360 mg, 1.15 mmol) underwent silylation to give the diol product **16a** (473 mg, 96% yield) as a colorless oil. IR (neat, cm^{-1}) 2955, 2932, 2876, 2856, 1459, 1093, 741. ^1H NMR (400 MHz, $CDCl_3$) δ 4.04 (d, J = 2.3 Hz, 1H), 3.39 (dd, J = 4.1, 2.2 Hz, 1H), 3.11 (dd, J = 4.0, 2.1 Hz, 2H), 2.90 (d, J = 2.0 Hz, 1H), 2.48 (s, 1H), 1.97 (dt, J = 13.3, 3.4 Hz, 1H), 1.79 (td, J = 13.8, 4.5 Hz, 1H), 1.68−1.61 (m, 1H), 1.44−1.34 (m, 3H), 1.27 (p, J = 6.2, 5.0 Hz, 10H), 1.07 (s, 3H), 1.04 (s, 3H), 1.00 (t, J = 7.9 Hz, 9H), 0.88 (t, J = 6.8 Hz, 3H),

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

0.71−0.61 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 87.2, 76.8, 71.9, 66.9, 60.3, 60.0, 38.8, 36.7, 35.6, 31.8, 29.7, 29.5, 29.2, 26.6, 25.6, 22.7, 21.5, 14.1, 6.9 (3C), 5.2 (3C). HRMS (CI$^+$) m/z calcd for $C_{24}H_{47}O_4Si$ $[M + H]^+$ 427.3238, found 427.3223.

Preparation of ***16b***. Following the procedure for synthesis of **5b**, **15b** (1.09 g, 3.5 mmol) underwent silylation to give the diol product, protected alcohol **16b** (1.45 g, 97% yield), as a colorless oil. IR (neat, cm^{-1}) 3509, 2956, 2930, 2876, 2857, 1464, 1239, 1091, 1014, 841, 740. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (d, J = 1.3 Hz, 1H), 3.35 (dd, J = 3.8, 1.3 Hz, 1H), 3.35−3.27 (m, 1H), 3.11 (d, J = 3.7 Hz, 1H), 2.90 (s, 1H), 2.30 (s, 1H), 1.92−1.77 (m, 2H), 1.79−1.70 (m, 1H), 1.44−1.35 (m, 3H), 1.26 (d, J = 7.8 Hz, 9H), 1.02−0.95 (m, 15H), 0.87 (t, J = 6.7 Hz, 3H), 0.64 (q, J = 7.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 85.9, 74.2, 72.7, 67.4, 61.7, 58.6, 39.4, 36.4, 33.8, 31.9, 29.6, 29.3, 28.2, 25.9, 25.7, 22.7, 20.6, 14.1, 6.9 (3C), 4.9 (3C). HRMS (CI$^+$) m/z calcd for $C_{24}H_{47}O_4Si$ $[M + H]^+$ 427.3238, found 427.3254.

Preparation of ***17a***. Following General Procedure A, **16a** (592 mg, 1.15 mmol) underwent PCC-mediated oxidative ring expansion to give the 10-membered lactone **17a** (372 mg, 73% yield) as a colorless oil. IR (neat, cm^{-1}) 2956, 2930, 2876, 2857, 1742, 1714, 1464, 1263, 1097, 745. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.89−4.80(m, 1H), 4.04 (d, J = 5.0 Hz, 1H), 3.43 (d, J = 4.3 Hz, 1H), 3.14 (t, J = 4.7 Hz, 1H), 2.82 (ddd, J = 13.6, 11.8, 1.6 Hz, 1H), 2.26−2.04 (m, 2H), 1.96−1.81 (m, 1H), 1.51−1.39 (m, 2H), 1.26 (d, J = 17.8 Hz, 13H), 1.12 (s, 3H), 0.99 (t, J = 7.9 Hz, 9H), 0.86 (t, J = 6.8 Hz, 3H), 0.69 (q, J = 7.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6, 175.3, 74.2, 69.1, 61.7, 60.5, 47.1, 36.9, 34.4, 31.7, 30.2, 29.4, 29.1, 25.0, 24.9, 22.6, 16.6, 14.1, 6.8 (3C), 4.7 (3C). HRMS (CI$^-$) m/z calcd for $C_{24}H_{44}O_5Si$ $[M]^-$ 440.2963, found 440.2970.

Preparation of ***17b***. Following General Procedure A, **16b** (1.00 g, 2.35 mmol) underwent PCC-mediated oxidative ring expansion to give **17b** (921 mg, 89% yield) as a colorless oil. IR (neat, cm^{-1}) 2955, 2931, 2876, 2858, 2732, 1729, 1466, 1265, 1152, 1090, 742. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.87−4.73 (m, 1H), 3.86 (d, J = 4.7 Hz, 1H), 3.55 (d, J = 8.1 Hz, 1H), 3.32 (dd, J = 8.1, 4.7 Hz, 1H), 2.74 (ddd, J = 15.4, 7.0, 2.9 Hz, 1H), 2.41 (ddd, J = 15.2, 11.9, 3.3 Hz, 1H), 2.22−2.13 (m, 1H), 2.04 (ddd, J = 15.3, 6.8, 3.2 Hz, 1H), 1.69 (dt, J = 14.9, 7.2 Hz, 1H), 1.51 (q, J = 6.5 Hz, 1H), 1.33−1.21 (m, 12H), 1.14 (s, 3H), 0.98 (t, J = 8.0 Hz, 9H), 0.85 (t, J = 6.7 Hz, 3H), 0.79−0.68 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6, 174.1, 74.7, 72.1, 60.8, 57.6, 47.1, 40.8, 34.2, 31.6, 29.6, 29.2, 29.0, 25.2, 23.3, 22.5, 17.9, 14.0, 6.8 (3C), 4.9 (3C). HRMS (CI$^-$) m/z calcd for $C_{24}H_{44}O_5Si$ $[M]^-$ 440.2963, found 440.2964.

Preparation of ***18a***. Following the procedure for synthesis of **7b**, **17a** (66 mg, 0.15 mmol) underwent SmI_2-mediated reductive epoxide ring opening to give **18a** (30 mg, 93% yield) as a colorless oil. IR (neat, cm^{-1}) 3517, 2955, 2928, 2876, 2857, 1730, 1711, 1613, 1465, 1260, 1166, 1067, 1006, 744. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.17−5.06 (m, 1H), 4.49−4.38 (m, 1H), 4.05 (d, J = 2.8 Hz, 1H), 2.76−2.61 (m, 2H), 2.41 (ddd, J = 13.1, 9.0, 4.4 Hz, 2H), 2.31−2.22 (m, 1H), 2.10−2.04 (m, 2H), 1.49 (d, J = 5.6 Hz, 1H), 1.25 (d, J = 3.3 Hz, 15H), 1.17 (s, 3H), 1.02 (t, J = 7.9 Hz, 9H), 0.87 (t, J = 6.8 Hz, 3H), 0.78−0.68 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.3, 176.6, 77.2, 74.7, 71.2, 45.8, 45.0, 40.1, 33.7, 31.9, 31.7, 29.3, 29.1, 27.6, 25.3, 22.6, 18.7, 14.1, 6.9 (3C), 5.1 (3C). HRMS (CI$^-$) m/z calcd for $C_{24}H_{46}O_5Si$ $[M]^-$ 442.3120, found 442.3109.

Preparation of ***18b***. Following the procedure for synthesis of **7d**, **17b** (66 mg, 0.15 mmol) underwent SmI_2-mediated reductive epoxide ring opening to give **18b** (31 mg, 94% yield) as a colorless oil. IR (neat, cm^{-1}) 3518, 2955, 2929, 2875, 2857, 1717, 1465, 1266, 1105, 738. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.85−4.76 (m, 1H), 4.12 (td, J = 7.9, 1.9 Hz, 1H), 3.74 (d, J = 8.4 Hz, 1H), 2.77 (dd, J = 17.6, 7.7 Hz, 1H), 2.69 (s, 1H), 2.56 (dd, J = 17.5, 1.9 Hz, 1H), 2.49−2.30 (m, 2H), 2.21−2.11 (m, 1H), 2.09−2.00 (m, 1H), 1.77−1.69 (m, 1H), 1.56−1.46 (m, 1H), 1.23 (d, J = 18.0 Hz, 13H), 1.07−0.95 (m, 12H), 0.87 (t, J = 6.8 Hz, 4H), 0.70 (q, J = 7.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.4, 176.4, 80.7, 76.0, 68.5, 46.9, 46.5, 40.0, 33.4, 31.7, 30.3, 29.2, 29.1, 26.8, 25.8, 22.6, 16.8, 14.1, 7.0 (3C), 5.5 (3C). HRMS (CI$^-$) m/z calcd for $C_{24}H_{46}O_5Si$ $[M]^-$ 442.3120, found 442.3109.

Preparation of [5,5]-Spiroacetal-cis-fused-γ-lactones ***19a*** *and* ***19b***. Following General Procedure D, **19a** (14.3 mg, 55% yield, colorless oil) and **19b** (6.5 mg, 25% yield, colorless oil) were obtained from **18a** (40 mg, 0.09 mmol).

