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Study of Cascade Ring-Closing Metathesis Reactions en Route to an Advanced Intermediate of Taxol

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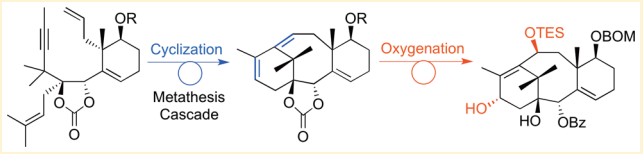
Supporting Information

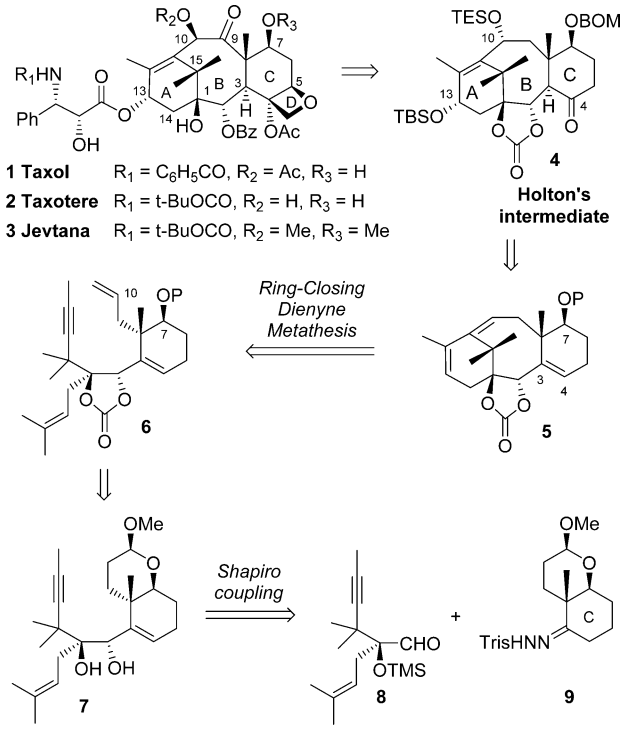
ABSTRACT: A highly functionalized intermediate in the synthesis of Taxol has been synthesized, which features the tricyclic core and the required oxygen substituents at C1, C2, C7, C10, and C13. The key step, a ring-closing dienyne metathesis (RCDEYM) reaction, has been thoroughly optimized to favor the tricyclic product over the undesired bicyclic product resulting from diene metathesis.



INTRODUCTION

Taxol (paclitaxel) **1**, Taxotere (docetaxel) **2**, and Jevtana (cabazitaxel) **3** are widely prescribed to treat a broad range of malignancies[1] (Scheme 1). Although Taxol is produced through plant cell fermentation while Taxotere and Jevtana are produced by semisynthesis from 10-deacetylbaccatin III, taxanes still trigger interest among synthetic organic chemists, as exemplified by the formal syntheses of Taxol recently reported by the groups of Nakada[2] as well as Sato and Chida,[3] and the synthesis of decinnamoyltaxinine E and taxabaccatin III by Baran et al.[4] Among the previous syntheses of Taxol,[5] compound **4** reported by Holton[5b] (Scheme 1) attracted our attention. In addition to being an intermediate en route to Taxol, it could also be rapidly transformed into taxoids with interesting activity; indeed, it has been shown that 9-deoxotaxol exhibits a similar cytotoxicity to Taxol and 10-*epi*-taxol and 10-*epi*-deacetyltaxol are approximately twice more active than the natural product.[6] A rapid synthesis of the tricyclic core of Taxol leading to Holton's intermediate would pave the way to a range of novel Taxol analogues with potential anticancer activity. In this article, we report our efforts toward this goal, with an in-depth study of a cascade metathesis reaction leading to the ABC tricyclic core of taxanes.

Scheme 1. Taxol and Derivatives; Retrosynthesis of the ABC Tricycle of Taxol Featuring a Ring-Closing Dienyne Metathesis (RCDEYM)



RESULTS AND DISCUSSION

Our retrosynthesis of Holton's intermediate **4** is shown in Scheme 1. The 2-ene-1,4-diol function at C10−C13 would be formed by a Ti(III) radical-mediated opening of the corresponding 1,3-*bis*epoxide, which can be synthesized by *bis* epoxidation of compound **5**,[7] and the ketone at C4 would be installed by a hydroboration/oxidation sequence of the C3−C4 olefin of **5**.[5d] Carbonate **5** would be formed by a ring-closing dienyne metathesis (RCDEYM) reaction from dienyne **6**. This cascade metathesis reaction was validated in our previous work on the synthesis of a 7-deoxy ABC tricycle of Taxol[8] as well as Granja et al.'s work on the construction of simplified Taxol analogues.[7b,c] The key step for the assembly of metathesis precursors is a Shapiro coupling reaction between aldehyde **8** and trisylhydrazone **9**. This reaction was shown to be incompatible with the presence of an olefin at C10 in the hydrazone C ring,[8b] so the olefin at C10 and the alcohol at C7 were masked as a methyl ketal in compound **9**.[9]

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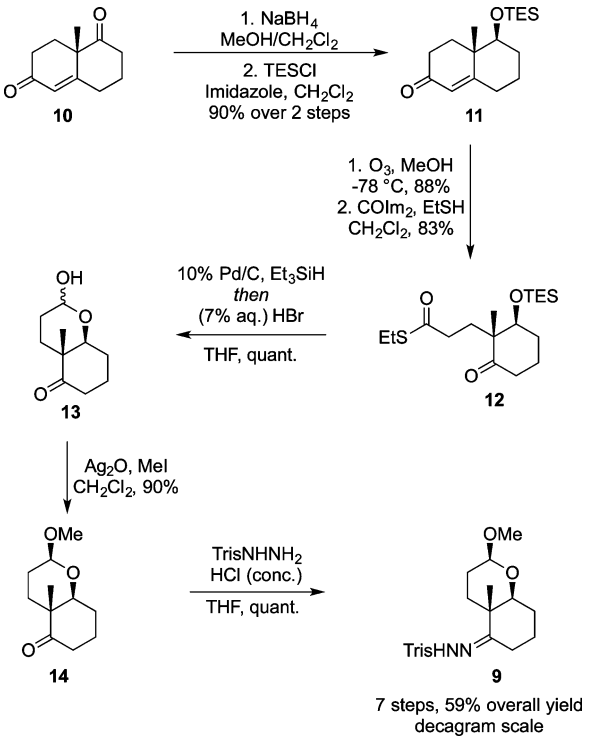
The synthesis of C ring **9** started from Wieland-Miescher ketone **10** (Scheme 2), which can be prepared on large scale

Scheme 2. Synthesis of C Ring 9[a]



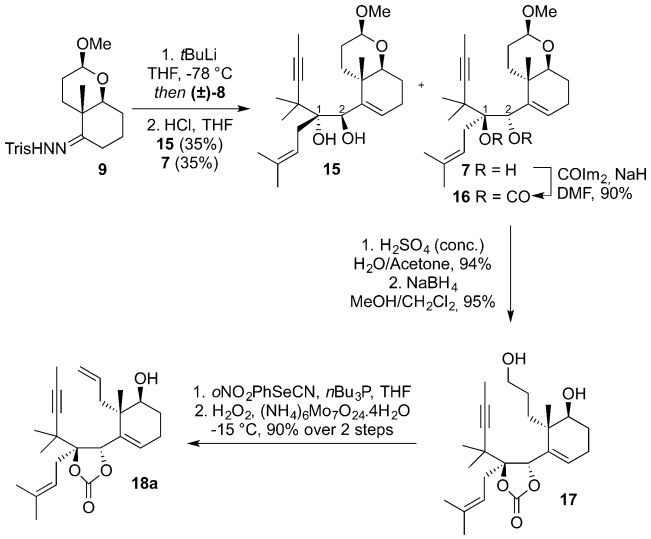
[a]TES = triethylsilyl; Im = imidazolyl; THF = tetrahydrofuran; Tris = triisopropylbenzenesulfonyl.

and excellent enantiomeric purity using the method described by Bonjoch et al.[10] Chemoselective and diastereoselective reduction of this ketone with sodium borohydride at low temperature followed by protection of the resulting alcohol as a triethylsilyl ether furnished compound **11** in excellent yield. Decarbonylative ozonolysis and subsequent formation of the thioester proceeded smoothly to give compound **12** in good yield over 2 steps. Thioester **12** was reduced with triethylsilane/Pd on carbon and the resulting aldehyde was treated with acid to form lactol **13** as a 1:1 mixture of epimers after cleavage of the TES ether. Purdie methylation of compound **13** using silver(I) oxide and methyl iodide afforded methyl ketal **14** as a single diastereomer. Finally, treatment of ketone **14** with trisylhydrazine and catalytic HCl led to the desired hydrazone **9** in 59% overall yield over 7 steps.

The aldehyde coupling partner (±)-**8** had been synthesized previously in 7 steps and 66% overall yield from ethyl isobutyrate and propargyl bromide.[8] Enantioenriched **8** (4:1 er) could also be prepared in 9 steps and 33% overall yield,[11] but the synthesis of the racemate was easier to perform on large scale, so the Shapiro coupling reaction was performed using (±)-**8** (Scheme 3).

This reaction proved to be very diastereoselective, giving only the *trans* 1,2-diols[12] after hydrolysis of the trimethylsilyl ether, as was observed with similar substrates in our previous synthetic routes to taxoids.[8,13] Diastereomer **7** was transformed into carbonate **16**, which was crystalline, and X-ray crystallographic analysis confirmed that it possessed the required configuration for Taxol at C1 and C2 (see Supporting Information for details).[14] The methyl ketal in **16** was then

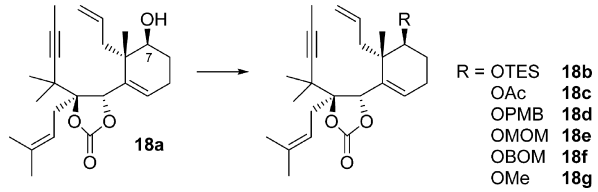
Scheme 3. Synthesis of Unprotected Metathesis Precursor 18a



hydrolyzed with concentrated sulfuric acid and the resulting hemiketal reduced with sodium borohydride to furnish diol **17** in excellent yield. The primary alcohol was selectively eliminated using the Grieco protocol[15] to furnish the unprotected metathesis precursor **18a**.

To study the cascade metathesis reaction in detail, diverse protecting groups were installed on the alcohol at C7 to give compounds **18b–f** (Scheme 4). Compound **18g** with a methyl ether at C7 was also prepared, as it constitutes an intermediate in the synthesis of Jevtana (Scheme 1).

Scheme 4. Synthesis of Diversely Protected Metathesis Precursor 18b–g[a]



[a]DMAP = 4-dimethylaminopyridine; PMB = *p*-methoxybenzyl; MOM = methoxymethyl; BOM = benzyloxymethyl; DMF = *N*,*N*-dimethylformamide.

We next attempted to perform the key metathesis reaction on compound **18a** with a free alcohol at C7 under the conditions that were optimized for the 7-deoxy derivative **18h** (R = H), with the Zhan-1B precatalyst (Table 1).[8] Unfortunately, only the bicyclic compound **20a** resulting from metathesis between the olefins at C10 and C13 was obtained, along with a complex mixture of side products. This poor result could be due to the deactivation of the carbene formed from the olefin at C10 by complexation with the hydroxyl group at C7. When the OH at C7 was protected as a silyl ether or an acetate, only **20b,c** were observed, albeit in good yields. The compounds possessing C7 ether groups (OPMB, OMOM, and OBOM) **18d–f** gave the desired products in about 30% yield, along with varying amounts of compounds **20d–f**. The methyl ether **18g** gave the highest yield (45%) of the desired tricycle **19g**, along with 30% of **20g**,

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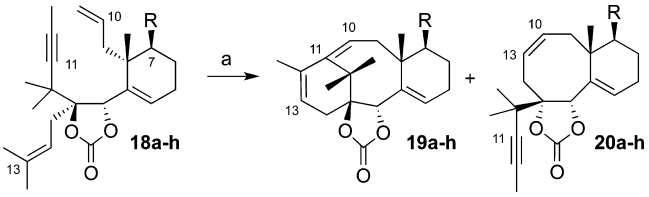
Table 1. Metathesis Reactions of Compounds 18[a]



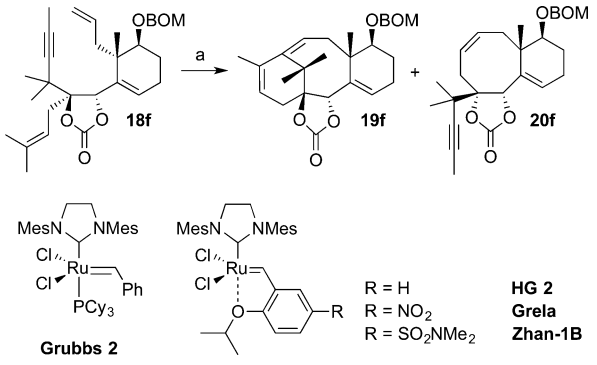
R	substrate	yield of **19a–h** (%)	yield of **20a–h** (%)
OH	**18a**	0	23
OTES	**18b**	0	77
OAc	**18c**	0	80
OPMB	**18d**	29	22
OMOM	**18e**	28	54
OBOM	**18f**	29	46
OMe	**18g**	45	30
H	**18h**	70	20

[a]Reaction conditions: 10 mol% Zhan-1B, toluene, 110 °C, 12 h. See Table 2 for structure of Zhan-1B precatalyst.

but this result was disappointing compared with the 70% yield obtained for the 7-deoxy compound **19h**. It seems that small substituents at C7 (R = H or OMe) favor the formation of the tricyclic compound; in the case of a larger R group, the gauche interaction between this substituent and the allyl group leads to a conformation of the dienyne in which the carbene at C10 is closer to the alkene at C13 than the alkyne at C11.[16]

In order to optimize the yield of the desired tricycle, we revisited the metathesis cascade of **18f** (R = OBOM) with different precatalysts (Table 2). The Grubbs 2 and the Hoveyda-Grubbs 2 (HG2) precatalysts gave poor yields of the tricyclic product **19f**, while the Grela complex led to a slight improvement. Although the overall yield is better with the Grela catalyst, the ratio of **19f**/**20f** is similar; therefore all the subsequent experiments were performed with the more readily available precatalyst Zhan-1B. The influence of the solvent and the temperature was also probed (Table 2); performing the metathesis reaction in 1,2-dichloroethane (DCE) at reflux improved the overall product yield of the reaction but not of the desired tricycle, while the reaction performed in xylene at reflux only produced 33% of the bicycle **20f**.

Table 2. Metathesis Reactions of Compound 18f with Different Precatalysts[a]

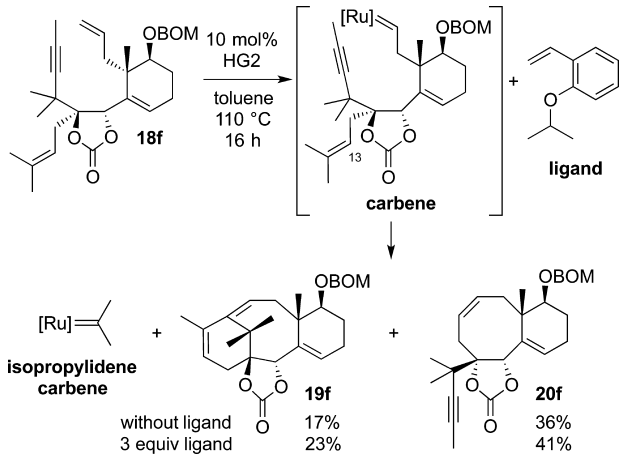


precatalyst	solvent	yield of **19f** (%)	yield of **20f** (%)
Grubbs 2	toluene	12	64
Hoveyda-Grubbs 2	toluene	17	36
Grela	toluene	33	57
Zhan-1B	toluene	29	46
Zhan-1B	1,2-dichloroethane	23	63
Zhan-1B	*p*-xylene	0	33

[a]Reaction conditions: 10 mol% precatalyst, solvent, reflux, 16 h.

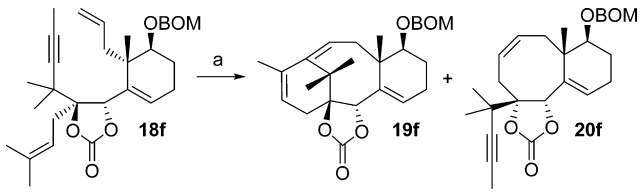
The different results observed between the reactions with the Hoveyda-Grubbs-type precatalysts can only be due to the presence of the styrene derivative released after formation of the first carbene derived from **18f**.[17] To assess the importance of this ligand, metathesis of **18f** was performed with HG2 in the presence of three equivalents of 2-isopropoxystyrene (Scheme 5). This led to a slight improvement in the yields of both **19f** and **20f**. In a parallel experiment, the isopropylidene carbene was preformed by stirring the Zhan-1B complex with 2-methyl-2-butene for 4 h,[18] and when **18f** was treated with this mixture under the standard conditions, only 3% of **19f** and 23% of **20f** were obtained. The exact roles of the ligand and the isobutene released after the second catalytic cycle are not clear, but clearly the presence of the former is beneficial and that of the latter deleterious to the outcome of the metathesis reaction.

Scheme 5. Metathesis Reaction of 18f with Added Ligand



With this observation in mind, the next parameter we changed was the amount of precatalyst used for the reaction. Increasing the amount of Zhan-1B to 100 mol% did improve the yield of **19f**, but at the expense of **20f** (Table 3). It became clear that compound **20f** was not very stable under the

Table 3. Influence of Catalyst Loading and Reaction Time on the Outcome of the Metathesis of 18f[a]



X (mol%)	time	yield of **19f** (%)	yield of **20f** (%)
10	16 h	29	46
50	16 h	27	20
100	16 h	35	traces
50	45 min	12	58
100	45 min	13	57

[a]Reaction conditions: *X* mol% Zhan-1B, toluene, 110 °C, time.

