JOC The Journal of Organic Chemistry

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Synthesis and Biological Evaluation of Kendomycin and Its Analogues

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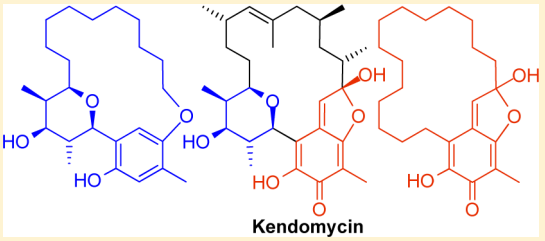
Supporting Information

ABSTRACT: Ansa compounds are gifts from microbes with intriguing molecular structures and highly potent bioactivities. One of the ansa compounds, kendomycin, has an oxa-metacyclophane skeleton with a quinone methide core and a fully substituted tetrahydropyran ring. Beyond a common synthetic strategy for construction of the ansa skeleton (i.e., elongation of an alkyl chain from an aromatic core followed by macrocyclization), we challenged a new method for construction of the ansa skeleton via simultaneous macrocyclization and benzannulation (using an intramolecular Dötz benzannulation). Understanding the reactivity of various Fischer-type ω-alkynyloxy chromium carbene complexes with kendomycin analogue syntheses led to achievement of the total synthesis of kendomycin. Investigations of structure−activity relationships revealed the need for an ansa skeleton for antimicrobial activity. Therefore, we envisage that this intramolecular Dötz benzannulation will enable divergent syntheses of ansa compounds which have important bioactive potential.



INTRODUCTION

Various secondary microbial metabolites have potent biological activities that arise from the structural complexity formed by combinations of substructures through natural selection of their producer, gene clusters.[1] Natural ansa compounds, consisting of an aromatic chromophore connected at nonadjacent positions by an aliphatic chain, are representative of such antibiotics created by a natural process. Numerous ansa compounds, including macrolactams of ansamycin family having a benzenic or naphthalenic core, have long fascinated synthetic organic chemists because of their intriguing structures and biochemists because of their biological activity.[2] Kendomycin (**1**), shown in Figure 1, is one of the hot ansa-type macrocycles which was first isolated from *Streptomyces* species as an endothelin receptor antagonist by Takeda Pharmaceutical Co. Ltd.[3] followed by a report of its antiosteoporotic activity by Su.[4] Zeeck reisolated this unique small molecule during screening for biological activity and discovered its potent antibacterial and cytotoxic activities.[5] An unprecedented unique ansa-type structure of kendomycin (**1**) attracted many synthetic organic chemists, providing five reports of the total syntheses by Lee,[6] Smith,[7] Panek,[8] Mulzer,[9] and our laboratories,[10] as well as a formal total synthesis by Rychnovsky[11] by 2010.[12] After a three year absence, the sixth total synthesis achieved by Arimoto[13] and a formal total synthesis by Fürstner[14] have recently been reported, which indicates a high interest in the fascinating kendomycin structure. Including synthetic studies by White[15] and Williams,[16] all of the syntheses realized originally developed tactics for both stereoselective synthesis of the characteristic tetrahydropyran (THP) ring and construction of the unique quinone methide moiety as well as for the assembly to the ansa structure by macrocyclization.

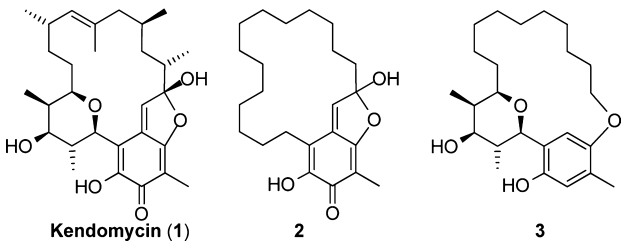


Figure 1. Kendomycin (**1**) and its analogues **2** and **3**.

Although total syntheses of kendomycin (**1**) would provide a variety of synthetic intermediates and analogues, few studies concerning the structure−activity relationship of **1** have been conducted.[5,17] Regarding our adventurous strategy with late-stage construction of the ansa skeleton by intramolecular Dötz benzannulation, we have examined the synthetic routes for two kendomycin analogues **2** and **3** in parallel with the total synthesis of **1** (Figure 1). These analogue syntheses provided not only important findings for the total synthesis of **1** but also interesting findings about bioactivities. The present report describes the syntheses of two types of kendomycin analogues **2** and **3** and the second-generation synthesis of kendomycin (**1**) based on the above-mentioned analogue synthesis. We also

Received: July 10, 2014
Published: August 19, 2014

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

describe the significant biological profiles of **1**, **2**, and **3** together with other two complemental analogues (vide infra).

RESULTS AND DISCUSSION

Synthetic Strategy of Kendomycin and Design of Its Analogues. Our perspective on the backbone of kendomycin (**1**) is an oxa-metacyclophane **4**, and our success for the total synthesis of **1** depended on utilizing intramolecular Dötz benzannulation of Fischer-type chromium carbene complex **5** to construct an ansa skeleton at once, through metal insertion into the alkyne terminus followed by CO insertion and electrocyclic ring closure (Figure 2).

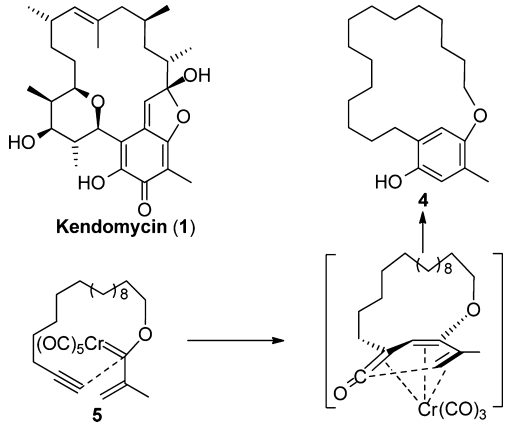


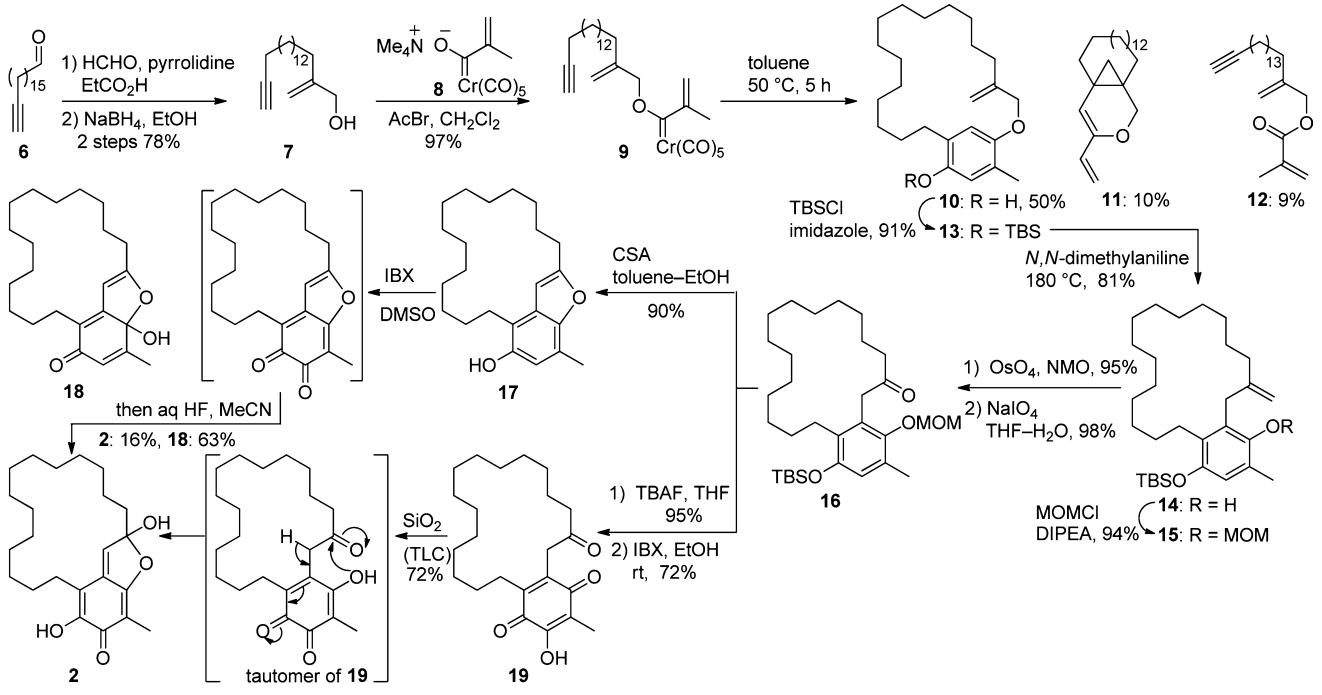
Figure 2. Intramolecular Dötz benzannulation strategy for the backbone synthesis of kendomycin (**1**).

Dötz developed this benzannulation in 1975 by heating a Fischer-type chromium carbene complex with an alkyne, producing hydroquinone monoalkyl ether via insertion of the alkyne into the carbene center.[18] Later, Semmelhack developed intramolecular benzannulation using short tethered ω-alkynyloxy aryl carbene complexes to give naphthadihydrofurans, naphthadihydropyrans, and naphthadihydroxepines produced by cyclization of aliphatic chain at the ortho position.[19] Intramolecular benzannulation of α- and β-tethered vinylidene chromium complexes have been studied intensely by Wulff and resulted in formation of various cyclophanes and cyclohexadienones.[20] Our previous study revealed that an alkynyl carbene complex **5**, having a sufficiently long alkynyloxy chain, provides the desired oxametacyclophane **4** in accordance with the regioselectivity manner of an intermolecular version.[21] Based on this success of the crucial reaction, we forwarded more complicated analogues **2** and **3** (Figure 1), which have the quinone methide core and the THP ring, respectively, specific to kendomycin (**1**).

Synthesis of Quinone Methide Analogue 2. The electrophilic quinone methide core of kendomycin (**1**) would be expected to be a major contributor for various bioactivities, and its construction would need ingenious synthetic tactic. Mulzer's success for construction of the quinone methide model involved a radical anion intermediate;[9d] later, he and all synthetic groups adopted either oxidation of 6-methoxybenzofuran-5-ol core followed by conjugate addition of water[6,9,13,14] or *o*-quinone formation from catechol monomethyl ether following by benzofuranol formation.[7,8] In view of our strategy featuring intramolecular Dötz benzannulation, the intermediate oxa-metacyclophane (e.g., **4**) needed ortho oxidation of its phenol moiety and a one-carbon prop for benzofuran core. Claisen rearrangement after benzannulation of ω-alkynyl allyl chromate would be suitable sequence for construction of the furan foothold.

Thus, synthesis of **2** started with α-methylenation of known aldehyde **6**[22] (Scheme 1). After 1,2-reduction of the obtained enal, the resulting allyl alcohol **7** was introduced to activated

Scheme 1. Synthesis of Quinone Methide Analogue 2[a]



[a]DIPEA = *N*,*N*-diisopropylethylamine, CSA = camphorsulfonic acid.

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

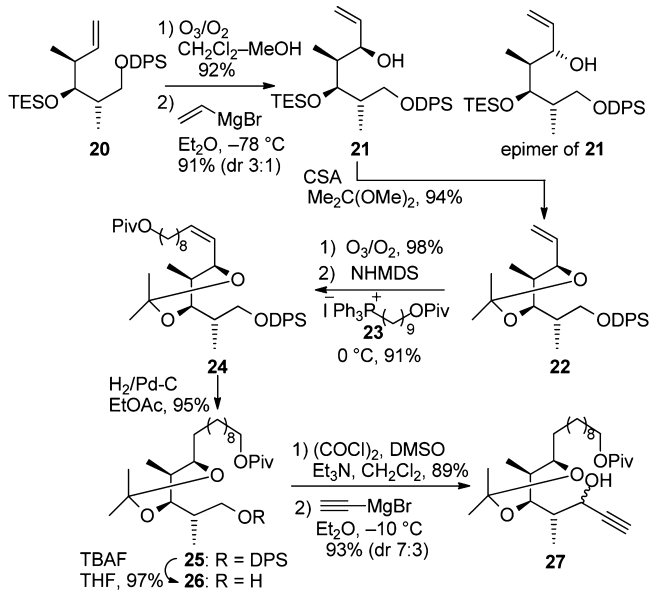
chromate[23] derived from chromate salt **8**[24] and acetyl bromide, giving chromium carbene complex **9** in 97% yield. This complex was heated in toluene to give the desired oxa-metacyclophane **10** in 50% yield along with cyclopropane **11** (10%) and oxygen-implanted ester **12** (9%). The cyclopropane side product **11** was probably produced via sequential metathesis through a vinylogue chromium carbene complex and metallacyclobutane followed by reductive elimination of chromium.[25] After protection of the phenolic hydroxy group in **10**, the silyl ether **13** was subjected to Claisen rearrangement in *N*,*N*-dimethylaniline, which accelerates the reaction rate and suppresses competitive air oxidation compared with xylene.[26,13] The rearrangement proceeded smoothly (81%) to give phenol **14** whose generated hydroxy group was protected as methoxymethyl ether, giving **15** (94%). Then the double bond of the fully protected hydroquinone **15** was cleaved by stepwise oxidation to give ketone **16** (93% in two steps).

Conversion of the resulting ketone **16** into quinone methide was investigated in two routes. An acidic treatment of ketone **16** gave benzofuran **17**, which was subjected to the next oxidation. Ortho oxidation of phenols can be accomplished by Fremy's salt[27] or benzeneselenic anhydride;[28] however, for *p*-alkoxyphenol it often competes with *p*-oxidation. An attempt to oxidize **17** with Fremy's salt resulted in no reaction, whereas in oxidation with benzeneselenic anhydride, formation of a *p*-quinone equivalent **18** was observed. In addition to these methods, Pettus reported highly regioselective ortho oxidation of phenols by IBX (2-iodoxybenzoic acid)[29] and this method was applicable to the substrate here, leading to unstable orthoquinone formation. Treatment of the red orthoquinone with aqueous HF/MeCN[6] produced the desired quinone methide analogue **2** in 16% yield for two steps along with **18** (63%). Alternatively, the silyl ether of ketone **16** was cleaved and the resulting *p*-hydroquinone monomethoxymethyl ether was subjected to ortho oxidation. The IBX oxidation in DMF using Pettus conditions afforded, accompanied by demethoxymethylation, 2-hydroxy-1,4-benzoquinone **19**, the tautomer of the desired orthoquinone, in 25% yield. After extensive solvent screening, ethanol was determined to be the best solvent, affording **19** in 72% yield. The final multistep conversion of 2-hydroxy-*p*-quinone into 2-hydroxy-*p*-quinone methide−benzofuranol was realized by a simple manipulation: applying *p*-quinone solution on silica gel.[10] A yellow solution of *p*-quinone **19** turned red when applied onto a silica gel TLC plate and then gradually became yellow. After the TLC plate was left for 12 h, the new yellow material was eluted with chloroform to give quinone methide analogue **2** in 72% yield along with the recovered *p*-quinone **19** (18%). Applying the isolated **2** on silica gel caused formation of **19** in ca. 20% yield, indicating that **2** and **19** are in equilibrium on silica gel TLC plate. No such equilibrium was observed under other conditions examined; treatment of **19** in acidic solution, on solid acid such as montmorillonite K-10, and even in an aqueous MeCN suspension of silica gel did not provide any quinone methide **2**. Even though the silica gel-specific effect on *p*-quinone−*p*-quinone methide transformation is still not well understood, the highly acidic nature[30] of 2-hydroxy-1,4-benzoquinone **19** causes dissociative adsorption on silica gel and that would account for rapid equilibrium with 4-hydroxy-1,2-quinone which can form an acetal and then can promote the following enolization to give *p*-quinone methide **2**.