Data for **19a**: IR (neat, cm^{-1}) 2927, 2855, 1780, 1462, 1139, 1124. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.10 (t, J = 5.2 Hz, 1H), 4.35 (d, J = 5.0 Hz, 1H), 4.16−3.90 (m, 1H), 2.45 (d, J = 14.1 Hz, 1H), 2.18−1.96 (m, 4H), 1.50 (d, J = 2.6 Hz, 1H), 1.47−1.39 (m, 2H), 1.25 (d, J = 3.0 Hz, 13H), 1.21 (s, 3H), 0.87 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.8, 115.0, 86.8, 80.0, 79.7, 44.3, 41.9, 35.4, 34.5, 31.9, 29.9, 29.7, 29.2, 26.0, 25.4, 22.7, 18.4, 14.1. HRMS (CI$^+$) m/z calcd for $C_{18}H_{31}O_4$ $[M + H]^+$ 311.2217, found 311.2232.

Data for **19b**: IR (neat, cm^{-1}) 2928, 2857, 1776, 1463, 1345, 1123, 1104. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.02 (ddd, J = 6.0, 3.7, 1.6 Hz, 1H), 4.30 (d, J = 3.7 Hz, 1H), 4.07−3.95 (m, 1H), 2.49 (dd, J = 14.9, 6.2 Hz, 1H), 2.33 (dd, J = 15.1, 1.5 Hz, 1H), 2.11−1.87 (m, 4H), 1.79−1.69 (m, 1H), 1.45 (dd, J = 10.7, 5.5 Hz, 1H), 1.31−1.28 (m, 6H), 1.26 (s, 6H), 1.22 (s, 3H), 0.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.0, 115.2, 85.0, 80.8, 80.4, 44.4, 41.9, 37.2, 37.0, 31.8, 30.6, 29.6, 29.2, 26.0, 23.1, 22.7, 18.1, 14.1. HRMS (CI$^+$) m/z calcd for $C_{18}H_{31}O_4$ $[M + H]^+$ 311.2217, found 311.2227.

Preparation of [5,5]-Spiroacetal-cis-fused-γ-lactones ***19c*** *and* ***19d***. Following General Procedure C, **19c** (4.2 mg, 30% yield, colorless solid) and **19d** (8.4 mg, 60% yield, colorless oil) were obtained from **18b** (16 mg, 0.045 mmol).

Data for **19c**: IR (neat, cm^{-1}) 2955, 2928, 2856, 1781, 1464, 1133, 1095. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.03 (ddd, J = 6.0, 3.7, 1.6 Hz, 1H), 4.29 (d, J = 3.7 Hz, 1H), 4.09−3.98 (m, 1H), 2.52 (dd, J = 15.0, 6.3 Hz, 1H), 2.36 (dd, J = 15.1, 1.6 Hz, 1H), 2.16−1.99 (m, 3H), 1.51 (dd, J = 14.6, 7.0 Hz, 1H), 1.27 (d, J = 4.8 Hz, 15H), 1.22 (s, 3H), 0.87 (t, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 181.0, 115.5, 85.3, 80.6, 79.1, 44.5, 42.4, 35.7, 35.6, 31.9, 30.1, 29.7, 29.3, 25.9, 23.2, 22.7, 18.2, 14.2. HRMS (CI$^+$) m/z calcd for $C_{18}H_{31}O_4$ $[M + H]^+$ 311.2217, found 311.2227.

Data for **19d**: IR (neat, cm^{-1}) 2928, 2856, 1777, 1464, 1348, 1171. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.07 (t, J = 4.9 Hz, 1H), 4.29 (d, J = 4.6 Hz, 1H), 4.03−3.92 (m, 1H), 2.44 (d, J = 14.1 Hz, 1H), 2.17−1.96 (m, 4H), 1.69−1.61 (m, 2H), 1.47−1.31 (m, 2H), 1.29 (s, 3H), 1.25 (s, 9H), 1.21 (s, 3H), 0.88 (d, J = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.6, 115.1, 87.1, 81.9, 79.8, 44.5, 41.7, 37.4, 36.3, 31.8, 30.9, 29.6, 29.2, 26.1, 24.9, 22.7, 18.3, 14.1. HRMS (CI$^+$) m/z calcd for $C_{18}H_{31}O_4$ $[M + H]^+$ 311.2217, found 311.2227.

Preparation of ***20***. Following the procedure for synthesis of **10**, **9** (5.29 g, 20 mmol) underwent nucleophilic addition of alkynyllithium (3.80 g, 26.0 mmol) to give **20** (7.46 g, 91% yield) as a colorless oil, which was used directly for next step without further purification. IR (neat, cm^{-1}) 3410, 3090, 3062, 3031, 2890, 2858, 1609, 1509, 1258, 1068, 916, 839, 781, 740, 697. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.27 (m, 5H), 7.06 (d, J = 8.1 Hz, 2H), 6.76 (d, J = 8.2 Hz, 2H), 4.61 (s, 2H), 4.41 (t, J = 6.6 Hz, 1H), 4.24 (s, 2H), 2.74 (t, J = 7.8 Hz, 2H), 2.07−1.94 (m, 2H), 0.98 (s, 9H), 0.19 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 137.3, 133.7, 129.3 (2C), 128.4 (2C), 128.1 (2C), 127.9, 120.0 (2C), 87.4, 81.1, 71.7, 61.7, 57.4, 39.3, 30.5, 25.7 (3C), 18.2, −4.4 (2C). HRMS (CI$^+$) m/z calcd for $C_{25}H_{34}O_3Si$ $[M]^+$ 410.2272, found 410.2289.

Preparation of ***21***. Following the procedure for synthesis of **E**, **20** (45.6 g, 111 mmol) underwent silylation to give **K** (57.0 g, 98% yield) as a colorless oil, which was used directly for next step without further purification. IR (neat, cm^{-1}) 3030, 2931, 2889, 2857, 1609, 1510, 1466, 1256, 1087, 916, 838, 779. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.27 (m, 5H), 7.07−7.01 (m, 2H), 6.78−6.72 (m, 2H), 4.61 (s, 2H), 4.41 (t, J = 6.4 Hz, 1H), 4.22 (d, J = 1.6 Hz, 2H), 2.70 (td, J = 7.5, 4.0 Hz, 2H), 2.03−1.90 (m, 2H), 0.98 (s, 9H), 0.92 (s, 9H), 0.18 (s, 6H), 0.12 (d, J = 11.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.7, 137.5, 134.2, 129.2 (2C), 128.4 (2C), 128.1 (2C), 127.8, 119.9 (2C), 88.2, 80.1, 71.4, 62.3, 57.4, 40.4, 30.6, 25.8 (3C), 25.7 (3C), 18.2, 18.2, −4.4 (3C), − 5.0. HRMS (CI$^+$) m/z calcd for $C_{31}H_{48}O_3Si_2$ $[M]^+$ 524.3136, found 524.3125.

To a solution of **K** (9.0 g, 17.1 mmol) in EtOH (90 mL) was added Raney nickel (50% in water, 18.0 g) under hydrogen atmosphere (1

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

atm, balloon). The resulting mixture was stirred for 2 h at rt, filtered through Celite, and concentrated under reduced pressure to give **L** (8.94 g, 99% yield) as a colorless oil, which was used directly for next step without further purification. IR (neat, cm^{-1}) 3061, 3029, 2931, 2888, 2857, 1609, 1510, 1466, 1362, 1256, 1074, 916, 836, 777. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 7.02 (d, J = 8.2 Hz, 2H), 6.75 (d, J = 8.4 Hz, 2H), 4.51 (s, 2H), 3.74−3.70 (m, 1H), 3.48 (t, J = 6.4 Hz, 2H), 2.66−2.50 (m, 2H), 1.78−1.52 (m, 6H), 0.99 (s, 9H), 0.91 (s, 9H), 0.19 (s, 6H), 0.05 (d, J = 4.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 138.6, 135.3, 129.1 (2C), 128.3 (2C), 127.6 (2C), 127.4, 119.8 (2C), 72.8, 71.6, 70.6, 39.1, 33.4, 30.8, 25.9 (3C), 25.7 (3C), 25.5, 18.2, 18.1, −4.4, −4.4 (3C). HRMS (CI^+) m/z calcd for $C_{31}H_{53}O_3Si_2$ $[M]^+$ 529.3528, found 529.3524.

Following the procedure for synthesis of **11**, **L** (40.4 g, 76.4 mmol) underwent desilylation to give **21** (30.7 g, 97% yield). IR (neat, cm^{-1}) 3402, 3065, 3030, 2930, 2856, 1614, 1514, 1454, 1252, 1072, 832, 774, 736. ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.26 (m, 5H), 7.03 (d, J = 8.4 Hz, 2H), 6.74 (d, J = 8.5 Hz, 2H), 4.51 (s, 2H), 3.72 (q, J = 5.6 Hz, 1H), 3.48 (t, J = 6.4 Hz, 2H), 2.62−2.50 (m, 2H), 1.71−1.67 (m, 4H), 1.61−1.51 (m, 2H), 0.90 (s, 9H), 0.04 (d, J = 4.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 138.5, 134.8, 129.3 (2C), 128.3 (2C), 127.6 (2C), 127.5, 115.1 (2C), 72.8, 71.6, 70.6, 39.2, 33.4, 30.7, 25.9 (3C), 25.5 (3C), 18.1, −4.4 (4C). HRMS (CI^+) m/z calcd for $C_{25}H_{39}O_3Si$ $[M + H]^+$ 415.2663, found 415.2650.