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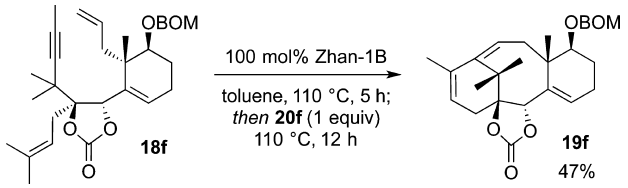
metathesis reaction conditions. This was confirmed by stirring a mixture of **19f** and **20f** with 10 mol% of Zhan-1B in toluene at reflux for 16 h. After that time, the tricycle was recovered almost entirely while more than half of the bicycle had degraded. When the metathesis reaction with 50 or 100 mol% of precatalyst was stopped after 45 min, **19f** and **20f** were obtained in 12−13% and 58−57% yield, respectively (Table 3), implying that bicycle **20f** is the kinetic product of this reaction and that it isomerizes slowly to tricycle **19f** (see Scheme 6 for proof of isomerization). Unfortunately, the decomposition of **20f** is faster than its conversion to **19f**. From a preparative point of view, the best conditions consisted of stirring **18f** with 100 mol% of Zhan-1B in toluene at reflux for 4 h, which reliably gave 35−40% yield of **19f**, along with 50% of recovered precatalyst.[19]

Scheme 6. Metathesis Reaction of 18f with Added 20f

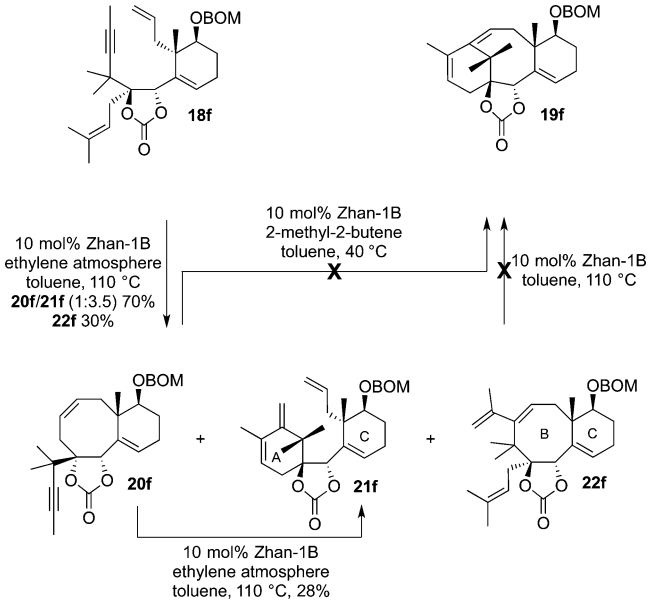


An additional experiment was performed to confirm the isomerization of **20f** into **19f** during the metathesis reaction. After treating **18f** with 100 mol% of Zhan-1B in toluene at reflux for 5 h, at which point there is no bicycle remaining in the reaction mixture, one equivalent of bicycle **20f** was added and the mixture was stirred for an additional 12 h (Scheme 6). Tricycle **19f** was isolated in 47% yield, indicating that around 10% of **20f** isomerized to **19f** and the rest of the bicycle decomposed.

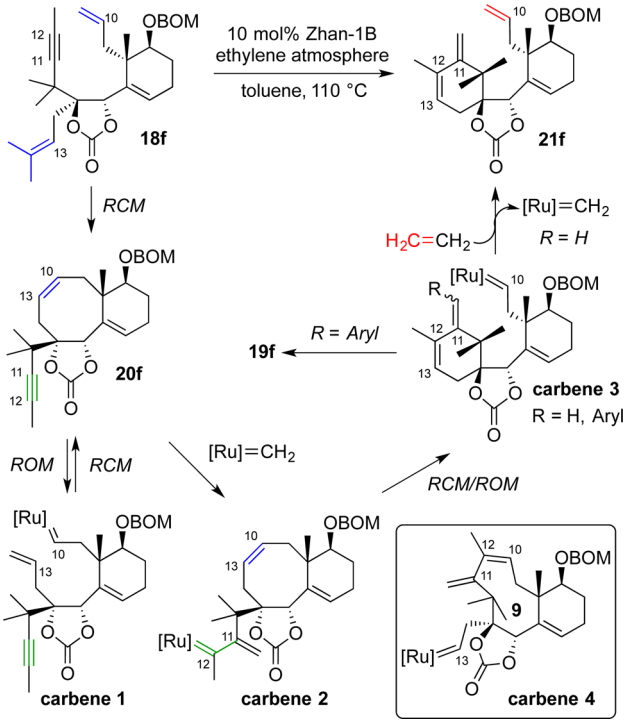
The beneficial influence of ethylene on ring-closing enyne metathesis (RCEYM) is well-known because it helps release the catalyst at the end of the cycle.[20] Although the presence of ethylene might not be necessarily helpful in a cascade process where the RCEYM is followed by a diene metathesis that achieves this release, it could help us identify intermediates in the metathesis cascade. Thus, compound **18f** was treated with 10 mol% of Zhan-1B in toluene at reflux under an ethylene atmosphere. A 1:3.5 inseparable mixture of **20f** and **21f**, which encompasses the AC ring system of Taxol, was obtained in 70% yield, along with 30% yield of **22f**, containing the BC bicycle of Taxol (Scheme 7). When **20f** was resubmitted to the metathesis reaction with ethylene,[21] it was converted into **21f** in 28% yield, with no trace of **22f** or the desired tricycle **19f**.

Bicycle **22f** is the product of simple RCEYM of **18f**, which is favored under ethylene atmosphere. A possible mechanism for the formation of compound **21f** is presented in Scheme 8. We believe that formation of **20f** occurs first by diene RCM, because the alkyne is hindered. Ring-opening metathesis (ROM) could produce carbene **1**, but since the olefin at C13 is unhindered, diene RCM would occur to form again **20f**.[8] Reaction of the methylidene carbene with **20f** leads to carbene **2**, which undergoes RCM/ROM to furnish carbene **3** (R = H) rather than carbene **4**, featuring a nine-membered ring. Carbene **3** then reacts with ethylene to furnish **21f** and releases the catalyst. When bicycle **20f** was submitted to Zhan-1b catalyst in the presence of 2-methyl-2-butene to regenerate the carbene shown in Scheme 5, no reaction occurred (see Scheme 7), suggesting that the isomerization of **20f** into **19f** does not start with ROM of **20f**. This isomerization could also be explained by the mechanism shown in Scheme 8, where carbene **3** (R = aryl coming from the precatalyst) would undergo RCM to furnish tricycle **19f**. This RCM is very challenging, which explains the poor conversion of **20f** to **19f** (around 10% with 100 mol% of precatalyst) vs decomposition (see Scheme 6).

Scheme 7. Metathesis of 18f under Ethylene Atmosphere and Conversion Experiments



Scheme 8. Possible Mechanism for the Formation of 21f and Isomerization of 20f into 19f



We next turned to the functionalization of tricycle **19f**. Epoxidation with one equivalent of *m*CPBA selectively oxidized the more reactive bridgehead olefin of **19f** to give **23** in excellent yield (Scheme 9), so we decided to pursue this route before exploring the *bis* epoxidation pathway. Expecting that

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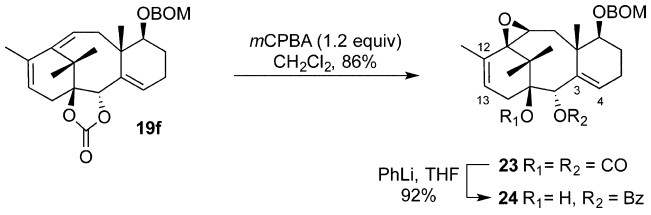
Scheme 9. Functionalization of 19f[a]

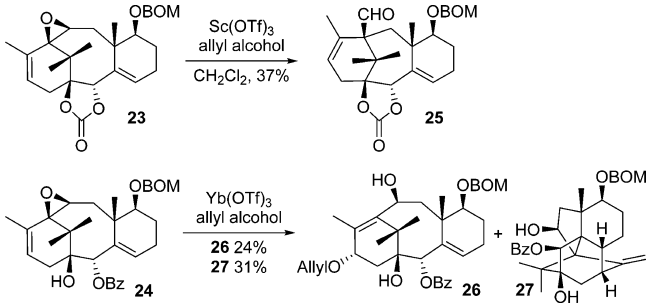


[a]*m*CPBA = *meta*-chloroperbenzoic acid.

the fused trisubstituted alkene at C3−C4 would be more reactive than the other trisubstituted alkene at C12−C13, we next submitted compound **23** to a range of standard hydroboration conditions (BH_3·THF or BH_3·Me_2S), but to our surprise no reaction occurred at ambient temperature and only decomposition was observed under forcing conditions (ten equivalents of reagent, reflux in THF). Compound **23** was then transformed into the corresponding benzoate **24** by addition of phenyllithium,[5b] but attempted hydroboration of **24** was equally unsuccessful.

Next, carbonate **23** was treated with allyl alcohol in the presence of diverse acids to open the epoxide in a vinylogous manner. No reaction occurred with $Yb(OTf)_3$ and in the presence of stronger Lewis acid $Sc(OTf)_3$ or Brønsted acids, such as camphorsulfonic acid, skeletal rearrangement took place to give aldehyde **25** (Scheme 10). Epoxide **24** proved to be

Scheme 10. Further Functionalization of 19f

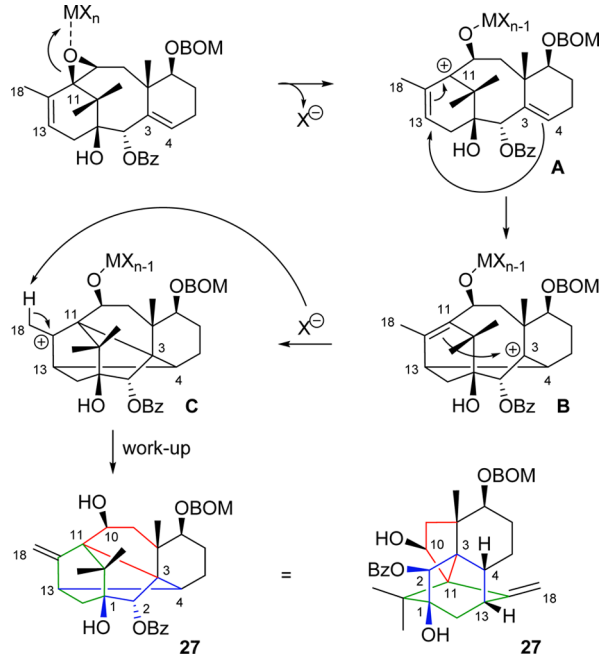


more reactive and gave the desired allylic alcohol **26** under $Yb(OTf)_3$ catalysis. However, this product was accompanied by the rearranged polycyclic compound **27**. The structure of **27** was determined by NMR studies (see the Supporting Information for details).

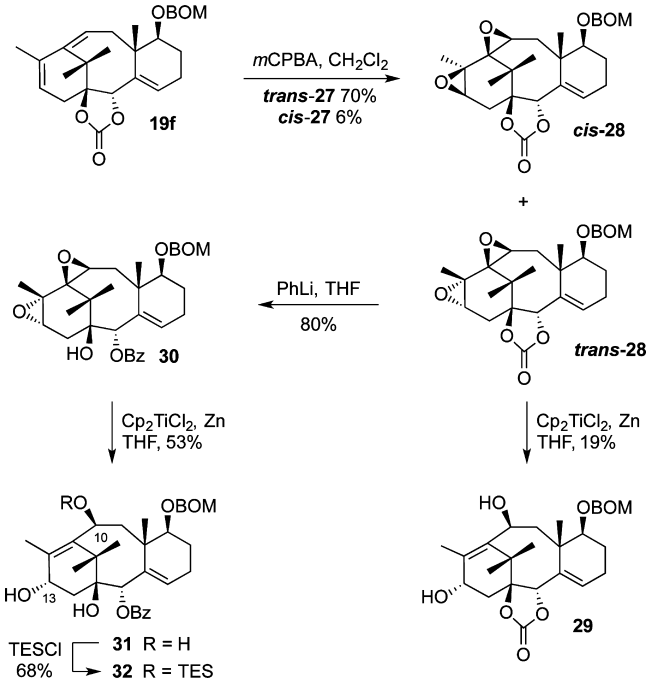
Formation of polycycle **27** can be explained by a cationic cyclization cascade reaction, as illustrated in Scheme 11. Opening of the activated epoxide forms carbocation **A**, where the C4 and C13 position are very close due to the convex shape of this tricycle. Cyclization of **A** between these two positions furnishes intermediate **B** encompassing an additional six-membered ring. Further cyclization between C3 and C11 leads to five-membered ring cation **C**. Finally, loss of proton and aqueous workup gives **27**.

Even mild acidic conditions such as the 3-chlorobenzoic acid contained in *m*CPBA promoted the rearrangement of epoxide **24** into polycycle **27**. Fortunately, treatment of compound **19f** with excess *m*CPBA furnished diepoxide *trans*-**28** in 70% yield, along with 6% of the minor diastereomer *cis*-**28** (Scheme 12).[22] Radical opening of this diepoxide using the conditions developed by Granja et al.[7a] on taxoids led to diol **29** in only 19% yield in refluxing THF;[23] however, the same reaction

Scheme 11. Possible Mechanism for the Formation of Compound 27



Scheme 12. Final Functionalization of 19f



performed on the corresponding benzoate **30** at ambient temperature gave diol **31** in 53% yield. The alcohols at C10 and C13 were easily differentiated by selective silyl ether formation at C10, but hydroboration of the C3−C4 olefin was once again unsuccessful. Under forcing conditions, only the C11−C12 alkene seems to react.

CONCLUSIONS

In summary, we have synthesized an advanced intermediate in the synthesis of Taxol with the required oxygen substituents at C1, C2, C7, C10, and C13. The key ring-closing dienyne

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metathesis (RCDEYM) step has been studied in detail, but the presence of a substituent at C7 seems to favor the diene metathesis reaction giving the undesired bicycle **20f** rather than the enyne metathesis leading to the tricyclic core of Taxol **19f**. Oxygenation of this compound was difficult because of the unpredictable reactivity of the strained tricycle, but we were able to install the 2-ene-1,4-diol function at C10−C13 with the required configurations for Taxol. The poor reactivity of the C3−C4 olefin suggests that it will be necessary to install the substituent at C4 before the formation of the tricycle by cascade metathesis, and we are currently working on this new approach.

EXPERIMENTAL SECTION

General Remarks. Reactions involving air-sensitive agents and dry solvents were performed in glassware that had been dried in an oven (150 °C) or flame-dried prior to use. These reactions were carried out with the exclusion of air using an argon atmosphere. Melting points were determined using a hot stage apparatus and are uncorrected. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 400 MHz/500 MHz and ^{13}C NMR at 100 MHz/126 MHz. Chemical shifts are reported in ppm. ^{1}H NMR spectra were recorded with $CDCl_3$ as the solvent using residual $CHCl_3$ (δ= 7.27) as internal standard, and for ^{13}C NMR spectra the chemical shifts are reported relative to the central resonance of $CDCl_3$ (δ = 77.0). Signals in NMR spectra are described as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), septet (spt), multiplet (m), broad (br), or combination of these, which refers to the spin−spin coupling pattern observed. Spin−spin coupling constants reported are uncorrected. Two dimensional (COSY, HSQC, HMBC, NOESY) NMR spectroscopy was used where appropriate to assist the assignment of signals in the ^{1}H and ^{13}C NMR spectra. For the description of NMR spectra, the numbering used follows the chain extension or Taxol numbering, not the IUPAC numbering rules. IR spectra were obtained employing a type IIa diamond as a single reflection element so that the IR spectrum of the compound (solid or liquid) could be detected directly (thin layer). High-resolution mass spectra were recorded under (ESI) (TOF-Q), (EI) (Quadrupole), and (CI) (Quadrupole) mass spectrometers. Flash column chromatography was performed using forced flow of the indicated solvent system on Silica Gel 60 as solid support and HPLC graded solvents as eluant. Reactions were monitored by thin layer chromatography (TLC) using silica gel 60 F254 precoated plates. TLC plates were developed under UV-light and/or with an acidic ethanolic anisaldehyde solution or a $KMnO_4$ solution. All reagents were purchased from commercial suppliers and used without further purification unless otherwise stated.

(4*S*,5*S*)-5-Hydroxy-methyl-4,4,5,6,7,8-hexahydronaphthalen-2(3H)-one. To a solution of ketone **10** (43.3 g, 243 mmol) in (1:1) MeOH/CH_2Cl_2 (700 mL) at −78 °C was added $NaBH_4$ (9.2 g, 243 mmol, 1.0 equiv). The reaction mixture was stirred for 15 min. Acetone (200 mL) and H_2O (200 mL) were added. The aqueous layer was extracted with CH_2Cl_2 (200 mL), and the combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/EtOAc: 6/4) to afford the title secondary alcohol (43.8 g, 243 mmol, 100%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 5.79 (d, J = 1.9 Hz, 1H), 3.44 (dd, J = 11.6, 3.6 Hz, 1H), 2.49−2.30 (m, 3H), 2.25−2.15 (m, 2H), 1.93−1.81 (m, 4H), 1.77−1.66 (m, 1H), 1.48−1.36 (m, 1H), 1.21 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 199.5, 168.4, 125.5, 78.3, 41.6, 34.2, 33.7, 32.0, 30.3, 23.1, 15.2. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C11H16O2Na 203.1043, found 203.1043. $[\alpha]^{25}_D$: + 185 (c 1.5, benzene).

