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Ring-Closing Metathesis in the Synthesis of BC Ring-Systems of Taxol

Cong Ma,[a] Stéphanie Schiltz,[a] Xavier F. Le Goff,[b] and Joëlle Prunet*[a]

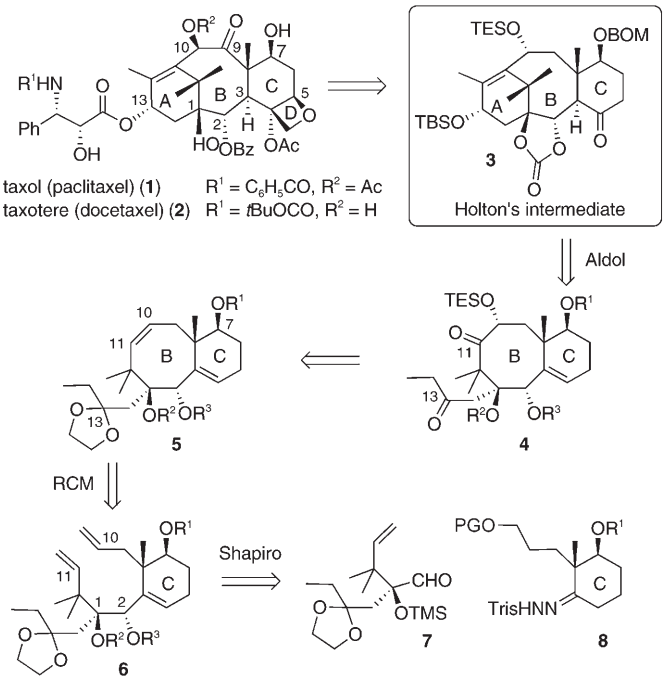
Abstract: BC ring-systems of taxol with different or no protecting group for the C1,C2-diol moiety have been efficiently synthesized. The eight-membered B ring is formed by a ring-closing metathesis reaction (RCM) between the C10 and C11 carbon atoms. The influence of the 1,2-diol protecting group on the RCM reaction has been studied in detail.

Keywords: metathesis · organic chemistry · ruthenium · synthesis · taxol

Introduction

Taxol (**1**) and Taxotere (**2**) are very effective agents for the treatment of breast and ovarian cancer worldwide.[1] In spite of numerous synthetic approaches, including six total syntheses,[2] they still constitute a remarkable challenge for organic chemists because of their sterically hindered and highly functionalized structures.

Ring-closing metathesis (RCM) has been shown to be a very versatile and efficient tool for the synthesis of natural products.[3] During our previous studies towards the synthesis of taxol, we observed the first formation of a *trans* cyclooctene by RCM, which closed the B-ring between C9 and C10.[4] We then envisioned a semiconvergent retrosynthesis of compound **3**, which is an intermediate described by Holton in his synthesis of taxol (Scheme 1). The A ring would be formed at a late stage by performing an intramolecular aldol reaction between the two ketone groups at C11 and C13 in compound **4**.[5] The B ring of **5** would be formed by ring-closing metathesis between the two alkenes at C10 and C11. The metathesis precursor **6** would be prepared by a Shapiro reaction between the lithium derivative of hydrazone **8** and aldehyde **7**. Here, we wish to report the synthesis of models of compound **5**, with no alkoxy group at C7 and no ketal function at C13. In addition to our preliminary study,[6] the influence of the group protecting the C1,C2-diol moiety has been thoroughly studied.



Scheme 1. Retrosynthesis of taxol.

Results and Discussion

Aldehyde **9** was prepared as a racemic mixture, according to our previous work.[6] Ketone **10** was synthesized in an excel-

[a] C. Ma, Dr. S. Schiltz, Dr. J. Prunet
Laboratoire de Synthèse Organique
CNRS UMR 7652, École Polytechnique, DCSO
91128 Palaiseau Cedex (France)
Fax: (+33) 169-335-972
E-mail: joelle.prunet@polytechnique.fr

[b] Dr. X. F. Le Goff
Laboratoire Hététoéléments et Coordination
CNRS UMR 7653, École Polytechnique, DCPH
91128 Palaiseau Cedex, (France)

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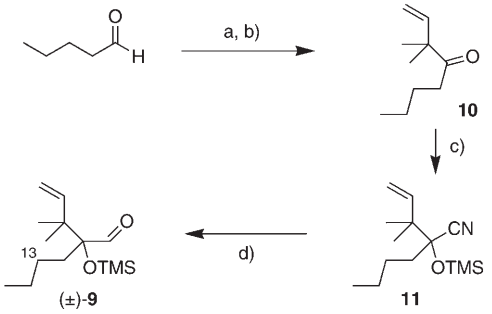
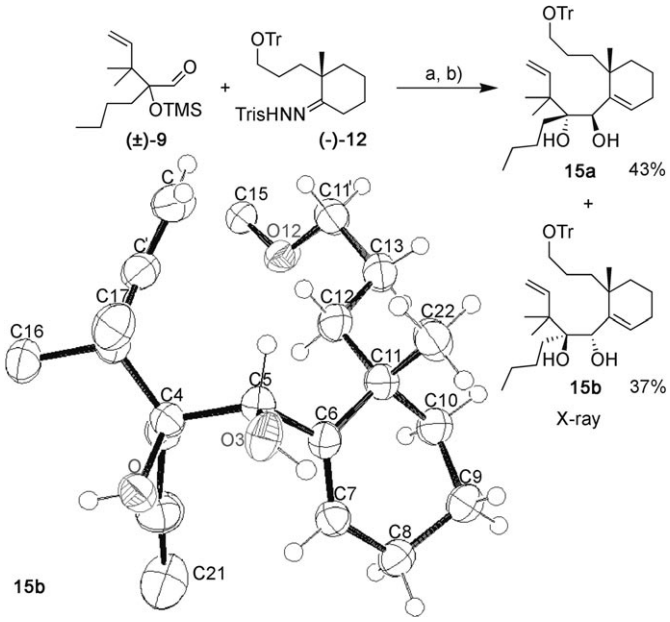
lent overall yield by a Barbier reaction between prenyl bromide and valeraldehyde,[7] followed by oxidation of the resulting alcohol with iodoxybenzoic acid.[8] Transformation of this ketone to aldehyde **9** was effected by conversion to cyanohydrin **11** with trimethylsilyl cyanide in the presence of ZnI_2, and reduction of the latter by DIBAL-H (Scheme 2).[9]

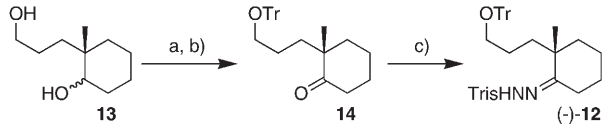


Scheme 2. Synthesis of racemic aldehyde **9**: a) Prenyl bromide, Zn, aq. NH_4Cl, THF, 20 °C; b) IBX, THF, 20 °C, 98 % over 2 steps; c) TMSCN, ZnI_2, CH_2Cl_2, reflux, 97 %; d) DIBAL-H, CH_2Cl_2, −78–0 °C; silica gel, −20 °C, 85 %. IBX = iodoxybenzoic acid, TMSCN = trimethylsilyl cyanide, DIBAL-H = diisobutyl aluminum hydride.



Scheme 4. Diastereoselective Shapiro coupling reaction. a) *t*BuLi, THF, −78 °C; b) HCl (1 N), 20 °C, 43 % for **15a**, 37 % for **15b**, respectively.

As shown in Scheme 3, the synthesis of optically active hydrazone **12** began with known diol **13**,[10] which could be synthesized according to d'Angelo's method.[11] Protection



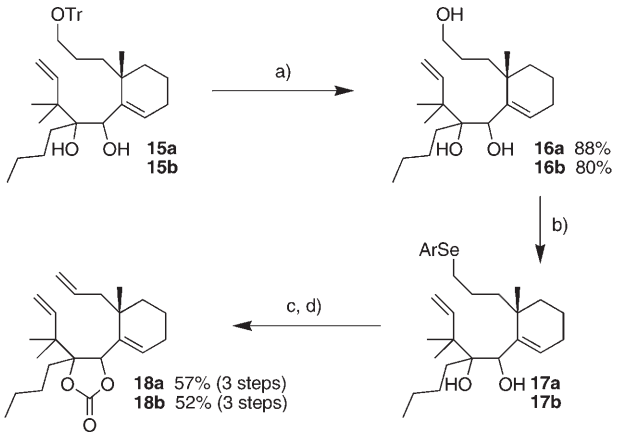
Scheme 3. Synthesis of enantiopure hydrazone (−)-**12**: a) DMAP·TrCl, CH_2Cl_2, reflux; IBX, THF, 20 °C, 77 % over 2 steps; b) $TrisNHNH_2$, concd HCl, THF, 20 °C, 96 %. DMAP = 4-dimethylaminopyridine, Tr = trityl, Tris = triisopropylbenzenesulfonyl.

of the primary alcohol of compound **13** as its trityl ether, followed by oxidation of the secondary alcohol provided ketone **14**, which was efficiently converted to hydrazone **12** with trisyl hydrazine under acidic conditions.

The Shapiro coupling reaction of racemic aldehyde **9** and enantiopure hydrazone **12** was then studied. Although *n*BuLi is a common choice for the base employed in the Shapiro reaction, use of *t*BuLi was proven necessary in our case. An unsuccessful trial with MeLi confirmed the impact of the pK_a of the base on our Shapiro coupling. The desired product was obtained as a mixture of two diastereomers. Deprotection of the tertiary hydroxy site by removal of the TMS group was then immediately performed to provide diols **15a** and **15b**, which were easily separated by column chromatography in very good yield (Scheme 4).

In our preliminary study,[6] ketone **14** was converted into the corresponding vinyl bromide in three steps, and the coupling reaction effected by lithium–halogen exchange to form the required vinyl lithium intermediate. Diols **15a** and **15b** were produced in 71 % combined yield after hydrolysis of the TMS ether. The present route saves two steps, and the Shapiro coupling, although a delicate reaction to perform, leads to the desired diols in a high yield (80 %).