Preparation of ***22***. Following the procedure for synthesis of **G**, **21** (6.21 g, 15.0 mmol) underwent PIDA-mediated dearomatization to give **M** (3.35 g, 52% yield) as a colorless oil. IR (neat, cm^{-1}) 3393, 3064, 3032, 2952, 2856, 1669, 1625, 1494, 1254, 1067, 860, 735, 774, 739. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 6.80 (d, J = 9.6 Hz, 2H), 6.17 (d, J = 9.8 Hz, 2H), 4.49 (s, 2H), 3.70 (t, J = 5.4 Hz, 1H), 3.45 (t, J = 6.1 Hz, 2H), 1.81 (t, J = 8.2 Hz, 2H), 1.65−1.40 (m, 6H), 0.88 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.5, 151.3, 151.1, 138.5, 128.3 (2C), 128.2 (2C), 127.6 (2C), 127.5, 72.9, 71.5, 70.3, 69.6, 35.1, 33.1, 30.4, 25.9 (3C), 25.6, 18.0, −4.4 (2C), −4.5 (2C). HRMS (CI^+) m/z calcd for $C_{25}H_{38}O_4Si$ $[M]^+$ 430.2534, found 430.2546.

Following the procedure for synthesis of **H**, **M** (2.87 g, 6.68 mmol) underwent desilylation to give **N** (2.01 g, 95% yield) as colorless oil, which was used directly for next step without further purification.

Following the procedure for synthesis of **12**, **N** (2.01 g, 6.34 mmol) underwent oxa-Michael cyclization to give tertiary alcohol **22** (1.80 g, 90% yield) as a colorless oil. IR (neat, cm^{-1}) 3416, 3066, 3031, 2931, 2861, 1673, 1495, 1363, 1080, 740 699. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41−7.25 (m, 5H), 6.47 (dd, J = 10.1, 2.5 Hz, 1H), 6.04 (d, J = 10.1 Hz, 1H), 4.47 (s, 2H), 3.78 (q, J = 2.9 Hz, 1H), 3.44 (q, J = 6.6 Hz, 2H), 3.35 (dq, J = 11.2, 5.5, 4.7 Hz, 1H), 2.95 (dd, J = 16.8, 3.0 Hz, 1H), 2.49 (dd, J = 16.9, 2.9 Hz, 1H), 2.26 (s, 1H), 2.02 (dt, J = 12.8, 3.4 Hz, 1H), 1.77 (td, J = 13.3, 4.0 Hz, 1H), 1.72−1.63 (m, 2H), 1.63−1.54 (m, 1H), 1.48 (td, J = 9.9, 9.0, 5.5 Hz, 2H), 1.35−1.21 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 148.0, 138.5, 131.3, 128.3 (2C), 127.6 (2C), 127.5, 78.7, 76.7, 72.8, 70.2, 66.1, 39.9, 37.5, 32.0, 29.3, 25.7. HRMS (CI^+) m/z calcd for $C_{19}H_{25}O_4$ $[M + H]^+$ 317.1747, found 317.1746.

Preparation of ***23***. Following the procedure for synthesis of **I**, **22** (6.32 g, 20.0 mmol) underwent silylation to give enone **O** (7.37 g, 95% yield) as a colorless oil. IR (neat, cm^{-1}) 3061, 3030, 2925, 2855, 1685, 1452, 1247, 1099. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.26 (m, 5H), 6.51 (dd, J = 10.1, 2.4 Hz, 1H), 6.02 (d, J = 10.1 Hz, 1H), 4.47 (s, 2H), 3.73 (d, J = 2.8 Hz, 1H), 3.43 (q, J = 6.8 Hz, 2H), 3.35 (dq, J = 11.2, 5.2 Hz, 1H), 2.96 (dd, J = 16.7, 2.8 Hz, 1H), 2.49−2.39 (m, 1H), 2.09−1.99 (m, 1H), 1.82 (td, J = 13.4, 4.2 Hz, 1H), 1.67 (dt, J = 12.8, 4.1 Hz, 1H), 1.61−1.57 (m, 1H), 1.50−1.43 (m, 2H), 1.33−1.18 (m, 2H), 0.12 (d, J = 1.2 Hz, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 149.0, 138.6, 131.0, 128.3 (2C), 127.6 (2C), 127.5, 79.6, 76.9, 72.8, 70.2, 68.4, 40.0, 37.9, 32.1, 29.1, 25.7, 2.6 (3C). HRMS (CI^+) m/z calcd for $C_{22}H_{33}O_4Si$ $[M + H]^+$ 389.2143, found 389.2151.

Following the procedure for synthesis of **J**, **O** (3.6 g, 9.28 mmol) underwent dimethylation to give **P** (3.74 g, 97% yield) as a colorless oil. IR (neat, cm^{-1}) 3063, 3029, 2951, 2858, 1686, 1452, 1252, 1100, 841. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.24 (m, 5H), 6.38 (dd, J = 10.1, 2.6 Hz, 1H), 5.93 (d, J = 10.1 Hz, 1H), 4.47 (s, 2H), 3.48−3.40 (m, 2H), 3.33 (d, J = 2.6 Hz, 1H), 3.31−3.17 (m, 1H), 2.02 (dt, J = 12.8, 3.5 Hz, 1H), 1.85 (td, J = 13.4, 4.3 Hz, 1H), 1.76−1.64 (m, 1H), 1.60−1.53 (m, 2H), 1.52−1.33 (m, 2H), 1.27 (s, 3H), 1.22 (s, 1H), 1.18 (s, 3H), 0.15 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.1, 147.1, 138.6, 129.2, 128.3 (2C), 127.6 (2C), 127.5, 86.4, 76.9, 72.8, 70.2, 70.0, 47.0, 39.4, 32.2, 29.5, 26.0, 25.9, 22.3, 2.8 (3C). HRMS (CI^+) m/z calcd for $C_{24}H_{37}O_4Si$ $[M]^+$ 417.2456, found 417.2457.

Following the procedure for synthesis of **13**, **P** (7.25 g, 17.3 mmol) underwent desilylation to give **23** (5.89 g, 99% yield). IR (neat, cm^{-1}) 3420, 3090, 3064, 3030, 2998, 2927, 2855, 1677, 1452, 1389, 1093, 740, 699. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45−7.24 (m, 5H), 6.33 (dd, J = 10.1, 2.6 Hz, 1H), 5.97 (d, J = 10.1 Hz, 1H), 4.47 (s, 2H), 3.48−3.40 (m, 2H), 3.39−3.35 (m, 1H), 3.29−3.22 (m, 1H), 2.09−1.95 (m, 1H), 1.78 (td, J = 13.3, 4.3 Hz, 1H), 1.73−1.66 (m, 1H), 1.60 (tt, J = 7.1, 2.7 Hz, 2H), 1.50−1.40 (m, 2H), 1.32 (s, 3H), 1.29−1.21 (m, 1H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.5, 146.1, 138.6, 129.7, 128.3 (2C), 127.6 (2C), 127.5, 86.0, 76.7, 72.8, 70.1, 67.6, 46.9, 39.6, 32.1, 29.5, 25.9, 21.9. HRMS (CI^+) m/z calcd for $C_{21}H_{29}O_4$ $[M + H]^+$ 345.2060, found 345.2066.

Preparation of ***24***. Following the procedure for synthesis of **14**, **23** (5.95 g, 17.7 mmol) underwent epoxidation to give **24** (6.09 g, 91% yield). IR (neat, cm^{-1}) 3441, 3031, 3002, 2930, 2857, 1713, 1637, 1092, 736, 899. ^1H NMR (400 MHz, $CDCl_3$) δ 7.47−7.15 (m, 5H), 4.47 (s, 2H), 3.50−3.35 (m, 4H), 3.19 (dt, J = 8.9, 5.6 Hz, 1H), 3.13 (d, J = 2.2 Hz, 1H), 2.54 (s, 1H), 2.10 (dt, J = 13.4, 3.5 Hz, 1H), 1.87 (td, J = 13.9, 4.5 Hz, 1H), 1.71 (dt, J = 15.7, 4.5 Hz, 2H), 1.63−1.43 (m, 3H), 1.37 (s, 3H), 1.34−1.24 (m, 1H), 1.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.2, 138.5, 128.3 (2C), 127.6 (2C), 127.5, 88.9, 77.1, 72.8, 70.0, 67.3, 62.6, 57.0, 47.2, 36.7, 32.1, 29.4, 25.9, 23.8, 23.3. HRMS (CI^+) m/z calcd for $C_{21}H_{29}O_5$ $[M + H]^+$ 361.2010, found 361.2003.

Preparation of ***25a*** *and* ***25b***. Following the procedure for synthesis of **15a** and **15b**, **24** (5.81 g, 17.68 mmol) underwent $NaBH_4$ reduction to give **Qa** (1.47 g, 23% yield, colorless oil) and **Qb** (4.67 g, 73% yield, colorless oil).

Data for **Qa**: IR (neat, cm^{-1}) 3438, 3089, 3063, 3030, 2930, 2855, 1723, 1643, 1451, 1363, 1094, 1029, 736, 699. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.25 (m, 5H), 4.50 (s, 2H), 3.97 (d, J = 2.3 Hz, 1H), 3.56 (dd, J = 4.1, 2.3 Hz, 1H), 3.46 (td, J = 6.6, 1.9 Hz, 2H), 3.20 (dd, J = 4.0, 2.0 Hz, 1H), 3.17−3.11 (m, 1H), 2.93 (d, J = 2.1 Hz, 1H), 2.36 (s, 1H), 1.98 (dt, J = 13.4, 3.5 Hz, 1H), 1.85−1.70 (m, 2H), 1.65−1.61 (m, 2H), 1.53−1.47 (m, 2H), 1.32−1.26 (m, 1H), 1.10 (d, J = 2.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 128.3 (2C), 127.6 (2C), 127.5, 86.9, 76.6, 72.9, 71.5, 70.2, 66.9, 60.7, 60.2, 38.2, 36.8, 32.3, 29.7, 26.2, 26.0, 20.9. HRMS (CI^+) m/z calcd for $C_{21}H_{31}O_5$ $[M + H]^+$ 363.2166, found 363.2160.

