JOC The Journal of Organic Chemistry

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Synthesis of the Purported *ent*-Pochonin J Structure Featuring a Stereoselective Oxocarbenium Allylation

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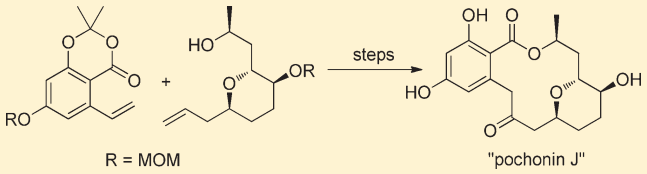
Supporting Information

ABSTRACT: The synthesis of the alleged natural product pochonin J is presented. Key steps of this convergent synthesis include a chemoselective Wacker oxidation, and an Evans' *anti*-reduction of the resulting ketone. Upon ozonolysis, this intermediate undergoes a 6-*exo*-*trig* cyclization to give a hemiketal intermediate, the key oxocarbenium precursor. The construction of the α-*C*-glycoside subunit is highlighted by a mismatched oxocarbenium cation formation/allylation sequence. An olefin metathesis afforded the 14-membered macrolactone, and final oxidation provided the "desired" compound that does not spectroscopically correlate to the initially described natural product.



INTRODUCTION

Terrestrially derived sources have long since been a repository for biologically relevant natural products.[1] In 2009, Shinonaga and co-workers disclosed four unique pochonin family structures (pochonins G−J) from the culture broth of *Pochonia chlamydosporia* var. *chlamydosporia*.[2] These compounds were isolated via bioassay-guided fractionation against WNT-5A expression in search of novel hair-growth stimulants. The structures of pochonins G−J were elucidated by means of a combination of 1D and 2D spectroscopic techniques. The entire family of pochonin natural products (A−P) has been shown to share a common structural motif of a 14-membered macrocyclic resorcylic acid lactone core. In addition, all pochonins except F and J are chlorinated at C13 of the aromatic ring analogous to radicicol and monorden.[3] Similarly, pochonins J (**1**) and F demonstrate more semblances to the aigialomycin family of natural products and hypothemycin, due in part to the lack of C13 chlorination as shown in Figure 1.[4,5] Because of their diverse biological functions and curious skeletal connectivities, members of these families of natural products have been met with interest giving rise to innovative synthetic approaches toward their assembly.[6]

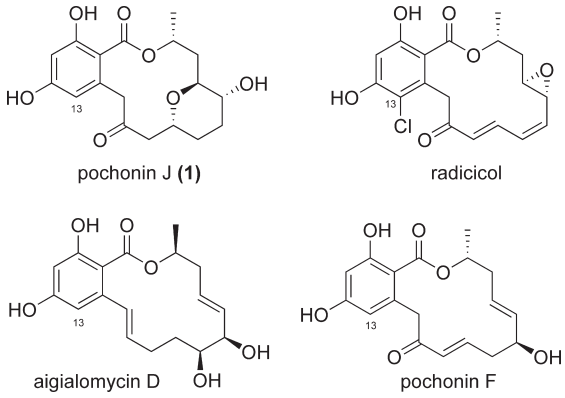


Figure 1. Resorcylic macrolide natural products.

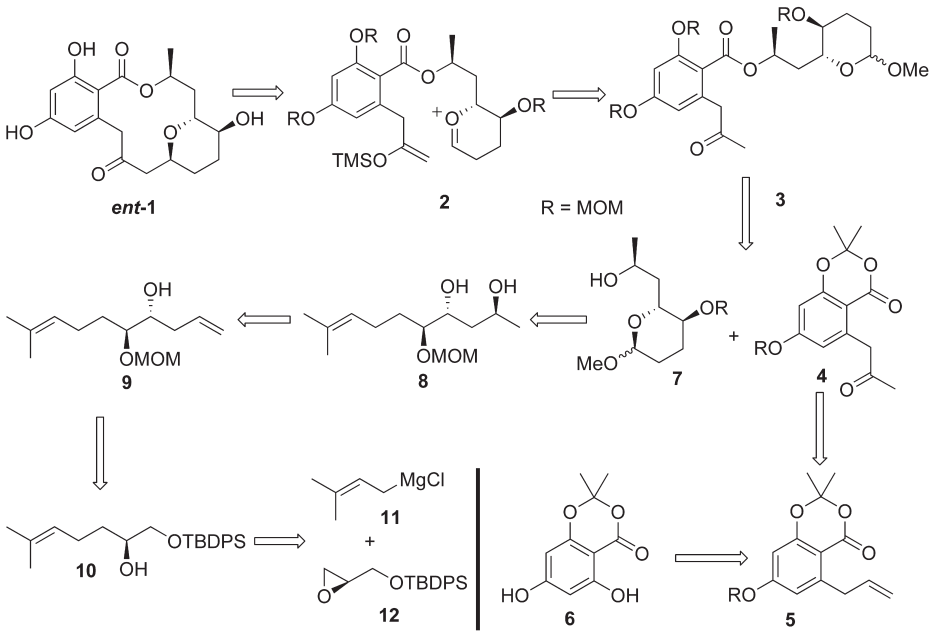
RESULTS AND DISCUSSION

Resorcylic acid lactones (RALs) of the type shown in Figure 1 are secondary metabolites that have been known since 1953 with the isolation of radicicol.[7] Despite great leaps forward in structure elucidation and characterization provided by NMR spectroscopy and other analytical methods, it is not uncommon to find errors in structure assignment. Nicolaou and Snyder reported the existence of over 300 structural revisions in the literature published between January 1990 and April 2004.[8] In over half of these cases, total synthesis of the presumed structure was required to identify a discrepancy and ultimately allowed for the determination of the correct structure. Surprisingly, these errors were not limited to molecules of great complexity as one would initially surmise, but include compounds of varying degrees of size and stereochemical complexity. Thus, total synthesis continues to play a very important role in structure elucidation of chemical entities by overcoming the gaps in technology that exist in the current state of spectroscopy.

As part of a research program aimed at expanding the diversity of RALs beyond the naturally occurring compounds, efforts made by the Winssinger group have also yielded significant contributions to the syntheses and biological studies of RALs. They have successfully synthesized aigialomycin D, pochonin A, C, and D, and through the application of solid-state chemistry, a library of pochonin and aigialomycin analogues that have been crucial in gaining valuable insight into their biological profiles.[9] Our attraction to **1** initially arose

Received: February 15, 2011
Published: April 15, 2011

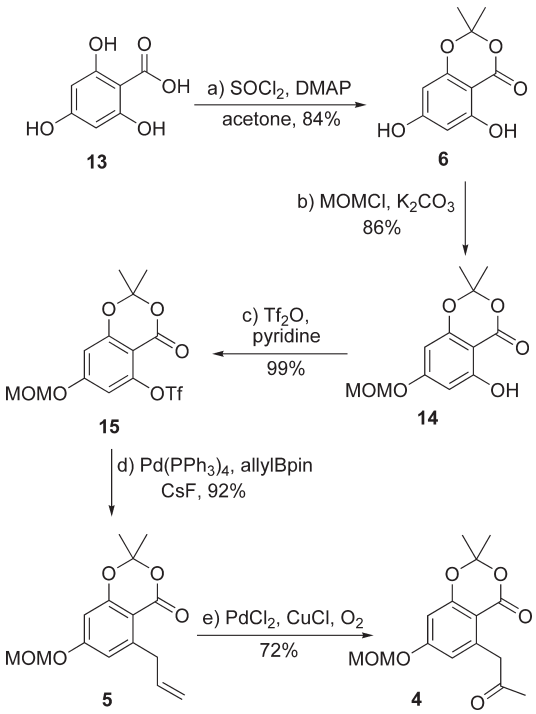
Scheme 1. First Generation Retrosynthetic Analysis of *ent*-Pochonin J



from the inclusion of an α-*C*-glycoside subunit in the 14-membered macrocyclic structure. Such structural motifs are extremely rare and have only been seen in aspergillide B and C.[10] On the basis of our previous synthetic work on resorcylic macrolides (i.e., aigialomycin D) and the synthesis of aspergillide B, we sought to merge our interests and investigate the synthesis of **1**.[11,12] Since we were uncertain of the absolute stereochemistry of **1** and considering its similarity to aigialomycin D, we initiated the synthetic venture toward **1** with the (*S*)-TBDPS protected glycidol starting chiral synthon (similar to our synthetic work with aigialomycin D). We were cognizant that the chiral starting material might lead to the enantiomer of **1** based on the initial disclosure by Shinogaga and co-workers.

Initial Retrosynthetic Analysis of *ent*-Pochonin J (1). Our initial retrosynthetic analysis of ***ent*-1** envisioned a late stage oxocarbenium cation formation, followed by intramolecular diastereoselective axial attack by the tethered TMS kinetic enolate **2** derived *in situ* from ketone **3** as delineated in Scheme 1. This approach was particularly attractive considering that formation of a stereogenic center to forge the α-*C*-glycoside moiety along with concomitant generation of the macrocyle could be theoretically achieved. If successful this strategy would further extend the scope of our oxocarbenium protocols as well as provide an alternative methodology for macrocyle construction. With this in mind, the macrocyclic/oxocarbenium precursor **3** was expected to arise from a trans-esterification reaction of the aromatic subunit **4** with methoxy ketal **7**. Aromatic precursor **4** was envisioned to be the product of a Wacker oxidation of the terminal alkene **5**. In turn, terminal alkene **5** would arise from the previously reported aromatic subunit **6** by means of a Pd-catalyzed cross coupling. The required methoxy ketal **7** could, in principle, be derived from reductive cleavage of the terminal alkene resident in triol **8**, leading to a 6-*exo*-*trig* cyclization followed by treatment with PPTS in MeOH. Compound **8** would be ultimately derived from diol **9** via a chemoselective Wacker oxidation of the least sterically hindered olefin and a subsequent intramolecular 1,3-*anti*-reduction of the corresponding ketone moiety. In turn, diol **9** would be the result of an asymmetric allylboration of an aldehyde intermediate resulting from TBDPS ether **10**. Lastly, **10** would arise from the union of the prenyl derived Grignard reagent **11** and TBDPS protected (*S*)-glycidol **12**.