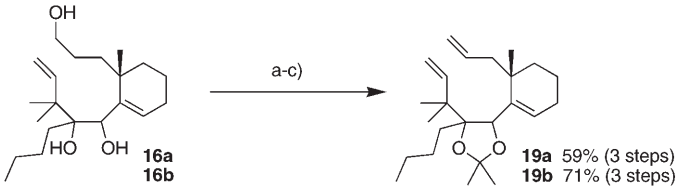
The coupling reaction is very diastereoselective in favor of the *trans* diols (two isomers are obtained because the aldehyde **9** is racemic).[12] This high diastereoselectivity had already been obtained for similar coupling reactions realized during previous studies on taxol precursors in our laboratory (Scheme 4).[13] The structure of diol **15b** was determined by X-ray analysis;[6] this diastereomer possesses the configuration found in taxol at the C1, C2, and C8 stereocenter. The structure of compound **15a** was secured by X-ray analysis of its triol derivative **16a** (Scheme 5).[6]



Scheme 5. Synthesis of metathesis precursors, carbonates **18a** and **18b**: a) Amberlyst H-15, MeOH, 20 °C; b) PBu_3, *o*-nitrophenylselenocyanate, THF, 20 °C; c) carbonyl diimidazole, toluene, reflux; d) H_2O_2, THF, 20 °C.

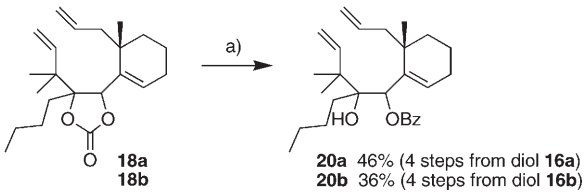
Both isomers **15a** and **15b** were converted to substrates for the metathesis reaction, to evaluate the influence of the relative stereochemistry of the diol motif and the C8 stereocenter on the metathesis reaction. All the following reactions have been performed on the two diastereomers separately. The primary trityloxy group had to be converted into a terminal olefin. For this purpose, triols **16a** and **16b** were first obtained by treatment of **15a** and **15b** with Amberlyst-15 resin in methanol (Scheme 5). The terminal olefin was then obtained by using Grieco's method: after selective transformation of the primary alcohol into the corresponding selenide (which also served as a temporary protecting group), diols **17a** and **17b** were protected as their carbonate derivatives, and final treatment with H_2O_2 led to the metathesis precursors **18a** and **18b**. The three steps (from the triols) were performed without any intermediate purification. This sequence is slightly more efficient than the one we previously used (protection of the diol as the carbonate, hydrolysis of the trityl group, and elimination of the alcohol with Grieco's procedure).[6]

Metathesis precursors **19a** and **19b**, in which the diol moiety is protected as an acetonide were also synthesized (Scheme 6). Treatment of triols **16a** and **16b** with 2,2-dimethoxypropane and CSA furnished the corresponding acetonides, then Grieco's method afforded the desired products **19a** and **19b** in good overall yields. Once again, no intermediate purification was necessary.



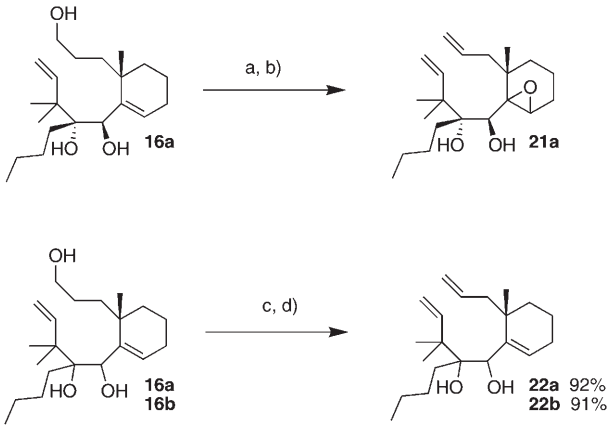
Scheme 6. Synthesis of metathesis precursors, acetonides **19a** and **19b**: a) 2,2-Dimethoxypropane, CSA, 20 °C; b) PBu_3, *o*-nitrophenylselenocyanate, THF, 20 °C; c) H_2O_2, THF, 20 °C. CSA = camphor-10-sulfonic acid.

Besides the two precursors **18** and **19**, which possess a five-membered protecting group for the C1,C2- diol, we decided to prepare two other types of precursors, in which the diol moiety was monoprotected or not protected at all, to test the influence of the conformation of the dienes on the ring-closing metathesis reaction. Simple treatment of dienes **18a** and **18b** with PhLi provided ring-opened products **20a** and **20b**, respectively (Scheme 7).



Scheme 7. Synthesis of metathesis precursors **20a** and **20b**: a) PhLi, THF, −78 °C.

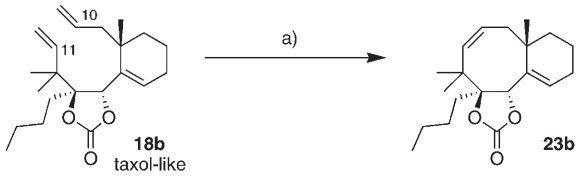
As shown in Scheme 8, direct transformation of triol **16a** into the corresponding diene by Grieco's method led to the corresponding epoxide product **21a** in modest yield, along with decomposition products. However, use of ammonium molybdate tetrahydrate in H_2O_2 at −10 °C for 5 min for the oxidation step afforded the desired dienes **22a** and **22b** in excellent yields.



Scheme 8. Synthesis of metathesis precursors **22a** and **22b**: a) PBu_3, *o*-nitrophenylselenocyanate, THF, 20 °C; b) H_2O_2, THF, 20 °C, 20 %; c) PBu_3, *o*-nitrophenylselenocyanate, THF, 20 °C; d) H_2O_2, $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$, THF, −10 °C.

The ring-closing metathesis experiments were first performed with the carbonate substrates. Diastereomer **18a**, which possesses the wrong stereochemistry for taxol at C1 and C2, did not furnish any cyclized product, either with Grubbs first- (Grubbs 1)[14] or second-generation (Grubbs 2)[15] catalysts in 1,2-dichloroethane at reflux. Longer reaction time (several days) with the latter complex only resulted in decomposition. However, when the other diastereomer **18b** was exposed to 30 mol % of Grubbs 1 catalyst, the corresponding cyclooctene **23b** was obtained in 65 % yield as the *Z* isomer exclusively after several days at ambient temperature (Table 1). No *trans* cyclooctene was detected, contrary to our previous study in which the metathesis closed the B ring between C9 and C10.[4a] Use of second-generation

Table 1. Metathesis of carbonates **18b**.[a]

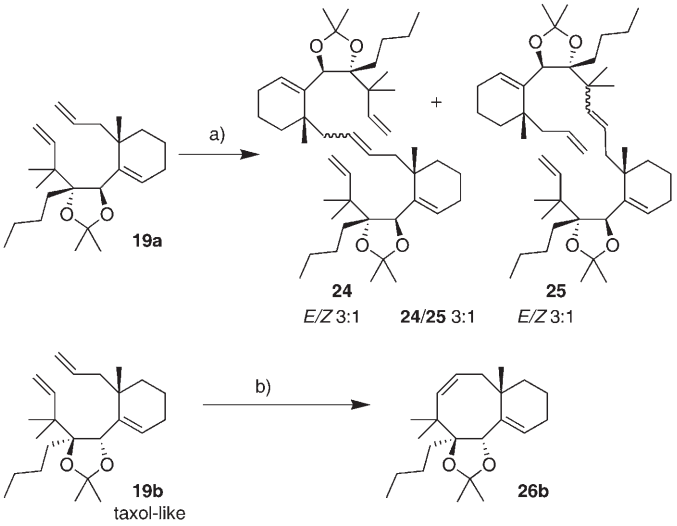


Catalyst ([mol %])	*T* [°C]	*t*	Yield [%]
Grubbs 1 (30)	20	5 d[b]	65
Grubbs 2 (10)	80	1 h	69
[RulMes] (5)	80	1 h	72

[a] Reaction conditions: a) catalyst, 1,2-dichloroethane. [b] The reaction was started with 10 mol % Grubbs 1, and 5 mol % additional catalyst was added every day.

catalysts Grubbs 2 or [RuIMes][16] also led to **23b** in a comparable yield (69 and 72%, respectively), but the reaction was complete in only 1 h.

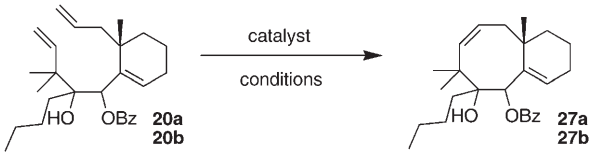
The acetonide derivatives were then subjected to Grubbs 2 catalyst. After 30 min in CH_2Cl_2 at reflux, diastereomer **19a** only led to dimeric products **24** and **25** in a 3:1 ratio, favoring the head-to-head dimer (Scheme 9). This result confirmed that the less-hindered C10 olefin is the site of initial carbene formation. A prolonged reaction time did not show a significant effect. Cyclization of the other diastereomer **19b** was exceptionally rapid, and bicycle **26b** was obtained in quantitative yield after only 5 min in 1,2-dichloroethane at reflux.



Scheme 9. Metathesis of acetonides **19a** and **19b**: a) 5 mol% Grubbs 2, CH_2Cl_2, reflux, 87% for the mixture of **24** and **25**; b) 5 mol% Grubbs 2, 1,2-dichloroethane, reflux, quant.