Synthesis of THP Analogue 3. Construction of the fully substituted THP ring is one of the key steps of kendomycin synthesis. Starting from chiral building blocks, aldol reaction[6,7,9,14,15] or crotylation[8,10,11,13] followed by cyclization realized stereoselective construction of the THP ring. In our case, both the reaction rate and the ease of the benzannulation/macrocyclization should be affected by the bulky THP ring adjacent to the triple bond which is a reaction site of benzannulation. Thus, the THP ring formation after Dötz benzannulation was first investigated in the course of the synthesis of the THP analogue **3**.

We used the racemic stereotriad **20**[31] prepared through diastereoselective crotylation for the construction of the substituents on the THP ring (Scheme 2). Oxidative cleavage

Scheme 2. Synthesis of Common Intermediate 27



of terminal olefin followed by addition of vinylmagnesium bromide afforded the Felkin adduct **21** along with the epimer of **21** (91% yield, dr 3:1). The major adduct **21** was transformed into acetonide **22** (94%), which was subjected to another ozone oxidation and subsequent carbon elongation by Wittig reaction with salt **23** to adjust the length of the ansa chain with **1**, affording **24** (89% in two steps). Hydrogenation of the resulting olefin furnished a saturated alphatic chain of THP analogue intermediate **25** (95%). Then the opposite side of the aliphatic chain was elaborated with three steps; after deprotection of DPS ether, primary alcohol **26** was subjected to Swern oxidation followed by addition of ethynylmagnesium bromide, giving propargyl alcohol **27** (83% in two steps, a 7:3 mixture of diastereomers). To examine the stability and reactivity of the corresponding chromium carbene complexes, the obtained common intermediate **27** was converted into the diverse alkynyl alcohols (Scheme 3).

Reductive removal of the pivaroyl group of **27** provided alkynyl alcohol **28a** (98%). Further acid treatment of **28a** served tetraol **28b** (82%). Treatment of **28b** with **8** and AcBr resulted in decomposition, giving no **29b**. The propargyl hydroxy group of **27** was subjected to etherification, affording methyl ether **28c** or PMB ether **28d** after depivaroylation or concomitant with depivaroylation, respectively. These alkynyl alcohols **28a**, **28c**, and **28d** were transformed into the corresponding chromium carbene complexes **29a**, **29c**, and **29d** in good yields (88%, 76%, and 64% yield, respectively).

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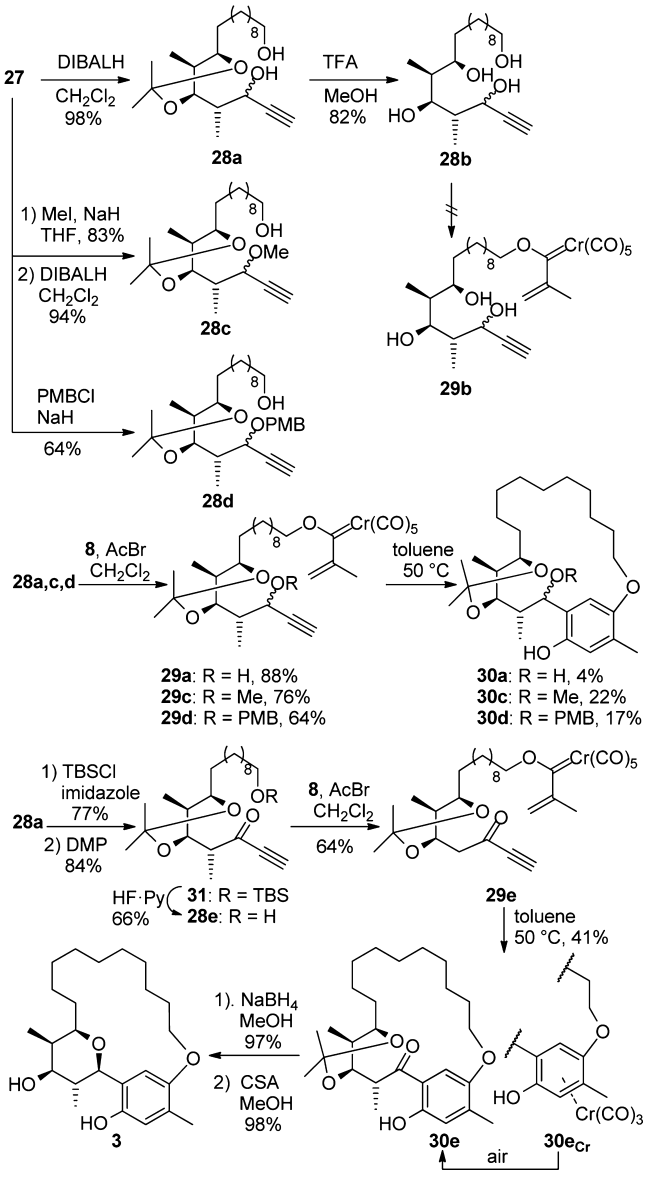
Scheme 3. Synthesis of THP Analogue 3



Next, the critical benzannulation step via heating of each dilute complex solution was examined. Complex **29a** with a propargyl hydroxy group caused some decomposition in an isolated yield of oxa-metacyclophane **30a** of only 4%. Methyl ether **29c** and PMB ether **29d** reduced the decomposition, giving the desired oxa-metacyclophane **30c** (22% yield) and **30d** (17% yield), respectively. Interesting behavior was observed in the case of the fifth substrate, ynone **28e**. This was derived from **28a** in 43% yield via selective silylation of the primary hydroxy group, oxidation of the propargyl hydroxy group with Dess–Martin periodinane (DMP), and desilylation of the resulting ynone **31**. After complexation of **28e** with **8** and AcBr in 64% yield, complex **29e** was subjected to the benzannulation conditions to give oxa-metacyclophane **30e** (4% yield) along with the unexpected arene chromium tricarbonyl complex $\mathbf{30e}_{Cr}$ (37% yield), which was stable relative to other arene complex formed via Dötz benzannulation.[21] The resulting complex $\mathbf{30e}_{Cr}$ gradually decomposed upon exposure to air to produce oxa-metacyclophane **30e** quantitatively. After reduction of the carbonyl group in **30e** (97% yield), acid-catalyzed deacetonization and thermodynamically controlled benzylic cyclization were performed to give the desired THP analogue **3** in 98% yield. These results indicate that a terminal ynone poised for THP-ring construction would be most suitable as an intermediate for the synthesis of **1**; the ynone carbonyl group is smaller than alkyl ethers, and the ynone-containing complex is more stable than the propargyl alcohol-containing complex under the conditions used for benzannulation. In addition, insertion of the carbene center to the alkyne having an electron-withdrawing group occurred smoothly, followed by CO insertion and electrocyclic reaction while the carbonyl group remained intact, providing oxa-metacyclophane **30e** in an acceptable yield.

Investigation of Benzannulation toward the Total Synthesis of Kendomycin (1). Based on the results from the two analogue syntheses, the total synthesis of kendomycin (**1**) was attempted featuring preparation of the ynone-containing alkynyl alcohol, Dötz benzannulation, Claisen rearrangement, and IBX oxidation.

We obtained the important synthetic intermediate **33** in an enantiomerically pure form from three segments, (−)- and (+)-**20** and alkyne (+)-**32**, through coupling at the broken lines in the structure of **33**, using the procedures previously reported[10] (Scheme 4). Desilylation of the alkyne terminus of **33** followed by oxidation of the propargyl hydroxy group afforded ynone **34**, which produced the most promising benzannulation precursor **35** by TBS deprotection. Introduction of the obtained alcohol **35** into complex **8** via activation by AcBr afforded the chromium carbene complex **36** in 90% yield. This was immediately heated in toluene at 50 °C to provide oxa-metacyclophane **37** in only 14% yield along with arene complex $\mathbf{37}_{Cr}$ (5%) and considerable amounts of ketone **38** (38%). The unexpected side product **38** would be formed by a metalla-Claisen type rearrangement of the carbene complex with the exo-olefin, followed by reductive elimination of the chromium carbonyl that has never seen in the synthesis of quinone methide analogue **2** (Scheme 1). Investigations using other solvents (hexane, THF) or lower reaction temperature (35 °C in toluene) did not produce any positive effect on the benzannulation, which indicates that this substrate designed based on the results of the model studies (Schemes 1–3) is not suitable for kendomycin synthesis. Therefore, modification of the substituents around the reaction sites (carbene center and the triple bond) was required.

Through several investigations of the substrates for benzannulation, our results, contrary to our expectations, indicated that THP-ring formation prior to benzannulation was most effective for assisting the desired Dötz benzannulation (Scheme 4). Propargyl alcohol **33** was oxidized with DMP to ynone **39** (98%), and the following acid treatment with CSA realized deprotection of both acetonide and TBS ether to give methyl acetal **40** in 89% yield. After deoxygenation of **40** with triethylsilane (71%), the THP-containing diol **41**[10] was subjected to disilylation and the resulting **42** was selectively deprotected to afford **43** in 77% yield. The resulting alkynyl alcohol **43** was subjected to complexation with the activated chromate from **8** followed by benzannulation to give the desired oxa-metacyclophane **44** as the sole isolated product in 50% yield in two steps.

Alternative Route for Synthesis of Alkynyl Alcohol 43: Potential of Dithiane Chemistry. Although we found the most suitable substrate for the intramolecular Dötz benzannulation, the early step of this synthetic route was faced with a

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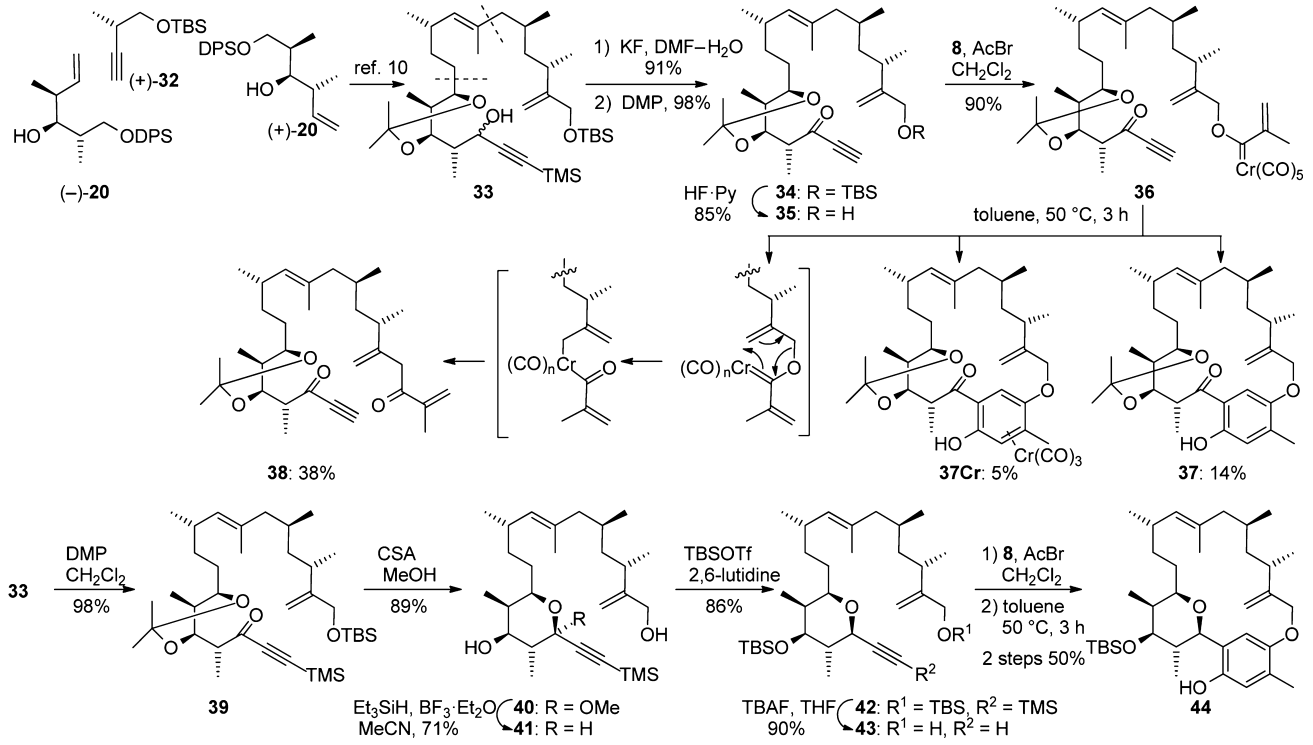
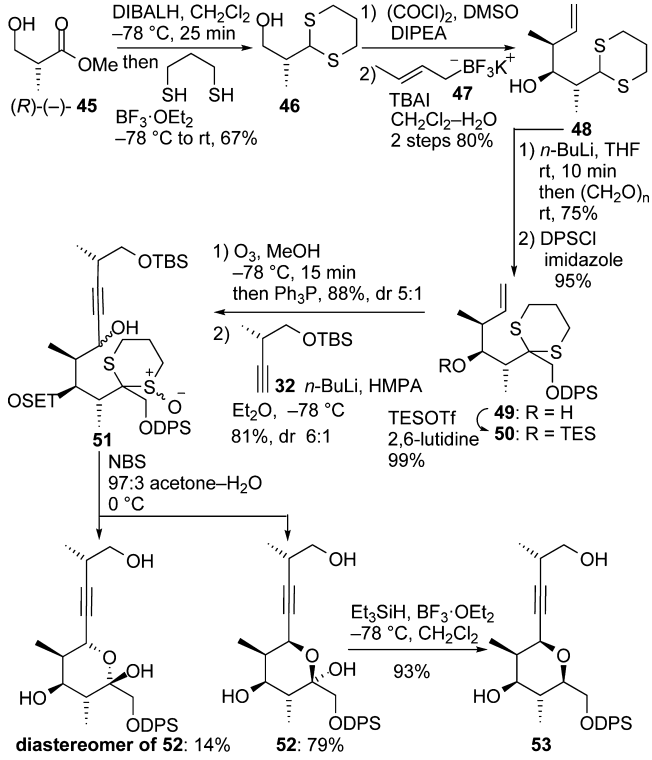
Scheme 4. Investigation of Benzannulation



dilemma. The starting substrates, both enantiomers (+)- and (−)-**20**, were readily prepared from the chiral Roche aldehydes using potassium *E*-crotyl trifluoroborate,[32] an easily handled reagent for practical synthesis; however, diastereoselectivity of this crotylation was moderate (dr 3:1).[33] As a breakthrough in the limitation due to the use of potassium crotyltrifluoroborate, we previously found that crotylation of α-dithianylpropionaldehyde derived from **46** with potassium *E*-crotyltrifluoroborate **47** gave the Felkin–Anh adduct **48** with high diastereoselectivity (dr 24:1).[33] In addition, the resulting homoallyl alcohol can be regarded as bisaldehyde synthon whose either terminal is available for further coupling reactions. Thus, a new route to alkynyl alcohol **43** involving the diastereoselective crotylation of α-dithianylpropionaldehyde was investigated (Scheme 5).