Scheme 2. Synthesis of Aromatic Subunit via a Wacker Oxidation



dx.doi.org/10.1021/jo200332d |*J. Org. Chem.* 2011, 76, 3898–3908

With the original retrosynthetic blueprint in mind, our initial focus was on the construction of aromatic subunit **4**, which commenced with acetonide formation of commercially available 2,4,6-trihydroxybenzoic acid **13** in the presence of $SOCl_2$, DMAP, and acetone to give aryl acetonide **6** in 84% yield as shown in Scheme 2.[13] A subsequent chemoselective protection of the more reactive phenol moiety as a MOM ether by employing MOMCl and K_2CO_3 afforded the desired product **14** in 86% yield. Next, aryl triflate **15** was obtained in near quantitative yield, and an ensuing Pd-catalyzed Suzuki–Miyaura allylation provided aromatic subunit **5** in a 92% yield.[14] Lastly, treatment of **5** under modified Wacker conditions, employing 50 mol % of $PdCl_2$ and excess quantities of CuCl (2.0 equiv) under an atmosphere of O_2 provided the desired aryl ketone **4** in 72% yield.[15]

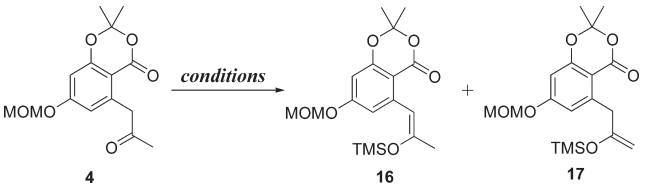
Prior to the attempted unification of fragments **4** and **7**, en route to the coveted trimethylsilyl enol ether **2** intermediate, we chose to explore conditions that would hopefully lead to the desired kinetic silyl enol ether **17** from ketone **4**. On the basis of early studies on the kinetic deprotonation of benzyl methyl ketone conducted by Yoshifuji and co-workers, we reasoned that it might be possible to obtain kinetic silyl enol ether **17** by using a sterically hindered lithium base, such as 1-lithio-2,4,6-tri-*tert*-butylbenzene, at low temperatures.[16] More recently, Kozlowski's group has also demonstrated that kinetic enolization at the least hindered position of highly substituted benzyl methyl ketones was indeed possible utilizing sterically hindered LiHMDS/Ph_3N adducts in toluene at −78 °C.[17] Despite the initial promise provided by these examples, careful implementation of literature procedures lead exclusively to the undesired thermodynamic silyl enol ether **16**. Summarized in Table 1 are the various attempts made to attain the required kinetic silyl enol ether **17**.

In retrospect, aryl ketone **4** possesses a carbonyl moiety that is locked in position through the cyclic acetonide subunit, a functionality not present in the substrates studied by Yoshifuji or Kozlowski. As shown in Scheme 3, one could envision a scenario where deprotonation at the more acidic benzylic position would lead to a lithium-stabilized six-membered chelate intermediate, somewhat similar to the one proposed during our synthesis of brussonol.[18] In addition to this stabilization, the generated anion might also be significantly delocalized given that the ester carbonyl group π-bond is aligned with the π-orbitals of the aromatic ring.

Unfortunately, TMS enol ether **17** eluded all attempts toward its synthesis and we were forced to abandon our initial synthetic strategy. Thus, we redesigned a second synthetic blueprint, this time taking advantage of a highly diastereoselective intermolecular oxocarbenium allylation reaction, which has been successfully employed in numerous synthetic ventures from our laboratory.[19]

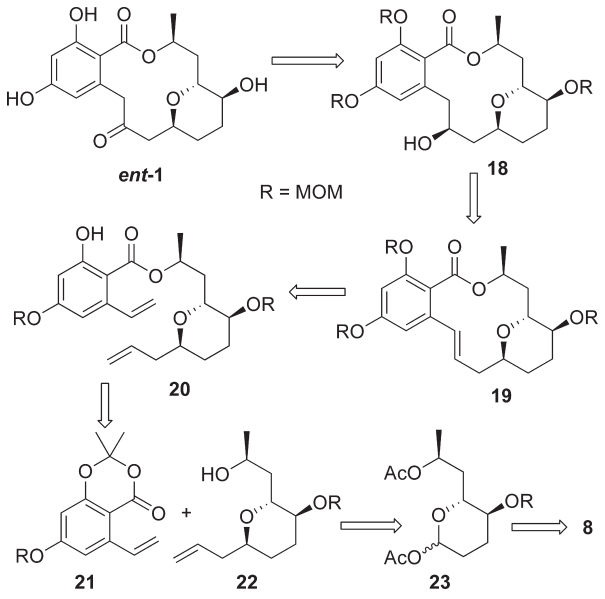
Second-Generation Retrosynthetic Analysis of Pochonin J (1). Disappointed, yet undaunted by the failure to obtain the key kinetic siyl enol ether **17**, we proceeded to revise our synthetic strategy. The second-generation retrosynthetic analysis envisioned a late stage alcohol oxidation of **18** that would be derived from the macrocyclic olefin **19** as delineated in Scheme 4. Synthesis of macrocycle **19** would be obtained from a ring-closing metathesis reaction of the acyclic diene **20**, followed by MOM protection of the free phenol moeity. In turn, a transesterification of the aromatic subunit **21** with α-*C*-glycoside **22** should provide diene **20**. Aromatic subunit **21** should be accessed starting from the previously synthesized aryl triflate **15** via a Pd-catalyzed coupling with potassium vinyl trifluoroborate. The

Table 1. Attempted Kinetic Enolization of Aromatic Ketone

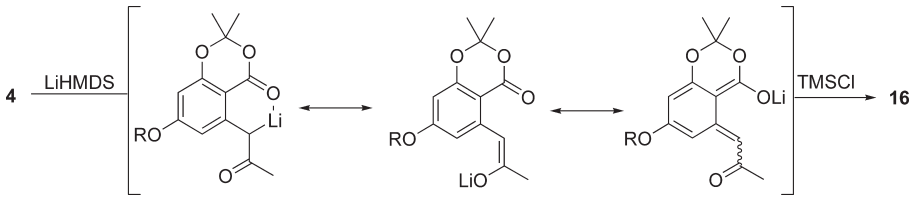


entry	solvent	time (h)	base (equiv)	additive (equiv)	TMSCl (equiv)	**16**:**17**
1	THF	0.5	ArLi (1.2)	NEt_3 (2.3)	2	>97:3
2	THF	1	ArLi (1.5)	NEt_3 (6.0)	5	>97:3
3	$PhCH_3$	1	LiHMDS (1.25)	Ph_3N (5.0)	3	>97:3
4	$PhCH_3$	1	LiHMDS (1.25)	Ph_3N (10.0)	4	>97:3
5	$PhCH_3$	1	LiHMDS (1.5)	Ph_3N (10.0)	5	>97:3
6	$PhCH_3$	1	LiHMDS (1.25)	Ph_3N (40.0)	5	>97:3
7	$PhCH_3$	1	LiHMDS (1.25)	Ph_3N (80.0)	5	>97:3

Scheme 4. Second Generation Synthetic Blueprint of Pochonin J



Scheme 3. Rationale for the Thermodynamic Enolate Formation of 16



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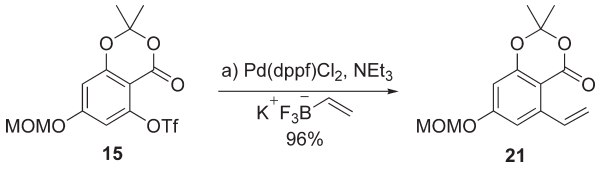
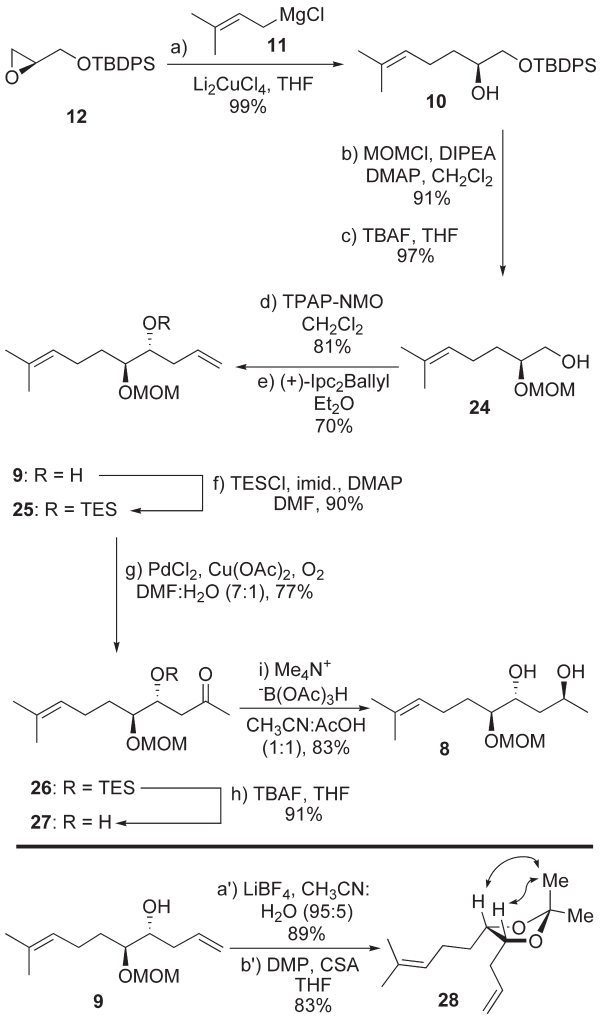
Scheme 5. Synthesis of Substituted Styrene 21 via Suzuki Cross-Coupling



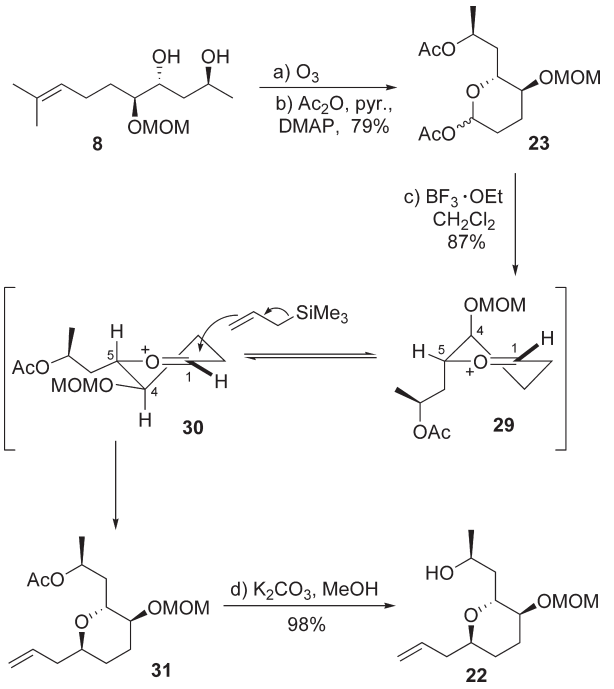
Scheme 6. Synthesis of Triol 8 via Wacker Oxidation



required alcohol **22** could, in principle, be derived from a highly stereoselective oxocarbenium allylation reaction process between precursor **23** and allyl trimethylsilane. Thus, acetal **23** would be envisioned to arise from an oxidative cleavage of the olefin resident in **8** followed by cyclization and capping of both hydroxy moieties with acetic anhydride.