(4*S*,5*S*)-4-Methyl-5-((triethylsilyl)oxy)-4,4,5,6,7,8-hexahydronaphthalen-2(3H)-one (11). To a solution of secondary alcohol (43.8 g, 243 mmol) in CH_2Cl_2 (150 mL) were added imidazole (41.3 g, 607 mmol, 2.5 equiv) and TESCl (61 mL, 364 mmol, 1.5 equiv). The reaction mixture was stirred for 16 h. A saturated aqueous solution of $NaHCO_3$ (100 mL) was added to quench the reaction. The aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL), and the combined organic extracts were washed with brine (300 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 9/1 to 7/3) to afford the title protected alcohol **11** (64.4 g, 219 mmol, 90%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 5.78 (d, J = 1.7 Hz, 1H), 3.40 (dd, J = 10.9, 4.9 Hz, 1H), 2.51−2.27 (m, 3H), 2.19 (ddt, J = 14.7, 4.1, 1.9 Hz, 1H), 2.13 (ddd, J = 13.6, 5.2, 3.8 Hz, 1H), 1.89−1.81 (m, 1H), 1.79−1.65 (m, 3H), 1.43−1.30 (m, 1H), 1.18 (s, 3H), 0.97 (t, J = 7.9 Hz, 9H), 0.61 (q, J = 7.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 199.8, 168.9, 125.3, 78.9, 42.2, 34.6, 33.9, 32.1, 30.8, 23.0, 15.5, 6.9, 5.2. IR (ν, cm^{-1}): 3019, 2960, 1670, 1625, 1460, 1255, 1100, 1056. HRMS (CI/ISO) m/z: $[M+H]^+$ Calcd for C17H31O2Si 295.2093, found 295.2092. $[\alpha]^{25}_D$: + 105 (c 1.0, $CHCl_3$). Spect. Reference: Ma, C.; Schiltz, S.; Prunet, J. *Collect. Czech. Chem. Commun.* **2011**, *76*, 1579−1594.

3-((1*R*,6*S*)-1-Methyl-2-oxo-6-((triethylsilyl)oxy)cyclohexyl)-propanoic acid. To a solution of **11** (5.0 g, 17 mmol) in MeOH (180 mL) at −78 °C was passed a stream of O_3 for 50 min. The reaction mixture was concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O/AcOH: 75/25/0.1) to afford the title acid (4.7 g, 15 mmol, 88%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: ^{1}H NMR (500 MHz, $CDCL_3$) δ 10.75 (br s, 1H), 3.82 (dd, J = 6.5, 2.2 Hz, 1H), 2.41−2.32 (m, 3H), 2.23 (ddd, J = 16.4, 11.3, 5.1 Hz, 1H), 2.09−1.96 (m, 3H), 1.88−1.74 (m, 2H), 1.71−1.60 (m, 1H), 1.09 (s, 3H), 0.95 (t, J = 8.0 Hz, 9H), 0.59 (q, J = 8.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 214.0, 178.6, 76.5, 54.3, 37.7, 30.1, 29.0, 29.0, 20.4, 17.6, 6.9, 5.0. IR (ν, cm^{-1}): 3250, 2980, 1740, 1715, 1250, 1058. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C16H30O4SiNa 337.1806, found 337.1794. $[\alpha]^{25}_D$: −10.5 (c 1.0, $CHCl_3$).

(S)-Ethyl 3-((1*R*,6*S*)-1-Methyl-2-oxo-6-((triethylsilyl)oxy)-cyclohexyl)propanethioate (12). To a solution of acid (26.1 g, 83.0 mmol) in CH_2Cl_2 (200 mL) was added carbonyl diimidazole (17.5 g, 107 mmol, 1.3 equiv) and the reaction mixture was stirred for 30 min. Then EtSH (12.0 mL, 166 mmol, 2.0 equiv) was added. The reaction mixture was stirred for 16 h. The volatiles were removed *in vacuo* and H_2O (150 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL), and the combined organic extracts were washed with brine (500 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 95/5) to afford the title thioester **12** (24.6 g, 68.6 mmol, 83%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 3.83 (dd, J = 6.1, 1.8 Hz, 1H), 2.87 (q, J = 7.4 Hz, 2H), 2.55 (ddd, J = 15.4, 11.4, 5.3 Hz, 1H), 2.42−2.32 (m, 3H), 2.10−1.98 (m, 3H), 1.88−1.80 (m, 1H), 1.79−1.72 (m, 1H), 1.72−1.64 (m, 1H), 1.25 (t, J = 7.4 Hz, 3H), 1.07 (s, 3H), 0.95 (t, J = 7.9 Hz, 9H), 0.59 (q, J = 7.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 213.7, 199.2, 76.8, 54.3, 39.1, 37.8, 31.1, 29.0, 23.3, 20.4, 17.6, 14.7, 6.9, 5.0. IR (ν, cm^{-1}): 3057, 2964, 2912, 2879, 1704, 1692, 1458, 1419, 1272, 1118, 1079, 1018, 1000. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C18H34O3NaSSi 381.1890, found 381.1878. $[\alpha]^{25}_D$: −21.1 (c 1.0, $CHCl_3$).

(4*R*,8*S*)-2-Hydroxy-4-methyloctahydro-5H-chromen-5-one (13). To a solution of thioester **12** (24.6 g, 68.6 mmol) in CH_2Cl_2 (150 mL) were added triethylsilane (21.8 mL, 137 mmol, 2.0 equiv) and 10% Pd/C (7.5 g) portionwise. The reaction mixture was stirred for 30 min. Then the reaction mixture was filtered through a short pad of Celite and the solvent was concentrated *in vacuo*. The crude mixture was dissolved in THF (150 mL) and at 0 °C was slowly added an aqueous solution of 7% HBr (150 mL). The resulting mixture was stirred at this temperature for 1 h. A saturated aqueous solution of $NaHCO_3$ (500 mL) was slowly added to quench the reaction, the aqueous layer was extracted with EtOAc (3 × 500 mL), the combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/EtOAc: 7/3 to 0/1) to afford the title hemiacetal **13** as a 1:1 mixture of diastereomers (12.6 g, 68.6 mmol, 100%) as a colorless solid. ^{1}H NMR (500 MHz, $CDCL_3$) δ

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ppm: 5.26 (t, J = 3.2 Hz, 0.5H), 4.74 (ddd, J = 9.5, 6.5, 2.7 Hz, 0.5H), 4.03 (dd, J = 11.9, 4.1 Hz, 0.5H), 3.38 (dd, J = 11.5, 4.2 Hz, 0.5H), 2.97 (br. s, 0.5H), 2.67 (td, J = 14.4, 7.1 Hz, 1H), 2.40 (br s, 0.5H), 2.26−2.16 (m, 1H), 2.06−1.68 (m, 6H), 1.66−1.50 (m, 2H), 1.27 (s, 1.5H), 1.23 (s, 1.5H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 213.6, 97.0, 91.5, 79.5, 71.7, 48.6, 48.4, 36.5, 29.3, 29.0, 26.0, 25.9, 24.7, 20.8, 16.3, 15.3. IR (ν, cm^{-1}): 3425, 2947, 2877, 1705, 1450, 1373, 1049, 964, 902. HRMS (EI) m/z: [M]$^+$ Calcd for C10H16O3 184.1099, found 184.1102. Spect. Reference: Ma, C.; Schiltz, S.; Prunet, J. *Collect. Czech. Chem. Commun.* **2011**, *76*, 1579−1594.

(2*S*,4*R*,8*S*)-2-Methoxy-4-methyloctahydro-5H-chromen-5-one (14). To a solution of hemiacetal **13** (12.6 g, 68.6 mmol) in CH_2Cl_2 (100 mL) were added Ag_2O (17.5 g, 75.5 mmol, 1.1 equiv) and MeI (12.8 mL, 206 mmol, 3.0 equiv). The reaction mixture was stirred for 16 h. Then the reaction mixture was filtered and the solvent was concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 8/2) to afford the title acetal **14** (12.2 g, 61.7 mmol, 90%) as a white foam. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 4.29 (dd, J = 9.7, 2.3 Hz, 1H), 3.50 (s, 3H), 3.32 (dd, J = 11.6, 4.1 Hz, 1H), 2.66 (td, J = 14.4, 7.0 Hz, 1H), 2.23−2.13 (m, 1H), 2.04−1.96 (m, 1H), 1.96−1.88 (m, 1H), 1.88−1.82 (m, 1H), 1.81−1.69 (m, 3H), 1.67−1.58 (m, 1H), 1.58−1.48 (m, 1H), 1.24 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 213.7, 104.0, 79.3, 56.5, 48.7, 36.5, 29.3, 27.3, 26.0, 20.9, 16.3. IR (ν, cm^{-1}): 2854, 2747, 2641, 1736, 1431, 1337, 1264, 1247, 1080, 984, 953. HRMS (CI/ISO) m/z: [M + H]$^+$ Calcd for C11H19O3 199.1334, found 199.1331. $[\alpha]^{25}_D$: +100 (c 1.5, $CHCl_3$). Spect. Reference: Ma, C.; Schiltz, S.; Prunet, J. *Collect. Czech. Chem. Commun.* **2011**, *76*, 1579−1594.

2,4,6-Triisopropyl-*N*′-((2*S*,4*S*,8*S*)-2-methoxy-4-methyloctahydro-5H-chromen-5-ylidene)benzenesulfonohydrazide (9). To a solution of acetal **14** (14.5 g, 73.2 mmol) in THF (100 mL) were added TrisNHNH$_2$ (23.8 g, 80.5 mmol, 1.1 equiv) and concentrated HCl (4 drops). The reaction mixture was stirred for 3 h. A saturated aqueous solution of $NaHCO_3$ (150 mL) was added to the reaction, the aqueous layer was extracted with Et_2O (3 × 150 mL), and the combined organic extracts were washed with brine (250 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 8/2) to afford the title hydrazone **9** (35.0 g, 73.2 mmol, 100%) as a white foam. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 7.30 (s, 1H), 7.16 (s, 2H), 4.22 (dd, J = 8.6, 3.2 Hz, 1H), 4.16 (spt, J = 6.8 Hz, 2H), 3.47 (s, 3H), 3.13 (dd, J = 9.9, 5.9 Hz, 1H), 2.92 (spt, J = 6.9 Hz, 1H), 2.51−2.45 (m, 1H), 2.00 (dd, J = 13.7, 6.3 Hz, 1H), 1.96−1.88 (m, 1H), 1.75−1.68 (m, 2H), 1.63−1.53 (m, 4H), 1.40−1.30 (m, 1H), 1.27 (d, J = 6.8 Hz, 6H), 1.26 (d, J = 6.9 Hz, 6H), 1.25 (d, J = 6.8 Hz, 6H), 1.03 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 161.8, 153.2, 151.1, 131.2, 123.5, 104.0, 79.4, 56.4, 42.1, 34.2, 31.3, 29.9, 27.5, 26.1, 24.8, 24.7, 23.6, 23.5, 21.5, 21.5, 17.3. IR (ν, cm^{-1}): 3240, 2954, 2872, 2836, 2752, 2635, 1712, 1629, 1596, 1550, 1453, 1384, 1326, 1252, 1203, 1160, 1067, 912. HRMS (ESI/TOF-Q) m/z: [M+Na]$^+$ Calcd for C26H42N2O4SNa 478.2865, found 478.2867. $[\alpha]^{29}_D$: +36.0 (c 1.0, $CHCl_3$).

((2*S*,4*S*,8*S*)-2-Methoxy-4-methyl-3,4,4,7,8,8-hexahydro-2H-chromen-5-yl)-5-methyl-2-(2-methylpent-3-yn-2-yl)hex-4-ene-1,2-diol (15) and (7). To a solution of hydrazone **9** (24 g, 50 mmol, 1.2 equiv) in THF (60 mL) at −78 °C was added dropwise *t*BuLi (68 mL, 1.47 M in hexane, 100 mmol, 2.4 equiv). The solution turned dark red. The solution was stirred at this temperature for 30 min and warmed for a few min to room temperature and intense nitrogen bubbling occurred. The mixture was then cooled down to −78 °C and a solution of aldehyde (±)-**8** (12 g, 42 mmol) in THF (30 mL) was added. The resulting mixture was stirred at −78 °C for 5 h and became yellow. The reaction was quenched with saturated aqueous $NaHCO_3$ (100 mL). The aqueous layer was extracted with Et_2O (3 × 150 mL), and the combined organic extracts were washed with brine (500 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was dissolved in THF (150 mL) and a 1N aqueous solution of HCl (63 mL, 63 mmol, 1.5 equiv) was then added. The resulting mixture was stirred at room temperature for 12 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (100 mL). The aqueous layer was extracted with EtOAc (3 × 200 mL), and the combined organic extracts were washed with brine (250 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (CH_2Cl_2/EtOAc: 97/3 to 9/1) to afford the title diol **15** (5.7 g, 15 mmol, 35%) and the title compound **7** (5.7 g, 15 mmol, 35%) as colorless highly viscous oils.

(1*R*,2*R*)-1-((2*S*,4*S*,8*S*)-2-Methoxy-4-methyl-3,4,4,7,8,8-hexahydro-2H-chromen-5-yl)-5-methyl-2-(2-methylpent-3-yn-2-yl)-hex-4-ene-1,2-diol (15). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 6.10 (t, J = 3.7 Hz, 1H), 5.37−5.29 (m, 1H), 4.41 (d, J = 4.8 Hz, 1H), 4.39−4.30 (m, 1H), 3.53 (s, 3H), 3.34 (dd, J = 10.7, 5.2 Hz, 1H), 3.11−3.04 (m, 2H), 2.36 (d, J = 6.8 Hz, 2H), 2.26−2.16 (m, 2H), 2.00−1.91 (m, 1H), 1.81 (s, 3H), 1.78−1.69 (m, 5H), 1.7 (d, J = 1.0 Hz, 3H), 1.58 (s, 3H), 1.30 (s, 3H), 1.28 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 143.7, 131.7, 126.4, 120.7, 104.0, 86.4, 79.2, 79.0, 78.1, 70.7, 56.3, 41.7, 37.0, 33.0, 32.7, 27.9, 26.2, 26.0, 26.0, 24.8, 23.4, 18.9, 17.9, 3.6. IR (ν, cm^{-1}): 3053, 2984, 2956, 2305, 1421, 1265, 1165, 1072. HRMS (EI) m/z: [M]$^+$ Calcd for C24H38O4 390.2770, found 390.2766. $[\alpha]^{26}_D$: −27.6 (c 1.0, $CHCl_3$).

(1*S*,2*S*)-1-((2*S*,4*S*,8*S*)-2-Methoxy-4-methyl-3,4,4,7,8,8-hexahydro-2H-chromen-5-yl)-5-methyl-2-(2-methylpent-3-yn-2-yl)-hex-4-ene-1,2-diol (7). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 5.99 (t, J = 3.8 Hz, 1H), 5.40−5.30 (m, 1H), 4.43 (d, J = 4.6 Hz, 1H), 4.35 (dd, J = 8.7, 3.8 Hz, 1H), 3.52 (s, 3H), 3.34 (dd, J = 12.1, 4.0 Hz, 1H), 3.20 (s, 1H), 2.90 (d, J = 4.6 Hz, 1H), 2.31 (dd, J = 15.6, 7.0 Hz, 1 H) 2.42 (dd, J = 15.6, 6.8 Hz, 1 H), 2.26−2.18 (m, 2H), 1.89 (dt, J = 12.6, 3.6 Hz, 1H), 1.81−1.68 (m, 4H), 1.79 (s, 3H), 1.71 (d, J = 1.1 Hz, 3H), 1.59 (s, 3H), 1.47 (td, J = 12.5, 5.7 Hz, 1H), 1.29 (s, 3H), 1.27 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 146.2, 131.5, 126.2, 121.2, 103.8, 86.6, 78.7, 78.3, 78.2, 69.5, 56.3, 41.8, 37.5, 33.4, 32.5, 28.1, 26.3, 26.2, 26.1, 24.6, 23.5, 19.9, 18.1, 3.6. IR (ν, cm^{-1}): 3245, 3054, 2984, 2305, 1868, 1717, 1669, 1557, 1421, 1265, 1065. HRMS (ESI/TOF-Q) m/z: [M+Na]$^+$ Calcd for C24H38O4Na 413.2662, found 413.2655. $[\alpha]^{25}_D$: −44.0 (c 1.0, $CHCl_3$).