Preparation of dithianyl alcohol **46** was readily performed by one-pot, two-step manipulation from commercially available Roshe ester **45** which was previously used for the synthesis of the same alcohol by five-step transformation by Smith.[34] After Swern oxidation, the resulting aldehyde was subjected to crotylation using crotyltrifluoroborate **47** to give the desired homoallyl alcohol **48** in 80% yield in two steps after the diastereomer separation. Then dithioacetal carbon was successfully metalated,[33] and the resulting dianion was exposed to hydroxymethylation (75%) followed by selective silylation, giving **49** (95%). The next challenging oxidative cleavage of the opposite terminus double bond of **49** in the presense of the dithiane moiety was realized by ozone oxidation of its triethylsilyl ether **50**, accompanying mono-oxidation of the dithiane sulfur atom, to afford an aldehyde in 88% yield as a 5:1 mixture of the diastereomers arose from the sulfoxide centers.[35] This sulfoxide functionality turned out to be intact after the following addition of the acetylide derived from **32**; the resulting adduct **51** was a mixture of the diastereomers at the new stereocenter having the hydroxy group and the sulfoxide centers. Dedithioacetalization of **51** with NBS[36] in wet acetone

Scheme 5. Alternative THP Ring Synthesis[a]



[a]TBAI = tetrabutylammonium iodide.

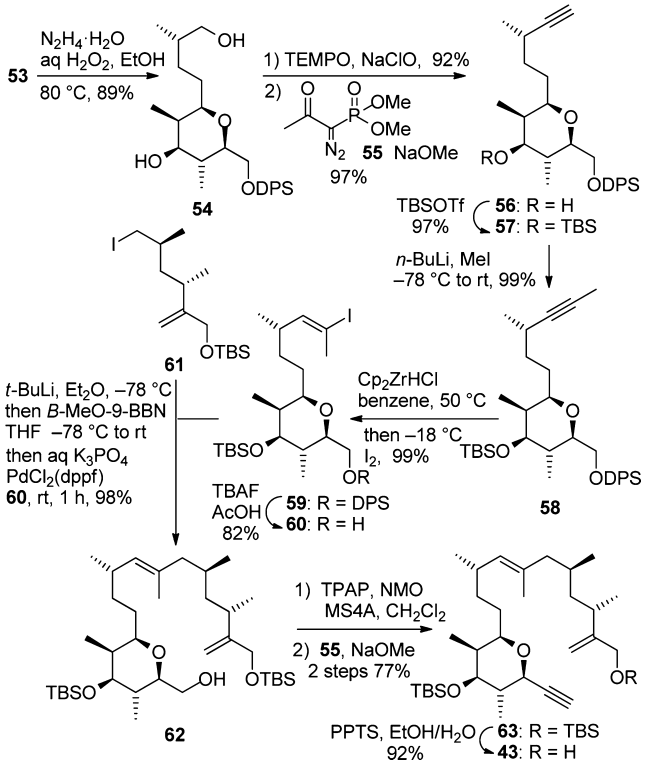
concomitant with desilylation and cyclization efficiently provided hemiacetal **52** (79%) and its diastereomer (14%), which revealed a 6:1 diastereoselectivity in the above acetylide addition reaction. Deoxygenation of the hemiacetal with

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922–9947

triethylsilane in the presence of $BF_3{\cdot}OEt_2$ afforded tetrahydropyran **53** with the desired stereochemistry.

The following transformations were done according to the previously developed sequences (Scheme 6).[10] After diimide reduction of **53** (89% yield), the hydroxymethyl terminus of the resulting **54** was converted to the triple bond via site-selective TEMPO oxidation and Ohira alkynylation (two steps, 85% yield), giving **56**. After the remaining hydroxy group was protected as the TBS ether, the alkyne terminus in **57** was methylated to afford **58** in 99% yield. Subsequent hydrozirconation/iodination[11,37] of **58** required a strict temperature control to provide the desired iodoolefin **59** in 99% yield without formation of its regioisomer. Subsequent selective deprotection of the DPS group in the presence of the TBS group furnished alcohol **60**, a precursor of the Suzuki–Miyaura coupling. The reliable Suzuki–Miyaura coupling[6,11,38] of iodoalkene **60** and alkyl borane derived from iodoalkane **61**[10] smoothly provided the trisubstituted alkene **62** in 98% yield. Following oxidation of the primary alcohol, alkynylation with **55** afforded the terminal alkyne **63**, selective desilylation of which realized second-generation synthesis of alkynyl alcohol **43**. Establishment of this new route demonstrated the utility of crotylation of the dithiane-containing aldehyde; the crotylation is highly diastereoselective to give the desired, stereotriad and the resulting dithiane-containing homoallyl alcohol can be used for further conversions at both termini in a flexible manner.

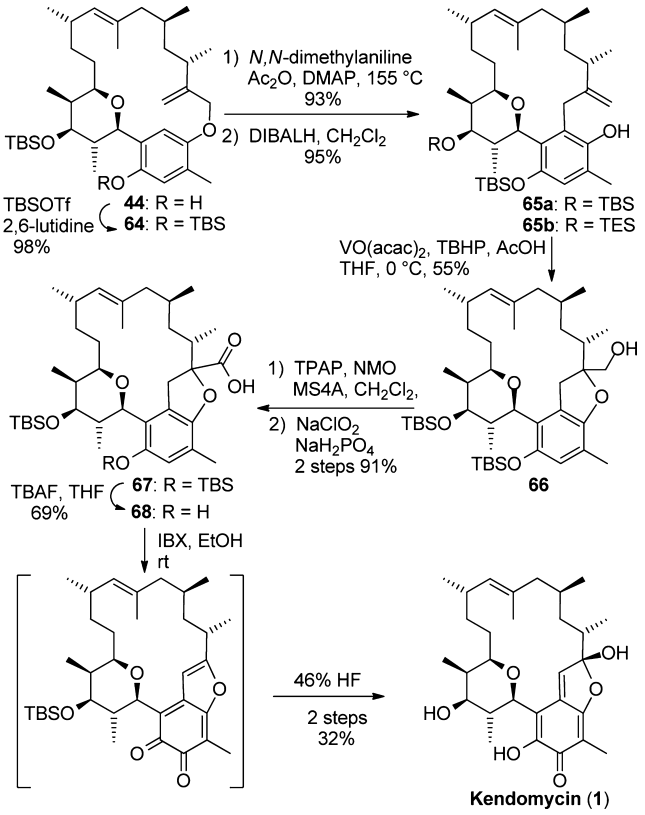
Scheme 6. Synthetic Route for Alkynyl Alcohol 43[a]



[a]dppf = 1,1′-bis(diphenylphosphino)ferrocene, TPAP = tetrapropylammonium perruthenate, MS = molecular sieves, PPTS = pyridinium *p*-toluenesulfonate.

Second-Generation Total Synthesis of Kendomycin (1) via Site-Selective Oxidation. Oxa-metacyclophane **44**, obtained through Dötz benzannulation in Scheme 4, was next converted to TBS ether **64**, and this was subjected to Claisen rearrangement (Scheme 7). In addition to the solvent choice based on the synthesis of analogue **2**, acetic anhydride and DMAP as additives were required to prevent formation of an unexpected side product formed by cyclization of the resulting phenolic hydroxy group into the exo-olefin.[39] After deacetylation with DIBALH, phenol **65a** was exploited for further conversion into the final target **1**.

Scheme 7. Total Synthesis of Kendomycin (1) via Decarboxylative Orthoquinone Formation



The previous total synthesis[10] featured methodology for the synthesis of quinone methide analogue **2** (Scheme 1) using triethylsilyl ether **65b** instead of TBS ether **65a**; however, this approach had one large obstacle. To complete the total synthesis, one-carbon degradation at the exomethylene position was necessary. The inner trisubstituted double bond was more reactive than the exomethylene under the oxidative scission conditions, requiring extra protection–deprotection of the inner double bond. Thus, reinvestigation of the late-stage sequence furnished a new total synthesis.

Hydroxy-directed, vanadium-catalyzed TBHP epoxidation[40] of 2-(2-alkenyl)phenol **65a** was used in the presence of acetic acid to afford 2,3-dihydrobenzofuran **66** in 55% yield. Removal of the hydroxymethyl group was realized as follows. Two-step oxidation of the primary hydroxy group of **66** with TPAP-NMO and $NaClO_2$ gave carboxylic acid **67**. Then selective desilylation of the aromatic TBS ether afforded **68** which was subjected to ortho-oxidation with IBX in EtOH. A transient red spot was observed in lower polarity areas on TLC (R_f of the red spot = 0.85 and R_f of **68** = 0.28 on SiO_2 TLC (2:1 hexane–acetone)), suggesting the formation of a highly unstable benzofuran–orthoquinone via simultaneous decarboxylation. The orthoquinone was treated immediately with concentrated aqueous HF solution[6] to achieve the second-generation total

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922–9947

synthesis of kendomycin (**1**) (32%, two steps). This new route from **65a** to kendomycin (**1**) is shorter with better yield (six steps, 11%) than the previous route from the corresponding triethylsilyl ether **65b** to **1** (nine steps, 4.6%).[10]

Kendomycin Macrocycle: Essential for Biological Activity. The broad activities[3−5,41,42] and multifunctional structures of **1** complicate the establishment of structure−activity relationships. The first example is a Zeeck's derivative[5a] that retains high antimicrobial activity and cytotoxicity despite the loss of a quinone methide core specific to **1**. Subsequently, two other biosynthetically derived analogues showed greater antimicrobial activity and lower cytotoxicity than **1**.[5b] These observations suggest the existence of a certain key element in the skeleton of **1** responsible for each bioactivity. The quinone methide analogue **2** and the THP analogue **3** are appropriate for pursuit of the key element; because each analogue has a characteristic moiety such as THP ring and quinone methide core, and each ansa-chain is expected to possess hydrophobic space similar to that of kendomycin (**1**). Thus, we attempted to narrow down precise structure essential to antimicrobial activity by use of analogues **2** and **3**. The optically pure **3**, instead of the racemate **3**, was separately prepared by the similar manner to the second synthetic route for **43** involving dithiane chemistry (Scheme 8).

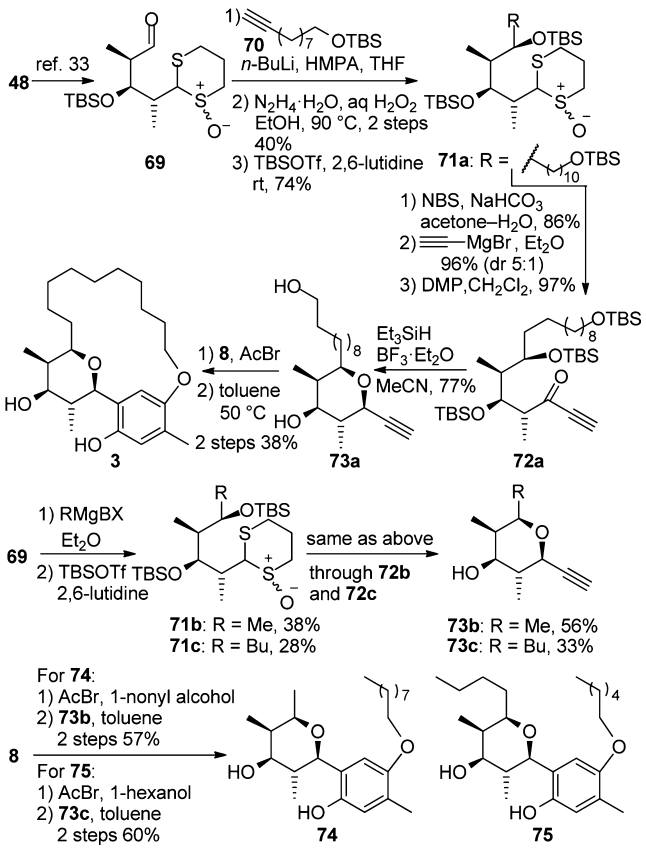
Aldehyde **69** synthesized from homoallyl alcohol **48** was subjected to addition of an acetylide derived from **70**,[43] giving a 5:1 mixture of adducts at the newly formed stereocenter. Prior to dedithioacetalization, diimide reduction with hydrazine hydrate and H_2O_2 followed by silylation was conducted to give tri-TBS ether **71a** after separation of diastereomers (three steps 29%). A subsequent three-step sequence including treatment with NBS, ethynylmagnesium bromide addition, and DMP oxidation provided ynone **72a** in 80% yield. THP formation was stereoselectively succeeded by using a combination of Et_3SiH and $BF_3{\cdot}Et_2O$ in MeCN instead of CH_2Cl_2 in kendomycin synthesis to give alkynyl alcohol **73a** in 77% yield. The reliable complexation and intramolecular Dötz benzannulation furnished the optically pure THP analogue **3**.

A preliminary antibacterial assay[44] against *Staphyrococcus aureus* including MRSA and *Enterococcus faecalis/faecium* including VRE indicated that both the quinone methide analogue **2** and the THP analogue **3** possessed activities similar to those of kendomycin (**1**) (Table 1). Next, focus was directed toward a common element, the macrocycle skeleton. To verify the effect of the macrocycle skeleton on biological activity, two open-chain THP analogues, **74** and **75**, were synthesized as new analogues by the similar synthetic route to **3**: addition of Grignard reagents to give **71b** and **71c**, THP formation in four steps, giving **73b** and **73c** through **72b** and **72c**, and intermolecular benzannulation with the corresponding alkyl chromates (Scheme 8). The net carbon numbers in the alkyl chain of **74** and **75** are same as those of THP analogue **3**. Comparison of **74** and **75** was done to determine whether the divided position affects bioactivity. These two analogues possessed no antimicrobial activities, which indicated the importance of the macrocycle skeleton for activity. A similar phenomenon was found in the rifamycin family, a representative ansamycin. The recently isolated open-chain analogue of rifamycin, salinisporamycin, exhibited much less potent antimicrobial activity than rifamycin S, though the authors mentioned that the decrease in activity was attributed to the different positions of the hydroxy groups necessary for binding to the target.[45] Furthermore, a previous report described the curious observation that a variety of chemical modifications of the rifamycin aromatic core did not reduce the antimicrobial activity and that the main requires feature for antimicrobial activity might be the ansa bridge.[46] The results presented here add additional evidence for the involvement of the ansa bridge in biological activity.

Table 1. Antimicrobial Activities of 1, Analogues 2 and 3, and Open-Chain Analogues 74 and 75

	MIC (μg/mL)				
organisms	**1**	**2**	**3**	**74**	**75**
S. aureus Smith	4	8	4	128	>64
S. aureus MRSA No.5	8	16	4	>128	>64
S. aureus MRSA No.17	8	8	4	>128	>64
E. faecalis JCM 5803	4	8	8	>64	>64
E. faecalis NCTC12203 (VRE)	4	2	4	>64	>64
E. faecium JCM 5804	8	8	4	>64	>64
E. faecium NCTC12202 (VRE)	4	4	8	>64	>64

Scheme 8. Synthesis of Optically Pure 3 and Open-Chain Analogues 74 and 75



■ CONCLUSIONS

We examined benzannulation of various alkyne-tethered Fischer-type chromium carbene complexes. Tuning of the substituent structures around the reaction sites realized the desired benzannulation of a complicated chromium carbene complex, allowing success of the total synthesis of kendomycin (**1**). In addition, incorporation of dithiane chemistry into the synthesis of the ansa-chain moiety and success of the site-selective oxidation of the double bonds in the late-stage rewrote

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

issues of the previous route. The result of antibacterial test comparing **3** with the open-chain analogues **74** and **75** revealed that the ansa skeleton is necessary for antimicrobial activity, which enhances the value of our method, simultaneous macrocyclization and benzannulation, supplying various ansa compound analogues with a variety of ansa chains.