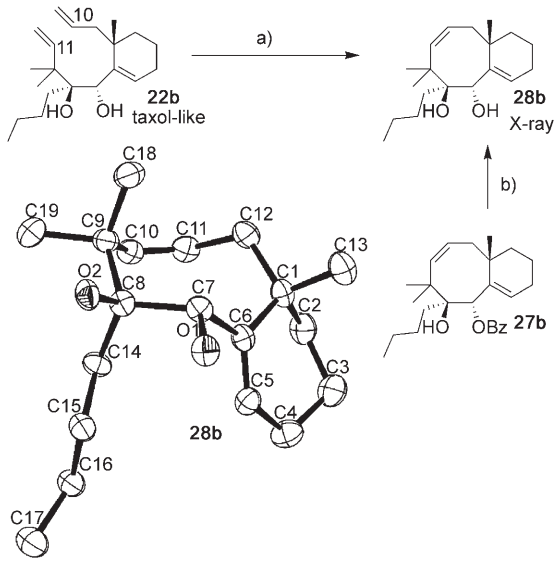
Our attempt at the ring-closing reaction with dienes **20a** and **20b** showed an interesting conformation/reactivity relationship. Treatment of benzoate **20a** (wrong diastereomer) with both Grubbs 1 and 2 catalysts provided the desired cyclized product (Table 2). These results tend to prove that the cyclic protecting groups lock the metathesis precursors in an unfavorable conformation for cyclization of the wrong diastereomer. Heating **20a** with Grubbs 1 in 1,2-dichloroethane at reflux for 36 h or with Grubbs 2 in dichloromethane at reflux for 18 h furnished the same cyclooctene **27a** in 71 and 84% yield, respectively. No product was observed at a lower temperature. Diastereomer **20b** (the desired diastereomer), when reacted with Grubbs 1 and 2, also afforded the corresponding cyclooctene **27b**, but the reaction conditions were milder. Bicycle **27b** was obtained in 78% yield by treatment with Grubbs 1 at 40°C and in quantitative yield by treatment with Grubbs 2 at ambient temperature after only 15 min (Table 2).

Table 2. Metathesis of monoprotected benzoates **20a** and **20b**.



Isomer series	Catalyst ([mol%])	T [°C]	t	Yield [%]
a	Grubbs 1 (5)	80	36 h	71
	Grubbs 2 (5)	40	18 h	84
b	Grubbs 1 (5)	40	12 h	78
	Grubbs 2 (5)	20	15 min	quant.

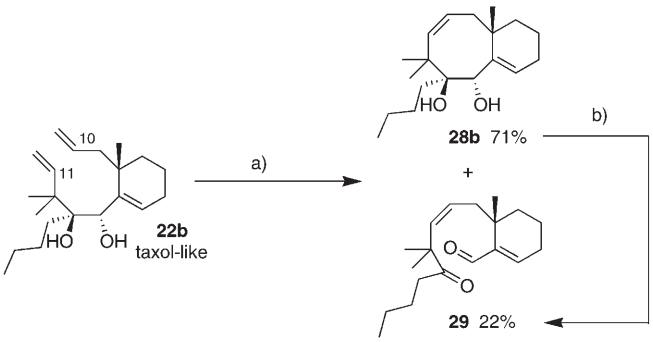
Finally, diols **22a** and **22b** were exposed to the different Grubbs catalysts. Unfortunately diol **22a** (the wrong diastereomer) only led to decomposition. However, diastereomer **22b** (the desired diastereomer) was successfully converted into the corresponding cyclooctene **28b** as colorless needle crystals in quantitative yield after 1 h in dichloromethane at reflux (Scheme 10). The structure of this cyclooctene was confirmed by X-ray analysis.[17] The decomposition or low reactivity[18] or occasional loss of methylene[19] in ring-closing metathesis reactions in the presence of a diol were not observed in our case.



Scheme 10. Metathesis of diol **22b**: a) 5 mol% Grubbs 2, CH_2Cl_2, reflux, quant.; b) $LiAlH_4$, THF, 0°C, 83%.

The ^{1}H NMR spectrum of cyclooctene **27b** exhibits a broadening of signals for the protons at C4 and C10, which is probably due to the presence of rotamers induced by the benzoate group. The expected NMR spectrum could be observed by heating **27b** at 65°C in deuterated DMSO. This compound was also correlated to cyclic diol **28b** by reduction of the benzoate ester with $LiAlH_4$ (Scheme 10).

An unusual oxidative fragmentation of the 1,2-diol moiety was observed in our attempt to form bicycle **28b** from unpurified diol **22b**. As shown in Scheme 11, the metathesis reaction on unpurified diol **22b** led to the desired cyclized product **28b** in 71% yield, along with keto aldehyde **29** in



Scheme 11. Oxidative cleavage of diol **22b** catalyzed by Grubbs 2 catalyst: a) 5 mol% Grubbs 2, *o*-nitrophenylselenocyanate (residue), CH_2Cl_2, reflux, 71% for **28b**, 22% for **29**, respectively; b) 5 mol% Grubbs 2, benzeneseleninic acid, CH_2Cl_2, reflux, 67%.

22% yield. We assumed that this oxidative cleavage was mediated by a high oxidation state ruthenium complex derived from the Grubbs 2 catalyst and the residual *o*-nitrophenyl seleninic acid from the Grieco reaction, which is the only oxidant present in the reaction.[20] To check this hypothesis, reaction of diol **28b** with Grubbs 2 catalyst was then carried out in the presence of stoichiometric phenyl seleninic acid, and the oxidized product **29** was obtained in 67% yield (Scheme 11).[21]

Finally, molecular modeling has been performed to try to explain the difference in behavior between the two diastereomers of the metathesis precursors bearing a cycling protecting group for the diol moiety. Systematic energy minimization experiments[22] led to the preferred conformations of carbonates **18a** and **18b** (Figure 1). Comparison between the C10–C11 distances in both diastereomers clearly shows that cyclization should be favored in the case of **18b**.

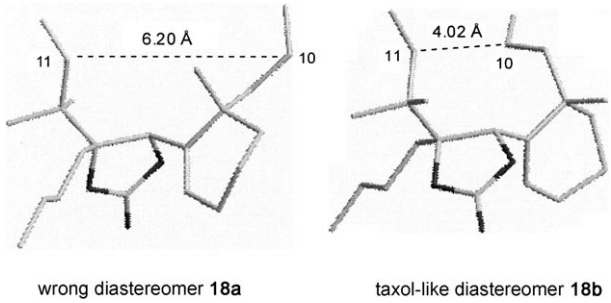


Figure 1. Conformations of carbonates **18a** and **18b**.

Conclusion

We have synthesized highly functionalized cyclooctenes by using a ring-closing metathesis reaction at C10–C11 to form the B ring. This key step was highly efficient for the diasteromer possessing the desired configuration for the C1 and C2 stereocenters of taxol, regardless of the diol protecting group. We even performed the RCM reaction on the unprotected diol in an excellent yield. On the other hand, the cyclic protecting groups, such as a carbonate or an acetonide, seem to lock the undesired diastereomer in a conformation which is unfavorable for cyclization, and only the monobenzoate **20a** is a good substrate for metathesis.

These results are in sharp contrast with those observed in our previous route involving a metathesis to close the B-ring between the C9 and the C10 carbon atom.[4] In this case, the cyclic protecting groups were mandatory for both diastereomers to obtain good yields in the RCM step.

We are currently synthesizing metathesis precursors with all the functionalities required for the ABC tricyclic core of taxol.

Experimental Section

Materials and methods: All solvents were reagent grade. Diethyl ether (Et_2O) and THF were freshly distilled from sodium/benzophenone under nitrogen. Dichloromethane, DMSO, toluene, and 1,2-dichloroethane were freshly distilled from calcium hydride. All reagents were purchased from commercial sources. Reactions were magnetically stirred and monitored by TLC with 0.25 mm precoated silica-gel plates. Flash chromatography was performed with silica gel (particle size 0.040–0.062 mm). Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise noted. IR spectra were recorded on a FTIR instrument. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer. Chemical shifts are reported relative to either chloroform ($\delta=$ 7.26 ppm) or [D_6]DMSO ($\delta=2.50$ ppm) for ^{1}H NMR spectra and chloroform ($\delta=77.0$ ppm) for ^{13}C NMR spectra. Optical rotations were measured on a polarimeter. X-ray structures were obtained on a diffractometer.

3,3-Dimethyloct-1-en-4-one (10): 1-Bromo-3-methylbut-2-ene (6.35 g, 42.6 mmol, 1.20 equiv) was added to a solution of valeraldehyde (3.8 mL, 36 mmol) in THF (20 mL). This was followed by the addition of aqueous ammonium chloride (sat. 100 mL). The resulting mixture was cooled to 0°C, and activated zinc dust (6.96 g, 106 mmol, 3.00 equiv) was slowly added. The mixture was then stirred vigorously at room temperature for 1 h (no inert atmosphere is necessary). After completion of the reaction, the mixture was filtered through a pad of Celite, the two phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. A solution of IBX (22 g, 100 mmol, 1.2 equiv) in DMSO (150 mL) was added slowly at 20°C to a stirred solution of the crude product (13 g, 83 mmol) in THF (150 mL). The resulting mixture was stirred at 20°C overnight. When the reaction was complete, water was added and the organic phase was diluted with diethyl ether. The biphasic system was stirred for at least 3 h. The white salts were then filtered through a pad of Celite. The aqueous phase was extracted with diethyl ether and the combined organic fractions were washed with water and brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 5:95 then 10:90) afforded the desired product **10** (12.6 g, 98% over two steps) as a pale-yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=5.90$ (dd, $J=17.5$, 10.5 Hz, 1H), 5.15–5.11 (d, m, 2H), 2.44 (t, $J=7.2$ Hz, 2H), 1.53–1.46 (m, 2H), 1.29–1.21 (m, 2H), 1.21 (s, 6H), 0.88 ppm (t, $J=7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=213.2$, 142.7, 114.1, 65.8, 50.8, 37.1, 26.1, 23.5, 15.2, 13.9 ppm; IR (film): $\tilde{\nu}=$ 3087, 2961, 2933, 2873, 1711, 1636, 1466, 1413, 1379, 1364, 1260 cm^{-1}; MS (CI, NH_3): m/z: 172 $[M+NH_4]^+$, 155 $[M+H]^+$, 105.