Data for **Qb**: IR (neat, cm^{-1}) 3501, 3087, 3062, 3029, 2929, 2856, 1637, 1478, 1452, 1096, 1025. ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.27 (m, 5H), 4.49 (s, 2H), 3.71−3.60 (m, 2H), 3.46 (q, J = 5.9 Hz, 2H), 3.30 (d, J = 11.5 Hz, 1H), 3.21−3.13 (m, 1H), 3.11 (dd, J = 3.7, 1.4 Hz, 1H), 3.01 (s, 1H), 2.36 (s, 1H), 2.10−2.01 (m, 1H), 1.90−1.79 (m, 1H), 1.78−1.68 (m, 2H), 1.62−1.56 (m, 3H), 1.38−1.27 (m, 1H), 1.16 (s, 3H), 1.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 128.4 (2C), 127.6 (3C), 85.8, 77.5, 72.9, 70.6, 69.8, 66.9, 59.4, 56.4, 36.9, 36.4, 32.5, 29.7, 26.0, 25.3, 24.9. HRMS (CI^+) m/z calcd for $C_{21}H_{31}O_5$ $[M + H]^+$ 363.2166, found 363.2162.

Following the procedure for synthesis of **16a**, **Qa** (1.94 g, 5.36 mmol) underwent silylation to give **25a** (2.47 g, 97% yield) as a colorless oil. IR (neat, cm^{-1}) 3587, 3088, 3064, 3030, 2953, 2875, 1455, 1361, 1097, 1010. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.50 (s, 2H), 4.03 (d, J = 2.3 Hz, 1H), 3.47 (td, J = 6.5, 2.6 Hz, 2H), 3.39 (dd, J = 4.0, 2.3 Hz, 1H), 3.19−3.08 (m, 2H), 2.90 (d, J = 1.9 Hz, 1H), 2.00−1.93 (m, 1H), 1.84−1.72 (m, 2H), 1.69−1.60 (m, 3H), 1.55−1.49 (m, 2H), 1.26 (d, J = 4.5 Hz, 1H), 1.07 (s, 3H), 1.01 (dd, J = 15.1, 7.1 Hz, 12H), 0.71−0.59 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 128.3 (2C), 127.6 (2C), 127.5, 87.3, 76.6, 72.8, 71.8, 70.2, 66.9, 60.2, 60.0, 38.7, 36.6, 32.3, 29.7, 26.7, 25.9, 21.5, 6.9 (3C), 5.1 (3C). HRMS (CI^+) m/z calcd for $C_{27}H_{45}O_5Si$ $[M + H]^+$ 477.3031, found 477.3043.

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

Following the procedure for synthesis of **16b**, **Qb** (2.9 g, 8.0 mmol) underwent silylation to give **25b** (3.65 g, 96% yield) as a colorless oil. IR (neat, cm^{-1}) 3455, 3087, 3063, 3029, 2954, 2876, 1456, 1362, 1239, 1099, 1012. ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.26 (m, 5H), 4.50 (s, 2H), 3.59 (d, J = 1.3 Hz, 1H), 3.46 (q, J = 6.5 Hz, 2H), 3.40−3.29 (m, 2H), 3.11 (d, J = 3.8 Hz, 1H), 2.89 (s, 1H), 2.30 (s, 1H), 1.88−1.75 (m, 3H), 1.70−1.60 (m, 2H), 1.55−1.45 (m, 2H), 1.41−1.32 (m, 1H), 1.06−0.92 (m, 15H), 0.64 (q, J = 7.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 128.3 (2C), 127.6 (2C), 127.4, 85.9, 73.8, 72.8, 72.7, 70.4, 67.4, 61.7, 58.6, 39.5, 33.6, 32.9, 28.1, 25.9, 25.9, 20.5, 6.9 (3C), 4.9 (3C). HRMS (CI^+) m/z calcd for $C_{27}H_{45}O_5Si$ $[M + H]^+$ 477.3031, found 477.3038.

Preparation of ***26a***. Following General Procedure B, **25a** (200 mg, 0.42 mmol) underwent microwave-assisted PCC-mediated oxidative ring expansion to give **26a** (162 mg, 81% yield) as a colorless oil and benzoate **R** (20 mg, 10% yield) as a colorless oil.

Data for **26a**: IR (neat, cm^{-1}) 2954, 2877, 1742, 1717, 1454, 1265, 1092, 740. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.26 (m, 5H), 4.88 (d, J = 10.7 Hz, 1H), 4.47 (s, 2H), 4.03 (d, J = 5.1 Hz, 1H), 3.43 (t, J = 4.3 Hz, 3H), 3.14 (t, J = 4.8 Hz, 1H), 2.82 (t, J = 12.8 Hz, 1H), 2.27−2.10 (m, 2H), 1.95−1.83 (m, 1H), 1.56 (s, 4H), 1.28 (s, 3H), 1.11 (s, 3H), 0.99 (t, J = 7.9 Hz, 9H), 0.68 (q, J = 7.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.5, 175.3, 138.5, 128.3 (2C), 127.6 (2C), 127.5, 73.9, 72.8, 69.8, 69.1, 61.7, 60.5, 47.1, 36.9, 31.2, 30.3, 25.4, 24.9, 16.6, 6.8 (3C), 4.7 (3C). HRMS (CI^+) m/z calcd for $C_{27}H_{43}O_6Si$ $[M + H]^+$ 491.2823, found 491.2822.

Data for **R**: IR (neat, cm^{-1}) 2992, 2960, 2926, 2856, 1731, 1454, 1258, 1077, 861, 751, 700. ^1H NMR (400 MHz, $CDCl_3$) δ 8.06−7.97 (m, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 4.95 (s, 1H), 4.28 (dt, J = 6.3, 3.8 Hz, 2H), 4.05 (d, J = 5.1 Hz, 1H), 3.44 (d, J = 4.3 Hz, 1H), 3.15 (t, J = 4.8 Hz, 1H), 2.85 (t, J = 13.0 Hz, 1H), 2.19 (td, J = 13.0, 11.9, 9.6 Hz, 2H), 1.96−1.86 (m, 1H), 1.79−1.69 (m, 2H), 1.66 (q, J = 7.8, 6.3 Hz, 2H), 1.29 (s, 3H), 1.13 (s, 3H), 0.99 (t, J = 7.9 Hz, 8H), 0.69 (q, J = 7.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.4, 175.4, 166.5, 132.9, 130.2, 129.5 (2C), 128.3 (2C), 73.5, 69.1, 64.5, 61.8, 60.5, 47.1, 36.8, 31.1, 30.3, 24.9, 24.5, 6.8 (3C), 4.7 (3C). HRMS (CI^+) m/z calcd for $C_{27}H_{43}O_6Si$ $[M + H]^+$ 505.2616, found 505.2625.

Preparation of ***27a***. Following the procedure for synthesis of **7b**, **26a** (671 mg, 1.37 mmol) underwent SmI_2-mediated reductive epoxide ring opening to give **27a** (30 mg, 93% yield) as a colorless oil. IR (neat, cm^{-1}) 3498, 3087, 3063, 3030, 2953, 2876, 1715, 1454, 1361, 1265, 1102, 736, 698. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 5.13 (q, J = 6.4 Hz, 1H), 4.48 (s, 2H), 4.46−4.38 (m, 1H), 4.04 (d, J = 2.2 Hz, 1H), 3.52−3.38 (m, 2H), 2.78−2.58 (m, 2H), 2.42−2.35 (m, 1H), 2.33−2.21 (m, 1H), 2.07 (dt, J = 11.2, 4.1 Hz, 2H), 1.67−1.58 (m, 4H), 1.24 (s, 3H), 1.16 (s, 3H), 1.01 (t, J = 7.9 Hz, 9H), 0.71 (qd, J = 7.9, 2.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.2, 176.6, 138.4, 128.4 (2C), 127.6 (3C), 74.4, 73.7, 72.9, 71.2, 69.6, 45.8, 45.0, 40.1, 31.9, 30.6, 27.6, 25.6, 18.7, 6.9 (3C), 5.1 (3C). HRMS (CI^+) m/z calcd for $C_{27}H_{45}O_6Si$ $[M + H]^+$ 493.2980, found 493.2981.

Preparation of ***26b***. Following General Procedure A, **25b** (1.12 g, 2.35 mmol) underwent PCC-mediated oxidative ring expansion to give **26b** (1.02 g, 89% yield) as a colorless oil. IR (neat, cm^{-1}) 3064, 3031, 2954, 2877, 1726, 1454, 1382, 1265, 1092, 1006, 826, 739. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.27 (m, 5H), 4.89−4.80 (m, 1H), 4.49 (s, 2H), 3.86 (d, J = 4.6 Hz, 1H), 3.57 (d, J = 8.1 Hz, 1H), 3.53−3.41 (m, 2H), 3.33 (dd, J = 8.1, 4.7 Hz, 1H), 2.79−2.70 (m, 1H), 2.48−2.39 (m, 1H), 2.25−2.15 (m, 1H), 2.10−2.01 (m, 1H), 1.82−1.74 (m, 1H), 1.73−1.63 (m, 1H), 1.59 (s, 2H), 1.24 (s, 3H), 1.15 (s, 3H), 0.99 (t, J = 7.9 Hz, 9H), 0.79−0.62 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.5, 174.2, 138.3, 128.4 (2C), 127.6 (3C), 74.5, 72.9, 72.1, 69.5, 60.9, 57.6, 47.2, 40.8, 31.1, 29.6, 25.6, 23.4, 17.9, 6.9 (3C), 5.0 (3C). HRMS (CI^+) m/z calcd for $C_{27}H_{43}O_6Si$ $[M + H]^+$ 491.2823, found 491.2831.