EXPERIMENTAL SECTION

General Methods. Melting points were uncorrected. Optical rotations were recorded on a polarimeter in an appropriate solvent. UV−vis absorptions were recorded on a UV−vis spectrophotometer. IR spectra were obtained on a NaCl cell or in a KBr pellet and recorded on a FT-IR spectrometer. ^{1}H NMR spectra were recorded at 300 or 500 MHz, and ^{13}C NMR spectra were recorded at 75 or 125 MHz at ambient temperature. Chemical shifts (δ) are reported in ppm referenced to TMS or residual solvent signal. When the nonequivalent carbons have the same chemical shift in ^{13}C NMR spectrum, the value of the chemical shift is doubly or triply written. High- and low-resolution mass spectra were recorded by EI or FAB with quadrupole mass analyzer. Analytical thin-layer chromatography (TLC) was performed on 0.25 mm silica gel plates, and visualization was accomplished with ethanolic phosphomolybudic acid. Column chromatography was performed on spherical silica gel (particle size 100 μm). Experiments requiring anhydrous conditions were performed under an argon atmosphere. Organic solvents were distilled by appropriate procedure and stored under argon atmosphere.

Pentacarbonyl[(16-heptadecyn-1-oxy)(isopropenyl)carbene]chromium(0) (5). To a stirred solution of tetramethylammonium salt **8**[24] (47.8 mg, 0.143 mmol) in dry CH_2Cl_2 (1.88 mL) was added AcBr (0.011 mL, 0.143 mmol) at −50 °C. After 1.5 h at −78 °C, a solution of 16-heptadecyn-1-ol[47] (30.0 mg, 0.119 mmol) in dry CH_2Cl_2 (0.50 mL) was added at −78 °C, and the resulting mixture was warmed to 0 °C in 1 h. After removal of solvent at 0 °C, the residue was dissolved in pentane (5 mL), filtered, and concentrated. The crude red mixture was purified by column chromatography on silica gel (2.0 g, 7:1 hexane−EtOAc) to afford **5** (58.0 mg, 98%) as a red syrup: R_f = 0.69 (5:1 hexane−EtOAc); IR (neat, cm^{-1}) 3313, 2927, 2855, 2361, 2341, 2062, 1934, 1460, 1279, 1228, 979; ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.21−1.42 (m, 20H), 1.50 (m, 4H), 1.87 (s, 3H), 1.91−2.00 (m, 3H), 2.18 (dt, J = 2.3, 6.9 Hz, 2H), 4.72 (br s, 2H), 4.89 (br s, 1H), 5.06 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 18.4, 19.3 (br), 25.7, 28.5, 28.8, 29.11, 29.11, 29.4, 29.49, 29.49, 29.60, 29.60, 29.63, 29.63, 68.0, 80.1(br), 84.8, 216.4, 224.0, 353.5 (br); LRMS (EI) m/z (M)$^+$ 496.3; HRMS (EI) m/z (M)$^+$ calcd for $C_{26}H_{36}O_6Cr$ 496.1917, found 496.1944.

18-Hydroxy-20-methyl-1-oxa[16]metacyclophane (4). A solution of **5** (58.0 mg, 0.117 mmol) in dry degassed toluene (58.4 mL) was stirred at 50 °C for 3 h and then cooled to rt. After 12 h in air, the mixture was concentrated. The residue was purified by column chromatography on silica gel (2 g, 5:1 hexane−EtOAc) to afford **4** (21.1 mg, 54%) as colorless plates: R_f = 0.47 (5:1 hexane−EtOAc); mp = 44−45 °C (not recrystallized); IR (neat, cm^{-1}) 3406, 2927, 2855, 1719, 1515, 1459, 1415, 1215, 1196, 1098, 1022, 867; ^{1}H NMR (500 MHz, $CDCl_3$, TMS = 0.00) δ 1.22−1.39 (m, 20H), 1.46 (m, 2H), 1.60 (m, 2H), 1.80 (tt, J = 6.4, 6.4 Hz, 2H), 2.16 (s, 3H), 2.57 (t, J = 6.4 Hz, 2H), 3.94 (t, J = 6.4 Hz, 2H), 4.26 (br s, 1H), 6.58 (br s, 1H), 6.60 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 15.8, 24.8, 27.1, 27.2, 27.4, 27.6, 27.68 27.71, 28.0, 28.2, 28.33, 28.34, 28.6, 28.7, 29.1, 68.8, 115.0, 117.7, 125.6, 125.8, 146.8, 151.1; LRMS (EI) m/z (M)$^+$ 332.3; HRMS (EI) m/z (M)$^+$ calcd for $C_{22}H_{36}O_2$ 332.2715, found 332.2717.

2-Methyleneoctadec-17-yn-1-ol (7). To a solution of octadec-17-yn-1-al (**6**, 13.9 mg, 0.0526 mmol)[48] in *i*-PrOH (0.426 mL) were added at rt 35% aqueous formaldehyde solution (0.009 mL, 0.1 mmol), 105 mM pyrrolidine in *i*-PrOH (0.050 mL, 0.0053 mmol), and 105 mM propionic acid in *i*-PrOH (0.050 mL, 0.0053 mmol). The solution was heated at 45 °C for 4 h, and then the reaction mixture was quenched with H_2O at rt. The mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1.5 g, 15:1 hexane−EtOAc) to afford 2-methyleneoctadec-17-yn-1-al (11.6 mg, 80%) as colorless needles: R_f = 0.79 (10:1 hexane−EtOAc); mp = 34−35 °C (not recrystallized); IR (KBr, cm^{-1}) 3255, 2918, 2849, 1679, 1463, 1328, 1101, 955, 850, 707; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.22−1.34 (m, 18H), 1.34−1.48 (m, 4H), 1.48−1.56 (m, 2H), 1.93 (t, J = 2.9 Hz, 1H), 2.18 (dt, J = 2.9, 7.2 Hz, 2H), 2.23 (br t, J = 7.5 Hz, 2H), 5.98 (br s, 1H), 6.24 (br d, J = 0.8 Hz, 1H), 9.53 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ 18.4, 27.74, 27.75, 28.5, 28.8, 29.1, 29.3, 29.4, 29.49, 29.54, 29.58, 29.61, 29.61,29.61, 68.0, 84.8, 133.9, 150.5, 194.8; LRMS (FAB) m/z (M + H)$^+$ 277.3; HRMS (FAB) m/z (M + H)$^+$ calcd for $C_{19}H_{33}O$ 277.2531, found 277.2506. To a stirred solution of this aldehyde (11.6 mg, 0.0420 mmol) in EtOH (0.084 mL) was added at 0 °C $NaBH_4$ (0.80 mg, 0.021 mmol). After 15 min at 0 °C, saturated aqueous NaCl was added, and the mixture was extracted with EtOAc. The extracts were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (1 g, 3:1 hexane−EtOAc) to afford **7** (11.4 mg, 97%) as colorless needles: R_f = 0.21 (5:1 hexane−EtOAc); mp = 37−38 °C (not recrystallized); IR (KBr, cm^{-1}) 3383, 3287, 2918, 2845, 1660, 1475, 1463, 1083, 1064, 1027, 891, 731, 720; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 1.16−1.59 (m, 24H), 1.94 (t, J = 2.2 Hz, 1H), 2.05 (t, J = 7.4 Hz, 2H), 2.18 (dt, J = 2.2, 7.4 Hz, 2H), 4.07 (br s, 2H), 4.86 (br d, J = 1.4 Hz, 1H), 5.01 (br d, J = 1.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 18.3, 27.7, 28.4, 28.7, 29.1, 29.4, 29.46, 29.46, 29.56, 29.56, 29.60, 29.60, 29.60, 32.9, 65.8, 68.0, 84.8, 108.8, 149.2; LRMS (EI) m/z (M)$^+$ 278.2; HRMS (EI) m/z (M)$^+$ calcd for $C_{19}H_{34}O$ 278.2610, found 278.2589.

Pentacarbonyl[(2-methyleneoctadec-17-yn-1-oxy)(isopropenyl)carbene]chromium(0) (9). To a stirred solution of tetramethylammonium salt **8**[24] (247 mg, 0.738 mmol) in CH_2Cl_2 (12.3 mL) was added AcBr (0.055 mL, 0.738 mmol) at −50 °C. After 1.5 h at −78 °C, a solution of **7** (171 mg, 0.615 mmol) in CH_2Cl_2 (1.5 mL) was added and gradually warmed to 0 °C for a period of 30 min. After 1 h at 0 °C, the mixture was concentrated at 0 °C. The residue was purified by column chromatography on silica gel (10 g, 5:1 hexane−EtOAc) to afford **9** (312 mg, 97%) as a red syrup: R_f = 0.62 (5:1 hexane−EtOAc); IR (neat, cm^{-1}) 3313, 2928, 2855, 2063, 1939, 1448, 1371, 1278, 1184, 971, 896; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.22−1.35 (m, 18H), 1.38 (m, 2H), 1.46−1.58 (m, 4H), 1.89 (s, 3H), 1.93 (t, J = 2.6 Hz, 1H), 2.18 (t, J = 7.2 Hz, 2H), 2.18 (dt, J = 2.6, 7.2 Hz, 2H), 4.84 (br, 1H), 5.05 (br s, 1H), 5.11 (br s, 1H), 5.11 (br, 2H), 5.16 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 18.4, 19.4, 27.4, 28.5, 28.8, 29.1, 29.3, 29.4, 29.5, 29.55, 29.62, 29.60, 29.60, 29.60, 33.1, 68.0, 81.7 (br), 84.8, 114.3, 143.1, 157 (br), 216.2, 224.0, 354.1; LRMS (EI) m/z (M)$^+$ 522.2.

19-Hydroxy-21-methyl-3-methylene-1-oxa[17]metacyclophane (10), 4-(Prop-1-en-2-yl)-3-oxatricyclo[14,4,1,0^{1,6}]henicosane-4-ene (11), and 2-Methyleneoctadec-17-ynyl methacrylate (12). A solution of **9** (312 mg, 0.597 mmol) in dry degassed toluene (307 mL) was stirred at 50 °C. After 5 h, the mixture was concentrated. The residue was purified by column chromatography on silica gel (12 g, 8:1 hexane−EtOAc) to afford **10** (108 mg, 50%), **11** (19.7 mg, 10%), and **12** (18.6 mg, 9%) as colorless syrups. **10**: R_f = 0.39 (5:1 hexane−EtOAc); IR (neat, cm^{-1}) 2925, 2857, 1505, 1461, 1402, 1253, 1208, 1128, 1038, 903, 838, 780; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 1.21−1.40 (m, 20H), 1.42−1.67 (m, 4H), 2.17 (br dt, J = 1.8, 8.0 Hz, 2H), 2.20 (s, 3H), 2.56 (t, J = 7.5 Hz, 2H), 4.25 (s, 1H), 4.39 (s, 2H), 4.97 (br s, 1H), 5.14 (br d, J = 1.8 Hz, 1H), 6.55 (s, 1H), 6.59 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 15.8, 27.37, 27.42, 27.5, 27.7, 27.80, 27.80, 27.88, 27.93, 28.1, 28.2, 28.4, 28.6, 29.3, 33.3, 70.7, 110.7, 113.8, 117.8, 125.3, 125.6, 145.2, 146.8, 150.8; LRMS (EI) m/z (M$^+$) 358.3; HRMS (EI) m/z (M$^+$) calcd for $C_{24}H_{38}O_2$ 358.2872, found 358.2848. **11**: R_f = 0.92 (5:1 hexane−EtOAc); IR (neat, cm^{-1}) 2927, 2855, 1735, 1458, 1375, 1244, 1112, 1046, 942, 896, 801, 760; ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.44 (d, J = 4.2 Hz, 1H), 1.14 (d, J = 4.2 Hz, 1H), 1.17−1.66 (m, 28H), 1.82 (s, 3H), 3.57 (d, J = 10.0 Hz, 1H), 4.06 (d, J = 10.0 Hz, 1H), 4.81 (br s, 1H), 5.27 (br d, J = 2.2 Hz, 1H), 5.33 (s, 1H); ^{13}C

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

NMR (300 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 19.0, 23.3, 23.6, 25.9, 26.1, 26.3, 26.5, 26.6, 26.7, 26.8, 26.9, 27.0, 27.2, 28.0, 28.1, 30.3, 32.9, 33.5, 67.0, 109.5, 110.1, 137.3, 150.0; LRMS (EI) m/z (M^+) 330.3; HRMS (EI) m/z (M^+) calcd for $C_{23}H_{38}O$ 330.2923, found 330.2915. **12**: R_f = 0.50 (5:1 hexane−EtOAc); IR (neat, cm^{-1}) 3316, 2924, 2856, 1721, 1458, 1320, 1297, 1160, 942, 907, 817; ^1H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 1.22−1.58 (m, 24H), 1.94 (t, J = 2.8 Hz, 1H), 1.97 (s, 3H), 2.08 (br t, J = 7.8 Hz, 2H), 2.18 (dt, J = 2.8, 7.2 Hz, 2H), 4.60 (br s, 2H), 4.94 (br s, 1H), 5.03 (br d, J = 1.1 Hz, 1H), 5.58 (t, J = 1.6 Hz, 1H), 6.15 (br s, 1H); ^{13}C NMR (300 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 18.3, 18.4, 27.5, 28.5, 28.8, 29.1, 29.3, 29.46, 29.49, 29.59, 29.59, 29.63, 29.63, 29.63, 33.3, 67.0, 68.0, 84.8, 111.8, 125.6, 136.3, 144.2, 167.1; LRMS (EI) m/z (M^+) 346.3; HRMS (EI) m/z (M^+) calcd for $C_{23}H_{38}O_2$ 346.2872, found 346.2893.

19-(*tert*-Butyldimethylsilyloxy)-21-methyl-3-methylene-1-oxa[17]metacyclophane (13). To a stirred solution of **10** (98.7 mg, 0.275 mmol) in CH_2Cl_2 (1.1 mL) were added at rt imidazole (56.3 mg, 0.826 mmol) and TBSCl (62.2 mg, 0.423 mmol). After 2 h at rt, saturated aqueous NH_4Cl was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (7 g, 2:1 hexane−$CHCl_3$) to afford **13** (119 mg, 91%) as a colorless syrup: R_f = 0.70 (5:1 hexane−EtOAc); IR (neat, cm^{-1}) 3408, 2922, 2855, 1518, 1459, 1416, 1196, 1111, 1042, 900, 863; ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.19 (s, 6H), 1.00 (s, 9H), 1.24−1.39 (m, 20H), 1.42−1.62 (m, 4H), 2.16 (t, J = 8.0 Hz, 2H), 2.19 (s, 3H), 2.53 (t, J = 7.8 Hz, 2H), 4.39 (s, 2H), 4.96 (br s, 1H), 5.14 (br d, J = 2.0 Hz, 1H), 6.56 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.2, 16.0, 18.2, 25.8, 27.38, 27.44, 27.5, 27.7, 27.78, 27.80, 27.94, 27.94, 28.1, 28.2, 28.4, 28.9, 29.9, 33.3, 70.5, 110.6, 113.6, 120.8, 124.5, 130.4, 145.3, 146.7, 150.8; LRMS (EI) m/z (M^+) 472.3; HRMS (EI) m/z (M^+) calcd for $C_{30}H_{52}O_2Si$ 472.3737, found 472.3766.