(4*S*,5*S*)-5-((2*S*,4*S*,8*S*)-2-Methoxy-4-methyl-3,4,4,7,8,8-hexahydro-2H-chromen-5-yl)-4-(3-methylbut-2-en-1-yl)-4-(2-methylpent-3-yn-2-yl)-1,3-dioxolan-2-one (16). To a solution of diol 7 (6.5 g, 17 mmol) in DMF (250 mL) was added sodium hydride (2 g, 60% in mineral oil, 50 mmol, 3 equiv) and carbonyl diimidazole (11 g, 67 mmol, 4 equiv). The mixture was stirred at room temperature for 30 min. The reaction was quenched with saturated aqueous NH_4Cl (150 mL). The aqueous layer was extracted with Et_2O (3 × 150 mL), and the combined organic extracts were washed with brine (2 × 350 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 8/2) to afford the title carbonate **16** (6.2 g, 15 mmol, 90%) as a colorless crystalline solid. m.p.: 120 °C. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 5.64 (dd, J = 4.8, 2.9 Hz, 1H), 5.36−5.29 (m, 1H), 5.15 (s, 1H), 4.37 (dd, J = 9.6, 2.8 Hz, 1H), 3.53 (s, 3H), 3.37 (dd, J = 10.7, 5.6 Hz, 1H), 2.75−2.62 (m, 2H), 2.40−2.21 (m, 2H), 2.02 (ddd, J = 12.8, 4.4, 2.8 Hz, 1H), 1.85−1.66 (m, 4H), 1.76 (s, 3H), 1.72 (d, J = 1.2 Hz, 3H), 1.62 (s, 3H), 1.45 (td, J = 13.2, 4.4 Hz, 1H), 1.31 (m, 6H), 1.22 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 155.0, 140.2, 132.8, 129.5, 118.8, 103.7, 90.0, 83.1, 79.7, 79.1, 77.9, 56.3, 41.2, 37.3, 32.4, 31.4, 28.0, 26.0, 25.0, 24.8, 24.5, 23.1, 19.5, 18.2, 3.5. IR (ν, cm^{-1}): 3055, 2954, 2857, 2239, 1793, 1450, 1373, 1327, 1265, 1180, 1118, 1056. HRMS (ESI/TOF-Q) m/z: [M+Na]$^+$ Calcd for C25H36O5Na 439.2455, found 439.2455. $[\alpha]^{26}_D$: −27.0 (c 1.0, $CHCl_3$).

(4*S*,5*S*)-5-((4*S*,8*S*)-2-Hydroxy-4-methyl-3,4,4,7,8,8-hexahydro-2H-chromen-5-yl)-4-(3-methylbut-2-en-1-yl)-4-(2-methylpent-3-yn-2-yl)-1,3-dioxolan-2-one. To a solution of carbonate **16** (6.2 g, 15 mmol) in acetone (200 mL) was added H_2O (100 mL) followed by slow addition of H_2SO_4 conc. (26 mL, 0.52 mol, 35 equiv). The reaction mixture was stirred at room temperature for 16 h. The reaction was quenched with saturated aqueous $NaHCO_3$ (250 mL). The aqueous layer was extracted with EtOAc (3 × 250 mL), and the combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then

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purified by flash chromatography (petroleum ether/EtOAc: 7/3) to afford the title hemiacetal as a 1:1 mixture of diastereomers (5.7 g, 14 mmol, 94%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 5.67−5.60 (m, 1H), 5.34−5.26 (m, 1.5H), 5.14 (s, 1H), 4.80 (ddd, J = 9.4, 6.3, 2.8 Hz, 0.5H), 4.09 (dd, J = 12.5, 3.9 Hz, 0.5H), 3.42 (dd, J = 11.3, 4.8 Hz, 1H), 2.76−2.60 (m, 2.5H), 2.37−2.19 (m, 2H), 2.06−1.93 (m, 1H), 1.80−1.63 (m, 4.5H), 1.76 (s, 1.5H), 1.75 (s, 1.5H), 1.71−1.69 (m, 3H) 1.61 (s, 1.5H), 1.60 (s, 1.5H), 1.46 (td, J = 13.3, 4.7 Hz, 0.5H), 1.30 (m, 6H), 1.22 (s, 1.5H), 1.19 (s, 1.5H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 155.1, 154.9, 140.4, 140.1, 133.0, 132.9, 129.5, 129.3, 118.7, 118.6, 96.8, 91.4, 90.2, 90.1, 83.1, 83.0, 79.7, 79.6, 79.1, 78.9, 78.2, 70.2, 41.2, 41.1, 37.3, 37.0, 32.3, 31.4, 31.3, 29.8, 27.8, 26.4, 26.0, 25.9, 25.0, 25.0, 24.8, 24.8, 24.5, 24.4, 23.2, 23.0, 19.4, 18.4, 18.2, 18.2, 3.5, 3.5. IR (ν, cm^{-1}): 3393, 3055, 2985, 2848, 2305, 1791, 1650, 1551, 1481, 1335, 1272, 1187, 1033. HRMS (CI/ISO) m/z: $[M+H]^+$ Calcd for C24H35O5 403.2484, found 403.2482.

(4*S*,5*S*)-5-((5*S*,6*S*)-5-Hydroxy-6-(3-hydroxypropyl)-6-methylcyclohex-1-en-1-yl)-4-(3-methylbut-2-en-1-yl)-4-(2-methylpent-3-yn-2-yl)-1,3-dioxolan-2-one (17). To a solution of hemiacetal (5.7 g, 14 mmol) in (1:1) MeOH/CH_2Cl_2 (200 mL) at 0 °C was added $NaBH_4$ (1.6 g, 42 mmol, 3.0 equiv). The reaction mixture was allowed to reach room temperature and stir for 2 h. Acetone (50 mL) and H_2O (50 mL) were added. The aqueous layer was extracted with EtOAc (3 × 100 mL), and the combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/EtOAc: 5/5 to 0/1) to afford the diol **17** (5.3 g, 13 mmol, 95%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 5.81 (t, J = 3.9 Hz, 1H), 5.35−5.26 (m, 2H), 3.84 (br d, J = 4.7 Hz, 1H), 3.67−3.56 (m, 2H), 2.72 (dd, J = 16.1, 6.0 Hz, 1H), 2.62 (dd, J = 16.1, 7.3 Hz, 1H), 2.35−2.24 (m, 1H), 2.23−2.13 (m, 1H), 1.90−1.83 (m, 1H), 1.81 (s, 3H), 1.79−1.74 (m, 1H), 1.73−1.68 (m, 1H), 1.70 (d, J = 0.9 Hz, 3H), 1.64 (br s, 1H), 1.60−1.52 (m, 4H, 2H9), 1.58 (s, 3H), 1.31 (s, 3H), 1.30 (s, 3H), 1.23 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 154.9, 138.5, 132.7, 130.5, 118.9, 90.0, 82.9, 81.8, 79.5, 71.5, 63.3, 41.9, 41.8, 35.4, 31.0, 26.8, 25.8, 24.9, 24.8, 24.7, 22.0, 20.4, 18.1, 3.6. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C24H36O5Na 427.2455, found 427.2440. $[\alpha]^{22}_D$: −12.5 (c 1.0, $CHCl_3$).

(4*S*,5*S*)-5-((5*S*,6*S*)-6-Allyl-5-hydroxy-6-methylcyclohex-1-en-1-yl)-4-(3-methylbut-2-en-1-yl)-4-(2-methylpent-3-yn-2-yl)-1,3-dioxolan-2-one (18a). To a solution of diol **17** (1.0 g, 2.5 mmol) in THF (70 mL) was added *o*-nitrophenylselenocyanate (680 mg, 3.0 mmol, 1.2 equiv) and tri-*n*-butylphosphine (0.78 mL, 3.0 mmol, 1.2 equiv). The mixture was stirred at room temperature for 20 min. The reaction was quenched with water (10 mL). The aqueous layer was extracted with Et_2O (3 × 15 mL) and the combined organic extracts were washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give a brown oil that was used without further purification. A solution of $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (90 mg) in water (7 mL) and hydrogen peroxide (2.9 mL, 30% solution) was then prepared. This solution was added at −15 °C to a solution of the previous compound in THF (60 mL). The mixture was stirred at this temperature for 20 min. The reaction was diluted with water (60 mL). The aqueous layer was extracted with EtOAc (3 × 60 mL), and the combined organic extracts were washed with brine (2 × 150 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/EtOAc: 8/2) to afford the title alcohol **18a** (0.87 g, 2.25 mmol, 90%) as a pale yellow viscous oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 5.94−5.83 (m, 1H), 5.81 (t, J = 4.0 Hz, 1H), 5.36−5.29 (m, 2H), 5.18−5.08 (m, 2H), 3.81 (ddd, J = 8.2, 5.7, 2.8 Hz, 1H), 2.77 (dd, J = 15.5, 6.2 Hz, 1H), 2.68 (dd, J = 15.5, 7.1 Hz, 1H), 2.54 (dd, J = 14.2, 6.7 Hz, 1H), 2.35−2.13 (m, 3H), 1.89−1.80 (m, 1H), 1.77 (s, 3H), 1.75−1.69 (m, 1H), 1.71 (d, J = 1.1 Hz, 3H) 1.62 (br s, 1H), 1.60 (s, 3H), 1.33−1.29 (s, 6H), 1.24 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 155.0, 138.8, 134.7, 132.6, 131.1, 118.9, 118.1, 89.8, 83.0, 81.0, 79.8, 72.4, 43.7, 42.7, 41.8, 31.2, 25.9, 24.9, 24.9, 24.6, 22.5, 19.7, 18.1, 3.5. IR (ν, cm^{-1}): 3220, 3054, 2985, 2306, 1792, 1550, 1412, 1265, 1040. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C24H34O4Na 409.2349, found 409.2331. $[\alpha]^{24}_D$: −29.0 (c 1.0, $CHCl_3$).

(4*S*,5*S*)-5-((5*S*,6*S*)-6-Allyl-6-methyl-5-((triethylsilyl)oxy)-cyclohex-1-en-1-yl)-4-(3-methylbut-2-en-1-yl)-4-(2-methylpent-3-yn-2-yl)-1,3-dioxolan-2-one (18b). To a solution of alcohol **18a** (150 mg, 0.39 mmol) in CH_2Cl_2 (3 mL) were added imidazole (66 mg, 0.97 mmol, 2.5 equiv), DMAP (5 mg, 0.04 mmol, 0.1 equiv), and TESCl (98 μL, 0.58 mmol, 1.5 equiv). The reaction mixture was stirred for 16 h. A saturated aqueous solution of $NaHCO_3$ (10 mL) was added to quench the reaction. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were washed with brine (25 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 95/5) to afford the title protected alcohol **18b** (195 mg, 0.39 mmol, 100%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 5.82−5.68 (m, 2H), 5.37−5.27 (m, 2H), 5.09−5.00 (m, 2H), 3.80 (dd, J = 6.7, 2.3 Hz, 1H), 2.84−2.74 (m, 1H), 2.62 (dd, J = 16.3, 8.2 Hz, 1H), 2.47 (dd, J = 14.5, 7.0 Hz, 1H), 2.33−2.21 (m, 1H), 2.17 (dd, J = 14.5, 7.6 Hz, 1H), 2.07 (ddt, J = 18.5, 6.3, 4.6 Hz, 1H), 1.87−1.80 (m, 1H), 1.78 (s, 3H), 1.69 (s, 3H), 1.67−1.61 (m, 1H), 1.60 (s, 3H), 1.28 (s, 3H), 1.28 (s, 3H), 1.16 (s, 3H), 0.94 (t, J = 8.0 Hz, 9H), 0.57 (q, J = 8.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 155.1, 138.4, 134.3, 132.0, 130.4, 119.5, 117.5, 90.0, 83.0, 82.8, 79.4, 72.4, 43.8, 42.5, 42.0, 31.1, 25.8, 25.4, 24.8, 24.5, 22.2, 20.7, 18.1, 7.0, 5.2, 3.6. IR (ν, cm^{-1}): 3054, 2955, 2877, 2350, 1792, 1457, 1412, 1280, 1010. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C30H48O4NaSi 523.3214, found 523.3192. $[\alpha]^{25}_D$: −20.0 (c 1.0, $CHCl_3$).

(1*S*,2*S*)-2-Allyl-2-methyl-3-((4*S*,5*S*)-5-(3-methylbut-2-en-1-yl)-5-(2-methylpent-3-yn-2-yl)-2-oxo-1,3-dioxolan-4-yl)-cyclohex-3-en-1-yl Acetate (18c). To a solution of alcohol **18a** (40 mg, 0.10 mmol) in CH_2Cl_2 (2 mL) were added Et_3N (98 μL, 0.7 mmol, 7.0 equiv), DMAP (1.0 mg, 10 μmol, 0.1 equiv), and Ac_2O (47 μL, 0.50 mmol, 5.0 equiv). The resulting mixture was allowed to stir for 4 h at room temperature. A saturated solution of $NaHCO_3$ (5 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic extracts were washed with a saturated aqueous solution of $CuSO_4$ (5 mL), brine (2 × 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 9/1) to afford the protected alcohol **18c** (43 mg, 0.10 mmol, 100%) as a colorless oil.^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 5.84−5.70 (m, 2H), 5.37−5.28 (m, 2H), 5.12−5.02 (m, 2H), 4.99 (dd, J = 6.6, 2.7 Hz, 1H), 2.76 (dd, J = 16.3, 6.0 Hz, 1H), 2.66 (dd, J = 16.3, 7.5 Hz, 1H), 2.45 (dd, J = 14.3, 6.6 Hz, 1H), 2.26−2.14 (m, 3H), 2.01 (s, 3H), 1.91−1.78 (m, 2H), 1.77 (s, 3H), 1.70 (d, J = 0.9 Hz, 3H), 1.60 (s, 3H), 1.30 (s, 6H), 1.20 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 170.5, 154.9, 138.1, 133.2, 132.5, 130.9, 118.9, 118.3, 89.8, 83.0, 81.4, 79.7, 74.4, 43.8, 41.9, 40.8, 31.2, 25.8, 24.8, 24.5, 22.1, 22.0, 21.1, 20.2, 18.1, 3.5. IR (ν, cm^{-1}): 3054, 2986, 2439, 1792, 1731, 1427, 1265, 1041. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C26H36O5Na 451.2455, found 451.2439. $[\alpha]^{26}_D$: −2.0 (c 2.0, $CHCl_3$).

(4*S*,5*S*)-5-((5*S*,6*S*)-6-Allyl-5-((4-methoxybenzyl)oxy)-6-methylcyclohex-1-en-1-yl)-4-(3-methylbut-2-en-1-yl)-4-(2-methylpent-3-yn-2-yl)-1,3-dioxolan-2-one (18d). To a solution of alcohol **18a** (0.10 g, 0.26 mmol) in CH_2Cl_2 (5 mL) were added PMB-trichloroacetimidate (0.22 g, 0.78 mmol, 3.0 equiv) and CSA (10 mg, 0.04 mmol, 0.15 equiv). The resulting mixture was refluxed for 24 h. A saturated aqueous solution of $NaHCO_3$ (5 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic extracts were washed with brine (15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 95/5) to afford the protected alcohol **18d** (80 mg, 0.16 mmol, 61%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 7.23 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 5.80−5.68 (m, 2H), 5.35−5.30 (m, 2H), 5.06−4.98 (m, 2H), 4.54 (d, J = 11.2 Hz, 1H), 4.32 (d, J = 11.2 Hz, 1H), 3.81 (s, 3H), 3.47 (dd, J = 7.4, 2.2 Hz, 1H), 2.82 (dd, J = 16.3, 5.5 Hz, 1H), 2.63 (dd, J = 16.3, 7.6 Hz, 1H), 2.53 (dd, J =

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14.4, 7.4 Hz, 1H), 2.32−2.19 (m, 2H), 2.10 (dq, J = 18.3, 5.9 Hz, 1H), 1.91−1.82 (m, 1H), 1.81−1.73 (m, 1H), 1.77 (s, 3H), 1.70 (s, 3H), 1.55 (s, 3H), 1.29 (s, 6H), 1.22 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 158.9, 155.0, 138.9, 134.5, 132.2, 131.2, 130.8, 128.8, 119.3, 117.4, 113.6, 89.9, 83.0, 82.2, 79.5, 79.0, 70.5, 55.3, 43.6, 42.5, 42.0, 31.1, 25.8, 24.8, 24.5, 22.7, 20.8, 20.7, 18.0, 3.5. IR (ν, cm^{-1}): 3054, 2978, 2936, 1794, 1666, 1605, 1520, 1438, 1280, 1172, 1025. HRMS (EI) m/z: $[M]^+$ Calcd for C32H42O5 506.3032, found 506.3029. $[\alpha]^{21}_D$: −3.0 (c 1.5, $CHCl_3$).

(4*S*,5*S*)-5-((5*S*,6*S*)-6-Allyl-5-(methoxymethoxy)-6-methylcyclohex-1-en-1-yl)-4-(3-methylbut-2-en-1-yl)-4-(2-methylpent-3-yn-2-yl)-1,3-dioxolan-2-one (18e). To a solution of alcohol **18a** (40 mg, 0.10 mmol) in CH_2Cl_2 (3 mL) were added DIPEA (0.12 mL, 0.70 mmol, 7.0 equiv), TBAI (7 mg, 0.02 mmol, 0.2 equiv), and MOMCl (35 μL, 92% solution, 0.40 mmol, 4.0 equiv). The resulting mixture was allowed to stir at room temperature for 16 h. A saturated aqueous solution of $NaHCO_3$ (5 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic extracts were washed with a saturated aqueous solution of $CuSO_4$ (2 × 10 mL). The aqueous cuprate solution was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic extracts were washed with brine (2 × 100 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 85/15) to afford the protected alcohol **18g** (37 mg, 0.09 mmol, 86%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 5.82−5.70 (m, 2H), 5.36−5.30 (m, 2H), 5.10−5.02 (m, 2H), 4.69 (d, J = 6.9 Hz, 1H), 4.61 (d, J = 6.9 Hz, 1H), 3.65 (dd, J = 6.8, 2.3 Hz, 1H), 3.38 (s, 3H), 2.81 (dd, J = 16.5, 5.9 Hz, 1H), 2.63 (dd, J = 16.5, 7.2 Hz, 1H), 2.48 (dd, J = 14.4, 7.0 Hz, 1H), 2.32−2.18 (m, 2H), 2.13 (ddt, J = 18.7, 6.0, 5.1 Hz, 1H), 1.90−1.74 (m, 2H), 1.78 (s, 3H), 1.70 (d, J = 1.1 Hz, 3H), 1.60 (s, 3H), 1.30 (s, 6H), 1.23 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 155.0, 138.4, 134.0, 132.3, 131.0, 119.1, 117.9, 95.9, 89.8, 83.0, 81.9, 79.5, 78.0, 55.7, 43.6, 42.0, 41.9, 31.0, 25.8, 24.8, 24.5, 22.5, 22.1, 20.8, 18.1, 3.6. IR (ν, cm^{-1}): 3055, 2986, 2306, 1792, 1541, 1507, 1421, 1260, 1038. HRMS (CI/ISO) m/z: $[M+H]^+$ Calcd for C26H39O5 431.2797, found 431.2794. $[\alpha]^{27}_D$: −12.0 (c 1.0, $CHCl_3$).