Preparation of ***27b***. Following the procedure for synthesis of **7d**, **26b** (980 mg, 2.0 mmol) underwent SmI_2-mediated reductive epoxide ring opening to give **27b** (915 mg, 94% yield) as a colorless oil. IR (neat, cm^{-1}) 3497, 3063, 3030, 2953, 2978, 1715, 1454, 1266, 1102, 736, 698. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.26 (m, 5H), 4.85 (dd, J = 8.6, 4.8 Hz, 1H), 4.48 (s, 2H), 4.12 (t, J = 7.8 Hz, 1H), 3.73 (d, J = 8.0 Hz 1H), 3.46 (q, J = 5.9 Hz, 2H), 2.77 (dd, J = 17.6, 7.7 Hz, 1H), 2.67 (s, 1H), 2.56 (dd, J = 17.6, 1.9 Hz, 1H), 2.39 (td, J = 9.8, 8.7, 3.9 Hz, 2H), 2.22−2.15 (m, 1H), 2.10−2.00 (m, 1H), 1.85−1.74 (m, 1H), 1.67 (dd, J = 10.7, 4.4 Hz, 3H), 1.20 (s, 3H), 1.07−0.94 (m, 12H), 0.70 (q, J = 7.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.3, 176.5, 138.3, 128.4 (2C), 127.6 (3C), 80.8, 75.7, 72.9, 69.6, 68.5, 46.8, 46.4, 40.0, 30.3, 26.8, 25.8, 16.8, 7.0 (3C), 5.5 (3C). HRMS (CI^+) m/z calcd for $C_{27}H_{45}O_6Si$ $[M + H]^+$ 493.2980, found 493.2977.

Preparation of [5,5]-Spiroacetal-cis-fused-γ-lactones (6S)-****28a*** *and (6R*)-****28b***. Following General Procedure D, (6S*)-**28a** (15.5 mg, 53% yield, colorless oil) and (6R*)-**28b** (7.6 mg, 26% yield, colorless oil) were obtained from **27a** (40 mg, 0.09 mmol).

Data for (6S*)-**28a**: IR (neat, cm^{-1}) 3086, 3062, 3030, 2935, 2866, 2795, 1776, 1494, 1352, 1096, 1054, 738, 699. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.25 (m, 5H), 5.10 (t, J = 5.2 Hz, 1H), 4.49 (s, 2H), 4.35 (d, J = 5.1 Hz, 1H), 4.05 (q, J = 6.3, 5.5 Hz, 1H), 3.51 (dd, J = 9.4, 5.5 Hz, 1H), 3.47−3.41 (m, 1H), 2.44 (d, J = 14.0 Hz, 1H), 2.16−2.01 (m, 4H), 1.74−1.61 (m, 3H), 1.58−1.50 (m, 2H), 1.23 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.8, 138.7, 128.3 (2C), 127.6 (2C), 127.4, 115.0, 86.7, 79.9, 79.3, 72.8, 70.1, 44.2, 41.8, 34.4, 32.0, 29.9, 26.2, 25.4, 18.3. HRMS (CI^+) m/z calcd for $C_{21}H_{29}O_5$ $[M + H]^+$ 361.2010, found 361.2008.

Data for (6R*)-**28b**: IR (neat, cm^{-1}) 3086, 3062, 3030, 2935, 2866, 1776, 1494, 1388, 1207, 1096, 1054, 738. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.27 (m, 5H), 5.01 (ddd, J = 6.0, 3.8, 1.5 Hz, 1H), 4.50 (s, 2H), 4.28 (d, J = 3.8 Hz, 1H), 4.04 (t, J = 7.1 Hz, 1H), 3.50 (t, J = 6.0 Hz, 2H), 2.48 (dd, J = 15.0, 6.3 Hz, 1H), 2.39−2.28 (m, 1H), 2.12−2.01 (m, 2H), 1.99−1.89 (m, 1H), 1.80−1.67 (m, 3H), 1.64−1.58 (m, 2H), 1.24 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.0, 138.5, 128.3 (2C), 127.6 (2C), 127.5, 115.2, 85.0, 80.4, 80.4, 72.8, 70.2, 44.4, 41.8, 36.9, 33.8, 30.6, 26.3, 23.1, 18.0. HRMS (CI^+) m/z calcd for $C_{21}H_{29}O_5$ $[M + H]^+$ 361.2010, found 361.2019.

Preparation of [5,5]-Spiroacetal-cis-fused-γ-lactones ***28c*** *and* ***28d***. Following General Procedure C, (6S*)-**28c** (10.4 mg, 32% yield, colorless oil) and (6R*)-**28d** (19.4 mg, 60% yield, colorless oil) were obtained from **27b** (44 mg, 0.09 mmol).

Data for (6S*)-**28c**: IR (neat, cm^{-1}) 3062, 3030, 2935, 2866, 1776, 1455, 1352, 1207, 1096, 1054, 739, 699. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.27 (m, 5H), 5.02 (ddd, J = 6.0, 3.8, 1.5 Hz, 1H), 4.50 (s, 2H), 4.27 (d, J = 3.7 Hz, 1H), 4.07 (p, J = 6.3 Hz, 1H), 3.48 (t, J = 6.0 Hz, 2H), 2.50 (dd, J = 15.0, 6.4 Hz, 1H), 2.35 (dd, J = 15.1, 1.5 Hz, 1H), 2.17−2.00 (m, 3H), 1.71−1.60 (m, 3H), 1.57−1.50 (m, 2H), 1.27 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.9, 138.5, 128.3 (2C), 127.6 (2C), 127.5, 115.5, 85.2, 80.5, 78.6, 72.9, 70.2, 44.4, 42.3, 35.6, 32.1, 30.0, 26.1, 23.1, 18.1. HRMS (CI^+) m/z calcd for $C_{21}H_{29}O_5$ $[M + H]^+$ 361.2010, found 361.2007.

Data for (6R*)-**28d**: IR (neat, cm^{-1}) 3086, 3030, 2935, 2866, 1776, 1455, 1207, 1096, 1054, ^1H NMR (400 MHz, $CDCl_3$) δ 7.36−7.26 (m, 5H), 5.07 (t, J = 4.9 Hz, 1H), 4.49 (s, 2H), 4.29 (d, J = 4.7 Hz, 1H), 4.08−3.93 (m, 1H), 3.54−3.47 (m, 1H), 3.43 (dt, J = 9.5, 6.1 Hz, 1H), 2.44 (d, J = 14.1 Hz, 1H), 2.17−1.96 (m, 4H), 1.76−1.65 (m, 3H), 1.65−1.61 (m, 2H), 1.28 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.6, 138.7, 128.3 (2C), 127.6 (2C), 127.4, 115.1, 87.1, 81.5, 79.8, 72.6, 70.1, 44.5, 41.6, 36.3, 34.0, 30.9, 26.4, 24.8, 18.3. HRMS (CI^+) m/z calcd for $C_{21}H_{29}O_5$ $[M + H]^+$ 361.2010, found 361.2008.

Preparation of (6S)-****29a*** *and (6R*)-****29b***. To a solution of (6S*)-**28a** (148 mg, 0.41 mmol) in EtOAc (10 mL) was added palladium on carbon (5%, 85 mg, 0.04 mmol). The flask was charged with hydrogen (1 atm, balloon), and the resulting mixture was stirred overnight at rt. The reaction mixture was filtered through Celite and concentrated under reduced pressure to give the alcohol (6S*)-**29a** (105 mg, 95% yield) as a colorless oil, which was used directly for next step without further purification. Data for (6S*)-**29a**: IR (neat, cm^{-1}) 3430, 2930, 2869, 1759, 1640, 1458, 1348, 1128. ^1H NMR (400 MHz, $CDCl_3$) δ 5.11 (t, J = 5.1 Hz, 1H), 4.35 (d, J = 4.9 Hz, 1H), 4.06 (dq, J = 11.0, 4.4, 3.5 Hz, 1H), 3.61 (q, J = 5.8 Hz, 2H), 2.44 (d, J = 14.1 Hz, 1H),

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

2.15−2.04 (m, 4H), 1.65−1.55 (m, 3H), 1.53−1.42 (m, 2H), 1.24 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.0, 115.0, 86.7, 80.0, 79.3, 62.6, 44.3, 41.8, 34.3, 31.6, 30.1, 29.3, 25.2, 18.3. HRMS (CI$^+$) m/z calcd for $C_{14}H_{23}O_5$ $[M + H]^+$ 271.1540, found 271.1532.

Following the procedure for preparation of (6*S**)-**29a**, (6*R**)-**28b** (44 mg, 0.09 mmol) underwent debenzylation to give (6*R**)-**29b** (31.6 mg, 96% yield). IR (neat, cm^{-1}) 3429, 2931, 2870, 1759, 1645, 1458, 1308, 1129, 1055. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.02 (ddd, J = 5.8, 3.9, 1.3 Hz, 1H), 4.30 (d, J = 3.7 Hz, 1H), 4.07 (d, J = 4.4 Hz, 1H), 3.70−3.63 (m, 2H), 2.50 (dd, J = 15.2, 6.3 Hz, 1H), 2.40−2.32 (m, 1H), 2.13−2.08 (m, 3H), 2.00−1.94 (m, 1H), 1.69−1.59 (m, 2H), 1.59−1.50 (m, 2H), 1.25 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.8, 115.5, 85.2, 80.7, 80.3, 62.8, 44.5, 41.9, 37.0, 33.9, 30.8, 29.6, 23.0, 18.0. HRMS (CI$^+$) m/z calcd for $C_{14}H_{23}O_5$ $[M + H]^+$ 271.1540, found 271.1530.