4-(*tert*-Butyldimethylsilyloxy)-2-methyl-19-methylene-5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-hexadecahydrobenzo[18]annulen-1-ol (14). A solution of **13** (151 mg, 0.320 mmol) in degassed *N*,*N*-dimethylaniline (32.0 mL) was stirred at 180 °C. After 8 h, 1.0 M aqueous HCl was added at rt, and the mixture was extracted with Et_2O. The extracts were washed with 1.0 M aqueous HCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (10 g, 20:1 hexane−acetone) to afford **14** (123 mg, 81%) as a colorless syrup: R_f = 0.49 (3:1 hexane−EtOAc); IR (neat, cm^{-1}) 3500, 2925, 2857, 1475, 1416, 1340, 1257, 1222, 1197, 1128, 1115, 1026, 965, 880, 840, 780; ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.21 (s, 6H), 1.00 (s, 9H), 1.26−1.46 (m, 20H), 1.49−1.62 (m, 4H), 2.11−2.20 (m, 2H), 2.17 (s, 3H), 2.42−2.52 (m, 2H), 3.33 (br s, 2H), 4.46 (br d, J = 1.8 Hz, 1H), 4.56 (s, 1H), 4.83 (br s, 1H), 6.50 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ −4.1, 16.1, 18.2, 25.3, 25.8, 25.9, 26.4, 26.6, 26.8, 27.3, 27.6, 27.68, 27.73, 28.1, 28.6, 29.6, 30.5, 33.2, 37.3, 110.1, 118.6, 121.9, 124.3, 130.5, 146.8, 147.0, 148.1; LRMS (EI) m/z (M^+) 472.3; HRMS (EI) m/z (M^+) calcd for $C_{30}H_{52}O_2Si$ 472.3737, found 472.3751.

***tert*-Butyl(4-(methoxymethoxy)-3-methyl-6-methylene-5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20-hexadecahydrobenzo[18]annulen-1-yloxy)dimethylsilane (15).** To a stirred solution of **14** (114 mg, 0.242 mmol) in CH_2Cl_2 (0.810 mL) were added at 0 °C *N*,*N*-diisopropylethylamine (0.110 mL, 6.04 mmol) and MOMCl (0.220 mL, 2.90 mmol). After 8 h at 40 °C, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (3 g, 5:1 hexane−EtOAc) to afford **15** (118 mg, 94%) as a colorless syrup: R_f = 0.50 (10:1 hexane−EtOAc); IR (neat, cm^{-1}) 2923, 2856, 1745 1648, 1474, 1397, 1340, 1255, 1226, 1197, 1160, 1063, 1036, 992, 878, 839, 780, 759; ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.21 (s, 6H), 1.00 (s, 9H), 1.23−1.47 (m, 20H), 1.50−1.64 (m, 4H), 2.16 (m, 2H), 2.23 (s, 3H), 2.40 (m, 2H), 3.32 (br s, 2H), 3.56 (s, 3H), 4.12 (br d, J = 1.8 Hz, 1H), 4.74 (br s, 1H), 4.86 (s, 2H), 6.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.1, 17.1, 18.2, 25.2, 25.6, 25.8, 26.5, 26.7, 26.8, 27.4, 27.6, 27.7, 27.9, 28.4, 28.8, 29.5, 30.4, 33.0, 38.3, 57.2, 99.5, 109.5, 118.7 128.5, 131.4, 131.8, 148.7, 149.5, 149.9; LRMS (EI) m/z (M^+) 516.2; HRMS (EI) m/z (M^+) calcd for $C_{32}H_{56}O_3Si$ 516.3999, found 516.4006.

1-(*tert*-Butyldimethylsilyloxy)-4-(methoxymethoxy)-3-methyl-7,8,9,10,11,12,13,14,15,16,17,18,19,20-tetradecahydrobenzo[18]annulen-6(5*H*)-one (16). To a stirred solution of **15** (10.3 mg, 0.0199 mmol) in 3:3:1 *t*-BuOH−H_2O−THF (0.16 mL) were added at rt NMO (2.8 mg, 0.024 mmol) and OsO_4 (0.25 mg, 0.0010 mmol). After 11 h at rt, saturated aqueous $Na_2S_2O_3$ was added, and the mixture was stirred at rt for 30 min and extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 2:1 hexane−EtOAc) to afford diol (10.4 mg, 95%) as a colorless syrup: R_f = 0.46 (2:1 hexane−EtOAc); IR (neat, cm^{-1}) 3465, 2930, 2857, 1602, 1574, 1464, 1395, 1328, 1256, 1216, 1163, 1046, 1007, 969, 853, 754; ^1H NMR (270 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.21 (s, 3H), 0.23 (s, 3H), 1.00 (s, 9H), 1.20−1.45 (m, 22H), 1.45−1.85 (m, 4H), 2.21 (s, 3H), 2.39−2.82 (m, 3H), 2.92 (d, J = 14.2 Hz, 1H), 3.00 (d, J = 14.2 Hz, 1H), 3.17 (dd, J = 11.5, 1.4 Hz, 1H), 3.32 (dd, J = 11.5, 1.8 Hz, 1H), 3.62 (s, 3H), 4.90 (d, J = 5.4 Hz, 1H), 4.94 (d, J = 5.4 Hz, 1H), 6.51 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.1, −4.0, 17.1, 18.3, 22.6, 25.4, 25.7, 25.9, 26.74, 26.74, 27.1, 27.6, 27.7, 28.2, 28.5, 29.3, 29.4, 30.2, 38.5, 52.3, 58.2, 75.7, 99.8, 119.3, 128.4, 129.5, 132.8, 148.5, 150.6; LRMS (EI) m/z (M^+) 550.5; HRMS (EI) m/z (M^+) calcd for $C_{32}H_{58}O_5Si$ 550.4054, found 550.4047. To a stirred solution of this diol (9.8 mg, 0.0180 mmol) in 1:1 THF−H_2O (0.90 mL) was added at rt $NaIO_4$ (10.7 mg, 0.0540 mmol). After 3 h at 40 °C, water was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 2:1 hexane−EtOAc) to afford **16** (9.1 mg, 98%) as colorless needles: R_f = 0.80 (2:1 hexane−EtOAc); mp = 42−43 °C (not recrystallized); IR (KBr, cm^{-1}) 2930, 2861, 1717, 1475, 1462, 1415, 1397, 1321, 1257, 1229, 1199, 1158, 1107, 1078, 1057, 984, 891, 841, 780; ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.21 (s, 6H), 1.00 (s, 9H), 1.21−1.45 (m, 22H), 1.66 (m, 2H), 2.21 (s, 3H), 2.37 (m, 2H), 2.49 (t, J = 7.6 Hz, 2H), 3.52 (s, 3H), 3.86 (s, 1H), 4.81 (s, 2H), 6.53 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.00) δ −4.2, 17.0, 18.1, 23.6, 25.7, 26.0, 26.5, 26.7, 27.0, 27.3, 27.9, 27.96, 28.09, 28.14, 29.5, 29.6, 41.8, 42.2, 57.2, 99.5, 119.0, 127.8, 128.2, 130.9, 148.9, 149.9, 208.9; LRMS (EI) m/z (M^+) 518.1; HRMS (EI) m/z (M^+) calcd for $C_{31}H_{54}O_4Si$ 518.3791, found 518.3788.

5,6,7,8,9,10,11,12,13,14,15,16,17,18-Tetradecahydro-2-methyl-1,19-epoxybenzo[18]-annulen-4-ol (17). To a stirred solution of **16** (128 mg, 0.246 mmol) in 1:4 toluene−EtOH (5.00 mL) was added at rt CSA (114 mg, 0.492 mmol). After 24 h at 50 °C, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (3 g, 6:1 hexane−EtOAc) to afford **17** (76.3 mg, 90%) as colorless needles: R_f = 0.43 (8:1 hexane−EtOAc); mp =105−106 °C (not recrystallized); IR (KBr, cm^{-1}) 3384, 2927, 2856, 1609, 1460, 1444, 1396, 1367, 1287, 1222, 1180, 1107, 906, 836, 794; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.14−1.39 (m, 20H), 1.63 (m, 2H), 1.73 (m, 2H), 2.42 (s, 3H), 2.75 (t, J = 7.2 Hz, 2H), 2.78 (t, J = 6.0 Hz, 2H), 4.10 (br s, 1H), 6.33 (s, 1H), 6.51 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 14.9, 26.6, 26.72, 26.72, 26.9, 27.3, 27.4, 27.85, 27.85, 27.85, 27.97, 28.01, 28.01, 28.5, 29.2, 101.7, 112.6, 116.2, 118.8, 129.4, 148.2, 148.4, 159.3; LRMS (EI) m/z (M^+) 342.0; HRMS (EI) m/z (M^+) calcd for $C_{23}H_{34}O_2$ 342.2559, found 342.2578.

5,6,7,8,9,10,11,12,13,14,15,16,17,18-Tetradecahydro-4,19-dihydroxy-2-methyl-1,19-epoxybenzo[18]annulen-3(5*H*)-one (Quinone Methide Analogue 2) and 5,6,7,8,9,10,11,12,13,14,15,16,17,18-Tetradecahydro-1-hydroxy-2-methyl-1,19-epoxybenzo[18]annulen-4(5*H*)-one (18). To a stirred solution of **17** (31.6 mg, 0.0923 mmol) in DMSO

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

(0.923 mL) was added at rt IBX (129 mg, 0.462 mmol). After 10 min at rt, water was added, and the mixture was extracted with 1:1 hexane−EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated to afford a crude red material. The crude product was used in the next reaction without further purification. For an analytical sample, a part of crude material was separated on silica gel (8:1 hexane−EtOAc) to give a red *o*-quinone solution: R_f = 0.34 (8:1 hexane−EtOAc); UV (2:1 hexane−acetone) λ_{max} 542 nm; LRMS (EI) *m*/*z* (M + 2H$^+$) 358.2, (M$^+$) 356.2; HRMS (EI) *m*/*z* (M$^+$) calcd for $C_{23}H_{32}O_3$ 356.2352, found 356.2356. To a stirred solution of the crude product in acetonitrile (15.4 mL) was added at rt 1.0 M aqueous HF solution (1.23 mL, 1.23 mmol). After 20 min at rt, saturated aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (3 g, 8:1 hexane−EtOAc) to afford **2** (5.6 mg, 16%) and **18** (21.1 mg, 63%). **2**: yellow solids; R_f = 0.46(8:1 hexane−EtOAc); mp = 112−115 °C (not recrystallized); IR (KBr, cm^{-1}) 3341, 2922, 2854, 1667, 1610, 1580, 1509, 1462, 1397, 1377, 1323, 1249, 1163, 1102, 1060, 993, 938, 900, 835, 797; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 1.16−1.40 (m, 22H), 1.40−1.62 (m, 2H), 1.90 (s, 3H), 2.01 (dt, *J* = 15.5, 7.8 Hz, 1H), 2.10 (dt, *J* = 15.5, 7.2 Hz, 1H), 2.21 (dt, *J* = 7.7, 7.0 Hz, 1H), 2.77 (dt, *J* = 8.0, 7.7 Hz, 1H), 4.08 (s, 1H), 6.62 (s, 1H), 7.19 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 7.7, 23.2, 25.7, 26.83, 26.83, 26.9, 27.0, 27.2, 27.7, 27.8, 28.1, 28.4, 28.5, 28.7, 37.6, 105.4, 111.7, 115.5, 133.3, 137.7, 146.2, 167.6, 183.0; LRMS (EI) *m*/*z* (M$^+$) 374.2; HRMS (EI) *m*/*z* (M$^+$) calcd for $C_{23}H_{34}O_4$ 374.2457, found 374.2483. **18**: yellow plates; R_f = 0.52 (8:1 hexane−EtOAc); mp = 60−62 °C (not recrystallized); IR (KBr, cm^{-1}) 3440, 2932, 2853, 1645, 1528, 1458, 1435, 1396, 1367, 1346, 1237, 1203, 1153, 942, 833; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 1.10−1.44 (m, 22H), 1.56−1.80 (m, 4H), 2.26 (d, *J* = 1.2 Hz, 3H), 2.67 (ddd, *J* = 14.8, 8.3, 4.8 Hz, 1H), 2.76 (ddd, *J* = 14.8, 6.4, 4.5 Hz, 1H), 3.16 (br s, 1H), 5.70 (d, *J* = 1.2 Hz,1H), 6.31 (s, 1H); (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 16.8, 22.4, 27.1, 27.2, 27.3, 27.35, 27.39, 27.7, 27.8, 27.9, 28.0, 28.2, 28.4, 28.5, 43.7, 107.6, 116.9, 131.5, 146.3, 147.1, 160. 1, 205.7; LRMS (EI) *m*/*z* (M$^+$) 358.2; HRMS (EI) *m*/*z* (M$^+$) calcd for $C_{23}H_{34}O_3$ 358.2508, found 358.2514.

7,8,9,10,11,12,13,14,15,16,17,18,19,20-Tetradecahydro-2-hydroxy-3-methylbenzo[18]annulene-1,4,6-trione (19). To a stirred solution of **16** (67.1 mg, 0.129 mmol) in THF (1.3 mL) was added at rt 1.0 M TBAF in THF (0.155 mL, 0.155 mmol). After 2 min at rt, saturated aqueous NH_4Cl was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (2 g, 2:1 hexane−EtOAc) to afford phenol (49.5 mg, 95%) as colorless needles: R_f = 0.43 (2:1 hexane−EtOAc); mp = 100−101 °C (not recrystallized); IR (KBr, cm^{-1}) 3475, 2927, 2858, 1695, 1459, 1423, 1395, 1319, 1227, 1194, 1160, 1119, 1065, 979, 946, 931, 850; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 1.22−1.48 (m, 22H), 1.68 (tt, *J* = 7.6, 7.5 Hz, 2H), 2.19 (s, 3H), 2.37 (m, 2H), 2.52 (t, *J* = 7.6 Hz, 2H), 3.52 (s, 3H), 3.90 (s, 2H), 4.80 (s, 2H), 4.88 (s, 1H), 6.47 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 16.8, 23.7, 25.7, 26.0, 26.5, 26.8, 26.9, 27.3, 27.4, 27.8, 28.1, 28.2, 29.5, 41.6, 42.4, 57.1, 99.6, 116.6, 126.6, 127.2, 128.6, 148.6, 150.2, 210.0; LRMS (EI) *m*/*z* (M$^+$) 404.2; HRMS (EI) *m*/*z* (M$^+$) calcd for $C_{25}H_{40}O_4$ 404.2927, found 404.2942. To a stirred solution of this phenol (15.9 mg, 0.0393 mmol) in EtOH (0.786 mL) was added at rt IBX (22.0 mg, 0.0786 mmol). After 2 min at rt, the solvent was removed. The residue was purified by column chromatography on silica gel (1 g, 5:1 hexane−EtOAc) to afford **19** (10.6 mg, 72%) as yellow amorphous solids: R_f = 0.57 (2:1 hexane−EtOAc); IR (KBr, cm^{-1}) 3360, 2926, 2851, 1707, 1653, 1638, 1460, 1393, 1361, 1319, 1208, 1167, 1118, 1077, 758; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 1.25−1.46 (m, 22H), 1.64 (tt, *J* = 7.1, 7.1 Hz, 2H), 1.92 (s, 3H), 2.36 (m, 2H), 2.57 (t, *J* = 7.1 Hz, 2H), 3.67 (s, 2H), 6.95 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 8.1, 23.3, 26.29, 26.34, 26.5, 26.6, 26.7, 27.1, 27.2, 27.86, 27.88, 27.92, 28.7, 29.0, 40.4, 42.7, 116.7, 140.3, 142.4, 151.0, 183.1, 187.0, 206.2; LRMS (EI) *m*/*z* (M$^+$) 374.2; HRMS (EI) *m*/*z* (M$^+$) calcd for $C_{23}H_{34}O_4$ 374.2457, found 374.2467.