2-(1,1-Dimethylallyl)-2-trimethylsiloxyhexanenitrile (11): A catalytic amount of zinc iodide was added to a solution of **10** (3.33 g, 21.6 mmol) in freshly distilled dichloromethane (70 mL). Then, TMSCN (4.32 mL, 32.4 mmol, 1.50 equiv) was added dropwise. The resulting mixture was refluxed for 2 h. The solvents and excess TMSCN were then evaporated at

reduced pressure (with a NaOCl/NaOH trap). Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 2:100 then 5:100) afforded the desired nitrile **11** (5.33 g, 97%) as a pale-yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.96 (dd, J = 17.3, 11.0 Hz, 1H), 5.14–5.09 (m, 2H), 1.67–1.61 (m, 2H), 1.52–1.46 (m, 2H), 1.38–1.30 (m, 2H), 1.16 (s, 3H), 1.13 (s, 3H), 0.92 (t, J = 7.3 Hz, 3H), 0.25 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 142.4, 120.4, 114.4, 79.7, 45.2, 36.5, 27.5, 22.7, 22.6, 22.4, 14.0, 1.73 ppm; IR (film): $\tilde{\nu}$ = 3087, 2961, 2875, 2361, 2342, 1639, 1468, 1417, 1381, 1365, 1254, 1127, 1112, 1066, 1005 cm^{-1}; MS (CI, NH_3): m/z: 271 $[M+NH_4]^+$, 227, 172, 91; elemental analysis calcd (%) for $C_{14}H_{27}NOSi$: C 66.34, H 10.74; found: C 66.31, H 10.87.

2-(1,1-Dimethylallyl)-2-trimethylsiloxyhexanal (9): The nitrile **11** (2.28 g, 8.99 mmol) was dissolved in diethyl ether (40 mL) and cooled to −78°C. DIBAL-H (22.1 mL, 1 M in hexanes, 22.1 mmol, 2.50 equiv) was then added dropwise. The reaction mixture was warmed to 0°C and stirred for 2 h. The reaction was quenched by the addition of ethyl acetate, diluted with diethyl ether, and allowed to warm to 20°C. Silica (40 g) was added to the solution, which was then placed at −20°C overnight. After completion of the reaction, the mixture was warmed to 20°C and the silica was filtered off. Solvents were evaporated at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 1:99) afforded the desired product **9** (1.96 g, 85%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.58 (s, 1H), 6.01 (dd, J = 17.5, 10.9 Hz, 1H), 5.07–4.99 (m, 2H), 1.83–1.76 (m, 1H), 1.65–1.57 (m, 2H), 1.29–1.23 (m, 3H), 1.04 (s, 3H), 1.03 (s, 3H), 0.87 (t, J = 7.2 Hz, 3H), 0.16 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 204.8, 144.0, 113.2, 87.7, 44.3, 31.9, 26.3, 23.2, 22.8, 22.4, 14.0, 2.9 ppm; IR (film): $\tilde{\nu}$ = 3086, 2960, 2874, 1735, 1638, 1468, 1416, 1380, 1364, 1254 cm^{-1}; MS (CI, NH_3): m/z: 274 $[M+NH_4]^+$, 257 $[M+H]^+$, 91; elemental analysis calcd (%) for $C_{14}H_{28}O_2Si$: C 65.57, H 11.00; found: C 65.38, H 10.99.

(2*S*)-2-Methyl-2-(3-trityloxypropyl)cyclohexanone (14): 4-Dimethylamino-*N*-triphenylmethyl pyridinium chloride (11.3 g, 27.9 mmol, 1.20 equiv) was added at 20°C to a solution of diol **13** (4.0 g, 23 mmol) in dichloromethane (60 mL). The resulting mixture was refluxed overnight. After cooling, diethyl ether (30 mL) was added, and the white salts were filtered off. The solution was dried over magnesium sulfate, filtered, and the solvent was evaporated at reduced pressure. A solution of IBX (7.79 g, 27.9 mmol, 1.20 equiv) in DMSO (15 mL) was added slowly at 20°C to a stirred solution of the crude product in THF (15 mL). The resulting mixture was stirred at 20°C overnight. When the reaction had gone to completion, water was added and the organic phase was diluted with diethyl ether. The biphasic system was stirred for 3 h. The white salts were then filtered on a pad of Celite. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with water then brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 50:50) afforded the desired product **14** (7.38 g, 77% over two steps) as a white solid. M.p. 117–118°C; $[\alpha]_D^{20}$ = −32.0 (c = 2.76 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.45–7.42 (m, 6H), 7.32–7.28 (m, 6H), 7.25–7.21 (m, 3H), 3.07–3.03 (m, 2H), 2.44–2.28 (m, 2H), 1.92–1.86 (m, 1H), 1.80–1.73 (m, 4H), 1.71–1.53 (m, 3H), 1.46–1.31 (m, 2H), 1.05 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 216.1, 144.3, 128.7, 127.7, 126.8, 86.4, 64.0, 48.4, 39.3, 38.8, 33.9, 27.5, 24.4, 22.6, 21.1 ppm; IR (CaF_2, CCl_4, 1 mg mL^{-1}): $\tilde{\nu}$ = 3087, 3061, 3034, 2935, 2867, 2360, 1708, 1491, 1449, 1378, 1314 cm^{-1}; MS (CI, NH_3): m/z: 243 (Ph_3C^+); elemental analysis calcd (%) for $C_{29}H_{32}O_2$: C 84.43, H 7.82; found: C 84.21, H 8.08.

***N*-[(*S*)-2-Methyl-2-(3-trityloxypropyl)cyclohex-1-ylidene]-*N*′-(2,4,6-triisopropylbenzenesulfono)hydrazone (12)**: Two drops of concentrated hydrochloric acid were added to a solution of ketone **14** (1.00 g, 2.42 mmol) and triisopropylbenzenesulfonyl hydrazine (723 mg, 2.42 mmol, 1.00 equiv) in THF (5.0 mL). The resulting solution was stirred at 20°C for 1 h, and the reaction was quenched by the addition of saturated aqueous sodium hydrogen carbonate. The phases were separated and then the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 20:80) yielded the desired pure hydrazone **12** as white crystals (1.62 g, 96%). M.p. 75–77°C; $[\alpha]_D^{20}$ = −59.6 (c = 1.67 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.42–7.39 (m, 7H), 7.31–7.22 (m, 9H), 7.11 (s, 2H), 4.19 (septet, J = 6.7 Hz, 2H), 2.88 (t, J = 6.2 Hz, 2H), 2.81 (septet, J = 6.9 Hz, 1H), 2.38 (dt, J = 14.5, 4.6 Hz, 1H), 1.93 (ddd, J = 14.6, 11.2, 5.1 Hz, 1H), 1.78–1.69 (m, 1H), 1.68–1.49 (m, 4H), 1.48–1.36 (m, 2H), 1.24 (dd, J = 10.4, 6.7 Hz, 12H), 1.17 (dd, J = 6.9, 2.8 Hz, 6H), 0.90 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 163.0, 152.9, 151.0, 146.8, 144.3, 131.3, 128.6, 127.6, 126.8, 123.3, 86.2, 63.9, 41.7, 39.2, 34.3, 34.0, 29.8, 25.8, 24.8, 24.2, 24.0, 23.5, 23.5, 22.8, 20.8, 14.0 ppm; IR (film): $\tilde{\nu}$ = 3243, 2957, 2869, 1600, 1563, 1496, 1454, 1384, 1323, 1152, 1108, 911, 733 cm^{-1}; MS (CI, NH_3): m/z: 539 $[M+H]^+$, 449, 300, 276, 259, 151, 108, 91.

(1*R*,2*R*)-2-(1,1-Dimethylallyl)-1-[(6*S*)-6-methyl-6-(3-trityloxypropyl)cyclohex-1-enyl]hexane-1,2-diol (15a) and (1*S*,2*S*)-2-(1,1-dimethylallyl)-1-[(6*S*)-6-methyl-6-(3-trityloxypropyl)cyclohex-1-enyl]hexane-1,2-diol (15b): *tert*-Butyllithium (2.48 mL, 4.51 mmol, 2.20 equiv, titrated 1.82 M) was added dropwise to a solution of hydrazone **13** (1.42 g, 2.05 mmol, 1.00 equiv) in THF (10 mL) at −78°C. The solution turned red and was stirred at −78°C for 30 min until the color turned dark red, then the temperature was allowed to warm to 0°C. When nitrogen evolution was finished and the color had turned to pale red, the solution was cooled again to −78°C. A cooled solution of aldehyde **5** (526 mg, 2.05 mmol) in THF (5.0 mL) was added dropwise by cannula. The resulting mixture became light yellow and was stirred at −78°C for 30 min. The reaction was quenched by addition of saturated aqueous sodium hydrogen carbonate. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. Aqueous HCl (1 N, 3.08 mL, 3.08 mmol, 1.50 equiv) was added at 0°C to a solution of the crude product in THF (20 mL). The resulting mixture was allowed to warm to 20°C over 1 h and stirred overnight. The reaction was quenched by addition of saturated aqueous sodium hydrogen carbonate. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 10:90) allowed separation of the two diastereomers to afford the desired diols diasteromer **15a** (364 mg, 43%) as a pale-yellow oil and diasteromer **15b** (313 mg, 37%) as a white solid (80% global yield over two steps).

Product ***15a***: $[\alpha]_D^{20}$ = +9.48 (c = 1.12 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.47–7.43 (m, 6H), 7.33–7.23 (m, 6H), 7.23–7.15 (m, 3H), 6.24–6.16 (m, 2H), 5.06–5.00 (m, 2H), 4.17 (d, J = 4.4 Hz, 1H), 3.18 (s, 1H), 3.11–3.00 (m, 2H), 2.05–1.99 (m, 2H), 1.86 (d, J = 4.4 Hz, 1H), 1.69–1.47 (m, 6H), 1.47–1.31 (m, 6H), 1.31–1.11 (m, 2H), 1.07, 1.06 (2s, 6H), 0.97 (s, 3H), 0.87 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 147.1, 146.9, 144.4, 129.0, 128.7, 128.2, 127.7, 126.8, 112.1, 86.4, 78.1, 69.5, 64.4, 47.0, 37.1, 36.4, 35.1, 33.3, 27.0, 25.9, 25.7, 24.5, 23.7, 22.9, 22.8, 18.8, 14.1 ppm; IR (CaF_2, CCl_4, 1 mg mL^{-1}): $\tilde{\nu}$ = 3610, 3534, 2959, 2931, 2871, 2289, 2002, 1854, 1549, 1449, 1380, 1252, 1217, 1067 cm^{-1}; MS (CI, NH_3): m/z: 243 $[Ph_3C]^+$.