As presented in Scheme 5, our revised synthetic blueprint required the synthesis of substituted styrene **21**. By analogy to our previous synthesis of *epi*-aigialomycin D, treatment of aryl triflate **15** with potassium trifluoroborate and $Pd(dppf)Cl_2$ under conditions reported by Molander, readily provided compound **21** in 96% yield.[11,20]

Scheme 7. Synthesis of α-*C*-Glycoside 22



With the aromatic segment **21** readily in hand, we proceeded to the synthesis of the α-*C*-glycoside segment of ***ent*-1**. Thus, the addition of prenyl derived Grignard reagent **11** to TBDPS protected (*S*)-glycidol **12** readily proceeded with a catalytic amount of Li_2CuCl_4 to provide diol **10** in virtually a quantitative yield as shown in Scheme 6. An ensuing protection of the free hydroxyl moiety as a MOM ether utilizing standard conditions (MOMCl, DMAP, and DIPEA) followed by fluorine mediated desilylation of the corresponding primary TBDPS ether furnished monoprotected diol **24** in 88% yield over two steps from **10**. Subsequent oxidation of the primary alcohol with TPAP afforded the requisite aldehyde, and a matched asymmetric allylation with Brown's (+)-Ipc_2Ballyl reagent provided homoallylic alcohol **9** in 57% yield over the two-step sequence with a >20:1 dr for the desired diastereomer.[21]

At this point in the synthesis, we deemed it prudent to verify the 1,2-*anti* relationship of the diol moiety resident in **9**. Thus, removal of the MOM ether with $LiBF_4$ furnished the free diol. This compound was immediately submitted to acetonide formation utilizing 2,2-dimethoxypropane (DMP) and CSA to afford compound **28** in 74% yield over the two steps. As depicted in Scheme 6, we observed very strong NOE crosspeak signals between the hydroxyl-methine signals and the axial methyl group, which strongly supports the notion that the stereochemistry of the 1,2-diol was indeed *anti* as expected. With **9** in hand, the stage was set for what we envisioned would be a chemoselective Wacker oxidation of the terminal olefin in the presence of the trisubstituted alkene. Initial attempts at terminal alkene oxidation in the presence of a free secondary alcohol, led to diminished yields of the desired product (~10%). Along this line, the hydroxyl group of **9** was protected as a TES ether under standard silylation conditions (TESCl, imidazole, and DMAP) and furnished **25** in 90% yield. Much to our delight, treatment of **25** with 10 mol % of $PdCl_2$ and 0.2 equiv of $Cu(OAc)_2$ under an atmosphere of O_2 chemoselectively provided the desired TES protected β-hydroxy ketone **26** in 77% yield. Removal of the TES

dx.doi.org/10.1021/jo200332d |*J. Org. Chem.* 2011, 76, 3898–3908

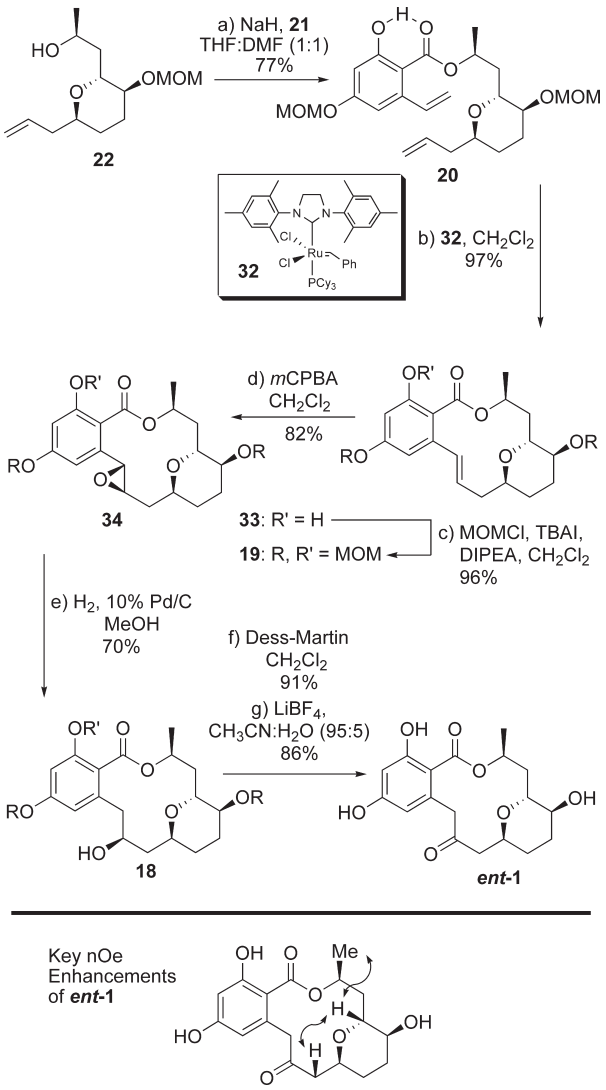
protecting group was readily accomplished with TBAF and afforded ketone **27.** An ensuing hydroxyl directed intramolecular 1,3-*anti* reduction of **27** with $NMe_4^+H(OAc)_3B^-$ provided the MOM protected triol **8** with a dr of >20:1 in 76% yield over two steps from ketone **26.**[22]

With triol **8** readily in hand, we were in position to proceed and cyclize the linear fragment through an oxidative cleavage reaction process as shown in Scheme 7. Hence, treatment of **8** under standard ozonolysis conditions allowed for oxidative cleavage of the alkene moiety followed by a 6-*exo-trig* cyclization of the corresponding *bis*-hydroxy aldehyde intermediate to afford the resultant hemiacetal product, which when directly treated with excess acetic anhydride and pyridine with catalytic amounts of DMAP provided the desired bis-acetyl hemiketal **23** as a mixture of diastereomers in a yield of 79% over two steps from triol **8**. With **23** in hand, addition of $BF_3\cdot OEt_2$ at −78 °C readily generated the endocyclic oxocarbenium cation and stereoselective allylation of reactive intermediate conformer **30** with allyltrimethylsilane provided the desired α-*C*-glycoside **31** in 87% yield as a single diastereomer. Presumably, alkylations of oxocarbenium cations occur through a stabilized chairlike transition state via axial addition of the allyl silane to afford the α-*C*-glycoside.[23] Of two possible reactive conformers (**29** and **30**) and based on the isolated α-*C*-glycoside, the proposed conformer **30** placed the substituents at C_4 and C_5 into pseudoequatorial positions. During our prior examination of stereoselective endocyclic oxocarbenium alkylation with respect to the synthesis of aspergillide B, the C_4 hydroxyl moiety was placed in the axial position and the C_5 substituent in the pseudo equatorial geometry and the allylation took only 1 h for completion.[12] Based on Woerpel's observations and in conjunction with our prior investigations, these C_4 axial and C_5 pseudoequatorial oxocarbenium conformations tend to represent a "matched" geometry.[12,24] However, the current reactive oxocarbenium conformer **30** placed the C_4 and C_5 substituents in the pseudoequatorial positions. Interestingly, the highly stereoselective oxocarbenium formation/alkylation reaction required ∼6 h for completion at −78 °C. Hence, it is alleged that conformer **30** represents a "mismatched" geometry for a highly stereoselective oxocarbenium allylation. Once again, the current results would suggest that the C5 substituent plays a dominant role with respect to reactive oxocarbenium conformation preference during an alkylation and/or reduction process.[24] Final hydrolysis of the acetate resident in **31** with K_2CO_3 and MeOH provided the requisite aliphatic portion (**22**) of ***ent*-1** in nearly quantitative yield as delineated in Scheme 7.

With the aliphatic α-*C*-glycoside subunit **22** readily in hand, our focus turned toward the completion of ***ent*-1** as summarized in Scheme 8. Consequently, convergent transesterification of **21** with the alkoxide anion derived from the treatment of **22** with NaH in a 1:1 THF/DMF solvent mixture proceeded to provide diene **20** in 77% yield. Similar to our previous work on aigialomycin D, we envisaged a macrocyclization to the 14-membered ring via a ring-closing metathesis at C10−C11.[11]

Thus, treatment of **20** with Grubbs' second generation catalyst (**32**) in refluxing CH_2Cl_2 led to the formation of the desired 14-membered macrocycle **33** in 97% yield. With the crude framework in place, we sought to install the final carbon−oxygen bond by means of an *m*-CPBA mediated epoxidation of the newly formed olefin in **33**. Since epoxidation of this intermediate proved problematic and led only to degradation of the starting material, we chose to protect the free phenol of **33** as a MOM acetal, and said reaction furnished the fully protected macrocycle **19** in 96% yield. Much to our surprise, treatment of **19** with *m*-CPBA, buffered in a 1:1 biphasic solvent