5,6,7,8,9,10,11,12,13,14,15,16,17,18-Tetradecahydro-4,19-dihydroxy-2-methyl-1,19-epoxybenzo[18]annulen-3(*5H*)-one (Quinone Methide Analogue 2). A solution of **19** (11.0 mg, 0.0294 mmol) in CH_2Cl_2 (0.060 mL) was applied on the silica gel TLC. After 12 h at rt, the adsorbed materials were eluted with $CHCl_3$ from silica gel and concentrated. The resulting mixture was chromatographed on silica gel (3 g, 5:1 hexane−EtOAc) to afford **2** (7.9 mg, 72%) and the recovered **19** (1.6 mg, 18%) as yellow crystals (the data of **2** are shown above).

(3*S,4*S**,5*R**,6*S**)-7-(*tert*-Butyldiphenylsilyloxy)-5-(triethylsilyloxy)-4,6-dimethylhept-1-en-3-ol (21) and (3*R**,4*S**,5*R**,6*S**)-7-(*tert*-Butyldiphenylsilyloxy)-5-(triethylsilyloxy)-4,6-dimethylhept-1-en-3-ol (C3-epimer of 21).** A stirred solution of **20**[31] (129 mg, 0.260 mmol) in 10:1 CH_2Cl_2−MeOH (10.0 mL) was cooled to −78 °C, and O_3/O_2 was bubbled through the solution until a blue color was observed. After 10 min at −78 °C, nitrogen was bubbled through the solution until no blue color remained. After the addition of triphenylphosphine (68.1 mg, 0.260 mmol), the reaction mixture was warmed to −40 °C. After 10 min at −40 °C, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with $CHCl_3$. The residue was purified by column chromatography on silica gel (10 g, 1:1 hexane−$CHCl_3$) to afford the known aldehyde[33] (119 mg, 92%) as a colorless syrup. To a stirred solution of this aldehyde (482 mg, 0.965 mmol) in dry Et_2O (9.65 mL) was added at −78 °C 1.0 M vinylmagnesium bromide in THF (1.93 mL, 1.93 mmol). After 50 min at −78 °C, saturated aqueous NH_4Cl was added at −78 °C, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (40 g, 2:1 $CHCl_3$−hexane) to afford **21** (330 mg, 68%) and **C3-epimer of 21** (111 mg, 23%) as a colorless syrup. **21**: R_f = 0.52 (5:1 hexane−EtOAc); IR (neat, cm^{-1}) 3450, 2958, 2880, 1592, 1475, 1460, 1424, 1390, 1222, 1113, 1008, 920, 825, 740; ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.64 (q, *J* = 7.8 Hz, 6H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.95 (t, *J* = 7.8 Hz, 9H), 0.99 (d, *J* = 7.0 Hz, 3H), 1.06 (s, 9H), 1.62 (m, 1H), 1.94 (m, 1H), 3.03 (d, *J* = 2.2 Hz, 1H), 3.48 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.59 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.90 (dd, *J* = 4.8, 4.8 Hz, 1H), 4.46 (br t, *J* = 2.0 Hz, 1H), 5.08 (dt, *J* = 10.0, 2.0 Hz, 1H), 5.17 (dt, *J* = 16.2, 2.0 Hz, 1H), 5.71 (ddd, *J* = 16.2, 10.0, 4.4 Hz, 1H), 7.34−7.47 (m, 6H), 7.61−7.68 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 5.4, 7.0, 11.1, 13.0, 19.2, 26.8, 39.4, 40.1, 66.5, 71.7, 78.2, 113.8, 127.6, 129.6, 133.6, 135.6, 140.1; LRMS (EI) *m*/*z* (M − *t*Bu)$^+$ 469.3; HRMS (EI) *m*/*z* (M − *t*Bu)$^+$ calcd for $C_{27}H_{41}O_3Si_2$ 469.2594, found 469.2601. **C3-epimer of 21**: R_f = 0.48 (5:1 hexane−EtOAc); IR (neat, cm^{-1}) 3470, 2960, 2880, 1590, 1475, 1460, 1425, 1390, 1240, 1115, 1005, 923, 824, 740,; ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.63 (q, *J* = 8.0 Hz, 3H), 0.64 (q, *J* = 8.0 Hz, 3H), 0.79 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 7.8 Hz, 3H), 0.95 (t, *J* = 8.0 Hz, 9H), 1.07 (s, 9H), 1.72 (m, 1H), 1.83 (m, 1H), 3.43 (d, *J* = 2.0 Hz, 1H), 3.47 (dd, *J* = 8.0, 5.4 Hz, 1H), 3.52 (dd, *J* = 8.0, 7.4 Hz, 1H), 3.99 (dd, *J* = 6.8, 2.0 Hz, 1H), 3.96−4.06 (br, 1H), 5.15 (dd, *J* = 10.0, 1.6 Hz, 1H), 5.25 (dd, *J* = 17.6, 1.6 Hz, 1H), 5.82 (ddd, *J* = 17.6, 10.0, 6.2 Hz, 1H), 7.32−7.46 (m, 6H), 7.61−7.70 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 5.2, 7.0, 10.7, 14.5, 19.1, 26.8, 39.7, 43.1, 66.3, 75.9, 76.1, 115.8, 127.6, 129.6, 133.6, 133.7, 135.56, 135.59, 139.1; LRMS (EI) *m*/*z* (M − Et)$^+$ 496.9; HRMS (EI) *m*/*z* (M − Et)$^+$ calcd for $C_{29}H_{45}O_3Si_2$ 497.2907, found 497.2911.

(3*S,4*R**,5*R**,6*S**)-7-(*tert*-Butyldiphenylsilyloxy)-3,5-(*O*-isopropylidenedioxy)-4,6-dimethylhept-1-ene (22).** To a stirred solution of **21** (587 mg, 1.11 mmol) in 2,2-dimethoxypropane (11.1 mL) was added at rt (1*S*)-10-camphorsulfonic acid (310 mg, 1.34 mmol). After 13.5 h at rt, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (6.0 g, 8:1 hexane−EtOAc) to afford **22** (474 mg, 94%) as a colorless syrup: R_f = 0.77 (5:1 hexane−EtOAc); IR (neat, cm^{-1}) 3430, 3078, 2960,

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

2935, 2860, 1648, 1475, 1460, 1425, 1380, 1224, 1180, 1160, 1115, 1030, 1000, 920, 885, 823, 740; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.83 (d, J = 7.8 Hz, 3H), 0.86 (d, J = 7.6 Hz, 3H), 1.05 (s, 9H), 1.32 (s, 3H), 1.35 (s, 3H), 1.76 (m, 1H), 1.89 (m, 1H), 3.50 (dd, J = 10.0, 5.4 Hz, 1H), 3.64 (dd, J = 10.0, 2.4 Hz, 1H), 3.66 (d, J = 8.2 Hz, 1H), 4.34 (dd, J = 6.0, 6.0 Hz, 1H), 5.16 (dd, J = 10.0, 1.8 Hz, 1H), 5.25 (dd, J = 16.6, 1.8 Hz, 1H), 5.98 (ddd, J = 16.6, 10.0, 6.0 Hz, 1H), 7.33−7.46 (m, 6H), 7.63−7.70 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 10.5, 12.6, 19.2, 23.9, 25.4, 26.8, 37.2, 38.7, 65.6, 71.2, 72.9, 100.4, 115.4, 127.6, 129.5, 133.9, 135.6, 136.2; LRMS (EI) m/z (M − Me)$^+$ 437.2; HRMS (EI) m/z (M − Me)$^+$ calcd for $C_{27}H_{37}O_3Si$ 437.2512, found 437.2514. The stereochemistry of the newly formed hydroxy group by the addition of vinylmagnesium bromide was determined according to ^{13}C NMR analysis of **22**: Rychnovsky−Evans rule (anti diol: 24.6 ± 0.76, 100.6 ± 0.25; found 23.86, 25.35, 100.41).[49]

9-(*tert*-Butylcarboxy)nonyl-1-triphenylphosphonium Iodide (23). To a stirred solution of 9-hydroxynonyl 2,2-dimethylpropionate[50] (1.80 g, 7.37 mmol) in 1:1 benzene−Et_2O (73.7 mL) were added at −10 °C triphenylphosphine (5.80 g, 0.022 mmol), imidazole (1.50 g, 0.022 mmol), and iodine (5.58 g, 0.022 mmol). After 10 min at −10 °C, the reaction mixture was warmed to rt. After 30 min at rt, saturated aqueous $Na_2S_2O_3$ was added, and the mixture was extracted with hexane. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (30 g, 2:1 hexane−$CHCl_3$) to iodide (2.30 g, 88%) as a colorless syrup: R_f = 0.33 (2:1 hexane−$CHCl_3$); IR (neat, cm^{-1}) 3430, 2935, 2855, 1730, 1480, 1460, 1399, 1365, 1285, 1156; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 1.20 (s, 9H), 1.26−1.44 (m, 10H), 1.56−1.68 (m, 2H), 1.82 (m, 2H), 3.18 (t, J = 7.6 Hz, 2H), 4.04 (t, J = 6.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 7.2, 25.8, 27.2, 28.4, 28.5, 29.1, 29.2, 30.4, 33.5, 38.7, 64.3, 178.6; LRMS (EI) m/z (M)$^+$ 354.1; HRMS (EI) m/z (M)$^+$ calcd for $C_{14}H_{27}O_2I$ 354.1056, found 354.1079. To a stirred solution of this iodide (3.14 g, 8.90 mmol) in xylene (22.0 mL) was added triphenylphosphine (4.70 g, 17.8 mmol). The reaction mixture was refluxed for 7 h. After the organic solvent was removed, the precipitate was washed with ether and dried under reduced pressure to afford **23** (2.30 g, 88%) as a colorless syrup: IR (neat, cm^{-1}) 2935, 2860, 2440, 1718, 1585, 1480, 1460, 1440, 1400, 1285, 1238, 1163, 1115, 1035, 998, 750; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.15 (s, 9H), 1.16−1.30 (m, 8H), 1.54 (m, 2H), 1.58−1.66 (br, 4H), 3.63 (m, 2H), 3.98 (t, J = 6.6 Hz, 2H), 7.66−7.73 (m, 6H), 7.76−7.84 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 22.6 (d, J = 4.8 Hz), 23.2 (d, J = 49.5 Hz), 25.7, 27.1, 28.5, 28.9, 30.3 (d, J = 15.5 Hz), 38.6, 64.3, 118.2 (d, J = 85.3 Hz), 130.5 (d, J = 12.5 Hz), 133.6 (d, J = 9.5 Hz), 135.0, 178.5. This Wittig salt was used in the next step without further purification.

(2*S,3*R**,4*R**,5*S**,6*Z*)-15-(*tert*-Butylcarboxy)-1-(*tert*-butyldiphenylsilyloxy)-3,5-(*O*-isopropylidenedioxy)-2,4-dimethylpentadec-6-ene (24).** A solution of **22** (822 mg, 1.82 mmol) in 9:1 CH_2Cl_2−MeOH (60 mL) was cooled to −78 °C, and ozone/oxygen was bubbled through the solution until a blue color was observed. After 10 min at −78 °C, oxygen was bubbled through the solution until no blue color remained. After addition of triphenylphosphine (476 mg, 1.82 mmol), the reaction mixture was gradually warmed to −30 °C for a period of 30 min. To this mixture was added saturated aqueous $NaHCO_3$ and the new mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (25 g, 1:1 hexane−$CHCl_3$) to afford aldehyde (809 mg, 98%) as a colorless syrup: R_f = 0.38 (5:1 hexane−EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.84 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.4 Hz, 3H), 1.04 (s, 9H), 1.34 (s, 3H), 1.42 (s, 3H), 1.76 (m, 1H), 2.32 (m, 1H), 3.50 (dd, J = 10.0, 5.6 Hz, 1H), 3.61 (dd, J = 10.0, 8.2 Hz, 1H), 3.74 (dd, J = 8.2, 2.6 Hz, 1H), 4.27 (d, J = 5.0 Hz, 1H), 7.30−7.46 (m, 6H), 7.62−7.69 (m, 4H), 9.68 (s, 1H). This aldehyde was immediately subjected to the next step. To a stirred solution of **23** (224 mg, 0.364 mmol) in dry THF (1.82 mL) was added at 0 °C 1.0 M NHMDS in THF (0.364 mL, 0.364 mmol). After 15 min at 0 °C, a solution of the crude aldehyde (55.1 mg, 0.12 mmol) in dry THF (0.18 mL) was added via a syringe at 0 °C. After 15 min at 0 °C, saturated aqueous NH_4Cl was added and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (3.5 g, 3:1 hexane−$CHCl_3$) to afford **24** (72.8 mg, 91%) as a colorless syrup: R_f = 0.69 (5:1 hexane−EtOAc); IR (neat, cm^{-1}) 2935, 2860, 1730, 1460, 1425, 1380, 1283, 1225, 1155, 1115, 1050, 1020, 890, 822, 740; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.86 (d, J = 6.8 Hz, 3H), 0.87 (d, J = 6.4 Hz, 3H), 1.05 (s, 9H), 1.20 (s, 9H), 1.24−1.44 (br, 10H), 1.34 (s, 3H), 1.34 (s, 3H), 1.53−1.68 (br, 2H), 1.68−1.92 (m, 2H), 1.92−2.20 (m, 2H), 3.50 (dd, J = 10.0, 5.8 Hz, 1H), 3.64 (dd, J = 10.0, 8.0 Hz, 1H), 3.70 (dd, J = 8.2, 2.8 Hz, 1H), 4.04 (t, J = 6.6 Hz, 2H), 4.66 (dd, J = 8.2, 5.0 Hz, 1H), 5.38−5.58 (m, 2H), 7.34−7.46 (m, 6H), 7.64−7.70 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 10.4, 12.5, 19.2, 23.9, 25.4, 25.9, 26.8, 27.2, 27.9, 28.6, 29.1, 29.2, 29.35, 29.44, 37.3, 38.6, 38.7, 64.4, 65.6, 66.4, 72.6, 100.3, 127.4, 127.5, 127.6, 129.5, 129.8, 132.1, 133.9, 135.5, 178.6; LRMS (EI) m/z (M − Me)$^+$ 649.4, (M − t-Bu)$^+$ 607.3; HRMS (EI) m/z (M − t-Bu)$^+$ calcd for $C_{37}H_{55}O_5Si$ 607.3819, found 607.3802.