Preparation of (6S)-**29c** and (6R*)-**29d**.* Following the procedure for preparation of (6*S**)-**29a**, (6*S**)-**28c** and (6*R**)-**28d** (148 mg, 0.41 mmol) underwent debenzylation to give (6*S**)-**29c** (105 mg, 95% yield, colorless oil) and (6*R**)-**29d** (105 mg, 95% yield, colorless oil), respectively.

Data for (6*S**)-**29c**: IR (neat, cm^{-1}): 3409, 2931, 2870, 1759, 1645, 1457, 1350, 1211, 1129, 1055. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.02 (ddd, J = 5.9, 3.9, 1.6 Hz, 1H), 4.27 (d, J = 3.7 Hz, 1H), 4.10 (q, J = 6.2 Hz, 1H), 3.66 (q, J = 4.0, 2.6 Hz, 2H), 2.52 (dd, J = 15.1, 6.4 Hz, 1H), 2.38 (d, J = 15.0 Hz, 1H), 2.18−2.00 (m, 3H), 1.63−1.53 (m, 3H), 1.27 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.8, 115.6, 85.3, 80.4, 78.8, 62.8, 44.5, 42.4, 35.6, 32.1, 30.2, 29.3, 23.1, 18.1. HRMS (CI$^+$) m/z calcd for $C_{14}H_{23}O_5$ $[M + H]^+$ 271.1540, found 271.1548.

Data for (6*R**)-**29d**: IR (neat, cm^{-1}) 3431, 2931, 2870, 1758, 1642, 1458, 1350, 1130, 1055. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.09 (t, J = 4.8 Hz, 1H), 4.29 (d, J = 4.5 Hz, 1H), 4.09−3.93 (m, 1H), 3.73−3.55 (m, 2H), 2.45 (d, J = 14.1 Hz, 1H), 2.17−2.01 (m, 3H), 1.75−1.60 (m, 6H), 1.30 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.0, 115.1, 87.0, 81.6, 80.0, 62.6, 44.7, 41.5, 36.2, 33.6, 31.1, 30.0, 24.7, 18.2. HRMS (CI$^+$) m/z calcd for $C_{14}H_{23}O_5$ $[M + H]^+$ 271.1540, found 271.1532.

Preparation of (6S)-**30a**.* To a solution of (6*S**)-**29a** (13.4 mg, 0.05 mmol) in dry CH_2Cl_2 (3 mL) at 0 °C were added sequentially imidazole (10.2 mg, 0.15 mmol), PPh_3 (21 mg, 0.08 mmol), and iodine (25.4 mL, 0.10 mmol) in CH_2Cl_2 (1 mL). The reaction mixture was allowed to warm to rt and stirred overnight. Standard workup (quenching with 3 mL of Na_2SO_3, extraction with 5 mL of CH_2Cl_2) gave the iodide **Sa** (18.8 mg, 95%) as a colorless oil, which was used directly for the next step without further purification.

To a solution of **Sa** (18.8 mg, 0.047 mmol) in DMF (2 mL) was added NaCN (5 mg, 0.1 mmol), and the resulting mixture was stirred overnight at rt. Standard workup (quenching with 3 mL of water and extraction with 5 mL of CH_2Cl_2) gave the nitrile **Ta** (12.9 mg, 94% yield) as a colorless oil, which was used directly for the next step without further purification.

To a solution of **Ta** (12.9 mg, 0.044 mmol) in EtOH (2 mL) were added NaOH (4 mg, 0.1 mmol) and H_2O_2 (30% in water, 0.01 mL, 0.1 mmol). The resulting mixture was heated to 60 °C and stirred for 1 h. After TLC analysis indicated complete conversion, the reaction mixture was concentrated under reduced pressure to remove EtOH. Water (5 mL) was added to the residue, which was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic fractions were concentrated to 1 mL under reduced pressure. To the resulting solution was added silica gel (50 mg), and the resulting mixture was stirred for 1 h at rt. Removal of the solvent under under reduced pressure gave the residue, which was purified by flash chromatography on silica gel (hexane/ethyl acetate = 1:4) to afford **30a** (12.5 mg, 90% yield) as a colorless oil. IR (neat, cm^{-1}) 3472, 2930, 2872, 2728, 1772, 1720, 1638, 1462, 1350, 1126, 1089, 1052. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.13 (t, J = 5.1 Hz, 1H), 4.36 (d, J = 4.9 Hz, 1H), 4.06 (d, J = 13.0 Hz, 1H), 2.46 (d, J = 14.3 Hz, 1H), 2.38 (dt, J = 16.4, 7.6 Hz, 2H), 2.16−2.05 (m, 4H), 1.69 (q, J = 7.4 Hz, 3H), 1.58 (t, J = 5.9 Hz, 1H), 1.51−1.47 (m, 1H), 1.25 (s, 3H), 1.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.4, 175.8, 115.2, 86.7, 80.2, 79.4, 44.5, 41.9, 34.3, 34.3, 33.5, 30.1, 25.2, 21.7, 18.3. HRMS (CI$^+$) m/z calcd for $C_{15}H_{22}O_6$ $[M]^+$ 298.1489, found 298.1499.

Preparation of (6R)-**30b**.* Following the procedure for synthesis of (6*S**)-**30a**, (6*R**)-**29b** (13 mg, 0.05 mmol) underwent Appel halogenation, S_N2 substitution with NaCN, and hydrolysis to give (6*R**)-**30b** (12.1 mg, 89% yield) as a colorless oil. IR (neat, cm^{-1}) 3472, 2930, 2872, 2728, 1772, 1721, 1638, 1462, 1350, 1126, 1089, 1052. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.02 (ddd, J = 6.1, 3.8, 1.5 Hz, 1H), 4.30 (d, J = 3.7 Hz, 1H), 4.10−4.00 (m, 1H), 2.49 (dd, J = 15.0, 6.3 Hz, 1H), 2.43−2.31 (m, 3H), 2.07 (dt, J = 17.6, 5.9 Hz, 3H), 1.99−1.91 (m, 1H), 1.75 (d, J = 8.9 Hz, 1H), 1.67 (dd, J = 8.5, 4.2 Hz, 2H), 1.56 (s, 2H), 1.25 (s, 3H), 1.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.9, 177.3, 115.3, 85.1, 80.4, 80.1, 44.4, 41.8, 36.8, 36.4, 33.5, 30.6, 23.0, 21.4, 18.0. HRMS (CI$^+$) m/z calcd for $C_{15}H_{22}O_6$ $[M]^+$ 298.1489, found 298.1490.

Preparation of (6S)-**30c**.* Following the procedure for synthesis of (6*S**)-**30a**, (6*S**)-**29c** (13 mg, 0.05 mmol) underwent Appel halogenation, S_N2 substitution with NaCN, and hydrolysis to give (6*S**)-**30c** (12.0 mg, 88% yield) as a colorless oil. IR (neat, cm^{-1}) 3472, 2930, 2872, 2728, 1772, 1720, 1638, 1462, 1350, 1126, 1089, 1052. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.02 (ddd, J = 6.1, 3.8, 1.5 Hz, 1H), 4.28 (d, J = 3.8 Hz, 1H), 4.06 (p, J = 6.5 Hz, 1H), 2.51 (dd, J = 15.0, 6.5 Hz, 1H), 2.44−2.31 (m, 3H), 2.18−1.96 (m, 4H), 1.73−1.64 (m, 2H), 1.58−1.49 (m, 3H), 1.27 (s, 3H), 1.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.9, 177.7, 115.6, 85.3, 80.5, 78.3, 44.5, 42.3, 35.5, 34.7, 33.5, 30.04, 23.1, 21.1, 18.1. HRMS (CI$^+$) m/z calcd for $C_{15}H_{22}O_6$ $[M]^+$ 298.1489, found 298.1493.

Preparation of (6R)-**30d**.* Following the procedure for synthesis of (6*S**)-**30a**, (6*R**)-**29d** (13 mg, 0.05 mmol) underwent Appel halogenation, S_N2 substitution with NaCN, and hydrolysis to give (6*R**)-**30d** (12.0 mg, 88% yield) as a colorless oil. IR (neat, cm^{-1}) 3497, 2929, 2872, 2728, 1772, 1720, 1638, 1350, 1268, 1125, 1089, 1052. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.09 (t, J = 4.8 Hz, 1H), 4.30 (d, J = 4.6 Hz, 1H), 3.97 (dd, J = 10.8, 5.5 Hz, 1H), 2.45 (d, J = 14.3 Hz, 2H), 2.33 (q, J = 8.6, 7.8 Hz, 1H), 2.17−1.98 (m, 5H), 1.69 (d, J = 6.6 Hz, 2H), 1.61 (dd, J = 7.9, 5.9 Hz, 2H), 1.29 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.1, 176.3, 115.3, 87.1, 81.5, 80.0, 44.7, 41.7, 36.2, 36.2, 33.6, 30.9, 24.7, 21.6, 18.3. HRMS (CI$^+$) m/z calcd for $C_{15}H_{22}O_6$ $[M]^+$ 298.1489, found 298.1499.