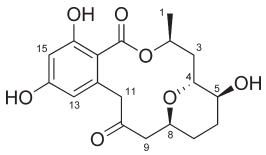
Scheme 8. Synthesis of the Proposed Structure of *ent*-Pochonin J



mixture of CH_2Cl_2 and 1 M aqueous solution of $NaHCO_3$, stereoselectively oxidized the olefin to afford epoxide **34** in a good yield of 82% as a single diastereomer. Although the generation of this stereogenic center is extraneous, as it is later oxidized to the requisite ketone, it is noteworthy that the epoxidation took place with such remarkable stereoselectivity. After meticulous experimentation and optimization of reaction parameters, reductive benzylic hydrogenolysis of the oxirane moiety of **34** with H_2 and 10% Pd/C in MeOH furnished the homobenzylic alcohol **18** in 70% yield. The stereochemistry of the secondary alcohol moiety resident in **18** was determined via NOE correlation spectroscopy, thus leading us to infer the epoxide stereochemistry as shown in Scheme 8. Initial screening of several oxidants (TPAP, IBX, and Swern) failed to provide the ketone and led only to starting material decomposition. Fortunately, the Dess−Martin periodinane reagent proved competent for the required oxidation of the secondary alcohol. Ensuing global deprotection of the three MOM acetal groups with $LiBF_4$ provided ***ent*-1** in 78% yield over two steps from **18**. Unfortunately, the spectral (^{1}H NMR, 500 MHz; ^{13}C NMR, 125 MHz) and optical rotation data of synthetic (+)-pochonin J did not agree with the

dx.doi.org/10.1021/jo200332d |*J. Org. Chem.* 2011, 76, 3898–3908

Table 2. ^{1}HNMR chemical shift comparison of natural vs synthetic pochonin J[a] in CD_3OD



natural pochonin J ppm, mult, *J* in Hz	carbon	synthetic *ent*-pochonin J ppm, mult, *J* in Hz
1.34, d, (6.7)	1	1.34, d, (6.0)
5.32, m	2	5.27, m
2.18, dd, (15.5, 2.4)	3a	2.04, m
1.58, ddd, (15.5, 7.3, 4.3)	3b	1.93, m
3.42, ddd, (10.0, 7.3, 2.4)	4	3.81, m
3.58, m	5	3.31, m
2.05, m	6a	1.96, m
1.94, m	6b	1.77, m
1.91, m	7a	1.83, m
1.74, m	7b	1.68, m
4.38, m	8	4.33, m
2.65, dd, (15.5, 10.0)	9a	3.21, dd, (13.9, 11.9)
2.40, dd, (15.5, 4.0)	9b	2.34, dd, (13.9, 3.8)
4.27, d, (18.3)	11a	4.44, d, (18.9)
3.85, d, (18.3)	11b	4.27, d, (18.9)
5.98, d, (2.4)	13	6.11, d, (2.5)
6.14, d, (2.4)	15	6.26, d, (2.5)

[a] Reference peak = 3.31 ppm.

natural sample.[2] The key NOE enhancements in Scheme 8 strongly suggest that ***ent*-1** is indeed an α-*C*-glycoside and the C1 methyl group has the presumed stereochemistry as illustrated. As shown in Table 2, many of the signals of ***ent*-1** in the ^{1}H NMR do not match that of the reported structure. A couple of significant ^{1}H NMR discrepancies lie at both C9 and C11 and these results might provide valuable insight into the true structure of pochonin J.

CONCLUSION

In summary, an efficient synthesis of ***ent*-1** has been achieved but unfortunately does not match the spectroscopic data of pochonin J as initially reported. The construction of the α-*C*-glycoside subunit is highlighted by a highly diastereoselective oxocarbenium cation formation/allylation sequence of a hemiketal intermediate. Convergent union of the elaborated subunits, through a trans-esterification and subsequent RCM reaction, forged the 14-membered macrolactone. Final oxidation of the resulting alkene provided "pochonin J", which did not spectroscopically correlate to the initially disclosed natural product. Further attempts at the structural verification of pochonin J are ongoing and will be reported in due course.

EXPERIMENTAL SECTION

General Procedure. All of the reactions were performed under an inert atmosphere of Ar in flame-dried glassware. Anhydrous tetrahydrofuran (THF) and dimethoxyethane (DME) were obtained from commercial sources and used without purification. Deuterated chloroform ($CDCl_3$) was stored over molecular sieves (4 Å). All of the NMR spectra were recorded on either a 360 or 500 MHz spectrometer. ^{1}H NMR spectra were obtained using $CDCl_3$ as the solvent with either tetramethylsilane (TMS, 0 ppm) or chloroform ($CHCl_3$, 7.26 ppm) as the internal standard. Column chromatography was performed using 60−200 μm silica gel. Analytical thin layer chromatography was performed on silica-coated glass plates with F-254 indicator. Visualization was accomplished by UV light (254 nm), $KMnO_4$, or ceric sulfate-PMA stain. All starting materials and solvents were commercially available and were used without further purification. Compounds **6** and **12** have been previously reported.[13,25]

1-(*tert*-Butyl-diphenyl-silanyloxy)-6-methyl-hept-5-en-2-ol (10). 1-Chloro-3-methyl-2-butene (1.10 mL, 9.60 mmol, 3.00 equiv) was added dropwise to a stirred suspension of preactivated Mg powder (466 mg, 19.2 mmol, 6.00 equiv) in THF (9.60 mL) at 0 °C under Ar and stirred for 1.5 h. Meanwhile to a solution of **12** (1.00 g, 3.20 mmol, 1.00 equiv) in THF (16.0 mL) at −40 °C under Ar was added Li_2CuCl_4 (0.10 M solution in THF, 0.16 mmol, 0.05 equiv). The previously made Grignard reagent was then added dropwise to the reaction mixture and allowed to stir for 1 h at −40 °C, at which time the reaction temperature was warmed to 0 °C and quenched with satd NH_4Cl (50.0 mL). The reaction mixture was then allowed to reach rt. The aqueous layer was extracted with EtOAc (3 × 30.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 2% ethyl acetate in hexanes) afforded **10** as a clear viscous oil (1.21 g, 99% yield): R_f at 5% ethyl acetate in hexanes 0.30; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (m, 4H), 7.44 (m, 6H), 5.13 (m, 1H), 3.77 (m, 1H), 3.71 (dd, 1H, *J* = 10.1, 3.5 Hz), 3.55 (dd, 1H, *J* = 10.1, 7.3 Hz), 2.11 (m, 2H), 1.71 (s, 3H), 1.62 (s, 3H), 1.54 (m, 1H), 1.46 (m, 1H), 1.12 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.5, 135.5, 133.2, 133.1, 131.8, 129.7, 127.7, 123.9, 71.4, 68.0, 32.8, 26.8, 25.6, 24.0, 19.2, 17.6. IR (CH_2Cl_2) 610, 703, 736, 825, 1006, 1109, 1427, 1471, 2857, 2928, 3050, 3068, 3456, 3578 cm^{-1}. $[\alpha]^{20}_D$ = +17.8 (*c* 0.40, CH_2Cl_2). HRMS (EI) calcd for $C_{24}H_{34}O_2Si$ (M − C_4H_9) 325.1624, found 325.1623.

2-Methoxymethoxy-6-methyl-hept-5-en-1-ol (24). To a stirred solution of **10** (300 mg, 0.78 mmol, 1.00 equiv) in CH_2Cl_2 (4.00 mL) were added DMAP (29 mg, 0.24 mmol, 0.30 equiv), DIPEA (0.68 mL, 3.92 mmol, 5.00 equiv), and MOMCl (0.18 mL, 2.35 mmol, 3.00 equiv) at 0 °C under Ar. The reaction mixture was stirred for 18 h at rt, at which time the temperature was lowered to 0 °C. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (10.0 mL) and deionized H_2O (10.0 mL) and then allowed to reach rt. The aqueous layer was extracted with Et_2O (3 × 20.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 1% ether in hexanes) afforded the MOM protected diol as a light yellow oil (304 mg, 91% yield): R_f at 1% ether in hexanes 0.30.;

To a solution of the MOM-protected diol (1.60 g, 3.75 mmol, 1.00 equiv) in THF (18.8 mL) was added TBAF (1.00 M solution in THF, 5.63 mmol, 1.50 equiv) at 0 °C under Ar. The reaction mixture was stirred for 6 h at rt, at which time the reaction temperature was lowered to 0 °C. The reaction was quenched with deionized H_2O (50.0 mL) and then allowed to reach rt. The aqueous layer was extracted with EtOAc (3 × 25.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 20% ethyl acetate in hexanes) afforded **24** as a yellow viscous oil (680 mg, 97% yield): R_f at 20% ethyl acetate in hexanes 0.20; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.08 (m, 1H), 4.74 (d, 1H, *J* = 6.9 Hz), 4.68 (d, 1H, *J* = 6.9 Hz), 3.54 (m, 3H), 3.43 (s, 3H), 3.13 (dd, 1H, *J* = 3.20, 8.8 Hz), 2.07 and 2.04 (ABq, 2H, *J* = 7.3 Hz), 1.68 (s, 3H), 1.60 (s, 3H), 1.56 (m, 1H), 1.46 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.2, 123.6, 97.1, 82.0, 65.8, 55.6, 31.7, 25.7, 23.9, 17.7. IR (CH_2Cl_2) 833, 917, 1035, 1105, 1146, 1213, 1375, 1453, 2932, 3445 cm^{-1}. $[\alpha]^{20}_D$ = +228 (*c* 0.33, CH_2Cl_2). HRMS (EI) calcd for $C_{10}H_{20}O_3$ (M - H) 187.1334, found 187.1335.

5-Methoxymethoxy-9-methyl-deca-1,8-dien-4-ol (9). To a stirred solution of **24** (2.00 g, 10.6 mmol, 1.00 equiv) in CH_2Cl_2 (106 mL) containing preactivated 4 Å molecular sieves (1.00 g/mmol) were added NMO (3.74 g, 31.9 mmol, 3.00 equiv) and TPAP (374 mg, 1.06 mmol, 0.10 equiv) at rt under Ar. The reaction mixture was allowed to stir for 1 h at rt, at which time the mixture was filtered through a plug of silica (ca. 3 mm) to afford the corresponding aldehyde as a clear oil (1.60 g, 81% yield): R_f at 40% ethyl acetate in hexanes 0.85.

To a stirred solution of (+)-Ipc$_2$BOMe (9.51 g, 30.1 mmol, 1.40 equiv) in Et_2O (75.0 mL) at −78 °C under Ar was added allylmagnesium bromide (1.00 M solution in Et_2O, 27.9 mmol, 1.30 equiv). The reaction mixture was allowed to reach rt and stirred for 1 h, after which time the mixture was recooled to −78 °C. The previously synthesized aldehyde (4.00 g, 21.5 mmol, 1.00 equiv) was then added dropwise to the reaction mixture, which was allowed to stir for 2 h. The reaction was warmed to 0 °C. To this mixture were added 3 M NaOH (7.50 mL), 30% aqueous H_2O_2 (15.0 mL), and deionized H_2O (50.0 mL) sequentially. The reaction mixture was allowed to stir at rt for 6 h, after which the aqueous layer was extracted with Et_2O (3 × 50.0 mL). The organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 10% ethyl acetate in hexanes) afforded **9** as a clear oil (3.43 g, 70% yield): R_f at 10% ethyl acetate in hexanes 0.20; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (m, 1H), 5.10 (m, 3H), 4.72 (d, 1H, J = 6.6 Hz), 4.62 (d, 1H, J = 6.9 Hz), 3.64 (m, 1H), 3.54 (m, 1H), 3.42 (s, 3H), 2.85 (m, 1H), 2.22 (m, 2H), 2.11 (m, 1H), 2.02 (m, 1H), 1.67 (s, 3H), 1.62 (m, 1H), 1.56 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.4, 132.1, 123.8, 117.1, 97.4, 83.2, 72.5, 55.8, 36.5, 30.6, 25.6, 24.2, 17.6. IR (CH_2Cl_2) 735, 915, 1033, 1263, 1446, 1641, 1686, 2927, 3060, 3438 cm^{-1}. $[\alpha]^{20}_D$ = +150 (c 0.14, CH_2Cl_2). HRMS (EI) calcd for $C_{13}H_{24}O_3$ (M+) 228.1725, found 228.1728.