Product ***15b***: M.p. 102–105°C; $[\alpha]_D^{20}$ = +9.42 (c = 1.00 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.53–7.48 (m, 6H), 7.38–7.32 (m, 6H), 7.32–7.26 (m, 3H), 6.31 (t, J = 4.0 Hz, 1H), 6.25 (dd, J = 17.6, 10.8 Hz, 1H), 5.08 (d, J = 17.6 Hz, 1H), 5.03 (d, J = 10.8 Hz, 1H), 4.28 (d, J = 4.4 Hz, 1H), 3.19 (s, 1H), 3.14–3.09 (m, 2H), 2.12–2.05 (m, 2H), 1.89 (d, J = 4.4 Hz, 1H), 1.70–1.52 (m, 8H), 1.52–1.40 (m, 3H), 1.35–1.14 (m, 3H), 1.15–1.10 (m, 9H), 0.89 ppm (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 147.9, 147.1, 144.4, 128.6, 127.7, 127.0, 126.8, 112.1, 86.2, 78.1, 70.0, 64.0, 46.9, 36.7, 36.2, 35.0, 33.4, 27.0, 25.7, 25.1, 24.4, 23.6, 22.9, 22.8, 18.6, 14.1 ppm; IR (CaF_2, CCl_4, 1 mg mL^{-1}): $\tilde{\nu}$ = 3610, 3537, 3061, 2959, 2930, 2871, 2291, 2004, 1856, 1550, 1449, 1379, 1252, 1217, 1067 cm^{-1}; MS (CI, NH_3): m/z: 243 $[Ph_3C]^+$.

(1*R*,2*R*)-2-(1,1-Dimethylallyl)-1-[(*S*)-6-(3-hydroxypropyl)-6-methylcyclohex-1-enyl]hexane-1,2-diol (16a) and (1*S*,2*S*)-2-(1,1-dimethylallyl)-1-[(*S*)-6-(3-hydroxypropyl)-6-methylcyclohex-1-enyl]hexane-1,2-diol (16b): Diol

15a (251 mg, 0.43 mmol) was dissolved in MeOH (5 mL) at 20 °C. Amberlyst H-15 (40 mg) was then added, and the mixture was stirred overnight at 20 °C. The resin was filtered off and the solvents were removed in vacuo. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 20:80 then 50:50 then 80:20) afforded the desired alcohol **16a** (128 mg, 88 %) as a white solid. The same procedure repeated with 223 mg of diol **15b** afforded the desired alcohol **16b** (104 mg, 80 %) as a yellow oil.

Product ***16a***: M.p. 47–49 °C; $[\alpha]_D^{20}=+1.03$ ($c=1.56$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=6.27$ (t, $J=4.0$ Hz, 1H), 6.18 (dd, $J=17.6$, 10.9 Hz, 1H), 5.06 (m, 2H), 4.18 (s, 1H), 3.70–3.65 (m, 1H), 3.58–3.53 (m, 1H), 3.01 (br s, 1H), 2.50 (br s, 1H), 2.12 (br s, 1H), 2.02–1.98 (m, 2H), 1.66–1.48 (m, 6H), 1.46–1.40 (m, 2H), 1.38–1.31 (m, 4H), 1.27–1.12 (m, 2H), 1.08 (s, 3H), 1.07 (s, 3H), 0.98 (s, 3H), 0.85 ppm (t, $J=7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=146.9$, 145.9, 128.0, 112.2, 78.2, 69.3, 63.1, 47.0, 37.4, 35.9, 35.2, 33.3, 27.1, 27.0, 26.7, 25.8, 23.6, 23.1, 22.8, 18.9, 14.1 ppm; IR (CaF_2, CCl_4, 1 mg mL^{-1}): $\tilde{\nu}=3380$, 2955, 2870, 1460, 1377, 785, 705, 603 cm^{-1}; HRMS: m/z: calcd for $C_{21}H_{38}O_3$: 338.2821; found: 338.2832.

Product ***16b***: $[\alpha]_D^{20}=+0.35$ ($c=1.15$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=6.24$–6.17 (m, 2H), 5.08–5.03 (m, 2H), 4.20 (s, $J=4.5$ Hz, 1H), 3.60 (t, $J=6.7$ Hz, 2H), 3.11 (s, 1H), 2.03–1.99 (m, 2H), 1.85 (d, $J=4.7$ Hz, 1H), 1.63–1.49 (m, 6H), 1.47–1.30 (m, 6H), 1.28–1.12 (m, 2H), 1.08–1.07 (m, 9H), 0.85 ppm (t, $J=7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=147.6$, 147.1, 127.2, 112.1, 78.2, 70.2, 63.7, 46.9, 36.6, 35.3, 35.1, 33.5, 27.2, 27.0, 25.7, 25.2, 23.6, 22.9, 22.8, 18.6, 14.1 ppm; IR (film): $\tilde{\nu}=3412$, 2954, 2867, 1461, 1377, 1055, 1011, 842, 737, 686, 625 cm^{-1}; HRMS: m/z: calcd for $C_{21}H_{38}O_3$: 338.2821; found: 338.2834.

(4*R*,5*R*)-5-[(6*S*)-6-Allyl-6-methylcyclohex-1-enyl]-4-butyl-4-(1,1-dimethylallyl)[1,3]dioxolan-2-one (18a) and (4*S*,5*S*)-5-[(6*S*)-6-allyl-6-methylcyclohex-1-enyl]-4-butyl-4-(1,1-dimethylallyl)[1,3]dioxolan-2-one (18b): *o*-Nitrophenylselenocyanate (55 mg, 0.24 mmol, 2.4 equiv) was added in one portion at 20 °C to a solution of alcohol **16a** (34 mg, 0.10 mmol) in THF (1.0 mL). Tributylphosphine (60 μL, 0.24 mmol, 2.4 equiv) was then added dropwise. The resulting mixture was stirred at 20 °C for 20 min. Completion of the reaction was checked by TLC. Water was then added, and the solution was diluted with diethyl ether. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. The crude product was used for the next step without purification. Carbonyl diimidazole (81 mg, 0.50 mmol, 5.0 equiv) was added at 20 °C to a solution of the crude product in toluene (5 mL). The resulting mixture was refluxed for 3 d. After cooling, the reaction was quenched by addition of saturated aqueous sodium hydrogen carbonate. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. The crude product was then dissolved in THF (1.0 mL). Aqueous hydrogen peroxide (1.5 mL, 10 % wt solution in water) was added dropwise at 0 °C. The mixture was stirred overnight. After this time, water was added and the solution was diluted with diethyl ether. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 10:90) afforded the desired diene **18a** (32 mg, 57 % over three steps) as a pale-yellow oil. The same procedure repeated with 30 mg of alcohol **16b** afforded the desired diene **18b** (16 mg, 52 % over three steps) as a pale-yellow oil.

Product ***18a***: $[\alpha]_D^{20}=+23.5$ ($c=0.92$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=5.95$ (dd, $J=17.6$, 10.6 Hz, 1H), 5.85 (t, $J=4.1$ Hz, 1H), 5.75 (ddt, $J=17.6$, 10.6, 7.6 Hz, 1H), 5.22 (d, $J=10.5$ Hz, 1H), 5.21 (d, $J=17.4$ Hz, 1H), 5.10 (d, $J=7.6$ Hz, 1H), 5.06 (d, $J=17.6$ Hz, 1H), 4.98 (s, 1H), 2.32–2.26 (m, 1H), 2.19–2.02 (m, 3H), 1.85–1.50 (m, 4H), 1.50–1.19 (m, 6H), 1.15 (s, 3H), 1.14 (s, 3H), 0.98 (s, 3H), 0.87 ppm (t, $J=7.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=155.7$, 141.9, 139.3, 133.9, 131.2, 118.1, 115.7, 90.7, 79.0, 46.6, 44.9, 36.9, 35.7, 31.0, 27.0, 26.2, 25.6, 23.2, 22.3, 20.8, 18.2, 13.8 ppm; IR (film): $\tilde{\nu}=3575$, 3076, 2960, 2368, 1984, 1790, 1638, 1538, 1456, 1417, 1380, 1326, 1198, 1042 cm^{-1}; MS (CI, NH_3): m/z: 364 $[M+NH_4]^+$, 347 $[M+H]^+$, 303, 285; HRMS: m/z: calcd for $C_{22}H_{34}O_3$: 346.2508; found: 346.2524.

Product ***18b***: $[\alpha]_D^{20}=-19.3$ ($c=1.01$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=5.95$ (dd, $J=17.6$, 11.2 Hz, 1H), 5.79 (t, $J=4.1$ Hz, 1H), 5.73 (ddt, $J=17.2$, 10.4, 7.1 Hz, 1H), 5.23 (d, $J=11.2$ Hz, 1H), 5.21 (d, $J=17.6$ Hz, 1H), 5.06 (dd, $J=17.0$, 10.6 Hz, 2H), 5.02 (s, 1H), 2.14–2.00 (m, 4H), 1.89–1.80 (m, 1H), 1.74–1.55 (m, 4H), 1.50–1.18 (m, 5H), 1.16 (s, 3H), 1.14 (s, 3H), 1.07 (s, 3H), 0.88 ppm (t, $J=7.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=155.5$, 141.9, 140.6, 133.8, 130.5, 118.1, 115.8, 90.6, 79.7, 46.5, 43.6, 36.9, 35.0, 31.1, 27.0, 25.7, 25.0, 23.2, 22.4, 20.8, 18.0, 13.8 ppm; IR (film): $\tilde{\nu}=3568$, 3077, 2956, 2254, 1790, 1638, 1539, 1456, 1417, 1379, 1326, 1200, 1117, 1044 cm^{-1}; MS (CI, NH_3): m/z: 364 $[M+NH_4]^+$, 347 $[M+H]^+$, 285; elemental analysis calcd (%) for $C_{22}H_{34}O_3$: C 76.26, H 9.89; found: C 76.01, H 9.98.