(4*S*,5*S*)-5-((5*S*,6*S*)-6-Allyl-5-((benzyloxy)methoxy)-6-methylcyclohex-1-en-1-yl)-4-(3-methylbut-2-en-1-yl)-4-(2-methylpent-3-yn-2-yl)-1,3-dioxolan-2-one (18f). To a solution of alcohol **18a** (1.4 g, 3.7 mmol) in CH_2Cl_2 (50 mL) were added DIPEA (4.8 mL, 28 mmol, 7.5 equiv), TBAI (1.6 g, 4.3 mmol, 1.1 equiv), and BOMCl (3.5 mL, 75% solution, 19 mmol, 5.0 equiv). The resulting mixture was allowed to reflux for 16 h. After the reaction mixture was cooled down to room temperature an aqueous solution of 1N NaOH (25 mL) was added and stirred for 5−10 min. The aqueous layer was extracted with Et_2O (3 × 50 mL), and the combined organic extracts were washed with a saturated aqueous solution of $CuSO_4$ (2 × 50 mL) The aqueous copper solution was extracted with Et_2O (3 × 100 mL) and the combined organic extracts were washed with brine (2 × 350 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 95/5 to 9/1) to afford the protected alcohol **18f** (1.7 g, 3.4 mmol, 95%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 7.38−7.29 (m, 5H), 5.81 (t, J = 3.8 Hz, 1H), 5.79−5.71 (m, 1H), 5.38−5.32 (m, 2H), 5.10−5.02 (m, 2H), 4.83 (d, J = 7.1 Hz, 1H), 4.75 (d, J = 7.1 Hz, 1H), 4.62 (s, 2H), 3.74 (dd, J = 6.5, 2.4 Hz, 1H), 2.87−2.79 (m, 1H), 2.64 (dd, J = 16.4, 7.3 Hz, 1H), 2.50 (dd, J = 14.5, 6.9 Hz, 1H), 2.33−2.19 (m, 2H), 2.18−2.09 (m, 1H), 1.94−1.81 (m, 2H), 1.78 (s, 3H), 1.70 (d, J = 1.0 Hz, 3H), 1.60 (s, 3H), 1.30 (s, 6H), 1.26 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 155.0, 138.3, 137.9, 134.0, 132.3, 130.9, 128.4, 127.8, 127.7, 119.2, 118.0, 93.9, 89.8, 83.0, 82.0, 79.5), 78.2, 69.7, 43.8, 42.0, 41.8, 31.0, 25.8, 24.8, 24.5, 22.4, 21.9, 20.8, 18.1, 3.6. IR (ν, cm^{-1}): 3054, 2986, 2306, 1792, 1558, 1421, 1265, 1041, 1033. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C32H42O5Na 529.2924, found 529.2916. $[\alpha]^{25}_D$: −10.0 (c 1.0, $CHCl_3$).

(4*S*,5*S*)-5-((5*S*,6*S*)-6-Allyl-5-methoxy-6-methylcyclohex-1-en-1-yl)-4-(3-methylbut-2-en-1-yl)-4-(2-methylpent-3-yn-2-yl)-1,3-dioxolan-2-one (18g). To a solution of alcohol **18a** (40 mg, 0.1 mmol) in DMF (1.5 mL) were added at 0 °C NaH (6.0 mg, 60% in mineral oil, 0.15 mmol, 1.5 equiv) and MeI (12 μL, 0.20 mmol, 2.0 equiv). The resulting mixture was allowed to stir for 16 h at room temperature. A saturated aqueous solution of $NaHCO_3$ (5 mL) was added and the aqueous layer was extracted with Et_2O (3 × 5 mL), then the combined organic extracts were washed with brine (15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was purified by flash chromatography (petroleum ether/Et_2O: 95/5) to afford the protected alcohol **18g** (35 mg, 0.09 mmol, 87%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 5.82−5.68 (m, 2H), 5.35−5.27 (m, 2H), 5.10−4.99 (m, 2H), 3.30 (s, 3H), 3.22 (dd, J = 8.0, 2.5 Hz, 1H), 2.81 (dd, J = 16.3, 6.0 Hz, 1H), 2.64 (dd, J = 16.3, 7.0 Hz, 1H), 2.49 (dd, J = 14.4, 7.5 Hz, 1H), 2.29−2.16 (m, 2H), 2.13−2.03 (m, 1H), 1.83 (dtd, J = 13.4, 6.5, 2.7 Hz, 1H), 1.76 (s, 3H), 1.73−1.67 (m, 1H), 1.70 (d, J = 1.2 Hz, 3H), 1.59 (s, 3H), 1.29 (s, 6H), 1.17 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 155.0, 138.9, 134.6, 132.3, 131.0, 119.1, 117.4, 89.7, 83.0, 81.6, 80.7, 79.6, 56.5, 43.2, 42.4, 41.9, 31.0, 25.8, 24.8, 24.5, 22.7, 20.5, 20.0, 18.0, 3.5. IR (ν, cm^{-1}): 3074, 2977, 2920, 2208, 1801, 1637, 1458, 1363, 1170, 1090. HRMS (ESI/TOF-Q) m/z: $[M + Na]^+$ Calcd for C25H36O4Na 423.2506, found 423.2488. $[\alpha]^{22}_D$: −28.0 (c 2.0, $CHCl_3$).

(3*S*,7*S*,8*S*,11*S*,*Z*)-8-Hydroxy-7-methyl-3-(2-methylpent-3-yn-2-yl)-3,4,7,7,8,9,10,11-octahydrobenzo[3,4]cycloocta[1,2][1,3]-dioxol-2-one (20a). A solution of alcohol **18a** (35 mg, 90 μmol) in toluene (30 mL) was thoroughly degassed under argon (using the freeze−thaw pump technique) and Zhan-1B catalyst (7.0 mg, 9.0 μmol, 0.1 equiv) was added and the mixture was stirred at reflux for 16 h. The resulting mixture was allowed to cool down and the solvent was removed *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/EtOAc: 85/15) to afford the title bicycle compound **20a** (9.5 mg, 29 μmol, 23%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 5.90 (t, J = 3.7 Hz, 1H), 5.87−5.79 (m, 1H), 5.69 (td, J = 9.0, 7.0 Hz, 1H), 5.28 (s, 1H), 3.57 (br s, 1H), 2.62−2.51 (m, 2H), 2.44−2.31 (m, 2H), 2.28 (dd, J = 13.5, 7.0 Hz, 1H), 2.10−2.02 (m, 1H), 1.87 (dd, J = 13.5, 9.0 Hz, 1H), 1.84−1.78 (m, 1H), 1.75 (s, 3H), 1.61 (br s, 1H), 1.40 (s, 3H), 1.34 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 154.9, 136.9, 128.7, 127.1, 126.8, 91.0, 83.1, 81.0, 80.6, 76.0, 44.5, 39.5, 39.1, 32.0, 25.6, 24.9, 23.7, 20.5, 18.7, 3.7. IR (ν, cm^{-1}): 3300, 3032, 2923, 2854, 2254, 1798, 1643, 1466, 1272, 1172, 1040. HRMS (CI/ISO) m/z: $[M+H]^+$ Calcd for C20H27O4 331.1909, found 331.1912. $[\alpha]^{25}_D$: + 143 (c 1.0, $CHCl_3$).

(3*S*,7*S*,8*S*,11*S*,*Z*)-7-Methyl-3-(2-methylpent-3-yn-2-yl)-8-((triethylsilyl)oxy)-3,4,7,7,8,9,10,11-octahydrobenzo[3,4]cyclo-octa[1,2][1,3]dioxol-2-one (20b). The same metathesis procedure was repeated with the protected alcohol **18b** (35 mg, 70 μmol). The crude mixture was purified by flash chromatography (petroleum ether/EtOAc: 97/3) to afford the title bicycle compound **20b** (24 mg, 54 μmol, 77%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 5.83−5.74 (m, 2H), 5.69−5.61 (m, 1H), 5.27 (s, 1H), 3.60 (dd, J = 4.6, 2.0 Hz, 1H), 2.61 (ddd, J = 14.0, 9.6, 0.9 Hz, 1H), 2.52 (dd, J = 14.0, 7.3 Hz, 1H), 2.40−2.30 (m, 1H), 2.27 (dd, J = 13.6, 6.5 Hz, 1H), 2.20−2.10 (m, 1H), 1.99−1.91 (m, 1H), 1.84 (dd, J = 13.6, 8.5 Hz, 1H), 1.75 (s, 3H), 1.65 (dddd, J = 14.0, 7.3, 4.8, 2.0 Hz, 1H), 1.39 (s, 3H), 1.34 (s, 3H), 1.10 (s, 3H), 0.96 (t, J = 8.0 Hz, 9H), 0.60 (q, J = 8.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm: 155.1, 136.4, 128.9, 126.9, 126.2, 91.2, 83.2, 80.7, 80.6, 76.3, 44.4, 39.3, 39.2, 32.1, 25.6, 24.9, 24.8, 21.7, 19.3, 7.0, 5.1, 3.7. IR (ν, cm^{-1}): 3055, 2955, 2877, 1796, 1466, 1427, 1265, 1187, 1056. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C26H40O4SiNa 467.2588, found 467.2568. $[\alpha]^{22}_D$: + 133 (c 2.0, $CHCl_3$).

(3*S*,7*S*,8*S*,11*S*,*Z*)-7-Methyl-3-(2-methylpent-3-yn-2-yl)-2-oxo-3,4,7,7,8,9,10,11-octahydrobenzo[3,4]cycloocta[1,2][1,3]-dioxol-8-yl Acetate (20c). The same metathesis procedure was repeated with the protected alcohol **18c** (36 mg, 84 μmol). The crude mixture was purified by flash chromatography (petroleum ether/Et_2O: 85/15) to afford the title bicycle **20c** (25 mg, 67 μmol, 80%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm: 5.90−5.81 (m,

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2H), 5.70−5.63 (m, 1H), 5.31 (s, 1H), 4.88 (dd, J = 3.8, 2.4 Hz, 1H), 2.64−2.52 (m, 2H), 2.36−2.25 (m, 3H), 2.05 (s, 3H), 2.04−1.99 (m, 1H), 1.96 (dd, J = 13.5, 8.7 Hz, 1H), 1.91−1.84 (m, 1H), 1.73 (s, 3H), 1.40 (s, 3H), 1.35 (s, 3H), 1.10 (s, 3H).b^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 170.9, 154.9, 136.3, 128.1, 127.5, 126.7, 91.1, 83.2, 80.9, 80.6, 77.6, 42.7, 39.4, 39.1, 32.0, 25.6, 24.9, 21.4, 21.3, 21.2, 18.5, 3.6. IR (ν, cm^{-1}): 3055, 3034, 2984, 2920, 1796, 1726, 1466, 1373, 1249, 1164, 1033. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C22H28O5Na 395.1829, found 395.1815. $[\alpha]^{26}_D$: + 126 (c 2.0, $CHCl_3$).

(3*S*,9*S*,10*S*,13*S*,*Z*)-10-((4-Methoxybenzyl)oxy)-6,9,14,14-tetramethyl-9,9,10,11,12,13-hexahydro-4H-3,7-methanobenzo[3,4]cyclodeca[1,2][1,3]dioxol-2-one (19d) and (3*S*,7*S*,8*S*,11*S*,*Z*)-8-((4-methoxybenzyl)oxy)-7-methyl-3-(2-methylpent-3-yn-2-yl)-3,4,7,7,8,9,10,11-octahydrobenzo[3,4]-cycloocta[1,2][1,3]dioxol-2-one (20d). The same metathesis procedure was repeated with the protected diol **18d** (50 mg, 0.10 mmol). The crude mixture was purified by flash chromatography (petroleum ether/Et_2O: 85/15) to afford the title tricycle **19d** (13 mg, 29 μmol, 29%) and the bicycle **20d** (9.9 mg, 22 μmol, 22%) as colorless oils.

(3*S*,9*S*,10*S*,13*S*,*Z*)-10-((4-Methoxybenzyl)oxy)-6,9,14,14-tetramethyl-9,9,10,11,12,13-hexahydro-4H-3,7-methanobenzo[3,4]cyclodeca[1,2][1,3]dioxol-2-one (19d). ^{1}H NMR (400 MHz, $CDCL_3$) δ ppm: 7.33−7.28 (m, 2H), 6.93−6.89 (m, 2H), 5.87 (dd, J = 5.7, 1.7 Hz, 1H), 5.10 (s, 1H), 5.03 (dd, J = 13.0, 6.1 Hz, 1H), 4.88 (tq, J = 3.3, 1.6 Hz, 1H), 4.70 (d, J = 11.9 Hz, 1H), 4.38 (d, J = 11.9 Hz, 1H), 3.81 (s, 3H), 3.30 (dd, J = 12.1, 3.3 Hz, 1H), 2.74 (ddq, J = 18.8, 3.3, 1.6 Hz, 1H), 2.61 (dd, J = 13.8, 6.1 Hz, 1H), 2.26 (dd, J = 13.8, 13.0 Hz, 1H), 2.25−2.19 (m, 1H), 2.14 (ddq, J = 18.8, 3.3, 1.6 Hz, 1H), 2.05−1.97 (m, 2H), 1.62 (q, J = 1.6 Hz, 3H), 1.66−1.60 (m, 1H), 1.53 (s, 3H), 1.28 (s, 3H), 1.14 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 159.3, 154.2, 146.1, 138.1, 134.9, 130.5, 129.9, 127.9, 127.4, 115.6, 113.8, 93.3, 78.9, 74.9, 69.8, 55.3, 47.7, 41.0, 32.6, 30.6, 25.1, 24.2, 21.7, 21.5, 21.2, 18.5. IR (ν, cm^{-1}): 3054, 2980, 2934, 1797, 1620, 1458, 1420, 1242, 1025. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C28H34O5Na 473.2298, found 473.2278. $[\alpha]^{21}_D$: +120 (c 1.0, $CHCl_3$).

(3*S*,7*S*,8*S*,11*S*,*Z*)-8-((4-Methoxybenzyl)oxy)-7-methyl-3-(2-methylpent-3-yn-2-yl)-3,4,7,7,8,9,10,11-octahydrobenzo[3,4]-cycloocta[1,2][1,3]dioxol-2-one (20d). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 7.25 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 5.84−5.75 (m, 2H), 5.64−5.56 (m, 1H), 5.31 (s, 1H), 4.59 (d, J = 11.8 Hz, 1H), 4.37 (d, J = 11.8 Hz, 1H), 3.82 (s, 3H), 3.28 (dd, J = 4.2, 2.2 Hz, 1H), 2.60 (dd, J = 13.7, 10.9 Hz, 1H), 2.53 (dd, J = 13.7, 7.3 Hz, 1H), 2.35−2.27 (m, 2H), 2.20 (ddt, J = 19.1, 6.3, 3.1 Hz, 1H), 1.93−1.82 (m, 3H), 1.73 (s, 3H), 1.39 (s, 3H), 1.33 (s, 3H), 1.15 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 159.0, 155.0, 136.9, 131.1, 129.1, 128.8, 126.9, 126.6, 113.7, 91.1, 83.2, 82.0, 80.6, 77.2, 70.3, 55.3, 43.8, 39.5, 39.2, 32.1, 25.6, 24.9, 21.7, 19.7, 19.2, 3.7. IR (ν, cm^{-1}): 3042, 2980, 2943, 2832, 1800, 1612, 1497, 1458, 1257, 1187, 1041. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C28H34O5Na 473.2298, found 473.2277. $[\alpha]^{21}_D$: +90.0 (c 1.0, $CHCl_3$).

(3*S*,9*S*,10*S*,13*S*,*Z*)-10-(Methoxymethoxy)-6,9,14,14-tetramethyl-9,9,10,11,12,13-hexahydro-4H-3,7-methanobenzo[3,4]cyclodeca[1,2][1,3]dioxol-2-one (19e) and (3*S*,7*S*,8*S*,11*S*,*Z*)-8-(Methoxymethoxy)-7-methyl-3-(2-methylpent-3-yn-2-yl)-3,4,7,7,8,9,10,11-octahydrobenzo[3,4]cyclooocta[1,2][1,3]dioxol-2-one (20e). The same metathesis procedure was repeated with the protected alcohol **18e** (33 mg, 76 μmol). The crude mixture was purified by flash chromatography (petroleum ether/Et_2O: 85/15) to afford the title tricycle compound **19e** (8.0 mg, 21 μmol, 28%) and the bicycle **20e** (15 mg, 41 μmol, 54%) as colorless oils.