(2*S,3*R**,4*S**,5*R**)-15-(*tert*-Butylcarboxy)-1-(*tert*-butyldiphenylsilyloxy)-3,5-(*O*-isopropylidenedioxy)-2,4-dimethylpentadecane (25).** A solution of **24** (211 mg, 0.318 mmol) in EtOAc (6.40 mL) and Pd/C (10 wt %, 211 mg) was stirred under H_2. After 1 h at rt, the mixture was filtered through Celite to afford **25** (202 mg, 95%) as a colorless syrup: R_f = 0.48 (5:1 hexane−EtOAc); IR (neat, cm^{-1}) 2935, 2855, 1730, 1460, 1425, 1380, 1285, 1225, 1160, 1115, 1020, 822, 760; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.82 (d, J = 5.6 Hz, 3H), 0.84 (d, J = 6.0 Hz, 3H), 1.04 (s, 9H), 1.20 (s, 9H), 1.24−1.50 (m, 22H), 1.52−1.68 (br, 2H), 1.68−1.82 (m, 2H), 3.49 (dd, J = 10.0, 6.0 Hz, 1H), 3.59 (dd, J = 8.0, 2.2 Hz, 1H), 3.62 (dd, J = 10.0, 8.0 Hz, 1H), 3.72 (m, 1H), 4.04 (t, J = 6.2 Hz, 2H), 7.34−7.46 (m, 6H), 7.64−7.69 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 10.5, 11.8, 19.2, 23.8, 25.1, 25.9, 26.1, 26.8, 27.2, 28.6, 29.2, 29.48, 29.50, 29.6, 29.7, 30.8, 36.6, 38.7, 38.9, 64.5, 65.7, 69.5, 73.2, 100.2, 127.5, 129.5, 134.0, 135.6, 135.5, 178.6; LRMS (EI) m/z (M − Me)$^+$ 651.4, (M − t-Bu)$^+$ 609.4; HRMS (EI) m/z (M − t-Bu)$^+$ calcd for $C_{37}H_{57}O_5Si$ 609.3975, found 609.3975.

(2*S,3*R**,4*S**,5*R**)-3,5-(*O*-Isopropylidenedioxy)-15-(*tert*-butylcarboxy)-2,4-dimethylpentadecan-1-ol (26).** To a stirred solution of **25** (65.8 mg, 0.0986 mmol) in THF (0.986 mL) was added 1.0 M TBAF in THF (0.295 mL, 0.295 mmol). After 24 h at rt, saturated aqueous NH_4Cl was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (3 g, 8:1 hexane−EtOAc) to afford **26** (40.9 mg, 97%) as a colorless syrup: R_f = 0.31 (5:1 hexane−EtOAc); IR (neat, cm^{-1}) 3450, 2938, 2858, 1730, 1480, 1460, 1382, 1285, 1225, 1160, 1035, 1020, 990, 758; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.84 (d, J = 6.6 Hz, 3H), 0.98 (d, J = 6.8 Hz, 3H), 1.20 (s, 9H), 1.24−1.34 (br, 16H),1.32 (s, 3H), 1.36 (s, 3H), 1.54−1.66 (m, 2H), 1.78−1.88 (m, 2H), 2.46 (m, 1H), 3.52 (dd, J = 8.0, 2.8 Hz, 1H), 3.64−3.70 (m, 2H), 3.74 (m, 1H), 4.04 (t, J = 6.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 10.7, 12.3, 23.7, 25.1, 25.9, 26.1, 27.2, 28.6, 29.2, 29.46, 29.48, 29.6, 29.7, 30.6, 35.9, 37.3, 38.7, 64.4, 67.2, 69.6, 77.6, 100.4, 178.7; LRMS (EI) m/z (M − Me)$^+$ 413.2; HRMS (EI) m/z (M − Me)$^+$ calcd for $C_{24}H_{45}O_5$ 413.3267, found 413.3269.

(3*R,*S**,4*S**,5*S**,6*S**,7*R**)-17-(*tert*-Butylcarboxy)-5,7-(*O*-isopropylidenedioxy)-4,6-dimethylheptadec-1-yn-3-ol (27).** To a stirred solution of oxalyl dichloride (0.139 mL, 1.64 mmol) in dry CH_2Cl_2 (5.30 mL) was added at −78 °C dimethyl sulfoxide (0.233 mL, 3.28 mmol). After 10 min at −78 °C, a solution of **26** (352 mg, 0.821 mmol) in dry CH_2Cl_2 (0.53 mL) was added and the resulting suspension was stirred at −78 °C for 20 min. After the addition of triethylamine (0.685 mL, 4.92 mmol), the mixture was gradually warmed to rt for a period of 1 h. To this mixture was added water and the new mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated.

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

The residue was purified by column chromatography on silica gel (7 g, 5:1 hexane−EtOAc) to afford aldehyde (313 mg, 89%) as a colorless syrup: R_f = 0.93 (5:3 hexane−EtOAc); IR (neat, cm^{-1}) 3440, 2932, 2858, 1730, 1483, 1460, 1380, 1285, 1224, 1160, 1020, 980; ^1H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.87 (d, J = 7.0 Hz, 3H), 1.05 (d, J = 6.8 Hz, 3H), 1.20 (s, 9H), 1.24−1.48 (m, 16H), 1.29 (s, 3H), 1.33 (s, 3H), 1.55−1.66 (m, 2H), 1.80−1.92 (m, 1H), 2.43 (m, 1H), 3.70 (m, 1H), 3.78 (dd, J = 8.0, 3.8 Hz, 1H), 4.04 (t, J = 6.0 Hz, 2H), 9.70 (d, J = 1.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 7.8, 11.9, 23.6, 24.7, 25.9, 26.0, 27.2, 28.6, 29.2, 29.43, 29.43, 29.5, 29.6, 30.6, 36.2, 38.7, 48.7, 64.4, 69.4, 73.6, 100.6, 178.6, 204.3; LRMS (EI) m/z (M − Me)$^+$ 411.3; HRMS (EI) m/z (M − Me)$^+$ calcd for $C_{24}H_{43}O_5$ 411.3113, found 411.3111. To a stirred solution of this aldehyde (624 mg, 1.46 mmol) in dry Et_2O (29.2 mL) was added at −78 °C 0.5 M ethynylmagnesium bromide in THF (8.70 mL, 4.35 mmol). After 30 min at −78 °C, the reaction mixture was warmed to −10 °C. After 1 h at −10 °C, saturated aqueous NH_4Cl was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (50 g, 10:1 hexane−EtOAc) to afford **27** (612 mg, 93%: a 7:3 mixture of diastereomers) as a colorless syrup. The NMR chemical shifts of each isomer were determined using the spectra of a mixture of two isomers. **Major isomer of 27**: R_f = 0.43 (3:1 hexane−EtOAc); ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.84 (d, J = 6.8 Hz, 3H), 1.14 (d, J = 7.0 Hz, 3H), 1.20 (s, 9H), 1.24−1.34 (m, 16H), 1.31 (s, 3H), 1.36 (s, 3H), 1.54−1.68 (m, 2H), 1.76−1.94 (m, 2H), 2.46 (d, J = 2.0 Hz, 1H), 3.06 (br d, J = 2.0 Hz, 1H), 3.59 (dd, J = 8.2, 2.0 Hz, 1H), 3.70−3.79 (m, 1H), 4.04 (t, J = 6.2 Hz, 2H), 4.52 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 7.6, 11.8, 23.8, 24.8, 25.8, 26.0, 27.1, 28.5, 29.1, 29.43, 29.44, 29.5, 29.6, 30.5, 36.4, 38.6, 41.1, 64.4, 66.9, 69.5, 72.9, 77.6, 83.9, 100.6, 178.6. **Minor isomer of 27**: R_f = 0.43 (3:1 hexane−EtOAc); ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.84 (d, J = 6.8 Hz, 3H), 1.12 (d, J = 7.2 Hz, 3H), 1.20 (s, 9H), 1.24−1.34 (m, 16H), 1.31 (s, 3H), 1.41 (s, 3H), 1.54−1.68 (m, 2H), 1.76−1.94 (m, 2H), 2.51 (d, J = 2.2 Hz, 1H), 3.54 (br d, J = 8.4 Hz, 1H), 3.70−3.79 (m, 1H), 4.03 (dd, J = 6.2, 2.0 Hz, 1H), 4.04 (t, J = 6.2 Hz, 2H), 4.38 (ddd, J = 6.8, 4.4, 2.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 10.7, 11.6, 24.0, 24.9, 25.8, 26.0, 27.1, 28.5, 29.1, 29.43, 29.44, 29.5, 29.6, 30.5, 36.0, 38.7, 39.9, 64.4, 66.6, 69.6, 73.3, 74.8, 84.6, 100.7, 178.6. **Mixture of two isomers of 27**: IR (neat, cm^{-1}) 3450, 3312, 2935, 2878, 1729, 1480, 1460, 1383, 1285, 1225, 1160, 1038, 1018, 993, 885, 758; LRMS (EI) m/z (M − Me)$^+$ 437.4; HRMS (EI) m/z (M − Me)$^+$ calcd for $C_{26}H_{45}O_5$ 437.3267, found 437.3258.

(11*R,12*S**,13*R**,14*S**,15*RS*)-11,13-(*O*-Isopropylidenedioxy)-12,14-dimethylheptadec-16-yne-1,15-diol (28a).** A solution of **27** (274 mg, 0.610 mmol) in dry CH_2Cl_2 (3.05 mL) was cooled to 0 °C, and 0.99 M DIBALH in toluene (2.68 mL, 2.68 mmol) was added. After 1 h at 0 °C, EtOAc, MeOH, potassium sodium (+)-tartrate tetrahydrate, and water were added, and the mixture was warmed to rt. After being stirred vigorously for 3 h at rt, the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (5 g, 1:1 hexane−EtOAc) to afford **28a** (220 mg, 98%: a 7:3 mixture of diastereomers) as a colorless syrup. The NMR chemical shifts of each isomer were determined using the spectra of a mixture of two isomers. **Major isomer of 28a**: R_f = 0.43 (1:1 hexane−EtOAc); ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.84 (d, J = 6.8 Hz, 3H), 1.14 (d, J = 6.6 Hz, 3H), 1.20−1.48 (m, 16H), 1.32 (s, 3H), 1.35 (s, 3H), 1.48−1.62 (m, 2H), 1.76−1.92 (m, 2H), 2.46 (d, J = 2.0 Hz, 1H), 3.20 (br, 1H), 3.59 (br dd, J = 10.0, 2.0 Hz, 1H), 3.62 (t, J = 6.4 Hz, 2H), 3.69−3.79 (m, 1H), 4.50 (br dd, J = 4.4, 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 7.8, 11.7, 23.8, 24.8, 25.7, 26.0, 29.3, 29.3, 29.50, 29.50, 29.6, 30.5, 32.7, 36.3, 41.0, 62.9, 66.7, 69.5, 72.9, 77.5, 83.9, 100.6. **Minor isomer of 28a**: R_f = 0.43 (1:1 hexane−EtOAc); ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.84 (d, J = 6.8 Hz, 3H), 1.12 (d, J = 6.4 Hz, 3H), 1.20−1.48 (m, 16H), 1.32 (s, 3H), 1.41 (s, 3H), 1.48−1.62 (m, 2H), 1.76−1.92 (m, 2H), 2.51 (d, J = 1.8 Hz, 1H), 3.62 (t, J = 6.4 Hz, 2H), 3.69−3.79 (m, 1H), 4.02 (br dd, J = 8.2, 1.8 Hz, 1H), 4.37 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 10.7, 11.6, 24.0, 24.9, 25.7, 26.0, 29.3, 29.46, 29.50, 29.50, 29.6, 30.5, 32.7, 36.0, 39.9, 62.9, 66.5, 69.6, 73.3, 74.8, 84.6, 100.7. **Mixture of two isomers of 28a**: IR (neat, cm^{-1}) 3390, 3310, 2935, 2855, 1460, 1382, 1225, 1178, 1044, 1017, 990, 885; LRMS (EI) m/z (M − Me)$^+$ 353.4; HRMS (EI) m/z (M − Me)$^+$ calcd for $C_{21}H_{37}O_4$ 353.2692, found 353.2690.

(11*R,12*S**,13*S**,14*R**,15*R***S**)-12,14-Dimethylheptadec-16-yn-1,11,13,15-tetraol (28b).** To a stirred solution of **28a** (32.7 mg, 0.0890 mmol) in MeOH (0.890 mL) was added at 0 °C trifluoroacetic acid (0.0020 mL, 0.027 mmol). After 30 min at 0 °C, saturated aqueous $NaHCO_3$ was added and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (2 g, 1:3 hexane−EtOAc) to afford **28b** (24.0 mg, 82%: a 7:3 mixture of diastereomers) as colorless solids. The NMR chemical shifts of each isomer were determined using the spectra of a mixture of two isomers. **Major isomer of 28b**: R_f = 0.10 (1:3 hexane−EtOAc); ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.78 (d, J = 7.6 Hz, 3H), 1.11 (d, J = 6.8 Hz, 1H), 1.20−1.44 (m, 16H), 1.44−1.62 (m, 2H), 1.76−1.92 (m, 2H), 2.49 (d, J = 2.0 Hz, 1H), 2.60−2.80 (br s, 4H), 3.63 (t, J = 6.2 Hz, 2H), 3.75−3.86 (m, 1H), 3.95 (br d, J = 10.0, 2.0 Hz, 1H), 4.64 (br dd, J = 2.0, 2.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 6.0, 11.8, 25.6, 26.6, 29.3, 29.4, 29.45, 29.48, 29.6, 32.3, 32.6, 39.9, 40.1, 62.9, 67.3, 73.4, 74.3, 76.9, 83.8. **Minor isomer of 28b**: R_f = 0.10 (hexane/EtOAc = 1:3); ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.78 (d, J = 7.6 Hz, 3H), 1.06 (d, J = 7.0 Hz, 1H), 1.20−1.44 (m, 16H), 1.44−1.62 (m, 2H), 1.76−1.92 (m, 2H), 2.52 (d, J = 2.0 Hz, 1H), 2.60−2.80 (br s, 4H), 3.63 (t, J = 6.2 Hz, 2H), 3.75−3.86 (m, 1H), 4.29 (br dd, J = 10.0, 2.0 Hz, 1H), 4.42 (br dd, J = 4.8, 2.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 9.4, 11.7, 25.6, 26.6, 29.3, 29.4, 29.45, 29.48, 29.6, 32.3, 32.6, 39.7, 40.0, 62.9, 66.4, 73.1, 73.6, 74.6, 84.5. **Mixture of two isomers of 28b**: IR (KBr, cm^{-1}) 3500−3300, 2977, 2917, 2850, 2119, 1629, 1464, 1403, 1325, 1295, 1128, 1056, 1036, 978; LRMS (EI) m/z (M)$^+$ 328.2; HRMS (EI) m/z (M)$^+$ calcd for $C_{19}H_{36}O_4$ 328.2614, found 328.2621.