(4*R*,5*R*)-5-[(*S*)-6-Allyl-6-methylcyclohex-1-enyl]-4-butyl-4-(1,1-dimethylallyl)-2,2-dimethyl[1,3]dioxolane (19a) and (4*S*,5*S*)-5-[(*S*)-6-allyl-6-methylcyclohex-1-enyl]-4-butyl-4-(1,1-dimethylallyl)-2,2-dimethyl-[1,3]dioxolane (19b): 2,2-Dimethoxypropane (5 mL) followed by a catalytic amount of CSA was added to triol **16a** (38 mg, 0.111 mmol) at 20 °C, and the resulting mixture was stirred overnight. After this time, the reaction was quenched by the addition of saturated aqueous sodium hydrogen carbonate, the phases were separated, and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. The crude product was used for the next step without purification. *o*-Nitrophenylselenocyanate (58 mg, 0.254 mmol, 2.4 equiv) was added in one portion at 20 °C to a solution of the crude product (40 mg, 0.106 mmol) in THF (1.0 mL). Tributylphosphine (64 μL, 0.254 mmol, 2.4 equiv) was then added dropwise. The resulting mixture was stirred at 20 °C for 20 min. Completion of the reaction was checked by TLC. Water was then added, and the solution was diluted with diethyl ether. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. The crude product thus obtained was then dissolved in THF (1.0 mL) and aqueous hydrogen peroxide (0.5 mL, 35 % wt solution in water) was added dropwise at 0 °C. The mixture was stirred overnight. After this time, water was added and the solution was diluted with diethyl ether. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 10:90) afforded the desired diene **19a** (25 mg, 63 % over three steps) as a colorless oil. The same procedure was repeated with 30 mg of alcohol **16b** to afford the desired diene **19b** (23 mg, 71 % over three steps) as a colorless oil.

Product ***19a***: $[\alpha]_D^{20}=-21.4$ ($c=1.5$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=6.20$ (dd, $J=17.6$, 10.9 Hz, 1H), 6.03–5.98 (m, 1H), 5.89–5.77 (m, 1H), 5.01–4.91 (m, 4H), 4.44 (s, 1H), 2.27 (d, $J=7.0$ Hz, 2H), 2.14–1.99 (m, 2H), 1.82–1.79 (m, 2H), 1.62–1.58 (m, 4H), 1.46 (s, 3H), 1.36 (s, 3H), 1.33–1.16 (m, 4H), 1.12–1.05 (m, 9H), 0.90 ppm (t, $J=7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=146.9$, 139.2, 136.2, 129.1, 116.5, 110.6, 104.3, 88.3, 77.1, 44.8, 43.3, 37.9, 35.9, 33.5, 28.0, 27.9, 26.3, 26.2, 26.1, 25.4, 24.0, 23.4, 17.9, 14.3 ppm; IR (film): $\tilde{\nu}=3076$, 2959, 2933, 2872, 1636, 1461, 1372, 1247, 1212, 1016, 910, 862, 793, 764, 626, 486 cm^{-1}; HRMS: m/z: calcd for $C_{24}H_{40}O_2$: 360.3028; found: 360.3028.

Product ***19b***: $[\alpha]_D^{20}=-1.23$ ($c=1.3$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=6.19$ (dd, $J=17.7$, 10.9 Hz, 1H), 5.92 (t, $J=3.8$ Hz, 1H), 5.82–5.72 (m, 1H), 5.05–4.92 (m, 4H), 4.44 (s, 1H), 2.32 (dd, $J=13.9$, 7.2 Hz, 1H), 2.19 (dd, $J=13.9$, 7.2 Hz, 1H), 2.10–2.05 (m, 2H), 1.82–1.76 (m, 2H), 1.65–1.53 (m, 4H), 1.46 (s, 3H), 1.37 (s, 3H), 1.32–1.22 (m, 4H), 1.09–1.08 (m, 9H), 0.89 ppm (t, $J=7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=146.9$, 139.2, 135.5, 128.4, 116.9, 110.7, 104.3, 88.3, 77.7, 44.0, 43.4, 37.8, 35.6, 33.5, 27.9, 27.8, 26.5, 26.3, 26.0, 25.5, 23.9, 23.5, 17.8, 14.3 ppm; IR (film): $\tilde{\nu}=2959$, 2931, 2869, 1636, 1459, 1373, 1253, 1017,

857, 802, 713, 695, 648, 632, 524, 462 cm^{-1}; HRMS: *m/z*: calcd for $C_{24}H_{40}O_2$: 360.3028; found: 360.3032.

(1*R*,2*R*)-1-[(*S*)-6-Allyl-6-methylcyclohex-1-enyl]-2-(1,1-dimethylallyl)-2-hydroxyhexylbenzoate (20a) and (1*S*,2*S*)-1-[(*S*)-6-allyl-6-methylcyclohex-1-enyl]-2-(1,1-dimethylallyl)-2-hydroxyhexylbenzoate (20b): A solution of phenyllithium in ether (0.3 M, 1.5 mL, 2.1 equiv) was added dropwise to a solution of crude diene **18a**, synthesized from **16a** (49 mg), in THF (5 mL) at −78 °C. After 10 min, the solution was poured into a saturated aqueous solution of sodium hydrogen carbonate, the phases were separated, and then the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 5:95) afforded diene **20a** (30 mg, 46 % over four steps from diol **16a**) as a colorless oil. The same procedure was repeated with 41 mg of triol **16b** to afford diene **20b** (19.5 mg, 36 % over four steps from **16b**) as a colorless oil.

Product ***20a***: $[\alpha]_D^{20}=+1.6$ ($c=1.30$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.97$–7.95 (m, 2H), 7.57–7.53 (m, 1H), 7.45–7.42 (m, 2H), 6.43 (t, $J=4.0$ Hz, 1H), 5.96 (dd, $J=17.6$, 10.9 Hz, 1H), 5.77 (s, 1H), 5.71–5.61 (m, 1H), 4.98–4.92 (m, 3H), 4.77 (dd, $J=10.9$, 1.2 Hz, 1H), 2.59 (s, 1H), 2.40 (dd, $J=14.0$, 7.5 Hz, 1H), 2.12–2.07 (m, 3H), 1.68–1.58 (m, 3H), 1.55–1.39 (m, 2H), 1.33–1.18 (m, 5H), 1.11 (s, 3H), 1.09 (s, 3H), 1.06 (s, 3H), 0.90 (t, $J=7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=$ 164.7, 145.1, 142.9, 135.1, 132.8, 131.0, 130.5, 129.6, 128.4, 117.1, 112.3, 79.3, 72.5, 46.6, 44.0, 36.9, 34.9, 33.3, 29.7, 26.9, 25.7, 25.5, 23.6, 23.2, 22.9, 18.0, 14.2 ppm; IR (film): $\tilde{\nu}=3965$, 3807, 3711, 2928, 2280, 1793, 1710, 1576, 1484, 1427, 1316, 1262, 1078, 976, 944, 919, 857, 835, 817, 765, 685, 602, 571, 509 cm^{-1}; HRMS: *m/z*: calcd for $C_{28}H_{40}O_3$: 424.2978; found: 424.2985.

Product ***20b***: $[\alpha]_D^{20}=+5.5$ ($c=1.30$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.98$–7.96 (m, 2H), 7.57–7.54 (m, 1H), 7.46–7.42 (m, 2H), 6.41 (t, $J=3.9$ Hz, 1H), 5.99 (dd, $J=17.6$, 10.9 Hz, 1H), 5.87–5.78 (m, 1H), 5.76 (s, 1H), 5.06–4.93 (m, 3H), 4.79 (dd, $J=10.9$, 1.2 Hz, 1H), 2.61 (s, 1H), 2.34 (dd, $J=13.1$, 7.0 Hz, 1H), 2.17–2.07 (m, 3H), 1.67–1.63 (m, 2H), 1.58–1.36 (m, 6H), 1.33–1.18 (m, 2H), 1.13 (s, 3H), 1.08 (s, 3H), 1.05 (s, 3H), 0.90 ppm (t, $J=7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=165.0$, 145.3, 142.8, 134.9, 132.8, 131.0, 130.7, 129.6, 128.4, 117.5, 112.3, 79.4, 73.9, 46.5, 44.5, 36.8, 35.8, 33.7, 26.8, 25.8, 25.7, 23.6, 23.4, 23.0, 18.0, 14.1 ppm; IR (film): $\tilde{\nu}=3681$, 2931, 2275, 1714, 1636, 1454, 1316, 1265, 1108, 964, 937, 902, 864, 844, 725, 694, 524 cm^{-1}; HRMS: *m/z*: calcd for $C_{28}H_{40}O_3$: 424.2978; found: 424.2964.