(3*S*,9*S*,10*S*,13*S*,*Z*)-10-(Methoxymethoxy)-6,9,14,14-tetramethyl-9,9,10,11,12,13-hexahydro-4H-3,7-methanobenzo[3,4]cyclodeca[1,2][1,3]dioxol-2-one (19e). ^{1}H NMR (400 MHz, $CDCL_3$) δ ppm: 5.91 (dd, J = 5.2, 2.0 Hz, 1H), 5.70 (dd, J = 12.9, 6.1 Hz, 1H), 5.15 (s, 1H), 4.95 (tq, J = 3.3, 1.6 Hz, 1H), 4.82 (d, J = 7.0 Hz, 1H), 4.65 (d, J = 7.0 Hz, 1H), 3.62 (dd, J = 12.1, 3.9 Hz, 1H), 3.45 (s, 3H), 2.79 (ddq, J = 18.9, 3.3, 1.6 Hz, 1H), 2.65 (dd, J = 13.8, 6.1 Hz, 1H), 2.40 (dd, J = 13.8, 12.9 Hz, 1H), 2.26−2.13 (m, 2H), 2.04 (dddd, J = 18.5, 11.6, 6.6, 2.0 Hz, 1H), 1.93−1.85 (m, 1H), 1.79 (q, J = 1.6 Hz, 3H), 1.75−1.65 (m, 1H), 1.59 (s, 3H), 1.34 (s, 3H), 1.15 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 154.1, 146.7, 138.2, 134.6, 128.1, 127.0, 115.8, 95.3, 93.4, 79.0, 75.7, 55.8, 47.5, 41.1, 32.8, 30.6, 25.2, 24.2, 23.1, 21.7, 21.3, 18.9. IR (ν, cm^{-1}): 3049, 2932, 1799, 1558, 1435, 1266, 1020. HRMS (CI/ISO) m/z: $[M+H]^+$ Calcd for C22H31O5 375.2171, found 375.2175. $[\alpha]^{24}_D$: +84.0 (c 1.0, $CHCl_3$).

(3*S*,7*S*,8*S*,11*S*,*Z*)-8-(Methoxymethoxy)-7-methyl-3-(2-methylpent-3-yn-2-yl)-3,4,7,7,8,9,10,11-octahydrobenzo[3,4]-cycloocta[1,2][1,3]dioxol-2-one (20e). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 5.87−5.79 (m, 2H), 5.71−5.60 (m, 1H), 5.31 (s, 1H), 4.74 (d, J = 7.0 Hz, 1H), 4.62 (d, J = 7.0 Hz, 1H), 3.52 (dd, J = 4.0, 2.4 Hz, 1H), 3.40 (s, 3H), 2.64−2.50 (m, 2H), 2.35−2.28 (m, 2H), 2.27−2.22 (m, 1H), 1.97−1.86 (m, 3H), 1.75 (s, 3H), 1.40 (s, 3H), 1.34 (s, 3H), 1.20 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 155.0, 136.8, 128.6, 127.1, 126.7, 95.4, 91.0, 83.2, 81.3, 80.7, 80.6, 55.8, 43.6, 39.7, 39.1, 32.1, 25.6, 24.9, 21.7, 21.0, 19.1, 3.7. IR (ν, cm^{-1}): 3056, 3034, 2987, 2941, 1798, 1527, 1450, 1257, 1041. HRMS (CI/ISO) m/z: $[M+H]^+$ Calcd for C22H31O5 375.2171, found 375.2168. $[\alpha]^{25}_D$: +157 (c 1.0, $CHCl_3$).

(3*S*,9*S*,10*S*,13*S*,*Z*)-10-((Benzyloxy)methoxy)-6,9,14,14-tetramethyl-9,9,10,11,12,13-hexahydro-4H-3,7-methanobenzo[3,4]cyclodeca[1,2][1,3]dioxol-2-one (19f) (3*S*,7*S*,8*S*,11*S*,*Z*)-8-((Benzyloxy)methoxy)-7-methyl-3-(2-methylpent-3-yn-2-yl)-3,4,7,7,8,9,10,11-octahydrobenzo[3,4]cycloocta[1,2][1,3]-dioxol-2-one (20f). Method A: The same metathesis procedure was repeated with the protected alcohol **18f** (20 mg, 39 μmol). The crude mixture was purified by flash chromatography (benzene/CH_2Cl_2: 75/25) to afford the title tricycle **19f** (5.3 mg, 12 μmol, 29%) and the bicycle **20f** (7.9 mg, 18 μmol, 46%) as colorless oils. Method B: A solution of **18f** (100 mg, 0.20 mmol) in toluene (65 mL) was thoroughly degassed under argon (using the freeze−thaw pump technique) and Zhan-1B catalyst (144 mg, 0.20 mmol, 1.0 equiv) was added and the mixture was stirred at reflux for 16 h while a gentle stream of argon was bubbling through the reaction mixture. The resulting mixture was allowed to cool down and the solvent was removed *in vacuo*. The crude mixture was then purified by flash chromatography (benzene/CH_2Cl_2: 75/25) to only afford the title tricycle compound **19f** (32−36 mg, 70−80 μmol, 35−40%) as a colorless oil. Method C: A solution of precursor **18f** (36 mg, 71 μmol) in toluene (24 mL) was thoroughly degassed under argon (using the freeze−thaw pump technique) and Zhan-1B catalyst (52 mg, 71 μmol, 1.0 equiv) was added and the mixture was stirred at reflux for 4 h while a gentle stream of argon was bubbling through the reaction mixture. Then a solution of bicycle **20f** (32 mg, 71 μmol, 1.0 equiv) in toluene (5 mL) was added to the reaction mixture, which was stirred at reflux for an additional 16 h while a gentle stream of argon was bubbling through. The resulting mixture was allowed to cool down and the solvent was removed *in vacuo*. The crude mixture was then purified by flash chromatography (benzene/CH_2Cl_2: 75/25) to afford the title tricycle compound **19f** (15 mg, 33 μmol, 47%) as a colorless oil.

(3*S*,9*S*,10*S*,13*S*,*Z*)-10-((Benzyloxy)methoxy)-6,9,14,14-tetramethyl-9,9,10,11,12,13-hexahydro-4H-3,7-methanobenzo[3,4]cyclodeca[1,2][1,3]dioxol-2-one (19f). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 7.38−7.29 (m, 5H), 5.91 (dd, J = 5.6, 2.1 Hz, 1H), 5.68 (dd, J = 13.2, 6.1 Hz, 1H), 5.16 (s, 1H), 4.96 (d, J = 7.2 Hz, 1H), 4.93 (ddq, J = 6.2, 3.6, 1.6 Hz, 1H), 4.82 (d, J = 7.2 Hz, 1H), 4.74 (d, J = 11.6 Hz, 1H), 4.65 (d, J = 11.6 Hz, 1H), 3.72 (dd, J = 12.1, 3.8 Hz, 1H), 2.78 (ddq, J = 19.0, 3.6, 1.6 Hz, 1H), 2.71 (dd, J = 13.2, 6.1 Hz, 1H), 2.42 (t, J = 13.2 Hz, 1H), 2.26−2.14 (m, 2H), 2.04 (dddd, J = 18.4, 11.7, 6.7, 2.1 Hz, 1H), 1.98−1.91 (m, 1H), 1.74−1.65 (m, 1H), 1.71 (dt, J = 3.3, 1.6 Hz, 3H), 1.59 (s, 3H), 1.33 (s, 3H), 1.17 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 154.1, 146.7, 138.3, 137.6, 134.6, 128.5, 128.1, 127.8, 127.7, 127.0, 115.8, 93.4, 93.2, 78.9, 75.5, 70.1, 47.5, 41.1, 32.8, 30.6, 25.2, 24.1, 22.9, 21.7, 21.3, 18.8. IR (ν, cm^{-1}): 3056, 3030, 2934, 1801, 1541, 1377, 1338, 1267, 1216, 1159, 1025. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C28H34O5Na 473.2298, found 473.2287. $[\alpha]^{21}_D$: +113 (c 1.0, $CHCl_3$).

(3*S*,7*S*,8*S*,11*S*,*Z*)-8-((Benzyloxy)methoxy)-7-methyl-3-(2-methylpent-3-yn-2-yl)-3,4,7,7,8,9,10,11-octahydrobenzo[3,4]-

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cycloocta[1,2][1,3]dioxol-2-one (20f). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 7.39−7.29 (m, 5H), 5.89−5.78 (m, 2H), 5.71−5.63 (m, 1H), 5.33 (s, 1H), 4.88 (d, J = 7.2 Hz, 1H), 4.78 (d, J = 7.2 Hz, 1H), 4.67 (d, J = 11.5 Hz, 1H), 4.63 (d, J = 11.5 Hz, 1H), 3.62 (t, J = 3.1 Hz, 1H), 2.61 (dd, J = 13.5, 10.3 Hz, 1H), 2.55 (dd, J = 13.5, 7.3 Hz, 1H), 2.41−2.29 (m, 2H), 2.28−2.20 (m, 1H), 2.00−1.86 (m, 3H), 1.75 (s, 3H), 1.41 (s, 3H), 1.35 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 155.0, 137.9, 136.8, 128.6, 128.5, 127.8, 127.7, 127.2, 126.7, 93.5, 91.0, 83.2, 81.5, 80.7, 80.6, 69.9, 43.7, 39.7, 39.2, 32.1, 25.6, 24.9, 21.7, 20.9, 19.1, 3.7. IR (ν, cm^{-1}): 3056, 3014, 2989, 2951, 1791, 1520, 1423, 1400, 1257, 1125, 1041. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C28H34O5Na 473.2298, found 473.2287. $[\alpha]^{25}_D$: +123 (c 1.0, $CHCl_3$).

(3*S*,9*S*,10*S*,13*S*,*Z*)-10-Methoxy-6,9,14,14-tetramethyl-9,9,10,11,12,13-hexahydro-4H-3,7-methanobenzo[3,4]cyclodeca[1,2][1,3]dioxol-2-one (19g) and (3*S*,7*S*,8*S*,11*S*,*Z*)-8-methoxy-7-methyl-3-(2-methylpent-3-yn-2-yl)-3,4,7,7,8,9,10,11-octahydrobenzo[3,4]cycloocta[1,2][1,3]dioxol-2-one (20g). The same metathesis procedure was repeated with the protected alcohol **18g** (34 mg, 85 μmol). The crude mixture was purified by flash chromatography (petroleum ether/Et_2O: 85/15) to afford the title tricycle **19g** (13 mg, 38 μmol, 45%) and the bicycle **20g** (8.8 mg, 25 μmol, 30%) as colorless oils.

(3*S*,9*S*,10*S*,13*S*,*Z*)-10-Methoxy-6,9,14,14-tetramethyl-9,9,10,11,12,13-hexahydro-4H-3,7-methanobenzo[3,4]cyclodeca[1,2][1,3]dioxol-2-one (19g). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 5.90 (dd, J = 5.0, 1.5 Hz, 1H), 5.65 (dd, J = 13.7, 6.2 Hz, 1H), 5.13 (s, 1H), 4.95 (tq, J = 3.5, 1.8 Hz, 1H), 3.43 (s, 3H), 3.18 (dd, J = 12.1, 3.4 Hz, 1H), 2.79 (ddq, J = 18.9, 3.5, 1.8 Hz, 1H), 2.68 (dd, J = 13.7, 6.2 Hz, 1H), 2.36 (t, J = 13.7 Hz, 1H), 2.28−2.15 (m, 2H), 2.06−1.94 (m, 2H), 1.80 (q, J = 1.8 Hz, 3H), 1.58 (s, 3H), 1.57−1.52 (m, 1H), 1.33 (s, 3H), 1.10 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 154.2, 146.5, 138.2, 134.7, 127.9, 127.3, 115.9, 93.3, 79.5, 79.0, 57.2, 47.8, 41.1, 32.8, 30.6, 25.2, 24.2, 21.6, 21.3, 21.3, 18.8. IR (ν, cm^{-1}): 3054, 2983, 2931, 1797, 1507, 1434, 1265, 1211, 1172, 1110, 1025. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C21H28O4Na 367.1880, found 367.1863. $[\alpha]^{25}_D$: +105 (c 1.5, $CHCl_3$).

(3*S*,7*S*,8*S*,11*S*,*Z*)-8-Methoxy-7-methyl-3-(2-methylpent-3-yn-2-yl)-3,4,7,7,8,9,10,11-octahydrobenzo[3,4]cycloocta[1,2][1,3]dioxol-2-one (20g). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 5.83−5.77 (m, 2H), 5.70−5.61 (m, 1H), 5.30 (s, 1H), 3.36 (s, 3H), 3.08 (dd, J = 4.4, 2.2 Hz, 1H), 2.59 (ddd, J = 13.6, 9.7, 1.0 Hz, 1H), 2.54 (dd, J = 13.6, 7.3 Hz, 1H), 2.35−2.25 (m, 2H), 2.23−2.15 (m, 1H), 1.95 (ddt, J = 14.2, 6.5, 2.2 Hz, 1H), 1.91−1.84 (m, 2H), 1.74 (s, 3H), 1.39 (s, 3H), 1.33 (s, 3H), 1.17 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 155.0, 136.9, 128.7, 127.1, 126.6, 91.0, 85.2, 83.2, 80.7, 80.6, 57.0, 43.8, 39.6, 39.2, 32.1, 25.6, 24.9, 21.5, 19.1, 18.9, 3.7. IR (ν, cm^{-1}): 3055, 2944, 2832, 1794, 1647, 1456, 1268, 1117, 1029. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C21H28O4Na 367.1880, found 367.1862. $[\alpha]^{25}_D$: +175 (c 1.0, $CHCl_3$).

(4*S*,5*S*)-4-((5*S*,6*S*)-6-allyl-5-((benzyloxy)methoxy)-6-methylcyclohex-1-en-1-yl)-8,10,10-trimethyl-9-methylene-1,3-dioxaspiro[4.5]dec-7-en-2-one (21f) and (3*S*,8*S*,9*S*,12*S*,*Z*)-3-Allyl-9-((benzyloxy)methoxy)-4,4,6,8-tetramethyl-5-methylene-3,5,8,8,9,10,11,12-octahydro-4H-benzo[3,4]cyclonona-[1,2][1,3]dioxol-2-one (22f). Ethylene was bubbled for 2 min through a thoroughly degassed (using the freeze−thaw pump technique) solution of precursor **18f** (20 mg, 39 μmol) in toluene (13 mL) and Zhan-1B catalyst (3 mg, 4 μmol, 0.1 equiv) was added then ethylene was bubbled through the reaction mixture for another 2 min. The resulting mixture was refluxed under an ethylene atmosphere for 2.5 h. The resulting mixture was allowed to cool down and the solvent was removed *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et2O: 85/15) to afford the title bicycle **22f** (6.0 mg, 12 μmol, 30%) and a 1:3.5 mixture of **20f**/**21f** (13 mg, 27 μmol, 70%) as colorless oils.

(3*S*,8*S*,9*S*,12*S*,*Z*)-3-Allyl-9-((benzyloxy)methoxy)-4,4,6,8-tetramethyl-5-methylene-3,5,8,8,9,10,11,12-octahydro-4H-benzo[3,4]cyclonona[1,2][1,3]dioxol-2-one (21f). ^{1}H NMR (400 MHz, $CDCL_3$) δ ppm: 7.40−7.33 (m, 4H), 7.33−7.29 (m, 1H), 5.99 (t, J = 4.0 Hz, 1H), 5.73−5.59 (m, 2H), 5.16 (s, 1H), 5.10−5.02 (m, 3H), 4.99 (s, 1H), 4.86 (d, J = 7.1 Hz, 1H), 4.77 (d, J = 7.1 Hz, 1H), 4.68−4.59 (m, 2H), 3.75 (dd, J = 7.8, 2.6 Hz, 1H), 2.73−2.58 (m, 2H), 2.42−2.33 (m, 1H), 2.29−2.22 (m, 1H), 2.21−2.09 (m, 2H), 1.98−1.87 (m, 1H), 1.91 (s, 3H), 1.85−1.76 (m, 1H), 1.32 (s, 3H), 1.24 (s, 3H), 1.23 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 154.8, 149.8, 139.6, 138.2, 137.8, 133.5, 130.6, 128.4, 127.8, 127.7, 123.0, 118.3, 113.1, 98.3, 94.0, 77.6, 76.4, 69.8, 52.9, 42.9, 42.2, 38.9, 23.3, 23.1, 22.7, 22.3, 21.1, 18.9. IR (ν, cm^{-1}): 3045, 2972, 2934, 1794, 1458, 1327, 1272, 1180, 1033. HRMS (ESI/TOF-Q) m/z: $[M+Na]^+$ Calcd for C30H38O5Na 501.2611, found 501.2602.

(3*S*,7*S*,8*S*,11*S*,*Z*)-8-((Benzyloxy)methoxy)-4,4,7-trimethyl-3-(3-methylbut-2-en-1-yl)-5-(prop-1-en-2-yl)-3,4,7,7,8,9,10,11-octahydrobenzo[3,4]cycloocta[1,2][1,3]dioxol-2-one (22f). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 7.36−7.29 (m, 5H), 6.07 (t, J = 3.6 Hz, 1H), 5.57 (dd, J = 10.7, 8.6 Hz, 1H), 5.38 (s, 1H), 5.23 (tq, J = 7.2, 0.9 Hz, 1H), 4.95 (d, J = 7.1 Hz, 1H), 4.82 (d, J = 7.1 Hz, 1H), 4.80−4.76 (m, 1H), 4.69 (d, J = 11.7 Hz, 1H), 4.65 (d, J = 11.7 Hz, 1H), 4.53 (d, J = 1.5 Hz, 1H), 3.71 (dd, J = 12.1, 4.4 Hz, 1H), 2.61 (dd, J = 15.1, 7.2 Hz, 1H), 2.54−2.45 (m, 2H), 2.40−2.32 (m, 1H), 2.29 (m, J = 16.9, 10.7 Hz, 1H), 2.24−2.19 (m, 1H), 2.08 (m, 1H), 1.88−1.79 (m, 1H), 1.77 (s, 3H), 1.72 (d, J = 0.9 Hz, 3H″), 1.59 (s, 3H), 1.55 (s, 3H), 1.39 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 154.0, 150.3, 150.1, 137.7, 136.3, 134.6, 128.4, 127.8, 127.7, 127.7, 127.6, 117.2, 113.6, 93.9, 93.8, 80.9, 76.2, 70.1, 43.8, 43.2, 33.6, 30.2, 26.2, 26.1, 26.0, 23.9, 23.7, 23.4, 23.1, 18.4. IR (ν, cm^{-1}): 3056, 3025, 2998, 2921, 2284, 1799, 1686, 1521, 1436, 1265, 1025. HRMS (CI/ISO) m/z: $[M+H]^+$ Calcd for C32H43O5 507.3110, found 507.3114. $[\alpha]^{25}_D$: +94.0 (c 1.0, $CHCl_3$).