(1-Allyl-2-methoxymethoxy-6-methyl-hept-5-enyloxy)-triethyl-silane (25). To a solution of **9** (400 mg, 1.74 mmol, 1.00 equiv) in DMF (8.60 mL) were added DMAP (65 mg, 0.52 mmol, 0.30 equiv), imidazole (475 mg, 6.95 mmol, 4.00 equiv), and TESCl (0.75 mL, 4.34 mmol, 2.50 equiv) at 0 °C under Ar. The reaction mixture was stirred for 24 h at rt, at which time the reaction temperature was lowered to 0 °C and quenched with deionized H_2O (50.0 mL) and then allowed to reach rt. The aqueous layer was extracted with Et_2O (3 × 25.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 1% ether in hexanes) afforded **25** as a light yellow oil (540 mg, 90% yield): R_f at 1% ether in hexanes 0.35; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (m, 1H), 5.11 (m, 1H), 5.05 (m, 2H), 4.76 (d, 1H, J = 6.6 Hz), 4.62 (d, 1H, J = 6.6 Hz), 3.73 (m, 1H), 3.51 (m, 1H), 3.39 (s, 3H), 2.26 (m, 2H), 2.13 (m, 1H), 2.02 (m, 1H), 1.68 (s, 3H), 1.61 (s, 3H), 1.58 (m, 1H), 1.47 (m, 1H), 0.95 (t, 9H, J = 7.6 Hz), 0.59 (q, 6H, J = 7.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.7, 131.7, 124.3, 116.7, 96.3, 80.2, 74.4, 55.7, 37.7, 30.8, 25.6, 24.5, 17.7, 6.9, 5.1. IR (CH_2Cl_2) 738, 915, 1006, 1036, 1102, 1150, 1238, 1381, 1414, 1458, 1642, 2880, 2912, 2953 cm^{-1}. $[\alpha]^{20}_D$ = −133 (c 0.33, CH_2Cl_2). HRMS (EI) calcd for $C_{19}H_{38}O_3Si$ (M+) 342.2590, found 342.2595.

4-Hydroxy-5-methoxymethoxy-9-methyl-dec-8-en-2-one (26). To a solution of **25** (75.0 mg, 0.22 mmol, 1.00 equiv) in DMF/H_2O (2.20 mL, 7:1) were added $PdCl_2$ (4.00 mg, 0.02 mmol, 0.10 equiv) and $Cu(OAc)_2$ (8.00 mg, 0.04 mmol, 0.20 equiv). The reaction mixture was allowed to stir under O_2 (1 atm) at rt for 48 h. The reaction was then diluted with EtOAc (10.0 mL) and water (20.0 mL). The aqueous layer was extracted with EtOAc (3 × 15.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 10% ethyl acetate in hexanes) afforded **26** as a yellow oil (60 mg, 77% yield): R_f at 10% ethyl acetate in hexanes 0.20; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.10 (m, 1H), 4.80 (d, 1H, J = 6.3 Hz), 4.64 (d, 1H, J = 6.3 Hz), 4.23 (m, 1H), 3.53 (m, 1H), 3.39 (s, 3H), 2.70 (dd, 1H, J = 16.4, 7.6 Hz), 2.49 (dd, 1H, J = 16.4, 3.8 Hz), 2.16 (s, 3H), 2.11 (m, 1H), 2.02 (m, 1H), 1.68 (s, 3H), 1.61 (s, 3H), 1.48 (m, 1H), 1.37 (m, 1H), 0.93 (t, 9H, J = 7.9 Hz), 0.59 (q, 6H, J = 8.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.5, 132.1, 123.9, 96.5, 80.7, 71.1, 55.7, 46.5, 31.6, 31.4, 25.6, 24.4, 17.7, 6. 8, 6.5, 5.8, 4.8. IR (CH_2Cl_2) 736, 839, 1032, 1098, 1150, 1239, 1357, 1375, 1412, 1460, 1719, 2880, 2912, 2957, 3438 cm^{-1}. $[\alpha]^{20}_D$ = −76.9 (c 0.13, CH_2Cl_2). HRMS (EI) calcd for $C_{19}H_{38}O_4Si$ (M+) 358.2539, found 358.2556.

4-Hydroxy-5-methoxymethoxy-9-methyl-dec-8-en-2-one (27). To a solution of **26** (480 mg, 1.34 mmol, 1.00 equiv) in THF (14.0 mL) was added TBAF (1.00 M solution in THF, 1.34 mmol, 1.00 equiv) at 0 °C under Ar. The reaction mixture was stirred for 6 h at rt, at which time the reaction temperature was lowered to 0 °C. The reaction was quenched with deionized H_2O (25.0 mL) and then allowed to reach rt. The aqueous layer was extracted with EtOAc (3 × 25.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 25% ethyl acetate in hexanes) afforded **27** as a clear viscous oil (297 mg, 91% yield): R_f at 25% ethyl acetate in hexanes 0.20; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.04 (m, 1H), 4.69 (d, 1H, J = 6.6 Hz), 4.58 (d, 1H, J = 6.6 Hz), 4.02 (m, 1H), 3.52 (m, 1H), 3.37 (s, 3H), 2.59 (dd, 1H, J = 16.7, 9.20 Hz), 2.52 (dd, 1H, J = 16.7, 3.20 Hz), 2.20 (s, 3H), 2.07 (m, 1H), 1.99 (m, 1H), 1.63 (s, 3H), 1.56 (s, 3H), 1.50 (m, 1H), 1.38 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.6, 131.9, 123.5, 97.1, 82.1, 69.4, 55.6, 45.2, 31.1, 30.5, 25.4, 23.8, 17.4. IR (CH_2Cl_2) 921, 1032, 1073, 1150, 1213, 1265, 1361, 1375, 1442, 1712, 2924, 3449 cm^{-1}. $[\alpha]^{20}_D$ = +277 (c 0.14, CH_2Cl_2). HRMS (EI) calcd for $C_{13}H_{24}O_4$ (M+) 244.1675, found 244.1668.

5-Methoxymethoxy-9-methyl-dec-8-ene-2,4-diol (8). To a solution of tetramethylammonium triacetoxyborohydride (11.8 g, 44.6 mmol, 10.0 equiv) in anhydrous CH_3CN (25.0 mL) was added anhydrous HOAc (25.0 mL), and the mixture was stirred at rt for 0.5 h under Ar. The mixture was cooled to −40 °C, and a solution of **27** (1.09 g, 4.46 mmol, 1.00 equiv) in anhydrous CH_3CN (45.0 mL) was added dropwise. The reaction mixture was then allowed to stir at −20 °C for 48 h. The reaction was quenched with a 0.5 M aqueous solution of sodium potassium tartrate (25.0 mL), and the mixture was allowed to warm to rt. The reaction mixture was then carefully neutralized with a saturated aqueous solution of $NaHCO_3$ (100 mL) at 0 °C and then allowed to warm to rt. The aqueous layer was extracted with CH_2Cl_2 (3 × 50.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 40% ethyl acetate in hexanes) afforded **8** as a clear viscous oil (910 mg, 83% yield): R_f at 40% ethyl acetate in hexanes 0.20; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.00 (m, 1H), 4.65 (d, 1H, J = 6.9 Hz), 4.53 (d, 1H, J = 6.6 Hz), 4.01 (m, 1H), 3.79 (m, 1H), 3.67 (d, 1H, J = 6.9 Hz), 3.44 (m, 1H), 3.32 (s, 3H), 3.22 (m, 1H), 2.02 (m, 1H), 1.94 (m, 1H), 1.59 (s, 3H), 1.51 (s, 3H), 1.50 (m, 2H), 1.37 (m, 2H), 1.14 (d, 3H, J = 6.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.8, 123.7, 97.3, 83.8, 69.7, 64.5, 55.6, 39.3, 30.8, 25.5, 24.1, 23.5, 17.5. IR (CH_2Cl_2) 833, 917, 1035, 1150, 1209, 1375, 1446, 1642, 1723, 2924, 3408 cm^{-1}. $[\alpha]^{20}_D$ = +115 (c 0.28, CH_2Cl_2). HRMS (EI) calcd for $C_{13}H_{26}O_4$ (M+) 246.1831, found 246.1831.

4-Allyl-2,2-dimethyl-5-(4-methyl-pent-3-enyl)-[1,3]dioxolane (28). To a solution of **9** (67.0 mg, 0.29 mmol, 1.00 equiv) in a 95:5 solvent mixture of CH_3CN/H_2O (5.87 mL) was added $LiBF_4$ (1.0 M solution in CH_3CN, 2.93 mmol, 10.0 equiv). The reaction mixture was then heated to reflux (75 °C) and allowed to stir for 1 h. After cooling, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (10.0 mL). The aqueous layer was extracted with EtOAc (3 × 10.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 15% ethyl acetate in hexanes) afforded the corresponding diol as a white crystalline solid (48.0 mg, 89% yield): R_f at 20% ethyl acetate in hexanes 0.20.