(1*S*,2*R*)-1-[(*S*)-2-Allyl-2-methyl-7-oxabicyclo[4.1.0]hept-1-yl]-2-(1,1-dimethylallyl)hexane-1,2-diol (21a): *o*-Nitrophenylselenocyanate (145 mg, 0.66 mmol, 2.40 equiv) was added in one portion at 20 °C to a solution of alcohol **16a** (90 mg, 0.28 mmol) in THF (5.0 mL). Tributylphosphine (159 μL, 0.66 mmol, 2.39 equiv) was then added dropwise. The resulting mixture was stirred at 20 °C for 20 min. Completion of the reaction was checked by TLC. Water was added and the solution was diluted with diethyl ether. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. The crude product thus obtained was dissolved in THF (1.0 mL) and aqueous hydrogen peroxide (0.5 mL, 35 % wt solution in water) was added dropwise at 0 °C. The mixture was then stirred overnight. After this time, water was added and the solution was diluted with diethyl ether. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 10:90) afforded the epoxide diene **21a** (20 mg, 20 %) as pale-yellow oil. $[\alpha]_D^{20}=-17.2$ ($c=1.40$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=6.12$ (dd, $J=$ 17.4, 11.0 Hz, 1H), 5.88–5.78 (m, 1H), 5.09–5.01 (m, 4H), 4.05 (d, $J=$ 5.3 Hz, 1H), 3.93 (t, $J=2.4$ Hz, 1H), 3.30 (d, $J=5.3$ Hz, 1H), 2.86 (s, 1H), 2.30 (dd, $J=13.6$, 7.5 Hz, 1H), 2.12 (dd, $J=13.6$, 7.5 Hz, 1H), 1.87–1.83 (m, 2H), 1.60–1.48 (m, 2H), 1.47–1.37 (m, 4H), 1.36–1.17 (m, 4H), 1.09–1.05 (m, 6H), 1.03 (s, 3H), 0.92 ppm (t, $J=7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=146.2$, 134.2, 117.9, 112.6, 76.6, 67.7, 66.7, 60.7, 47.1, 43.2, 36.6, 32.7, 32.0, 27.6, 23.9, 23.9, 23.2, 22.3, 21.9, 16.1, 14.1 ppm; IR (film): $\tilde{\nu}=3494$, 2958, 2874, 1636, 1460, 1381, 1077, 1000, 907, 878, 826, 804, 771, 708, 632, 591 cm^{-1}; HRMS: *m/z*: calcd for $C_{21}H_{36}O_3$: 336.2665; found: 336.2665.

(1*R*,2*R*)-1-[(*S*)-6-Allyl-6-methylcyclohex-1-enyl]-2-(1,1-dimethylallyl)hexane-1,2-diol (22a) and (1*S*,2*S*)-1-[(*S*)-6-allyl-6-methylcyclohex-1-enyl]-2-(1,1-dimethylallyl)hexane-1,2-diol (22b): *o*-Nitrophenylselenocyanate (282 mg, 1.24 mmol, 2.40 equiv) was added in one portion at 20 °C to a solution of alcohol **16a** (175 mg, 0.52 mmol) in THF (1.0 mL). Tributylphosphine (49 μL, 0.2 mmol, 2.4 equiv) was then added dropwise. The resulting mixture was stirred at 20 °C for 20 min. Completion of the reaction was checked by TLC. Water was then added and the solution was diluted with diethyl ether. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. The crude product thus obtained was dissolved in THF (1.0 mL) and aqueous ammonium molybdate in solution (6 M) of hydrogen peroxide (1.5 mL, 10 % wt solution in water) was added dropwise at −10 °C. The mixture was then stirred for 5 min. Water was added and the solution was diluted with diethyl ether. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 20:80) afforded the desired diene **22a** (152 mg, 92 %) as a pale-yellow oil. The same procedure was repeated with 115 mg of alcohol **16b** to afford the desired diene **22b** (99 mg, 91 %) as a pale-yellow oil.

Product ***22a***: $[\alpha]_D^{20}=+3.3$ ($c=1.0$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=6.26$–6.17 (m, 2H), 5.91–5.80 (m, 1H), 5.08–5.04 (m, 4H), 4.20 (d, $J=3.4$ Hz, 1H), 3.16 (s, 1H), 2.23 (dq, $J=14.0$, 7.4 Hz, 2H), 2.04–2.00 (m, 2H), 1.90 (d, $J=3.8$ Hz, 1H), 1.66–1.48 (m, 4H), 1.43–1.32 (m, 4H), 1.28–1.22 (m, 2H), 1.09 (s, 3H), 1.08 (s, 3H), 0.99 (s, 3H), 0.86 ppm (t, $J=7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=147.1$, 146.2, 135.4, 128.1, 117.3, 112.1, 78.1, 69.5, 47.0, 45.1, 37.4, 35.6, 33.3, 27.0, 26.1, 25.7, 23.7, 22.9, 22.8, 18.6, 14.1 ppm; IR (film): $\tilde{\nu}=2929$, 2278, 1587, 1511, 1450, 1328, 1304, 1096, 1030, 924, 890, 850, 810, 772, 648, 587, 532 cm^{-1}; HRMS: *m/z*: calcd for $C_{21}H_{36}O_2$: 320.2715; found: 320.2716.

Product ***22b***: $[\alpha]_D^{20}=+4.6$ ($c=1.20$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=6.28$–6.19 (m, 2H), 5.85–5.74 (m, 1H), 5.10–5.01 (m, 4H), 4.22 (d, $J=4.3$ Hz, 1H), 3.09 (s, 1H), 2.09 (d, $J=7.4$ Hz, 2H), 2.02 (dt, $J=6.2$, 4.2 Hz, 2H), 1.83 (d, $J=4.5$ Hz, 1H), 1.66–1.60 (m, 1H), 1.57–1.49 (m, 3H), 1.45–1.33 (m, 4H), 1.33–1.12 (m, 2H), 1.10 (s, 3H), 1.09 (s, 3H), 1.07 (s, 3H), 0.86 ppm (t, $J=7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=147.1$, 134.7, 127.5, 117.6, 112.2, 78.2, 70.1, 47.0, 44.0, 37.0, 35.2, 33.5, 27.0, 25.7, 25.2, 23.6, 22.9, 22.8, 18.4, 14.1 ppm; IR (film): $\tilde{\nu}=2956$, 2867, 1716, 1638, 1587, 1508, 1328, 1300, 1095, 1026, 910, 859, 828, 782, 694, 642, 603, 517, 478 cm^{-1}; HRMS: *m/z*: calcd for $C_{21}H_{36}O_2$: 320.2715; found: 320.2728.

(*Z*)-(2*R*,6*S*,11*S*)-6-Butyl-7,7,11-trimethyl-3,5-dioxatricyclo[9.4.0.02]pentadeca-1(15),8-dien-4-one (23b): Diene **18b** (10 mg, 30 μmol) was dissolved in 1,2-dichloroethane (2.0 mL). The mixture was thoroughly degassed three times while stirring. Second-generation Grubbs catalyst (2.6 mg, 3.0 μmol, 10 mol %) was added and the mixture was refluxed for 1 h. After cooling, the solvent was evaporated at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 10:90) afforded the desired product **23b** (6.4 mg, 69 %) as a pale-yellow oil. The same procedure repeated with [RuIMes] catalyst (1.3 mg, 1.5 μmol, 5 mol %) afforded compound **23b** (6.6 mg, 72 %). $[\alpha]_D^{20}=+112.5$ ($c=1.17$ in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=6.06$ (t, $J=4.4$ Hz, 1H), 5.66 (ddd, $J=11.8$, 10.6, 8.1 Hz, 1H), 5.39 (s, 1H), 5.36 (d, $J=11.8$ Hz, 1H), 2.58 (dd, $J=14.2$, 10.6 Hz, 1H), 2.26 (dt, $J=$ 18.7, 5.8 Hz, 1H), 2.12–1.70 (m, 8H), 1.46 (s, 3H), 1.33 (s, 3H), 1.32–1.25 (m, 4H), 1.18 (s, 3H), 0.93 ppm (t, $J=7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=138.3$, 134.9, 129.7, 128.5, 93.5, 80.1, 40.4, 39.0, 38.8, 34.1, 31.1, 28.8, 28.5, 27.7, 24.5, 23.3, 21.8, 18.0, 13.9 ppm; IR (film): $\tilde{\nu}=3588$, 2961, 2870, 2345, 1803, 1654, 1560, 1458, 1380, 1248 cm^{-1}; MS (CI, NH_3):

m/z: 336 $[M+NH_4]^+$, 319 $[M+H]^+$, 258, 257; HRMS: *m/z*: calcd for $C_{20}H_{30}O_3$: 318.2195; found: 318.2206.

Mixture of 24 and 25: Diene **19a** (24 mg, 0.067 mmol) was dissolved in dichloromethane (7.0 mL). The mixture was thoroughly degassed three times while stirring. Second-generation Grubbs catalyst (2.8 mg, 3.3 μmol, 5 mol%) was added and the mixture was refluxed for 15 min. After cooling, the solvent was evaporated at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 10:90) afforded the mixture of **24** (15 mg, *E*/*Z* 3:1) and **25** (5 mg, *E*/*Z* 3:1) (87% global yield) with a ratio of 3:1 as a pale-yellow oil.

Fractions ***24***: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 6.37–6.12 (m, 2H), 6.04–6.01 (m, 2H), 5.55–5.46 (m, 3H), 5.02–4.91 (m, 3H), 4.49 (s, 0.75H), 4.21 (s, 0.25H), 2.54–2.42 (m, 2H), 2.26–2.20 ppm (m, 2H).

Fractions ***25***: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 6.24–6.16 (m, 2H), 6.01–5.96 (m, 2H), 5.50–5.48 (m, 0.5H), 5.40–5.38 (m, 1.5H), 4.98–4.90 (m, 4H), 4.43 (s, 2H), 2.34–2.26 (m, 2H), 2.21–2.13 ppm (m, 2H).