(1*S*,4*S*,7*S*,10*R*,11*S*,12*S*)-1-((Benzyloxy)methoxy)-10,12,13,13-tetramethyl-1,3,4,11,12,12-hexahydro-2H,8H-7,10-methanobenzo[3,4]oxireno[2′,3′:6,7]cyclodeca[1,2][1,3]dioxol-6-one (23). To a solution of triene **19f** (93 mg, 0.20 mmol) in CH_2Cl_2 (3 mL) was added at 0 °C a solution of *m*CPBA (55 mg, 0.24 mmol, 1.2 equiv) in CH_2Cl_2 (1 mL). The resulting mixture was stirred at the same temperature for 30 min. The reaction mixture was washed with a 10% aqueous solution of Na_2SO_3 (2 × 4 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with a saturated aqueous solution of $NaHCO_3$ (25 mL), washed with brine (25 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 8/2) to afford the title vinyl epoxide **23** (80 mg, 0.17 mmol, 86%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 7.38−7.29 (m, 5H), 6.10 (dd, J = 5.3, 1.5 Hz, 1H), 5.20 (tq, J = 3.4, 1.7 Hz, 1H), 5.10 (s, 1H), 4.97 (d, J = 7.3 Hz, 1H), 4.82 (d, J = 7.3 Hz, 1H), 4.73 (d, J = 11.4 Hz, 1H), 4.64 (d, J = 11.4 Hz, 1H), 3.86 (dd, J = 12.1, 3.7 Hz, 1H), 2.96 (ddq, J = 18.8, 3.4, 1.7 Hz, 1H), 2.72 (dd, J = 14.4, 4.0 Hz, 1H), 2.63 (dd, J = 12.5, 4.0 Hz, 1H), 2.34 (ddq, J = 18.8, 3.4, 1.7 Hz, 1H), 2.30−2.24 (m, 1H), 2.11 (dddd, J = 18.3, 11.7, 6.3, 1.5 Hz, 1H), 2.03−1.97 (m, 1H), 1.75 (dddd, J = 18.3, 12.1, 8.5, 6.3 Hz, 1H), 1.56 (dd, J = 14.4, 12.5 Hz, 1H), 1.40 (q, J = 1.7 Hz, 3H), 1.35 (s, 3H), 1.26 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 153.9, 137.8, 137.4, 133.7, 129.6, 128.6, 127.9, 127.9 117.7, 93.2, 91.4, 78.4, 75.0, 70.4, 64.8, 58.8, 43.2, 39.2, 31.7, 30.3, 24.2, 24.2, 23.0, 22.6, 18.9, 15.7. IR (ν, cm^{-1}): 3053, 2980, 2944, 2834, 1798, 1466, 1427, 1265, 1018. HRMS (CI/ISO) m/z: $[M+H]^+$ Calcd for C28H35O6 467.2434, found 467.2433. $[\alpha]^{25}_D$: +82.0 (c 1.0, $CHCl_3$).

(1*R*,5*S*,6*S*,10*S*,10*S*,11*S*)-10-((benzyloxy)methoxy)-5-hydroxy-2,10,12,12-tetramethyl-5,6,8,9,10,10,11,11-octahydro-4H-1,5-methanobenzo[4,5]cyclodeca[1,2]oxiren-6-yl Benzoate (24). To a solution of **23** (20 mg, 43 μmol) in THF (2 mL) at −78 °C was added phenyllithium (0.4 mL, 2 M in nBu_2O, 0.4 mmol, 10 equiv). The mixture was stirred at this temperature for 2 h. A solution of saturated aqueous $NaHCO_3$ (5 mL) was then added and the aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 8/2) to afford the title benzoate **24** (21 mg, 39 μmol, 92%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCL_3$) δ ppm: 8.10−8.05 (m, 2H), 7.64−7.55

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(m, 1H), 7.53−7.44 (m, 2H), 7.39−7.35 (m, 4H), 7.34−7.28 (m, 1H), 6.16 (dd, J = 5.8, 2.4 Hz, 1H), 5.94 (s, 1H), 5.37 (tq, J = 3.3, 1.8 Hz, 1H), 4.93 (d, J = 7.2 Hz, 1H), 4.81 (d, J = 7.2 Hz, 1H), 4.72 (d, J = 11.5 Hz, 1H), 4.64 (d, J = 11.5 Hz, 1H), 3.81 (dd, J = 10.5, 3.1 Hz, 1H), 3.08 (ddq, J = 18.7, 3.3, 1.8 Hz, 1H), 2.81 (dd, J = 12.2, 4.4 Hz, 1H), 2.49 (dd, J = 14.2, 4.4 Hz, 1H), 2.23−2.09 (m, 2H), 2.07 (s, 1H), 2.01−1.90 (m, 1H), 1.95 (dd, J = 14.2, 12.2 Hz, 1H), 1.89−1.80 (m, 1H), 1.69−1.56 (m, 1H), 1.46 (q, J = 1.8 Hz, 3H), 1.32 (s, 3H), 1.28 (s, 6H). ^{13}C NMR (100 MHz, $CDCL_3$) δ ppm: 165.7, 140.2, 137.6, 136.4, 133.1, 130.4, 129.7, 128.8, 128.5, 128.5, 127.9, 127.8, 120.9, 93.6, 79.8, 78.7, 74.1, 70.1, 65.6, 60.3, 43.4, 41.0, 34.2, 33.1, 24.5, 24.1, 23.1, 22.0, 19.2, 16.0. IR (ν, cm^{-1}): 3050, 2967, 2939, 2870, 1721, 1560, 1468, 1267, 1115, 1063. HRMS (ESI/TOF-Q) m/z: [M+Na]$^+$ Calcd for C34H40O6Na 567.2717, found 567.2697. $[\alpha]^{25}_D$: + 226 (c 1.0, $CHCl_3$).

(3*S*,7*R*,8*S*,9*S*,12*S*)-9-((Benzyloxy)methoxy)-6,8,13,13-tetramethyl-2-oxo-8,8,9,10,11,12-hexahydro-3,7-methanobenzo[3,4]cyclonona[1,2][1,3]dioxole-7(4H)-carbaldehyde (25). To a solution of vinyl epoxide **23** (8.0 mg, 17 μmol) in CH_2Cl_2 (0.5 mL) were added allyl alcohol (3.5 μL, 51 μmol, 3.0 equiv) and $Sc(OTf)_3$ (2.0 mg, 4.3 μmol, 0.25 equiv). The mixture was stirred at room temperature for 16 h. A solution of saturated aqueous $NaHCO_3$ (2 mL) was then added and the aqueous phase was extracted with EtOAc (3 × 5 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/EtOAc: 95/5 to 85/15) to afford the title aldehyde **25** (2.9 mg, 6.3 μmol, 37%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 9.65 (s, 1H), 7.38−7.28 (m, 5H), 5.85 (dd, J = 3.9, 1.5 Hz, 1H), 5.55−5.45 (m, 1H), 5.05 (s, 1H), 4.88 (d, J = 7.2 Hz, 1H), 4.77 (d, J = 7.2 Hz, 1H), 4.66 (d, J = 11.8 Hz, 1H), 4.63 (d, J = 11.8 Hz, 1H), 3.42 (dd, J = 11.8, 3.9 Hz, 1H), 2.66 (d, J = 17.2 Hz, 1H), 2.49 (dd, J = 18.0, 3.1 Hz, 1H), 2.35−2.29 (m, 1H), 2.27−2.19 (m, 1H), 2.07−1.94 (m, 2H), 1.76−1.70 (m, 1H), 1.69 (s, 3H), 1.60 (d, J = 17.2 Hz, 1H), 1.35 (s, 3H), 1.21 (s, 3H), 1.16 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 203.7, 153.7, 137.6, 132.9, 131.3, 128.4, 127.9, 127.7, 124.0, 121.6, 93.6, 88.0, 78.3, 78.2, 70.0, 59.5, 39.6, 39.4, 30.6, 30.1, 25.9, 24.3, 23.7, 21.0, 20.7, 17.9. IR (ν, cm^{-1}): 3049, 2989, 2953, 1801, 1717, 1632, 1446, 1425, 1345, 1267, 1190, 1026. HRMS (ESI/TOF-Q) m/z: [M+Na]$^+$ Calcd for C28H34O6Na 489.2248, found 489.2235. $[\alpha]^{20}_D$: +32.0 (c 0.75, $CHCl_3$).

(1*S*,5*S*,6*S*,8*S*,11*S*,12*S*)-8-(Allyloxy)-1-((benzyloxy)methoxy)-6,11-dihydroxy-9,12,13,13-tetramethyl-1,2,3,5,6,7,8,11,12,12-decahydro-6,10-methanobenzo[10]annulen-5-yl Benzoate (26) and (1*S*,2*S*,3*S*,5*R*,6*R*,8*S*,11*S*)-3-((Benzyloxy)methoxy)-1,8-dihydroxy-2,9,9-trimethyl-10-methylenedecahydro-1H-2,8:6,9-dimethanobenzoazulen-11-yl Benzoate (27). To a solution of vinyl epoxide **24** (13 mg, 24 μmol) in allyl alcohol (0.5 mL) was added $Yb(OTf)_3$ (1.5 mg, 2.4 μmol, 0.1 equiv) The mixture was stirred at room temperature for 16 h. A solution of saturated aqueous $NaHCO_3$ (2 mL) was then added and the aqueous phase was extracted with EtOAc (3 × 5 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (CH_2Cl_2/EtOAc: 95/5) to afford the title alcohol **26** (3.5 mg, 5.8 μmol, 24%) and pentacycle **27** (4.1 mg, 7.4 μmol, 31%) as colorless oils.

(1*S*,5*S*,6*S*,8*S*,11*S*,12*S*)-8-(Allyloxy)-1-((benzyloxy)methoxy)-6,11-dihydroxy-9,12,13,13-tetramethyl-1,2,3,5,6,7,8,11,12,12-decahydro-6,10-methanobenzo[10]annulen-5-yl Benzoate (26). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 8.13−8.08 (m, 2H), 7.63−7.57 (m, 1H), 7.52−7.46 (m, 2H), 7.37−7.32 (m, 4H), 7.32−7.28 (m, 1H), 6.11 (s, 1H), 5.98 (ddt, J = 17.3, 10.5, 5.4 Hz, 1H), 5.68 (t, J = 3.5 Hz, 1H), 5.34 (dq, J = 17.3, 1.5 Hz, 1H), 5.22 (dq, J = 10.5, 1.5 Hz, 1H), 4.85 (d, J = 7.2 Hz, 1H), 4.76 (d, J = 7.2 Hz, 1H), 4.69 (d, J = 11.6 Hz, 1H), 4.62 (d, J = 11.6 Hz, 1H), 4.60−4.56 (m, 2H), 4.14−4.02 (m, 2H), 3.44 (dd, J = 6.8, 3.0 Hz, 1H), 2.81 (dd, J = 13.6, 6.7 Hz, 1H), 2.18−2.06 (m, 1H), 2.00−1.71 (m, 5H), 1.66 (s, 3H), 1.58 (br. s, 1H), 1.55 (dd, J = 13.6, 7.2 Hz, 1H), 1.48 (s, 3H), 1.44 (br. s, 1H), 1.39 (s, 3H), 1.12 (s, 3H). ^{1}H NMR (500 MHz, C_6D_6) δ ppm: 8.25 (dd, J = 1.4, 8.3 Hz, 2H), 7.33−7.25 (m, 3H), 7.10−7.04 (m, 5H), 6.51 (s, 1H), 5.93 (ddt, J = 17.2, 10.4, 5.2 Hz, 1H), 5.71 (t, J = 3.3 Hz, 1H), 5.34 (dq, J = 17.2, 1.8 Hz, 1H), 5.10 (dq, J = 10.4, 1.8 Hz, 1H), 4.65 (d, J = 7.1 Hz, 1H), 4.62 (dd, J = 6.9, 6.5 Hz, 1H), 4.54 (d, J = 7.1 Hz, 1H), 4.53 (d, J = 12.1 Hz, 1H), 4.54−4.50 (m, 1H), 4.47 (d, J = 12.1 Hz, 1H), 4.00 (ddt, J = 13.1, 5.2, 1.8 Hz, 1H), 3.91 (ddt, J = 13.1, 5.2, 1.8 Hz, 1H), 3.40 (dd, J = 7.9, 3.1 Hz, 1H), 2.92 (dd, J = 13.7, 6.9 Hz, 1H), 2.04−1.92 (m, 3H), 1.78 (s, 3H), 1.73−1.66 (m, 2H), 1.65 (s, 3H), 1.61 (dd, J = 13.7, 6.5 Hz, 1H), 1.61−1.57 (m, 1H), 1.46 (s, 3H), 1.35−1.29 (m, 2H), 1.14 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 164.6, 145.6, 141.7, 137.9, 135.4, 133.0, 130.6, 129.5, 128.5, 128.4, 128.1, 127.8, 127.7, 117.3, 116.6, 94.0, 91.2, 84.0, 79.7, 72.3, 70.8, 70.1, 69.9, 65.3, 43.0, 41.5, 32.9, 25.6, 24.8 22.6, 22.2, 21.9, 10.9. HRMS (ESI/TOF-Q) m/z: [M+Na−H_2O]$^+$ Calcd for C37H44O6Na 607.3030, found 607.3020. $[\alpha]^{22}_D$: −36.0 (c 0.5, $CHCl_3$).

(1*S*,2*S*,3*S*,5*R*,6*R*,8*S*,11*S*)-3-((Benzyloxy)methoxy)-1,8-dihydroxy-2,9,9-trimethyl-10-methylenedecahydro-1H-2,8:6,9-dimethanobenzoazulen-11-yl Benzoate (27). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 8.09 (dd, J = 8.3, 1.2 Hz, 2H, ***H*$_{Ar}$**), 7.65−7.59 (m, 1H, ***H*$_{Ar}$**), 7.53−7.46 (m, 2H, ***H*$_{Ar}$**), 7.39−7.34 (m, 4H, ***H*$_{Ar}$**), 7.33−7.29 (m, 1H, ***H*$_{Ar}$**), 6.00 (d, J = 1.7 Hz, 1H, ***H2***), 4.87 (s, 1H, ***H18***), 4.85 (d, J = 7.1 Hz, 1H, ***Ha***), 4.81 (s, 1H, ***H18***), 4.74 (d, J = 7.1 Hz, 1H, ***Ha***), 4.70 (d, J = 12.1 Hz, 1H, ***Hb***), 4.61 (d, J = 12.1 Hz, 1H, ***Hb***), 4.48 (dd, J = 12.0, 6.0 Hz, 1H, ***H10***), 3.29 (dd, J = 11.8, 3.0 Hz, 1H, ***H7***), 2.73 (s, 1H, ***OH***), 2.58 (dd, J = 12.1, 6.9 Hz, 1H, ***H4***), 2.42 (t, J = 2.8 Hz, 1H, ***H13***), 2.27 (dd, J = 12.0, 6.0 Hz, 1H, ***H9***), 1.99 (t, J = 12.0 Hz, 1H, ***H9***), 1.91 (ddd, J = 12.7, 2.8, 1.7 Hz, 1H, ***H14***), 1.81 (dd, J = 12.7, 2.8 Hz, 1H, ***H14***), 1.76−1.66 (m, 2H, ***H5***, ***H6***), 1.55 (s, 3H, ***H17***), 1.37−1.28 (m, 1H, ***H6***), 1.25 (br s, 1H, ***OH***), 1.21−1.14 (m, 1H, ***H5***), 0.99 (s, 3H, ***H16***), 0.99 (s, 3H, ***H19***). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 167.7 (***COPh***), 157.5 (***C12***), 137.9 (***C*$_{Ar}$**), 133.4 (***C*$_{Ar}$**), 129.9 (***C*$_{Ar}$**), 129.7 (***C*$_{Ar}$**), 128.6 (***C*$_{Ar}$**), 128.5 (***C*$_{Ar}$**), 127.7 (***C*$_{Ar}$**), 127.6 (***C*$_{Ar}$**), 103.5 (***C18***), 93.5 (***Ca***), 81.7 (***C7***), 80.5 (***C2***), 80.0 (***C1***), 75.8 (***C10***), 69.6 (***Cb***), 63.6 (***C11***), 62.4 (***C3***), 50.9 (***C15***), 49.6 (***C8***), 45.1 (***C13***), 42.4 (***C9***), 39.0 (***C4***), 35.1 (***C14***), 26.0 (***C5***), 24.9 (***C6***), 21.8 (***C16***), 21.0 (C***17***), 14.8 (***C19***). IR (ν, cm^{-1}): 3321, 3034, 2965, 2929, 1733, 1698, 1565, 1463, 1267, 1113. HRMS (ESI/TOF-Q) m/z: [M+Na]$^+$ Calcd for C34H40O6Na 567.2717, found 567.2706. $[\alpha]^{23}_D$: −38.0 (c 0.5, $CHCl_3$).