To a stirred solution of the synthesized diol (25.0 mg, 0.14 mmol, 1.00 equiv) in THF (2.70 mL) were added CSA (3.20 mg, 0.02 mmol, 0.10 equiv) and 2,2-dimethoxypropane (0.17 mL, 1.36 mmol, 10.0 equiv) at 0 °C under Ar. The reaction mixture was allowed to stir at rt for

5 h, at which time the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (5.00 mL). The aqueous layer was extracted with Et_2O (3 × 5.00 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 1% ether in hexanes) afforded **28** as a yellow oil (25.0 mg, 83% yield): R_f at 1% ether in hexanes 0.40; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.84 (m, 1H), 5.10 (m, 3H), 4.08 (m, 2H), 2.28 (m, 1H), 2.18 (m, 2H), 2.04 (m, 1H), 1.69 (s, 3H), 1.62 (s, 3H), 1.57 (m, 1H), 1.45 (s, 3H), 1.40 (m, 1H), 1.34 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.9, 132.3, 123.7, 117.0, 107.6, 77.4, 77.3, 34.6, 29.8, 28.5, 25.9, 25.7, 24.7, 17.7. IR (CH_2Cl_2) 911, 1059, 1214, 1377, 1449, 1639, 1729, 2858, 2927 cm $^{-1}$. $[\alpha]^{20}_D$ = +56.7 (*c* 0.03, CH_2Cl_2). HRMS (EI) calcd for $C_{14}H_{24}O_2$ (M+) 224.1776, found 224.1781.

Acetic Acid 6-(2-Acetoxy-propyl)-5-methoxymethoxy-tetrahydro-pyran-2-yl Ester (23). A stream of ozone was bubbled through a solution of **8** (750 mg, 3.05 mmol, 1.00 equiv) dissolved in CH_2Cl_2 (60.0 mL) at −78 °C until complete consumption of starting material was observed by TLC analysis (30 min). To the reaction mixture was added PPh_3 (4.00 g, 15.3 mmol, 5.00 equiv) at −78 °C, and the resulting mixture was stirred initially for 0.5 h and then for an additional 2.5 h at rt. The solution was concentrated in vacuo, and flash chromatography (silica, 70% ethyl acetate in hexanes) afforded the hemiacetal as a clear viscous oil (535 mg, 80% yield): R_f at 70% ethyl acetate in hexanes 0.20.

To a solution of the synthesized hemiacetal (700 mg, 3.18 mmol, 1.00 equiv) in CH_2Cl_2 (16.0 mL) were added DMAP (117 mg, 0.95 mmol, 0.30 equiv), pyridine (0.78 mL, 9.54 mmol, 3.00 equiv), and Ac_2O (0.75 mL, 7.95 mmol, 2.50 equiv) at 0 °C under Ar. The reaction mixture was stirred for 12 h at rt, at which time the reaction temperature was lowered to 0 °C. The reaction was quenched with saturated aqueous solution of $NaHCO_3$ (25.0 mL) and then allowed to warm to rt. The aqueous layer was extracted with EtOAc (3 × 25.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 20% ethyl acetate in hexanes) afforded **23** as a yellow oil (765 mg, 79% yield): R_f at 20% ethyl acetate in hexanes 0.20; ^{1}H NMR (500 MHz, $CDCl_3$), Minor diastereomer: δ 5.59 (dd, 1H, *J* = 8.5, 1.3 Hz), 5.04 (m, 1H), 4.59 (d, 2H, *J* = 6.9 Hz), 3.45 (m, 1H), 3.34 (d, 3H, *J* = 1.0 Hz), 3.26 (m, 1H), 2.21 (m, 1H), 2.08 (m, 1H), 1.99 (s, 3H), 1.98 (s, 3H), 1.78 (m, 2H), 1.53 (m, 2H), 1.20 (d, 3H, *J* = 6.30 Hz). Major diastereomer: δ 5.99 (s, 1H), 5.05 (m, 1H), 4.70 (dd, 2H, *J* = 6.9, 1.0 Hz), 3.64 (t, 1H, *J* = 10.1 Hz), 3.36 (d, 3H, *J* = 1.0 Hz), 3.26 (m, 2H), 2.08 (m, 1H), 2.03 (s, 3H), 2.02 (s, 3H), 1.78 (m, 2H), 1.53 (m, 2H), 1.19 (d, 3H, *J* = 6.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8, 138.5, 128.3, 127.8, 127.6, 112.9, 76.8, 71.3, 65.9, 46.3, 40.1, 35.9, 22.4, 18.6, 14.2. IR (CH_2Cl_2) 944, 1043, 1109, 1249, 1374, 1443, 1737, 2938, 3452 cm $^{-1}$. $[\alpha]^{20}_D$ = +463 (*c* 0.40, CH_2Cl_2). HRMS (EI) calcd for $C_{14}H_{24}O_7$ (M+) 305.1600, found 305.1602.

Acetic Acid 2-(6-Allyl-3-methoxymethoxy-tetrahydro-pyran-2-yl)-1-methyl-ethyl Ester (31). To a stirred solution of **23** (550 mg, 1.81 mmol, 1.00 equiv) in CH_2Cl_2 (11.0 mL) were added allylTMS (1.20 mL, 7.24 mmol, 4.00 equiv) and $BF_3 \cdot OEt_2$ (0.45 mL, 3.62 mmol, 2.00 equiv) at −78 °C under Ar. The reaction mixture was stirred for 3 h, at which time the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (25.0 mL) at −78 °C and slowly allowed to reach rt. The aqueous layer was extracted with CH_2Cl_2 (3 × 25.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 10% ethyl acetate in hexanes) afforded **31** as a light yellow oil (440 mg, 87% yield): R_f at 10% ether in hexanes 0.20; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.76 (m, 1H), 5.02 (m, 3H), 4.71 (d, 1H, *J* = 6.9 Hz), 4.63 (d, 1H, *J* = 6.9 Hz), 3.68 (m, 2H), 3.37 (s, 3H), 3.32 (m, 1H), 2.40 (m, 1H), 2.16 (m, 1H), 2.00 (s, 3H), 1.86 (m, 2H), 1.69 (m, 2H), 1.61 (m, 2H), 1.24 (d, 3H, *J* = 6.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 134.8, 116.5, 94.7, 73.9, 70.6, 70.3, 67.8, 55.3, 37.3, 37.2, 26.0, 24.3, 21.1, 20.5. IR (CH_2Cl_2) 607, 917, 1035, 1106, 1150, 1242, 1375, 1442, 1642, 1734, 2935, 3072, 3534 cm $^{-1}$. $[\alpha]^{20}_D$ = +288 (*c* 0.40, CH_2Cl_2). HRMS (EI) calcd for $C_{15}H_{26}O_5$ (M − C_3H_5) 245.1389, found 245.1397.

1-(6-Allyl-3-methoxymethoxy-tetrahydro-pyran-2-yl)-propan-2-ol (22). To a stirred solution of **31** (300 mg, 1.05 mmol, 1.00 equiv) in MeOH (21.0 mL) was added K_2CO_3 (872 mg, 6.29 mmol, 6.00 equiv) in four portions at 5 min intervals at 0 °C. The reaction mixture was allowed to stir at rt for 5 h, at which time the reaction was quenched with deionized H_2O (50.0 mL) and then allowed to reach rt. The aqueous layer was extracted with EtOAc (3 × 75.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 30% ethyl acetate in hexanes) afforded **22** as a clear viscous oil (250 mg, 98% yield): R_f at 30% ethyl acetate in hexanes 0.20; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 (m, 1H), 5.08 (m, 2H), 4.72 (d, 1H, *J* = 6.9 Hz), 4.62 (d, 1H, *J* = 6.9 Hz), 4.03 (m, 1H), 3.88 (m, 1H), 3.80 (m, 1H), 3.39 (m, 1H), 3.36 (s, 3H), 2.60 (broad s, 1H), 2.51 (m, 1H), 2.19 (m, 1H), 1.92 (m, 1H), 1.76 (m, 2H), 1.65 (m, 3H), 1.20 (d, 3H, *J* = 6.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.2, 117.0, 94.8, 73.9, 71.4, 70.8, 64.6, 55.5, 39.0, 36.9, 26.4, 24.5, 23.3. IR (CH_2Cl_2) 917, 1035, 1102, 1220, 1368, 1446, 1642, 2355, 2942, 3083, 3430 cm $^{-1}$. $[\alpha]^{20}_D$ = +242 (*c* 0.60, CH_2Cl_2). HRMS (EI) calcd for $C_{13}H_{24}O_4$ (M - OH) 227.1647, found 227.1646.

5-Hydroxy-7-methoxymethoxy-2,2-dimethyl-benzo[1,3]-dioxin-4-one (14). To a stirred solution of 5,7-dihydroxy-2,2-dimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (**6**) (2.10 g, 10.1 mmol, 1.00 equiv) in anhydrous acetone (50.0 mL) were added K_2CO_3 (4.17 g, 30.1 mmol, 3.00 equiv) and MOMCl (1.53 mL, 20.1 mmol, 2.00 equiv) at 0 °C under Ar. The reaction mixture was stirred for 18 h at rt, at which time the reaction temperature was lowered to 0 °C and quenched with a saturated aqueous solution of $NaHCO_3$ (50.0 mL) and then allowed to reach rt. The aqueous layer was extracted with EtOAc (3 × 50.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 5% ethyl acetate in hexanes) afforded **14** as a white crystalline solid (2.30 g, 90% yield): R_f at 5% ethyl acetate in hexanes 0.20; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.4 (s, 1H), 6.28 (d, 1H *J* = 2.2 Hz), 6.12 (d, 1H, *J* = 2.2 Hz), 5.17 (s, 2H), 3.47 (s, 3H), 1.73 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 165.1, 162.8, 156.8, 119.9, 106.9, 97.9, 95.8, 94.1, 93.7, 56.4, 25.6. IR (CH_2Cl_2) 747, 847, 906, 1142, 1279, 1320, 1512, 1627, 1678, 2337, 2362, 2954, 3001, 3105 cm $^{-1}$. HRMS (EI) calcd for $C_{12}H_{14}O_6$ (M+) 254.0790, found 254.0799.

Trifluoro-methanesulfonic Acid 7-Methoxymethoxy-2,2-dimethyl-4-oxo-4*H*-benzo[1,3]dioxin-5-yl Ester (15). To a stirred solution of **14** (2.14 g, 8.42 mmol, 1.00 equiv) in anhydrous pyridine (42.0 mL) was added Tf_2O (2.13 mL, 12.6 mmol, 1.50 equiv) at 0 °C under Ar. The reaction mixture was stirred for 18 h at rt, at which time the reaction temperature was lowered to 0 °C and quenched with a saturated aqueous solution of $NaHCO_3$ (50.0 mL) and deionized H_2O (50.0 mL) and then allowed to reach rt. The aqueous layer was extracted with EtOAc (3 × 75.0 mL), and the combined organic extracts were washed with a saturated aqueous solution of $CuSO_4$ (300 mL) to remove excess pyridine, dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 15% ethyl acetate in hexanes) afforded **15** as a white crystalline solid (3.22 g, 99% yield): R_f at 15% ethyl acetate in hexanes 0.20; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.67 (d, 1H, *J* = 2.2 Hz), 6.64 (d, 1H, *J* = 2.2 Hz), 5.21 (s, 2H), 3.49 (s, 3H), 1.73 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 158.5, 157.0, 149.6, (q, CF_3, *J* = 321 Hz), 106.5, 118.4, 106.3, 103.6, 101.5, 94.6, 56.5, 25.3. IR (CH_2Cl_2) 588, 731, 815, 863, 1010, 1083, 1138, 1201, 1377. 1428, 1572, 1627, 1737, 2835, 2960, 3008, 3100 cm $^{-1}$. HRMS (EI) calcd for $C_{13}H_{13}O_8F_3S$ (M+) 386.0283, found 386.0274.