Preparation of (6S)-**31a**.* To a solution of alcohol (6*S**)-**29a** (32 mg, 0.12 mmol) in CH_2Cl_2 (4 mL) at 0 °C were added $NaHCO_3$ (50 mg, 0.58 mmol) and Dess−Martin periodinane (DMP; 100 mg, 0.23 mmol). The resulting mixture was stirred for 1 h at 0 °C. Standard workup (quenching with 5 mL of Na_2SO_3 and extraction with 10 mL of ethyl acetate) and purification (hexane/ethyl acetate = 1:4) gave (6*S**)-**31a** (29 mg, 90% yield) as a colorless oil. Data for **31a**: IR (neat, cm^{-1}) 2931, 2875, 2728, 1776, 1721, 1444, 1136, 1091, 1052. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 5.11 (t, J = 5.1 Hz, 1H), 4.35 (d, J = 5.0 Hz, 1H), 4.14−3.95 (m, 1H), 2.67−2.60 (m, 1H), 2.56−2.46 (m, 1H), 2.42 (d, J = 14.1 Hz, 1H), 2.10 (dt, J = 9.6, 5.3 Hz, 4H), 1.95−1.85 (m, 1H), 1.69−1.58 (m, 1H), 1.48 (m, 1H), 1.21 (d, J = 2.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 180.9, 114.9, 86.6, 79.9, 78.1, 44.3, 41.7, 40.5, 34.3, 29.9, 27.5, 25.3, 18.2. HRMS (CI$^+$) m/z calcd for $C_{14}H_{20}O_5$ $[M]^+$ 268.1305, found 268.1311.

Preparation of (6R)-**31b**, (6S*)-**31c**, and (6R*)-**31d**.* Following the procedure for synthesis of (6*S**)-**31a**, (6***R****)-**31b**, (6*S**)-**31c**, and (6*R**)-**31d** were obtained in nearly the same yields from (6*R**)-**29b**, (6*S**)-**29c**, and (6*R**)-**29d**, respectively.

Data for (6*R**)-**31b**: IR (neat, cm^{-1}) 2931, 2875, 2728, 1775, 1721, 1464, 1444, 1136, 1052. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (d, J = 1.5 Hz, 1H), 5.01 (ddd, J = 6.2, 3.7, 1.5 Hz, 1H), 4.26 (d, J = 3.7 Hz, 1H), 4.13−3.99 (m, 1H), 2.62−2.45 (m, 3H), 2.35 (dd, J = 15.1, 1.5 Hz, 1H), 2.08 (td, J = 12.7, 6.2 Hz, 2H), 1.99−1.85 (m, 3H), 1.83−1.71 (m, 1H), 1.25 (s, 3H), 1.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 180.8, 115.5, 85.2, 80.3, 79.5, 44.5, 41.8, 40.5, 37.0, 30.4, 29.3, 23.0, 18.0. HRMS (CI$^+$) m/z calcd for $C_{14}H_{21}O_5$ $[M + H]^+$ 269.1384, found 269.1384.

Data for (6*S**)-**31c**: IR (neat, cm^{-1}) 2931, 2874, 2727, 1776, 1721, 1462, 1444, 1249, 1052. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (d, J = 1.7 Hz, 1H), 5.01 (ddd, J = 6.2, 3.7, 1.5 Hz, 1H), 4.26 (d, J = 3.7 Hz,

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

1H), 4.12−4.05 (m, 1H), 2.57−2.44 (m, 3H), 2.36 (d, J = 15.0 Hz, 1H), 2.20−2.10 (m, 1H), 2.05 (tt, J = 12.8, 6.0 Hz, 2H), 1.91−1.80 (m, 2H), 1.56−1.51 (m, 1H), 1.26 (d, J = 1.7 Hz, 3H), 1.22 (d, J = 1.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.0, 180.8, 115.5, 85.2, 80.4, 77.6, 44.4, 42.0, 40.2, 35.5, 29.8, 27.8, 23.0, 18.0. HRMS (CI$^+$) m/z calcd for $C_{14}H_{20}O_5$ [M]$^+$ 268.1305, found 268.1296.

Data for (6*R**)-**31d**: IR (neat, cm^{-1}) 2931, 2875, 2728, 1775, 1721, 1638, 1464, 1444, 1206, 1136, 1052. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (d, J = 1.1 Hz, 1H), 5.09 (t, J = 4.8 Hz, 1H), 4.29 (d, J = 4.5 Hz, 1H), 3.99 (tt, J = 9.2, 4.3 Hz, 1H), 2.71−2.61 (m, 1H), 2.61−2.50 (m, 1H), 2.44 (d, J = 14.1 Hz, 1H), 2.18−2.01 (m, 4H), 1.96−1.90 (m, 1H), 1.78−1.66 (m, 2H), 1.26 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 180.7, 115.1, 87.0, 80.2, 79.7, 44.6, 41.5, 40.8, 36.1, 30.8, 29.3, 24.6, 18.0. HRMS (CI$^+$) m/z calcd for $C_{14}H_{20}O_5$ [M]$^+$ 268.1305, found 268.1305.

Preparation of (6S)-**32a**.* To a round-bottom flask (10 mL) was added $CrCl_2$ (40 mg, 0.33 mmol), and the flask was heated with a heat gun under high vacuum. The flask was filled with argon while cooling. The reaction flask was then cooled to 0 °C and a degassed solution of THF (1 mL) was added. The reaction flask was shielded from light by wrapping with aluminum foil. After 15 min, a solution of (6*S**)-**31a** (13 mg 0.05 mmol) in THF (1 mL) was added, followed by slow addition of allyl bromide (40 mg, 0.10 mmol) over 15 min via a syringe pump. The resulting mixture was stirred at 0 °C for 2 h. The reaction was quenched by addition of aqueous saturated $NaHCO_3$, the organic layer was collected, and the aqueous layer was extracted with Et_2O (3 × 5 mL). The combined organic fractions were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to give the alcohol **Ua** (14 mg, 90% yield), which was used directly for the next step without further purification.

To a solution of **Ua** (14 mg, 0.045 mmol) in EtOAc (10 mL) was added palladium on carbon (5%, 85 mg, 0.04 mmol). The flask was charged with hydrogen (1 atm, balloon), and the resulting mixture was stirred overnight at rt. The reaction mixture was filtered through Celite and concentrated in vacuo to give the alcohol **Va** (13.9 mg, 99% yield) as a colorless oil, which was used directly for the next step without further purification.

Following the procedure for synthesis of (6*S**)-**31a**, **Va** (13.9 mg, 0.045 mmol) underwent Dess−Martin oxidation to give (6*S**)-**32a** (12.5 mg, 90% yield) as a colorless oil. IR (neat, cm^{-1}) 2957, 2924, 2872, 2854, 1777, 1710, 1462, 1133, 1091, 1051. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.10 (t, J = 5.1 Hz, 1H), 4.34 (d, J = 4.9 Hz, 1H), 4.01 (dd, J = 7.6, 4.0 Hz, 1H), 2.60−2.50 (m, 1H), 2.49−2.37 (m, 4H), 2.15−2.05 (m, 4H), 1.92−1.83 (m, 1H), 1.59 (q, J = 7.4 Hz, 3H), 1.46 (d, J = 4.4 Hz, 1H), 1.21 (s, 3H), 1.19 (s, 3H), 0.91 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.3, 180.8, 114.9, 86.6, 79.9, 78.5, 44.8, 44.3, 41.7, 39.0, 34.2, 30.1, 29.1, 25.3, 18.3, 17.2, 13.7. HRMS (CI$^+$) m/z calcd for $C_{17}H_{27}O_5$ [M + H]$^+$ 311.1853, found 311,1857.

Preparation of (6R)-**32b**, (6S*)-**32c**, and (6R*)-**32d**.* Following the procedure for synthesis of (6*S**)-**32a**, (6*R**)-**32b**, (6*S**)-**32c**, and (6*R**)-**32d** were obtained in nearly the same yields (80−81%, three steps) from (6*R**)-**31b**, (6*S**)-**31c**, and (6*R**)-**31d**, respectively.

Data for (6*R**)-**32b**: IR (neat, cm^{-1}) 2957, 2924, 2872, 2854, 1777, 1710, 1462, 1133, 1091, 1051. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.02 (ddd, J = 6.0, 3.8, 1.5 Hz, 1H), 4.27 (d, J = 3.7 Hz, 1H), 4.08−3.96 (m, 1H), 2.58−2.42 (m, 3H), 2.42−2.31 (m, 3H), 2.10−2.00 (m, 3H), 1.99−1.89 (m, 1H), 1.82 (q, J = 7.3 Hz, 2H), 1.78−1.69 (m, 1H), 1.64−1.59 (m, 3H), 1.25 (s, 3H), 1.23 (s, 3H), 0.92 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.7, 180.9, 115.3, 85.1, 80.3, 79.7, 44.8, 44.4, 41.8, 39.1, 37.0, 30.8, 30.4, 23.1, 18.1, 17.3, 13.8. HRMS (CI$^+$) m/z calcd for $C_{17}H_{27}O_5$ [M + H]$^+$ 311.1853, found 311.1850.

Data for (6*S**)-**32c**: IR (neat, cm^{-1}) 2957, 2924, 2875, 2854, 1777, 1710, 1462, 1133, 1091, 1051. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.02 (ddd, J = 6.0, 3.8, 1.5 Hz, 1H), 4.26 (d, J = 3.8 Hz, 1H), 4.09−4.00 (m, 1H), 2.51−2.42 (m, 3H), 2.41−2.32 (m, 3H), 2.18−2.08 (m, 1H), 2.08−1.97 (m, 2H), 1.76 (dt, J = 14.9, 7.3 Hz, 2H), 1.60 (d, J = 7.5 Hz, 2H), 1.26 (s, 3H), 1.22 (s, 3H), 0.91 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.5, 180.8, 115.6, 85.3, 80.5, 78.01, 44.8, 44.5, 42.2, 39.1, 35.6, 30.0, 29.4, 23.1, 18.1, 17.31, 13.8. HRMS (CI$^+$) m/z calcd for $C_{17}H_{27}O_5$ [M]$^+$ 310.1775, found 310.1778.