(1*R*,3*S*,6*S*,10*S*,10*S*,11*S*)-10-((Benzyloxy)methoxy)-1,10,12,12-tetramethyl-1,2,6,8,10,10,11,11-octahydro-3H,9H-1,3-methanobenzo[3,4]bis(oxireno)[2′,3′:6,7;2″,3″:8,9]cyclodeca-[1,2][1,3]dioxol-5-one (*trans*-28) and (*cis*-28). To a solution of triene **19f** (50 mg, 0.11 mmol) in CH_2Cl_2 (3 mL) was added at 0 °C a solution of *m*CPBA (76 mg, 0.33 mmol, 3.0 equiv) in CH_2Cl_2 (1 mL). The resulting mixture was stirred at room temperature for 16 h. The reaction mixture was washed with a 10% aqueous solution of Na_2SO_3 (2 × 2 mL) and the aqueous layer was extracted with CH_2Cl_2 (10 mL). The combined organic extracts were washed with a saturated aqueous solution of $NaHCO_3$ (10 mL) washed with brine (10 mL) and dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 6/4) to afford the title epoxide *trans*-**28** (37 mg, 77 μmol, 70%) and the epoxide *cis*-**28** (3.2 mg, 6.6 μmol, 6%) as colorless oils.

(1*R*,1*S*,2*S*,3*S*,6*S*,10*S*,10*S*,11*S*)-10-((Benzyloxy)methoxy)-1b,10,12,12-tetramethyl-1b,2,6,8,10,10,11,11-octahydro-3H,9H-1,3-methanobenzo[3,4]bis(oxireno)[2′,3′:6,7;2″,3″:8,9]-cyclodeca[1,2][1,3]dioxol-5-one (*trans*-28). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 7.40−7.34 (m, 4H), 7.33−7.28 (m, 1H), 6.04 (dd, J = 4.9, 2.5 Hz, 1H), 4.97 (s, 1H), 4.96 (d, J = 7.1 Hz, 1H), 4.83 (d, J = 7.1 Hz, 1H), 4.74 (d, J = 11.6 Hz, 1H), 4.65 (d, J = 11.6 Hz, 1H), 4.03 (dd, J = 12.1, 3.9 Hz, 1H), 3.26 (d, J = 4.8 Hz, 1H), 3.05 (dd, J = 12.5, 4.1 Hz, 1H), 3.04 (d, J = 16.6 Hz, 1H), 2.66 (dd, J = 14.7, 4.1 Hz, 1H), 2.36−2.21 (m, 2H), 2.12 (dd, J = 16.6, 4.8 Hz, 1H), 2.06−1.99 (m, 1H), 1.77 (qd, J = 12.1, 6.9 Hz, 1H), 1.38 (s, 3H), 1.37 (m, J = 14.7, 12.5 Hz, 1H), 1.19 (s, 6H), 1.16 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 153.4, 137.6, 132.4, 130.8, 128.5, 127.8, 127.8, 93.4, 91.4, 78.6, 75.1, 70.2, 65.1, 60.4, 60.1, 59.3, 42.8, 39.7, 30.8, 28.4, 24.0, 23.5, 23.4, 22.8, 19.0, 16.7. IR (ν, cm^{-1}): 3049, 2987, 2958, 1801, 1684, 1543, 1400, 1214, 1093. HRMS (CI/ISO) m/z: [M+H]$^+$ Calcd

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for C28H35O7 483.2383, found 483.2379. $[\alpha]^{21}_{D}$: + 70.0 (*c* 1.0, $CHCl_3$).

(1*R*,1*R*,2*R*,3*S*,6*S*,10*S*,10*S*,11*S*)-10-((Benzyloxy)methoxy)-1,10,12,12-tetramethyl-1,2,6,8,10,10,11,11-octahydro-3H,9H-1,3-methanobenzo [3,4]bis(oxireno)[2′,3′:6,7;2″,3″:8,9]cyclodeca[1,2][1,3]dioxol-5-one (*cis*-28). ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 7.37−7.34 (m, 4H), 7.32−7.28 (m, 1H), 5.76 (t, *J* = 3.5 Hz, 1H), 5.09 (s, 1H), 4.93 (d, *J* = 7.0 Hz, 1H), 4.83 (d, *J* = 7.0 Hz, 1H), 4.74 (d, *J* = 11.8 Hz, 1H), 4.67 (d, *J* = 11.8 Hz, 1H), 3.80 (dd, *J* = 11.9, 4.5 Hz, 1H), 3.48 (d, *J* = 3.4 Hz, 1H), 2.96 (dd, *J* = 7.8, 6.5 Hz, 1H), 2.76 (dd, *J* = 15.2, 6.5 Hz, 1H), 2.38 (d, *J* = 15.4 Hz, 1H), 2.36−2.31 (m, 2H), 2.07 (dd, *J* = 15.4, 3.4 Hz, 1H), 2.07−2.01 (m, 1H), 1.85−1.74 (m, 1H), 1.71 (s, 3H), 1.53 (s, 3H), 1.11 (dd, *J* = 15.2, 7.8, 1H), 1.08 (s, 3H), 1.02 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 149.3, 137.6, 134.4, 128.5, 127.8, 127.6, 126.8, 93.5, 87.5, 75.7, 73.4, 70.0, 68.2, 64.3, 62.4, 55.5, 55.2, 42.6, 33.7, 28.4, 26.4, 24.8, 23.3, 23.1, 22.9, 12.5. HRMS (EI) *m*/*z*: $[M]^+$ Calcd for C28H34O7 482.2305, found 482.2307. $[\alpha]^{25}_{D}$: + 59.0 (*c* 0.75, $CHCl_3$).

(3*S*,5*S*,8*S*,9*S*,10*S*,13*S*)-10-((Benzyloxy)methoxy)-5,8-dihydroxy-6,9,14,14-tetramethyl-5,8,9,9,10,11,12,13b-octahydro-4H-3,7-methanobenzo[3,4]cyclodeca[1,2][1,3]dioxol-2-one (29). Zinc dust (0.20 g, 3.0 mmol) was added to a solution of Cp_2TiCl_2 (0.25 g, 1.0 mmol) in anhydrous and degassed THF (2.5 mL). The suspension was vigorously stirred for 2 h. The freshly made green solution of $[Cp_2TiCl]_2$ (0.83 mL, 0.2 M in THF, 0.16 mmol, 5 equiv) was added to a solution of diepoxide *trans*-**28** (16 mg, 33 μmol) in THF (1.5 mL). The resulting mixture was stirred at reflux for 16 h. A 1N aqueous solution of HCl (5 mL) was added and the resulting mixture was stirred for 5 min. The aqueous layer was extracted with EtOAc (3 × 10 mL), drier over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/EtOAc: 3/7) to afford the title 1,4-diol **29** (3 mg, 6.3 μmol, 19%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 7.42−7.35 (m, 4H), 7.34−7.29 (m, 1H), 5.65 (t, *J* = 3.3 Hz, 1H), 5.47 (s, 1H), 4.91 (d, *J* = 7.3 Hz, 1H), 4.79 (d, *J* = 7.3 Hz, 1H), 4.78 (d, *J* = 11.9 Hz, 1H), 4.66 (d, *J* = 11.9 Hz, 1H), 4.67−4.63 (m, 1H), 4.59 (dd, *J* = 11.6, 6.1 Hz, 1H), 3.41 (dd, *J* = 11.8, 4.6 Hz, 1H), 2.32 (dd, *J* = 14.6, 6.1 Hz, 1H), 2.35−2.27 (m, 1H), 2.24 (dd, *J* = 13.3, 6.5 Hz, 1H), 2.25−2.15 (m, 1H), 1.98−1.94 (m, 1H), 1.83−1.78 (m, 1H), 1.79 (s, 3H), 1.78 (dd, *J* = 13.3, 7.8 Hz, 1H), 1.68 (dd, *J* = 14.6, 11.6 Hz, 1H), 1.61 (s, 3H), 1.43 (s, 1H), 1.32 (s, 3H), 1.15 (s, 3H), 1.11 (br s, 1H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 150.5, 150.4, 137.9, 135.2, 135.2, 128.5, 127.9, 127.2, 123.2, 93.3, 92.1, 76.1, 75.3, 73.8, 70.0, 63.5, 59.9, 39.9, 39.3, 37.2, 26.9, 25.4, 24.2, 23.1, 22.8, 11.5. IR (ν, cm^{-1}): 3366, 3054, 2986, 2927, 1744, 1543, 1427, 1280. HRMS (ESI/TOF-Q) *m*/*z*: $[M+Na]^+$ Calcd for C28H36O7Na 507.2353, found 507.2332. $[\alpha]^{21}_{D}$: +43.0 (*c* 0.75, $CHCl_3$).

(1*R*,1*S*,2*S*,4*S*,5*S*,9*S*,9*S*,10*S*)-9-((Benzyloxy)methoxy)-4-hydroxy-1,9,11,11-tetramethyl-1,2,4,5,7,8,9,9,10,10-decahydro-3H-1,4-methanobenzo[6,7]cyclodeca[1,2:3,4]bis(oxirene)-5-yl Benzoate (30). To a solution of diepoxide *trans*-**28** (25 mg, 51 μmol) in THF (2.5 mL) at −78 °C was added phenyllithium (0.22 mL, 2 M in nBu_2O, 0.45 mmol, 9.0 equiv). The mixture was stirred at this temperature for 2 h. A solution of saturated aqueous $NaHCO_3$ (2 mL) was then added and the aqueous phase was extracted with Et_2O (3 × 5 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 7/3) to afford the title benzoate **30** (23 mg, 41 μmol, 80%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 8.08−8.02 (m, 2H), 7.64−7.57 (m, 1H), 7.52−7.44 (m, 2H), 7.40−7.35 (m, 4H), 7.33−7.28 (m, 1H), 6.13 (dd, *J* = 5.5, 2.5 Hz, 1H), 5.75 (s, 1H), 4.95 (d, *J* = 7.1 Hz, 1H), 4.83 (d, *J* = 7.1 Hz, 1H), 4.75 (d, *J* = 11.7 Hz, 1H), 4.66 (d, *J* = 11.7 Hz, 1H), 3.96 (dd, *J* = 11.4, 3.4 Hz, 1H), 3.22 (d, *J* = 4.6 Hz, 1H), 3.14 (dd, *J* = 12.0, 4.1 Hz, 1H), 3.12 (d, *J* = 16.6 Hz, 1H), 2.48 (dd, *J* = 14.4, 4.1 Hz, 1H), 2.34 (s, 1H), 2.26−2.13 (m, 2H), 2.01 (dd, *J* = 16.6, 4.6 Hz, 1H), 1.89 (ddt, *J* = 11.4, 5.6, 2.8 Hz, 1H), 1.70−1.60 (m, 1H), 1.64 (dd, *J* = 14.4, 12.0 Hz, 1H), 1.31 (s, 3H), 1.26 (s, 3H), 1.21 (s, 6H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 165.4, 138.0, 137.7, 133.2, 131.1, 130.2, 129.7, 128.5, 128.5, 127.9, 127.7, 93.6, 79.8, 77.6, 74.4, 70.1, 64.3, 61.1, 60.2, 59.9, 42.9, 41.4, 31.5, 31.3, 24.2, 23.6, 23.0, 22.6, 19.2, 17.7. IR (ν, cm^{-1}): 3054, 2986, 1717, 1520, 1421, 1265, 1020. HRMS (ESI/TOF-Q) *m*/*z*: $[M+Na]^+$ Calcd for C34H40O7Na 583.2666, found 583.2652. $[\alpha]^{25}_{D}$: +28.0 (*c* 1.0, $CHCl_3$).

(1*S*,5*S*,6*S*,8*S*,11*S*,12*S*)-1-((Benzyloxy)methoxy)-6,8,11-trihydroxy-9,12,13,13-tetramethyl-1,2,3,5,6,7,8,11,12,12-decahydro-6,10-methanobenzo[10]annulen-5-yl Benzoate (31). Zinc dust (0.20 g, 3.0 mmol) was added to a solution of Cp_2TiCl_2 (0.25 g, 1.0 mmol) in anhydrous and degassed THF (2.5 mL). The suspension was vigorously stirred for 2 h. The freshly made green solution of $[Cp_2TiCl]_2$ (0.93 mL, 0.2 M in THF, 0.19 mmol, 5.0 equiv) was added to a solution of diepoxide **30** (21 mg, 37 μmol) in THF (1.5 mL). The resulting mixture was stirred at room temperature for 4 h. A 1N aqueous solution of HCl (5 mL) was added and the resulting mixture was stirred for 5 min. The aqueous layer was extracted with EtOAc (3 × 10 mL), drier over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/EtOAc: 3/7) to afford the title 1,4-diol **31** (11 mg, 20 μmol, 53%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 8.09−8.03 (m, 2H), 7.62−7.56 (m, 1H), 7.50−7.44 (m, 2H), 7.44−7.36 (m, 4H), 7.34−7.28 (m, 1H), 5.90 (dd, *J* = 4.9, 2.5 Hz, 1H), 5.70 (s, 1H), 5.08 (dd, *J* = 11.8, 5.2 Hz, 1H), 4.98 (d, *J* = 7.3 Hz, 1H), 4.87 (d, *J* = 12.2 Hz, 1H), 4.82 (d, *J* = 7.3 Hz, 1H), 4.68 (d, *J* = 12.2 Hz, 1H), 4.61−4.53 (m, 1H), 3.86 (dd, *J* = 12.2, 3.9 Hz, 1H), 2.50−2.46 (m, 2H), 2.36 (dd, *J* = 14.5, 5.2 Hz, 1H), 2.28 (s, 1H), 2.23−2.15 (m, 2H), 2.14−2.09 (m, 2H), 1.96−1.89 (m, 1H), 1.84 (d, *J* = 1.1 Hz, 3H), 1.70−1.63 (m, 1H), 1.65 (s, 3H), 1.57 (br s, 1H), 1.17 (s, 3H), 1.07 (s, 3H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 165.5, 144.8, 138.0, 137.1, 136.3, 133.1, 130.3, 129.7, 128.5, 128.5, 127.7, 127.2, 123.4, 93.1, 79.3, 75.5, 74.1, 70.0, 69.2, 67.7, 42.6, 41.4, 38.5, 38.2, 28.2, 24.2, 23.9, 22.8, 19.9, 16.8. HRMS (ESI/TOF-Q) *m*/*z*: $[M+Na]^+$ Calcd for C34H42O7Na 585.2823, found 585.2808. $[\alpha]^{21}_{D}$: +60.0 (*c* 1.0, $CHCl_3$).

(1*S*,5*S*,6*S*,8*S*,11*S*,12*S*)-1-((Benzyloxy)methoxy)-6,8-dihydroxy-9,12,13,13-tetramethyl-11-((triethylsilyl)oxy)-1,2,3,5,6,7,8,11,12,12-decahydro-6,10-methanobenzo[10]-annulen-5-yl Benzoate (32). To a solution of diol **31** (6.7 mg, 12 μmol) in CH_2Cl_2 (1 mL) were added imidazole (8.2 mg, 0.12 mmol, 10 equiv) and TESCl (10 μL, 60 μmol, 5 equiv). The reaction mixture was stirred for 16 h. A saturated aqueous solution of $NaHCO_3$ (1 mL) was added to quench the reaction. The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography (petroleum ether/Et_2O: 65/35) to afford the title mono protected alcohol **32** (5.5 mg, 8.2 μmol, 68%) as a colorless oil.^{1}H NMR (500 MHz, $CDCL_3$) δ ppm: 8.08−8.04 (m, 2H), 7.61−7.54 (m, 1H), 7.50−7.44 (m, 2H), 7.39−7.34 (m, 4H), 7.33−7.28 (m, 1H), 5.88 (dd, *J* = 5.8, 2.3 Hz, 1H), 5.72 (s, 1H), 4.99 (d, *J* = 6.7 Hz, 1H), 4.96 (dd, *J* = 11.4, 5.7 Hz, 1H), 4.90 (d, *J* = 6.7 Hz, 1H), 4.79 (d, *J* = 11.8 Hz, 1H), 4.59−4.54 (m, 1H), 4.53 (d, *J* = 11.8 Hz, 1H), 3.75 (dd, *J* = 12.2, 4.0 Hz, 1H), 2.48 (d, *J* = 6.7 Hz, 2H), 2.27−2.18 (m, 1H), 2.23 (dd, *J* = 15.0, 5.7 Hz, 1H), 2.17−2.09 (m, 3H), 2.08 (s, 1H), 1.86 (d, *J* = 1.0 Hz, 3H), 1.81−1.71 (m, 1H), 1.69 (s, 3H), 1.54 (br s, 1H), 1.14 (s, 3H), 1.07 (s, 3H), 0.97 (t, *J* = 8.0 Hz, 9H), 0.60 (d, *J* = 8.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCL_3$) δ ppm: 165.6, 145.2, 137.8, 136.9, 134.9, 133.1, 130.4, 129.7, 128.5, 128.5, 127.8, 127.7, 122.9, 95.8, 79.4, 78.9, 74.1, 69.6, 69.2, 68.0, 42.8, 41.5, 39.4, 38.5, 27.9, 24.5, 24.4, 23.9, 19.7, 16.8, 6.9, 4.9. IR (ν, cm^{-1}): 3421, 3049, 2984, 2961, 2882, 1717, 1675, 1430, 1409, 1206, 1095, 1005. HRMS (ESI/TOF-Q) *m*/*z*: $[M+Na]^+$ Calcd for C40H56O7SiNa 699.3688, found 699.3653. $[\alpha]^{26}_{D}$: +10.0 (*c* 0.75, $CHCl_3$).

■ ASSOCIATED CONTENT

Supporting Information

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^{1}H and ^{13}C NMR spectra for all new compounds, and X-ray structure and crystal data and structure refinement for compound **16** (PDF)
X-ray crystallographic data of compound **16** (CIF)

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Notes

The authors declare no competing financial interest.

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