5-Allyl-7-(methoxymethoxy)-2,2-dimethyl-4*H*-benzo[*d*][1,3]-dioxin-4-one (5). To a stirred solution of **15** (5.73 g, 14.8 mmol, 1.00 equiv) in THF (926 mL) were added CsF (4.50 g, 29.7 mmol, 2.00 equiv), $Pd(PPh_3)_4$ (1.72 g, 1.48 mmol, 0.10 equiv), and stirred for

30 min at room temperature under Ar. Allyl boronic acid pinacol ester (5.60 mL, 29.7 mmol, 2.00 equiv) was then added and the reaction mixture was stirred for 18 h at reflux (40 °C) and allowed to reach rt, at which time the reaction was quenched with deionized H_2O (400 mL). The aqueous layer was extracted with EtOAc (3 × 250 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 1% ethyl ether in hexanes) afforded **5** as a white solid (3.80 g, 92% yield): R_f at 1% ethyl ether in hexanes 0.35; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (d, 1H, J = 2.52 Hz), 6.49 (d, 1H, J = 2.52 Hz), 6.00 (m, 1H), 5.18 (s, 2H), 5.07 (m, 1H), 5.05 (m, 1H), 3.85 (s, 1H), 3.84 (s, 1H), 3.47 (s, 3H), 1.68 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 159.9, 158.9, 147.2, 136.4, 116.2, 113.4, 105.6, 104.9, 101.8, 94.1, 56.4, 38.4, 25.6. IR (CH_2Cl_2) 858, 910, 1017, 1079, 1147, 1209, 1279, 1438, 1580, 1612, 1734, 2828, 2943, 2998, 3080 cm $^{-1}$. HRMS (EI) calcd for $C_{15}H_{18}O_5$ (M+) 278.1154, found 278.1161.

7-(Methoxymethoxy)-2,2-dimethyl-5-(2-oxopropyl)-4*H*-benzo-[*d*][1,3]dioxin-4-one (4). To a solution of **5** (300 mg, 1.08 mmol, 1.00 equiv) in DMF/H_2O (10.8 mL, 7:1) were added $PdCl_2$ (48.0 mg, 0.27 mmol, 0.50 equiv) and CuCl (160 mg, 1.62 mmol, 2.00 equiv). The reaction mixture was allowed to stir under O_2 (1 atm) at rt for 48 h. The reaction was then diluted with EtOAc (10.0 mL) and water (20.0 mL). The aqueous layer was extracted with EtOAc (3 × 15.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 10% ethyl acetate in hexanes) afforded **4** as a pale yellow solid (230 mg, 72% yield): R_f at 10% ethyl acetate in hexanes 0.30; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.51 (s, 1H), 6.47 (s, 1H), 5.15 (s, 2H), 4.09 (s, 2H), 3.44 (s, 3H), 2.27 (s, 3H), 1.67 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.8, 201.4, 162.5, 160.6, 158.6, 140.6, 115.1, 105.4, 102.6, 94.1, 56.3, 49.2, 30.0, 25.5 IR (CH_2Cl_2) 727, 913, 1010, 1081, 1153, 1209, 1286, 1353, 1442, 1581, 1611, 1723, 2252, 2826, 2941, 2997 cm $^{-1}$. HRMS (EI) calcd for $C_{15}H_{18}O_6$ (M+) 294.1103, found 294.1117.

7-Methoxymethoxy-2,2-dimethyl-5-vinyl-benzo[1,3]dioxin-4-one (21). To a stirred solution of **15** (3.08 g, 8.03 mmol, 1.00 equiv) in EtOH (54.0 mL) were added Et_3N (1.45 mL, 10.4 mmol, 1.30 equiv), $PdCl_2$(dppf)·$CHCl_3$ (655 mg, 0.81 mmol, 0.10 equiv), and potassium vinyltrifluoroborate (1.20 g, 8.83 mmol, 1.10 equiv) at rt under Ar. The reaction mixture was stirred for 18 h at reflux (75 °C) at which time the reaction was concentrated in vacuo. The crude solid was redissolved in EtOAc (50.0 mL) and deionized H_2O (50.0 mL) and allowed to stir for 30 min at rt. The aqueous layer was then extracted with EtOAc (3 × 50.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 2% ethyl acetate in hexanes) afforded **21** as a white solid (2.08 g, 98% yield): R_f at 2% ethyl acetate in hexanes 0.25; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (dd, 1H, J = 17.3, 10.7 Hz), 6.83 (d, 1H, J = 1.9 Hz), 6.49 (d, 1H, J = 2.5 Hz), 5.63 (dd, 1H, J = 17.3, 1.26 Hz), 5.33 (dd, 1H, J = 11.1, 1.26 Hz), 5.15 (s, 2H), 3.42 (s, 3H), 1.64 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 160.1, 158.4, 144.0, 135.3, 117.7, 109.8, 105.1, 104.7, 102.9, 94.1, 56.4, 25.6. IR (CH_2Cl_2) 862, 910, 988, 1039, 1150, 1209, 1275, 1386, 1430, 1575, 1605, 1730, 2828, 2994, 3090 cm $^{-1}$. HRMS (EI) calcd for $C_{14}H_{16}O_5$ (M+) 264.0998, found 264.0989.

2-Hydroxy-4-methoxymethoxy-6-vinyl-benzoic Acid 2-(6-Allyl-3-methoxymethoxy tetrahydro-pyran-2-yl)-1-methyl-ethyl Ester (20). To a stirred solution of **22** (300 mg, 1.23 mmol, 1.00 equiv) in a 1:1 mixture of DMF/THF (54.0 mL) was added NaH (60% dispersion in mineral oil, 210 mg, 4.30 mmol, 3.50 equiv) at 0 °C under Ar. To this mixture was added **21** (422 mg, 1.60 mmol, 1.25 equiv), and the resulting mixture was allowed to stir at rt. At 5 h intervals, additional (4 times) **21** (80 mg, 0.31 mmol, 0.25 equiv) was added to the reaction mixture. After 30 h, the resulting suspension was cooled to 0 °C and quenched with deionized H_2O (100 mL). The mixture was allowed to stir at rt for 30 min, at which time the aqueous layer was extracted with EtOAc (3 × 75.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 15% ethyl acetate in hexanes) afforded **20** as a yellow viscous oil (425 mg, 77% yield): R_f at 15% ethyl acetate in hexanes 0.20; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.7 (s, 1H), 7.30 (dd, 1H, J = 17.1, 10.7 Hz), 6.56 (s, 2H), 5.72 (m, 1H), 5.41 (d, 1H, J = 17.1 Hz), 5.30 (m, 1H), 5.20 (m, 1H), 5.18 (s, 2H), 4.95 (m, 2H), 4.71 (d, 1H, J = 6.9 Hz), 4.61 (d, 1H, J = 6.9 Hz), 3.74 (m, 2H), 3.46 (s, 3H), 3.36 (s, 3H), 3.32 (m, 1H), 2.40 (m, 1H), 2.09 (m, 2H), 1.89 (m, 1H), 1.75 (m, 1H), 1.64 (m, 3H), 1.38 (d, 3H, J = 6.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 164.5, 161.4, 143.8, 138.7, 134.8, 116.7, 115.4, 109.0, 105.2, 102.9, 94.8, 93.9, 74.2, 70.7, 70.3, 70.1, 56.2, 55.4, 37.5, 36.8, 26.3, 24.5, 20.8. IR (CH_2Cl_2) 813, 921, 1024, 1146, 1261, 1323, 1375, 1571, 1612, 1652, 2938, 3397 cm $^{-1}$. $[\alpha]^{20}_D$ = +288 (*c* 0.08, CH_2Cl_2). HRMS (EI) calcd for $C_{24}H_{34}O_8$ (M+) 450.2254, found 450.2265.

7,9,16-Tris-methoxymethoxy-13-methyl-12,19-dioxa-tricyclo-[13.3.1.0^{5,10}]nonadeca 3,5,7,9-tetraen-11-one (33). To a refluxing solution of **20** (310 mg, 0.69 mmol, 1.00 equiv) in CH_2Cl_2 (68.8 mL, 40 °C) under Ar was added a solution of Grubbs' second-generation catalyst (**32**) (59.0 mg, 0.07 mmol, 0.10 equiv) in CH_2Cl_2 (7.00 mL) dropwise over a period of 2 h. The reaction mixture was allowed to stir at 40 °C for 18 h, at which time the reaction was concentrated in vacuo. Flash chromatography (silica, 15% ethyl acetate in hexanes) afforded **33** as a viscous oil (280 mg, 97% yield): R_f at 15% ethyl acetate in hexanes 0.15; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.2 (s, 1H), 6.83 (d, 1H, J = 15.5 Hz), 6.49 (d, 1H, J = 2.5 Hz), 6.41 (d, 1H, J = 2.5 Hz), 5.63 (dd, 1H, J = 10.4, 4.1 Hz), 5.28 (m, 1H), 5.15 (s, 2H), 4.75 (d, 1H, J = 6.9 Hz), 4.61 (d, 1H, J = 6.9 Hz), 3.98 (m, 1H), 3.80 (m, 1H), 3.43 (s, 3H), 3.38 (s, 3H), 3.25 (m, 1H), 2.91 (q, 1H, J = 12.3 Hz), 2.09 (m, 1H), 2.00 (m, 1H), 1.90 (m, 3H), 1.72 (m, 1H), 1.59 (m, 1H), 1.37 (d, 3H, J = 6.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 163.8, 161.3, 143.8, 134.6, 127.9, 108.6, 106.0, 102.2, 95.2, 93.9, 76.0, 71.3, 70.2, 67.7, 56.1, 55.6, 37.7, 33.4, 27.6, 25.9, 19.9. IR (CH_2Cl_2) 736, 851, 950, 1028, 1146, 1213, 1261, 1317, 1453, 1575, 1612, 1649, 2935 cm $^{-1}$. $[\alpha]^{20}_D$ = −44.0 (*c* 0.25, CH_2Cl_2). HRMS (EI) calcd for $C_{22}H_{30}O_8$ (M+) 422.1941, found 422.1945.