(*Z*)-(2*S*,6*S*,11*S*)-6-Butyl-4,4,7,7,11-pentamethyl-3,5-dioxatricyclo[9.4.0.02]-pentadeca-1(15),8-diene (26b): Diene **19b** (20 mg, 56 μmol) was dissolved in 1,2-dichloroethane (5.0 mL). The mixture was thoroughly degassed three times while stirring. Second-generation Grubbs catalyst (2.4 mg, 2.8 μmol, 5 mol%) was added and the mixture was refluxed for 5 min. After cooling, the solvent was evaporated at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 10:90) afforded the desired bicycle **26b** (19 mg, quantitative yield) as a pale-yellow oil. $[\alpha]_D^{20}$ = +124.0 (*c* = 1.3 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 6.04 (m, 1H), 5.55–5.47 (m, 1H), 5.34 (d, *J* = 12.0 Hz, 1H), 4.69 (s, 1H), 2.65 (dd, *J* = 13.7, 10.7 Hz, 1H), 2.15 (dt, *J* = 18.3, 5.0 Hz, 1H), 1.98–1.90 (m, 1H), 1.87–1.62 (m, 5H), 1.59–1.51 (m, 2H), 1.47 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H), 1.30–1.22 (m, 4H), 1.17 (s, 3H), 1.12 (s, 3H), 0.86 ppm (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 141.2, 137.6, 127.7, 125.8, 104.5, 89.1, 75.5, 40.5, 38.9, 38.8, 34.4, 34.4, 29.7, 29.6, 28.8, 28.3, 26.5, 24.9, 24.0, 22.5, 18.4, 14.2 ppm; IR (film): $\tilde{\nu}$ = 2929, 2866, 2360, 1701, 1666, 1594, 1458, 1372, 1247, 1041, 897, 833, 738, 539 cm^{-1}; HRMS: *m/z*: calcd for $C_{22}H_{36}O_2$: 332.2715; found: 332.2714.

(*Z*)-(5*R*,6*R*,10a*S*)-6-Butyl-6-hydroxy-7,7,10a-trimethyl-1,2,3,5,6,7,10,10a-octahydrobenzocycloocten-5-ylbenzoate (27a): Diene **20a** (15 mg, 35 μmol) was dissolved in dichloromethane (2.0 mL). The mixture was thoroughly degassed three times while stirring. Second-generation Grubbs catalyst (1.5 mg, 1.8 μmol, 5 mol%) was added and the mixture was refluxed for 18 h. After cooling, the solvent was evaporated at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 5:95) afforded the desired bicycle **27a** (13 mg, 84%) as a pale-yellow oil. The same procedure repeated with first-generation Grubbs catalyst (1.5 mg, 1.8 μmol, 5 mol%) in 1,2-dichloroethane (2.0 mL) refluxed for 36 h afforded compound **27a** (9.0 mg, 71%). $[\alpha]_D^{20}$ = +0.5 (*c* = 1.10 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.10–8.08 (m, 2H), 7.62–7.58 (m, 1H), 7.51–7.47 (m, 2H), 5.95–5.91 (m, 1H), 5.83 (s, 1H), 5.80–5.72 (m, 1H), 5.42 (d, *J* = 11.7 Hz, 1H), 3.26 (t, *J* = 11.9 Hz, 1H), 2.20–2.12 (m, 1H), 2.05–1.94 (m, 1H), 1.86–1.78 (m, 2H), 1.72–1.67 (m, 2H), 1.61 (s, 3H), 1.54 (s, 3H), 1.29–1.20 (m, 7H), 0.99 (s, 3H), 0.84 ppm (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 166.0, 139.8, 138.0, 133.0, 132.8, 131.5, 130.4, 129.8, 128.6, 83.5, 80.2, 43.3, 41.3, 37.6, 36.7, 31.9, 30.9, 29.4, 25.5, 23.8, 23.4, 18.3, 14.1 ppm; IR (film): $\tilde{\nu}$ = 3544, 3435, 2926, 2866, 2360, 1722, 1453, 1264, 1099, 913, 861, 842, 778, 655, 563, 532 cm^{-1}; HRMS: *m/z*: calcd for $C_{26}H_{36}O_3$: 396.2665; found: 396.2656.

(*Z*)-(5*S*,6*S*,10a*S*)-6-Butyl-6-hydroxy-7,7,10a-trimethyl-1,2,3,5,6,7,10,10a-octahydrobenzocycloocten-5-ylbenzoate (27b): Diene **20b** (9.0 mg, 21 μmol) was dissolved in dichloromethane (2.0 mL). The mixture was thoroughly degassed three times while stirring. Second-generation Grubbs catalyst (0.9 mg, 1.1 μmol, 5 mol%) was added and the mixture was stirred for 15 min at 20°C. The solvent was evaporated at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 5:95) afforded the desired bicycle **27b** (9.0 mg, quantitative yield) as a pale-yellow oil. The same procedure repeated with first-generation Grubbs catalyst (0.9 mg, 1.1 μmol, 5 mol%) in dichloromethane (2.0 mL) refluxed for 12 h afforded the compound **27b** (7.2 mg, 78%). $[\alpha]_D^{20}$ = +42.3 (*c* = 1.30 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.04–8.02 (m, 2H), 7.58–7.54 (m, 1H), 7.47–7.43 (m, 2H), 6.13 (s, 1H), 6.11–6.05 (m, 1H), 5.74–5.60 (m, 1H), 5.48–5.36 (m, 1H), 2.80–2.60 (br s, 1H), 2.12–2.02 (m, 3H), 1.94 (t, *J* = 12.5 Hz, 1H), 1.76–1.66 (m, 2H), 1.62–1.58 (m, 2H), 1.54 (s, 3H), 1.36–1.31 (m, 2H), 1.36–1.26 (m, 4H), 1.23 (s, 3H), 1.18 (s, 3H), 0.95 ppm (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 166.1, 142.4, 139.7, 132.8, 130.6, 129.7, 129.1, 128.4, 81.3, 77.2, 38.4, 31.9, 30.3, 28.1, 28.1, 27.6, 25.9, 25.8, 23.9, 22.7, 18.5, 14.2 ppm; IR (film): $\tilde{\nu}$ = 3920, 3704, 3548, 2926, 2867, 2360, 1723, 1656, 1599, 1454, 1273, 1110, 1025, 873, 857, 840, 697, 518 cm^{-1}; HRMS: *m/z*: calcd for $C_{26}H_{36}O_3$: 396.2665; found: 396.2678.

(*Z*)-(5*S*,6*S*,10a*S*)-6-Butyl-7,7,10a-trimethyl-1,2,3,5,6,7,10,10a-octahydrobenzocyclooctene-5,6-diol (28b): Diene **22b** (6 mg, 19 μmol) was dissolved in dichloromethane (2.0 mL). The mixture was thoroughly degassed three times while stirring. Second-generation Grubbs catalyst (0.8 mg, 1.0 μmol, 5 mol%) was added and the mixture was refluxed for 1 h. The solvent was evaporated at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 20:80) afforded the desired bicycle **28b** (6 mg, quantitative yield) as pale-yellow needles. Bicycle **27b** (9.0 mg, 21 μmol) in THF (1.0 mL) was added dropwise to a suspension of $LiAlH_4$ (2.0 mg, 53 μmol, 2.3 equiv) in THF (5 mL) at 0°C, and the resulting mixture was stirred for 15 min at 0°C. Ethyl acetate was then added, and the reaction was quenched by addition of aqueous sodium and potassium tartrate solution (10%, 10 mL), and the mixture was stirred for 3 h. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 20:80) afforded the same bicycle **28b** (5.5 mg, 83%) as pale-yellow needles. M.p. 105–107°C; $[\alpha]_D^{20}$ = +28.5 (*c* = 1.0 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.96 (dd, *J* = 4.8, 2.8 Hz, 1H), 5.62–5.55 (m, 1H), 5.35 (d, *J* = 11.7 Hz, 1H), 4.51 (s, 1H), 2.66–2.38 (br s, 1H), 2.36–1.92 (m, 4H), 1.84–1.48 (m, 4H), 1.34 (s, 3H), 1.29–1.24 (m, 6H), 1.18 (s, 3H), 1.15 (s, 3H), 0.91 ppm (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 145.8, 140.1, 128.8, 126.5, 81.4, 73.0, 42.3, 38.4, 31.4, 30.3, 29.7, 28.2, 27.7, 25.6, 23.9, 22.7, 22.3, 18.6, 14.2 ppm; IR (film): $\tilde{\nu}$ = 3791, 3477, 2927, 2866, 1718, 1588, 1514, 1452, 1330, 1265, 914, 885, 810, 788, 718, 685, 572 cm^{-1}; HRMS: *m/z*: calcd for $C_{19}H_{32}O_2$: 292.2402; found: 292.2405.

(*S*)-6-[(*Z*)-4,4-Dimethyl-5-oxonon-2-enyl]-6-methylcyclohex-1-enecarbaldehyde (29): Benzeneseleninic acid (12 mg, 66 μmol, 2.0 equiv) was added to a solution of bicycle **28b** (9.6 mg, 33 μmol) in dichloromethane (5 mL) followed by second-generation Grubbs catalyst (2.8 mg, 3.3 μmol, 10 mol%) at 20°C, and the mixture was refluxed for 6 h. The solvent was evaporated at reduced pressure. Purification of the crude product by flash chromatography (diethyl ether/petroleum ether 10:90) afforded ketoaldehyde **29** (6.4 mg, 67%) as a colorless oil. $[\alpha]_D^{20}$ = −7.5 (*c* = 0.4 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.32 (s, 1H), 6.81 (t, *J* = 3.9 Hz, 1H), 5.45 (dt, *J* = 11.5, 2.1 Hz, 1H), 5.19–5.13 (m, 1H), 2.52 (ddd, *J* = 15.7, 5.2, 2.4 Hz, 1H), 2.46 (t, *J* = 7.5 Hz, 2H), 2.37–2.27 (m, 2H), 2.09 (ddd, *J* = 15.7, 8.8, 1.3 Hz, 1H), 1.67–1.58 (m, 4H), 1.34–1.25 (m, 4H), 1.23 (s, 3H), 1.22 (s, 3H), 1.17 (s, 3H), 0.90 ppm (t, *J* = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 214.3, 194.6, 155.1, 146.8, 135.8, 129.4, 128.0, 49.1, 37.6, 36.7, 35.8, 27.2, 26.5, 26.3, 25.9, 25.6, 22.5, 18.0, 14.1 ppm; IR (film): $\tilde{\nu}$ = 3532, 2930, 2869, 2360, 1688, 1516, 1368, 1333, 998, 954, 908, 829, 802, 788, 755, 664, 624, 542, 493 cm^{-1}; HRMS: *m/z*: calcd for $C_{19}H_{30}O_2$: 290.2246; found: 290.2244.

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