Data for (6*R**)-**32d**: IR (neat, cm^{-1}) 2957, 2924, 2875, 2854, 1777, 1710, 1462, 1133, 1091, 1051. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.08 (t, J = 4.8 Hz, 1H), 4.29 (d, J = 4.6 Hz, 1H), 3.96 (dt, J = 10.1, 5.3 Hz, 1H), 2.69−2.60 (m, 1H), 2.53−2.36 (m, 4H), 2.12 (dd, J = 9.5, 4.6 Hz, 1H), 2.10−1.98 (m, 3H), 1.93−1.85 (m, 1H), 1.72 (s, 1H), 1.67−1.58 (m, 3H), 1.25 (d, J = 2.9 Hz, 3H), 1.21 (s, 3H), 0.91 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.4, 180.8, 115.1, 87.0, 80.6, 79.8, 44.8, 44.6, 41.6, 39.2, 36.1, 31.1, 30.9, 24.8, 18.1, 17.3, 13.8. HRMS (CI$^+$) m/z calcd for $C_{17}H_{27}O_5$ [M]$^+$ 310.1775, found 310.1777.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00788.

X-ray data for **4b**, **7a**, **7c**, **8b**, and **8d**; six tables and six figures showing NMR spectral comparison of synthetic stereostructures and natural products; ^{1}H and ^{13}C NMR spectra of new compounds (PDF)

Crystallographic file for **4b** (CCDC 1469936) (CIF)

Crystallographic file for **7a** (CCDC 1469937) (CIF)

Crystallographic file for **7c** (CCDC 1469938) (CIF)

Crystallographic file for **8b** (CCDC 1469945) (CIF)

Crystallographic file for **8d** (CCDC 1469944) (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail rtong@ust.hk.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was financially supported by The Hong Kong University of Science and Technology (HKUST, R9309), Research Grant Council of Hong Kong (ECS 605912, GRF 605113, and GRF 16305314), and National Natural Science Foundation of China (NSFC 21472160). We are very grateful to Professor Ian Williams (HKUST) and Dr. Herman Sung (HKUST) for single-crystal X-ray diffraction analysis.

■ REFERENCES

(1) (a) Ackland, M. J.; Hanson, J. R.; Hitchcock, P. B.; Ratcliffe, A. H. *J. Chem. Soc., Perkin Trans. 1* **1985**, *1*, 843. (b) Farooq, A.; Gordon, J.; Hanson, J. R.; Takahashi, J. A. *Phytochemistry* **1995**, *38*, 557. (c) Rukachaisirikul, V.; Pramjit, S.; Pakawatchai, C.; Isaka, M.; Supothina, S. *J. Nat. Prod.* **2004**, *67*, 1953. (d) Oller-López, J. L.; Iranzo, M.; Mormeneo, S.; Oliver, E.; Cuerva, J. M.; Oltra, J. E. *Org. Biomol. Chem.* **2005**, *3*, 1172. (e) Herath, H. M.; Jacob, M.; Wilson, A. D.; Abbas, H. K.; Nanayakkara, N. P. *Nat. Prod. Res.* **2013**, *27*, 1562.

(2) Li, X.; Yao, Y. H.; Zheng, Y. A.; Sattler, I.; Lin, W. H. *Arch. Pharmacal Res.* **2007**, *30*, 812.

(3) Li, X.; Sattler, I.; Lin, W. *J. Antibiot.* **2007**, *60*, 191.

(4) Seibert, S. F.; Krick, A.; Eguereva, E.; Kehraus, S.; König, G. M. *Org. Lett.* **2007**, *9*, 239.

(5) (a) Ramana, C. V.; Suryawanshi, S. B.; Gonnade, R. G. *J. Org. Chem.* **2009**, *74*, 2842. (b) Chang, S.; Britton, R. *Org. Lett.* **2012**, *14*, 5844. (c) Tlais, S. F.; Dudley, G. B. *Beilstein J. Org. Chem.* **2012**, *8*, 1287. (d) Brimble, M. A.; Finch, O. C.; Heapy, A. M.; Fraser, J. D.; Furkert, D. P.; O'Connor, P. D. *Tetrahedron* **2011**, *67*, 995. (e) Fernandes, R. A.; Ingle, A. B. *Synlett* **2010**, *2010*, 158. (f) Chaudhari, D. A.; Kattanguru, P.; Fernandes, R. A. *RSC Adv.* **2015**, *5*, 42131. (g) Cortezano-Arellano, O.; Quintero, L.; Sartillo-

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339

Piscil, F. *J. Org. Chem.* **2015**, *80*, 2601. (h) Song, L.; Liu, Y.; Tong, R. *Org. Lett.* **2013**, *15*, 5850.
(6) (a) Tlais, S. F.; Dudley, G. B. *Org. Lett.* **2010**, *12*, 4698. (b) Fernandes, R. A.; Halle, M. B. *Asian J. Org. Chem.* **2013**, *2*, 593. (c) Li, J.; Zhao, C.; Liu, J.; Du, Y. *Tetrahedron* **2015**, *71*, 3885. Brimble and co-workers achieved the synthesis of the tricyclic SAFL core of CesH: (d) Finch, O. C.; Furkert, D. P.; Brimble, M. A. *Tetrahedron* **2014**, *70*, 590. (e) See ref 5c..
(7) (a) Abraham, E.; Cooke, J. W. B.; Davies, S. G.; Naylor, A.; Nicholson, R. L.; Price, P. D.; Smith, A. D. *Tetrahedron* **2007**, *63*, 5855. (b) Rios, M.-Y.; Velazquez, F.; Olivo, H. F. *Tetrahedron* **2003**, *59*, 6531.
(8) Posner, G. H.; Loomis, G. L. *J. Chem. Soc., Chem. Commun.* **1972**, 892.
(9) For a representative review, see (a) Roche, S. P.; Porco, J. A., Jr. *Angew. Chem., Int. Ed.* **2011**, *50*, 4068. For selected recent examples, see (b) Zhao, K.; Cheng, G.-J.; Yang, H.; Shang, H.; Zhang, X.; Wu, Y.-D.; Tang, Y. *Org. Lett.* **2012**, *14*, 4878. (c) Brown, P. D.; Willis, A. C.; Sherburn, M. S.; Lawrence, A. L. *Org. Lett.* **2012**, *14*, 4537.
(10) (a) Nising, C. F.; Bräse, S. *Chem. Soc. Rev.* **2008**, *37*, 1218. (b) Barradas, S.; Urbano, A.; Carreño, M. C. *Chem. - Eur. J.* **2009**, *15*, 9286.
(11) Kolaczkowski, L.; Reusch, W. *J. Org. Chem.* **1985**, *50*, 4766.
(12) Zhang, L.; Koreeda, M. *Org. Lett.* **2002**, *4*, 3755.
(13) Myers, A. G.; Herzon, S. B. *J. Am. Chem. Soc.* **2003**, *125*, 12080.
(14) Weitz, E.; Scheffer, A. *Ber. Dtsch. Chem. Ges. B* **1921**, *54*, 2344.
(15) For the related oxidative ring expansion, see (a) Ferraz, H. M. C.; Longo, L. S., Jr. *Org. Lett.* **2003**, *5*, 1337. (b) Ferraz, H. M. C.; Longo, L. S., Jr. *J. Org. Chem.* **2007**, *72*, 2945. (c) See ref 10b..
(16) Molander, G. A.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 2596.
(17) A similar furan product was coisolated with cephalosporolides E and F; see ref 1d.
(18) (a) Posner, G. H.; Hatcher, M. A.; Maio, W. A. *Org. Lett.* **2005**, *7*, 4301. (b) Hatcher, M. A.; Borstnik, K.; Posner, G. H. *Tetrahedron Lett.* **2003**, *44*, 5407. (c) Wipf, P.; Li, W. *J. Org. Chem.* **1999**, *64*, 4576.
(19) Piccialli, V.; Zaccaria, S.; Oliviero, G.; D'Errico, S.; D'Atri, V.; Borbone, N. *Eur. J. Org. Chem.* **2012**, *2012*, 4293.
(20) For reviews, see (a) Larhed, M.; Moberg, C.; Hallberg, A. *Acc. Chem. Res.* **2002**, *35*, 717. (b) Lew, A.; Krutzik, P. O.; Hart, M. E.; Chamberlin, A. R. *J. Comb. Chem.* **2002**, *4*, 95. (c) Lidstrom, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225. (d) Perreux, L.; Loupy, A. *Tetrahedron* **2001**, *57*, 9199. (e) Kappe, C. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250. (f) Dudley, G. B.; Richert, R.; Stiegman, A. E. *Chem. Sci.* **2015**, *6*, 2144.
(21) Appel, R. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 801.
(22) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155.
(23) Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179.
(24) Knochel, P.; Millot, N.; Rodriguez, A. L.; Tucker, C. E. *Org. Reac.* **2001**, *58*, 417.
(25) Yatagai, H.; Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 4548.
(26) Cornil, J.; Gonnard, L.; Guérinot, A.; Reymond, S.; Cossy, J. *Eur. J. Org. Chem.* **2014**, *2014*, 4958.

DOI: 10.1021/acs.joc.6b00788
J. Org. Chem. 2016, 81, 4325−4339