7,9,16-Tris-methoxymethoxy-13-methyl-12,19-dioxa-tricyclo-[13.3.1.0^{5,10}]nonadeca-3,5,7,9-tetraen-11-one (19). To a stirred solution of **33** (43.0 mg, 0.11 mmol, 1.00 equiv) in CH_2Cl_2 (1.00 mL) were added TBAI (8.00 mg, 0.02 mmol, 0.20 equiv), DIPEA (0.06 mL, 0.31 mmol, 3.00 equiv), and MOMCl (0.02 mL, 0.21 mmol, 2.00 equiv) at 0 °C under Ar. The reaction mixture was stirred for 24 h at rt, at which time the reaction temperature was lowered to 0 °C and quenched with a saturated aqueous solution of $NaHCO_3$ (5.00 mL) and deionized H_2O (5.00 mL) and then allowed to reach rt. The aqueous layer was extracted with CH_2Cl_2 (3 × 10.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 25% ether in hexanes) afforded **19** as a light yellow oil (45.0 mg, 96% yield): R_f at 25% ethyl acetate in hexanes 0.15; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.69 (d, 1H, J = 2.2 Hz), 6.50 (m, 1H), 5.89 (dd, 1H, J = 10.7, 2.8 Hz), 5.41 (m, 1H), 5.19 (d, 1H, J = 6.6 Hz), 5.13 (s, 3H), 4.69 (d, 1H, J = 6.9 Hz), 4.56 (d, 1H, J = 6.9 Hz), 4.13 (m, 1H), 3.56 (m, 1H), 3.46 (s, 3H), 3.44 (s, 3H), 3.34 (s, 3H), 3.18 (m, 1H), 2.76 (m, 1H), 2.30 (m, 1H), 2.15 (m, 1H), 2.04 (m, 1H), 1.84 (m, 1H), 1.69 (m, 1H), 1.48 (m, 2H), 1.26 (d, 3H, J = 6.3 Hz), 1.25 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 158.3, 155.6, 138.5, 131.1, 130.3, 118.2, 108.6, 102.6, 95.2, 94.8, 94.3, 77.4, 69.1, 66.9, 66.7, 56.2, 56.1, 55.5, 39.2, 34.8, 27.6, 25.2, 20.8. IR (CH_2Cl_2) 925, 977, 1032, 1098, 1150, 1223, 1267, 1447, 1597, 1723, 2935, 3430 cm $^{-1}$. $[\alpha]^{20}_D$ = +120 (*c* 0.40, CH_2Cl_2). HRMS (EI) calcd for $C_{24}H_{34}O_9$ (M+) 466.2203, found 466.2192.

Epoxy-macrocycle (34). To a stirred solution of **19** (260 mg, 0.56 mmol, 1.00 equiv) in a 1:1 biphasic mixture of CH_2Cl_2 (5.60 mL) and a 1 M $NaHCO_3$ aqueous solution (5.60 mL) was added *m*CPBA (77% max., 275 mg, 1.12 mmol, 2.00 equiv) at 0 °C under Ar. The reaction mixture

was stirred for 3 h at rt, at which time the reaction temperature was quenched with saturated aqueous solutions of $NaHCO_3$ (10.0 mL) and $Na_2S_2O_3$ (10.0 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 25.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 35% ethyl acetate in hexanes) afforded **34** as a clear viscous oil (220 mg, 82% yield): R_f at 35% ethyl acetate in hexanes 0.20; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (d, 1H, J = 2.2 Hz), 6.71 (d, 1H, J = 2.2 Hz), 5.17 (m, 5H), 4.73 (d, 1H, J = 6.6 Hz), 4.60 (d, 1H, J = 6.9 Hz), 4.11 (m, 1H), 4.04 (s, 1H), 3.69 (m, 1H), 3.49 (s, 3H), 3.44 (s, 3H), 3.38 (s, 3H), 3.26 (m, 1H), 2.89 (m, 1H), 2.02 (m, 4H), 1.90 (m, 2H), 1.61 (m, 2H), 1.37 (d, 3H, J = 6.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 159.6, 156.9, 138.9, 116.3, 105.9, 103.9, 95.3, 95.2, 94.2, 76.3, 70.4, 69.3, 67.9, 60.6, 57.6, 56.3, 56.2, 55.6, 37.3, 33.6, 27.9, 25.5, 20.0. IR (CH_2Cl_2) 732, 921, 1032, 1150, 1265, 1446, 1605, 1723, 2935, 3527 cm^{-1}. $[\alpha]^{20}_D$ = +278 (c 0.04, CH_2Cl_2). HRMS (EI) calcd for $C_{24}H_{34}O_{10}$ (M+) 482.2152, found 482.2151.

3-Hydroxy-7,9,16-tris-methoxymethoxy-13-methyl-12,19-dioxa-tricyclo[13.3.1.0^{5,10}]nonadeca-5,7,9-trien-11-one (18). To a solution of **34** (65.0 mg, 0.14 mmol, 1.00 equiv) in MeOH (13.5 mL) was added 10% Pd/C (20.0 mg). The reaction vessel was evacuated under vacuum and placed under atmospheric H_2 balloon pressure. The reaction mixture was allowed to stir at rt for 12 h, at which time additional 10% Pd/C (20.0 mg) was added. After 12 h, additional 10% Pd/C (20.0 mg) was added and the suspension was stirred for 12 h. The reaction was then filtered through a plug of Celite and concentrated in vacuo. Flash chromatography (silica, 60% ethyl acetate in hexanes) afforded **18** as a clear viscous oil (45.0 mg, 70% yield): R_f at 60% ethyl acetate in hexanes 0.25; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.71 (d, 1H, J = 2.2 Hz), 6.54 (d, 1H, J = 2.2 Hz), 5.35 (m, 1H), 5.15 (s, 4H), 4.71 (d, 1H, J = 6.9 Hz), 4.61 (d, 1H, J = 6.9 Hz), 4.09 (m, 2H), 3.83 (m, 1H), 3.47 (m, 6H), 3.37 (m, 4H), 3.07 (dd, 1H, J = 13.9, 6.0 Hz), 2.92 (dd, 1H, J = 13.9, 8.5 Hz), 2.25 (broad s, 1H), 2.10 (m, 2H), 1.88 (m, 1H), 1.81 (dd, 1H, J = 8.8, 2.5 Hz), 1.68 (m, 2H), 1.60 (m, 2H), 1.38 (d, 3H, J = 6.3 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8, 158.7, 155.9, 138.6, 118.9, 111.4, 102.1, 94.9, 94.8, 94.4, 75.7, 69.2, 69.0, 68.8, 68.6, 56.2, 56.1, 55.5, 42.5, 37.9, 35.7, 26.9, 25.4, 19.7. IR (CH_2Cl_2) 843, 924, 1035, 1150, 1265, 1438, 1605, 1719, 2938, 3430 cm^{-1}. $[\alpha]^{20}_D$ = +205 (c 0.10, CH_2Cl_2). HRMS (EI) calcd for $C_{24}H_{36}O_{10}$ (M+) 484.2308, found 484.2320.

***ent*-Pochonin J (*ent*-1).** To a stirred solution of **18** (33.0 mg, 0.07 mmol, 1.00 equiv) in CH_2Cl_2 (1.00 mL) was added Dess−Martin periodinane (58.0 mg, 0.14 mmol, 2.00 equiv) at 0 °C. The reaction mixture was allowed to stir at rt for 5 h, at which time the reaction was quenched with saturated aqueous solutions of $NaHCO_3$ (5.00 mL) and $Na_2S_2O_3$ (5.00 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 40% ethyl acetate in hexanes) afforded the ketone macrocycle as a light yellow oil (28.0 mg, 91% yield): R_f at 50% ethyl acetate in hexanes 0.25.

To a stirred solution of the corresponding ketone (30.0 mg, 0.06 mmol, 1.00 equiv) in a 95:5 solvent mixture of CH_3CN/H_2O (1.30 mL) was added $LiBF_4$ (1.0 M solution in CH_3CN, 1.25 mmol, 20.0 equiv). The reaction mixture was then heated to reflux (75 °C) and allowed to stir for 1.5 h. After cooling, the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (10.0 mL). The aqueous layer was extracted with EtOAc (3 × 10.0 mL), and the organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash chromatography (silica, 60% ethyl acetate in hexanes) afforded ***ent*-1** as a white solid (19.0 mg, 86% yield): R_f at 70% ethyl acetate in hexanes 0.25; ^{1}H NMR (500 MHz, CD_3OD) δ 6.26 (d, 1H, J = 2.5 Hz), 6.11 (d, 1H, J = 2.5 Hz), 5.27 (m, 1H), 4.44 (d, 2H, J = 18.9 Hz), 4.35 (m, 1H), 4.27 (d, 2H, J = 18.9 Hz), 3.81 (m, 1H), 3.31 (m, 1H), 3.21 (dd, 1H, J = 13.9, 11.9 Hz), 2.34 (dd, 1H, J = 14.2, 3.80 Hz), 1.97 (m, 3H), 1.83 (m, 1H), 1.76 (m, 1H), 1.68 (m, 1H), 1.34 (d, 3H, J = 6.0 Hz). ^{13}C NMR (125 MHz, CD_3OD) δ 210.1, 173.6, 166.8, 164.6, 140.7, 114.3, 108.5, 103.7, 73.6, 72.9, 71.4, 71.1, 52.3, 46.0, 37.1, 29.8, 29.3, 20.0. IR (CH_2Cl_2) 1026, 1255, 1373, 1453, 1646, 1730, 2832, 2946, 3376 cm^{-1}. $[\alpha]^{20}_D$ = +144 (c 0.08, MeOH). HRMS (EI) calcd for $C_{18}H_{22}O_7$ (M+) 350.1366, found 350.1375.

■ ASSOCIATED CONTENT

Supporting Information. Full characterization (^{1}H and ^{13}C NMR) data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENT

Support for this project was provided by the University of Alabama and the National Science Foundation CAREER program under CHE-0845011.

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