(11*R,12*S**,13*R**,14*S**,15*R***S**)-11,13-(*O*-Isopropylidenedioxy)-15-methoxy-12,14-dimethylheptadec-16-yn-1-ol (28c).** To a stirred solution of **27** (131 mg, 0.289 mmol) in dry THF (2.60 mL) was added at 0 °C NaH (25 mg, 0.58 mmol). After 5 min at 0 °C, iodomethane (0.36 mL, 0.58 mmol) was added and the mixture was warmed to rt. After being stirred for 2 h at rt. To this mixture was added water and the new mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (10 g, 5:1 hexane−EtOAc) to afford methyl ether (112 mg, 83%: a 7:3 mixture of diastereomers) as a colorless syrup. The NMR chemical shifts of each isomer were determined using the spectra of a mixture of two isomers. **Major isomer**: R_f = 0.42 (5:1 hexane−EtOAc); ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.80 (d, J = 6.4 Hz, 3H), 1.02 (d, J = 7.0 Hz, 3H), 1.17 (s, 9H), 1.22−1.40 (m, 22H), 1.54−1.64 (m, 2H), 1.68−1.84 (m, 2H), 2.45 (d, J = 2.0 Hz, 1H), 3.40 (s, 3H), 3.62 (dd, J = 8.0, 2.4 Hz, 1H), 3.66−3.74 (m, 1H), 3.84 (dd, J = 8.6, 2.0 Hz, 1H), 4.02 (t, J = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 10.1, 11.6, 23.8, 25.0, 25.9, 26.1, 27.2, 28.6, 29.2, 29.4, 29.46, 29.54, 29.7, 30.7, 36.4, 38.7, 41.1, 56.5, 64.4, 69.4, 73.8, 74.3, 74.6, 82.0, 100.2, 178.6. **Minor isomer**: R_f = 0.42 (5:1 hexane−EtOAc); ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.78 (d, J = 6.6 Hz, 3H), 1.01 (d, J = 6.8 Hz, 3H), 1.17 (s, 9H), 1.22−1.40 (m, 22H), 1.54−1.64 (m, 2H), 1.68−1.84 (m, 2H), 2.42 (d, J = 2.0 Hz, 1H), 3.39 (s, 3H), 3.60 (dd, J = 8.2, 2.2 Hz, 1H), 3.66−3.74 (m, 1H), 3.81 (dd, J = 9.4, 2.0 Hz, 1H), 4.02 (t, J = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 10.2, 11.6, 23.5, 24.9, 25.9, 26.1, 27.2, 28.6, 29.2, 29.4, 29.46, 29.54, 29.7, 30.7, 36.3, 38.7, 40.4, 56.7, 64.4, 69.6, 71.8, 72.7, 74.1, 82.6, 100.3, 178.6. **Mixture of two isomers**: IR (neat, cm^{-1}) 3440, 3310, 2935, 2820, 1732, 1483, 1460, 1382, 1338, 1285, 1225, 1158, 1098, 1018; LRMS (EI) m/z (M − Me)$^+$ 451.1; HRMS (EI) m/z (M − Me)$^+$ calcd for $C_{27}H_{47}O_5$

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

451.3424, found 451.3443. A solution of a mixture of these methyl ethers (165 mg, 0.365 mmol) in dry CH_2Cl_2 (1.83 mL) was cooled to 0 °C, and 0.99 M DIBALH in toluene (1.60 mL, 1.61 mmol) was added. After 15 min at 0 °C, EtOAc, MeOH, potassium sodium-(+)-tartrate tetrahydrate, and water were added, and the mixture was warmed to rt. After being stirred vigorously for 1 h at rt, the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (10 g, 1:1 hexane−EtOAc) to afford **28c** (127 mg, 94%: a 7:3 mixture of diastereomers) as a colorless syrup. The NMR chemical shifts of each isomer were determined using the spectra of a mixture of two isomers. **Major isomer of 28c**: R_f = 0.42 (1:1 hexane−EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.82 (d, J = 6.6 Hz, 3H), 1.04 (d, J = 6.4 Hz, 3H), 1.18−1.48 (m, 22H), 1.50−1.62 (m, 2H), 1.70−1.86 (m, 2H), 2.48 (d, J = 2.0 Hz, 1H), 3.43 (s, 3H), 3.59−3.67 (m, 1H), 3.63 (t, J = 6.0 Hz, 3H), 3.68−3.76 (m, 1H), 3.86 (dd, J = 8.4, 2.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 10.1, 11.6, 23.8, 25.0, 25.7, 26.1, 29.4, 29.49, 29.52, 29.6, 29.7, 30.7, 32.7, 36.4, 41.0, 56.5, 63.0, 69.5, 73.8, 74.3, 74.6, 82.0, 100.2. **Minor isomer of 28c**: R_f = 0.42 (1:1 hexane−EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.79 (d, J = 6.2 Hz, 3H), 1.03 (d, J = 7.2 Hz, 3H), 1.18−1.48 (m, 22H), 1.50−1.62 (m, 2H), 1.70−1.86 (m, 2H), 2.44 (d, J = 2.0 Hz, 1H), 3.42 (s, 3H), 3.59−3.67 (m, 1H), 3.63 (t, J = 6.0 Hz, 3H), 3.68−3.76 (m, 1H), 3.84 (dd, J = 9.6, 2.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 10.2, 11.6, 23.5, 24.9, 25.7, 26.1, 29.4, 29.49, 29.52, 29.6, 29.7, 30.7, 32.7, 36.2, 40.4, 56.7, 63.0, 69.7, 71.8, 72.8, 74.1, 82.5, 100.3.**Mixture of two isomers of 28c**: IR (neat, cm^{-1}) 3440, 3310, 2935, 2850, 1458, 1381, 1225, 1098, 1018; LRMS (EI) m/z (M − Me)$^+$ 367.1; HRMS (EI) m/z (M − Me)$^+$ calcd for $C_{22}H_{39}O_4$ 367.2848, found 367.2878.

(11*R,12*S**,13*R**,14*S**,15*R***S**)-11,13-(*O*-Isopropylidenedioxy)-15-(4-methoxybenzyloxy)-12,14-dimethylheptadec-16-yn-1-ol (28d).** To a stirred solution of **27** (97.8 mg, 0.216 mmol) in THF (1.96 mL) were added at 0 °C NaH (18.9 mg, 0.430 mmol), MPMCl (0.027 mL, 0.43 mmol), and TBAI (8.0 mg, 0.022 mmol). After 10 min at 0 °C, the mixture was warmed to rt. After being stirred for 4 days at rt, saturated aqueous NH_4Cl was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (6.0 g, 5:2 hexane−EtOAc) to afford **28d** (67.6 mg, 64%: a 7:3 mixture of diastereomers) as a colorless syrup. The NMR chemical shifts of each isomer were determined using the spectra of a mixture of two isomers. **Major isomer of 28d**: R_f = 0.20 (5:1 hexane−EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.81 (d, J = 6.6 Hz, 3H), 1.06 (d, J = 4.3 Hz, 3H), 1.19−1.43 (m, 22 H), 1.56 (dq, J = 6.6, 6.6 Hz, 2H), 1.83 (m, 2H), 2.50 (d, J = 2.0 Hz, 1H), 3.63 (t, J = 6.9 Hz, 2H), 3.68 (dd, J = 8.3, 2.6 Hz, 1H), 3.70 (m, 1H), 3.80 (s, 3H), 4.03 (dd, J = 8.9, 2.0 Hz, 1H), 4.41 (d, J = 11.2 Hz, 1H), 4.75 (d, J = 10.9 Hz, 1H), 6.87 (d, J = 8.9 Hz, 2H), 7.28 (d, J = 8.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 10.3, 11.6, 23.9, 25.0, 25.7, 26.1, 29.4, 29.51, 29.54, 29.6, 29.7, 30.7, 32.8, 36.4, 41.1, 55.2, 63.0, 69.5, 70.6, 71.7, 74.3, 74.7, 82.3, 100.2, 113.7, 129.5, 129.7, 159.2. **Minor isomer of 28d**: R_f = 0.20 (5:1 hexane−EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.79 (d, J = 6.9 Hz, 3H), 1.05 (d, J = 6.9 Hz, 3H), 1.19−1.43 (m, 22 H), 1.56 (dq, J = 6.6, 6.6 Hz, 2H), 1.83 (m, 2H), 2.48 (d, J = 2.0 Hz, 1H), 3.63 (t, J = 6.9 Hz, 2H), 3.68 (dd, J = 8.3, 2.6 Hz, 1H), 3.70 (m, 1H), 3.79 (s, 3H), 4.01 (dd, J = 6.9, 2.0 Hz, 1H), 4.42 (d, J = 11.2 Hz, 1H), 4.73 (d, J = 9.5 Hz, 1H), 6.86 (d, J = 9.5 Hz, 2H), 7.28 (d, J = 9.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 10.3, 11.6, 23.8, 24.9, 25.7, 26.1, 29.4, 29.51, 29.54, 29.6, 29.7, 30.7, 32.8, 36.5, 40.8, 55.2, 63.0, 69.6, 70.1, 70.4, 72.1, 74.4, 82.7, 100.2, 113.7, 130.0, 130.2, 159.2. **Mixture of two isomers of 28d**: IR (neat, cm^{-1}) 3410, 3306, 2935, 2855, 1614, 1514, 1460, 1382, 1302, 1250, 1225, 1175, 1060, 1040, 1020, 948, 822, 758; LRMS (EI) m/z (M − Me)$^+$ 473.1; HRMS (EI) m/z (M − Me)$^+$ calcd for $C_{29}H_{45}O_5$ 473.3267, found 473.3273.

(4*R,5*S**,6*S**,7*R**)-17-(*tert*-Butyldimethylsilyloxy)-5,7-(*O*-isopropylidenedioxy)-4,6-dimethylheptadec-1-yn-3-one (31).** To a stirred solution of **28a** (310 mg, 0.841 mmol) in dry CH_2Cl_2 (3.36 mL) were added at 0 °C imidazole (172 mg, 2.52 mmol) and TBSCl (151 mg, 1.00 mmol). After 25 min at 0 °C, saturated aqueous NH_4Cl was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (6 g, 7:1 hexane−EtOAc) to afford TBS ether (313 mg, 77% a 7:3 mixture of diastereomers) as a colorless syrup. The NMR chemical shifts of each isomer were determined using the spectra of the mixture of two isomers. **Major isomer**: R_f = 0.62 (1:1 hexane−$CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 6H), 0.82 (d, J = 6.9 Hz, 3H), 0.89 (s, 9H), 1.14 (d, J = 6.9 Hz, 3H), 1.20−1.46 (m, 16H), 1.31 (s, 3H), 1.35 (s, 3H), 1.46−1.54 (m, 2H), 1.78−1.90 (m, 2H), 2.45 (d, J = 1.7 Hz, 1H), 2.98 (br, 1H), 3.58 (dd, J = 11.0, 4.3 Hz, 1H), 3.59 (t, J = 6.6 Hz, 2H), 3.73 (dt, J = 9.2, 4.6 Hz, 1H), 4.52 (br dd, J = 2.2, 2.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.3, 7.7, 11.8, 18.4, 23.9, 24.8, 25.97, 25.97, 26.04, 29.4, 29.5, 29.58, 29.58, 29.7, 30.6, 32.9, 36.4, 41.1, 63.3, 67.0, 69.5, 72.9, 77.8, 83.9, 100.6. **Minor isomer**: R_f = 0.62 (1:1 hexane−$CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 6H), 0.83 (d, J = 6.9 Hz, 3H), 0.89 (s, 9H), 1.12 (d, J = 7.2 Hz, 3H), 1.20−1.46 (m, 16H), 1.31 (s, 3H), 1.40 (s, 3H), 1.46−1.54 (m, 2H), 1.78−1.90 (m, 2H), 2.49 (d, J = 2.0 Hz, 1H), 3.48 (d, J = 8.3 Hz, 1H), 3.59 (t, J = 6.6 Hz, 2H), 3.73 (dt, J = 9.2, 4.6 Hz, 1H), 4.02 (dd, J = 8.6, 2.8 Hz, 1H), 4.36 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.3, 10.8, 11.7, 18.4, 24.1, 24.9, 25.8, 26.0, 27.2, 29.4, 29.5, 29.58, 29.58, 29.7, 30.6, 32.9, 36.1, 40.0, 63.3, 66.7, 69.5, 72.9, 74.9, 84.7, 100.8. **Mixture of two isomers**: IR (neat, cm^{-1}) 3440, 3310, 2930, 2855, 1462, 1383, 1255, 1225, 1175, 1148, 1100, 1040, 1018, 993, 838, 778, 760; LRMS (EI) m/z (M)$^+$ 482.4, (M − Me)$^+$467.3; HRMS (EI) m/z (M − Me)$^+$ calcd for $C_{27}H_{51}O_4Si$ 467.3557, found 467.3538. To a stirred solution of this TBS ether (23.2 mg, 0.0481 mmol) in dry CH_2Cl_2 (0.48 mL) was added at rt Dess−Martin periodinane (27.1 mg, 0.0643 mmol). After 1.5 h at rt, the resulting mixture was directly subjected to column chromatography on silica gel (2 g, 6:1 hexane−EtOAc) to afford **31** (19.2 mg, 84%) as a colorless syrup: R_f = 0.58 (3:1 hexane−EtOAc); IR (neat, cm^{-1}) 3256, 2930, 2858, 2095, 1688, 1462, 1384, 1255, 1225, 1170, 1100, 1020, 839, 776; ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 6H), 0.88 (d, J = 6.6 Hz, 3H), 0.89 (s, 9H), 1.21 (d, J = 6.6 Hz, 3H), 1.24−1.62 (m, 24H), 1.85 (m, 1H), 2.62 (qd, J = 6.6, 3.6 Hz, 1H), 3.24 (s, 1H), 3.59 (t, J = 6.4 Hz, 2H), 3.75 (m, 1H), 3.97 (dd, J = 8.0, 3.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.3, 8.9, 11.8, 18.3, 23.7, 24.6, 25.7, 25.9, 26.0, 29.4, 29.49, 29.53, 29.53, 29.6, 30.6, 32.8, 36.6, 50.8, 63.2, 69.3, 74.1, 79.2, 80.8, 100.6, 188.7; LRMS (EI) m/z (M)$^+$ 480.4, (M − Me)$^+$ 465.4; HRMS (EI) m/z (M − Me)$^+$ calcd for $C_{27}H_{49}O_4Si$ 465.3400, found 465.3401.

(4*R,5*S**,6*S**,7*R**)-17-Hydroxy-5,7-(*O*-isopropylidenedioxy)-4,6-dimethylheptadec-1-yn-3-one (28e).** To a stirred solution of **31** (7.5 mg, 0.015 mmol) in dry THF (0.15 mL) was added at 0 °C 1.0 M HF−pyridine (0.063 mL, 0.063 mmol). After 10 min at 0 °C, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (2 g, 2:1 hexane−EtOAc) to afford **28e** (3.6 mg, 66%) as a colorless syrup: R_f = 0.48 (1:1 hexane−EtOAc); IR (neat, cm^{-1}) 3410, 3300, 2985, 2930, 2858, 2095, 1682, 1460, 1383, 1225, 1170, 1020, 883, 758; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.89 (d, J = 6.6 Hz, 3H), 1.21 (d, J = 7.0 Hz, 3H), 1.24−1.50 (m, 22H), 1.50−1.64 (m, 2H), 1.86 (m, 1H), 2.63 (qd, J = 6.6, 3.6 Hz, 1H), 3.28 (s, 1H), 3.63 (t, J = 6.8 Hz, 2H), 3.75 (dt, J = 9.4, 4.7 Hz, 1H), 3.98 (dd, J = 8.0, 3.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 8.9, 11.8, 23.7, 24.7, 25.7, 26.0, 29.4, 29.47, 29.51, 29.51, 29.6, 30.6, 32.7, 36.6, 50.8, 62.9, 69.3, 74.1, 79.2, 80.8, 100.6, 188.8; LRMS (EI) m/z (M − Me) $^+$ 351; HRMS (EI) m/z (M − Me)$^+$ calcd for $C_{21}H_{35}O_4$ 351.2535, found 351.2537.

Pentacarbonyl[((11*R,12*S**,13*R**,14*S**,15*R***S**)-15-hydroxy-11,13-(*O*-isopropylidenedioxy)-12,14-dimethylheptadec-16-yn-1-oxy)(isopropenyl)carbene]chromium(0) (29a).** To a stirred solution of tetramethylammonium salt **8**[24] (33.5 mg, 0.0909 mmol) in

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

dry CH_2Cl_2 (1.34 mL) was added at −50 °C AcBr (0.006 mL, 0.08 mmol). After 1.5 h at −78 °C, a solution of **28a** (24.7 mg, 0.0670 mmol) in dry CH_2Cl_2 (0.20 mL) was added at −78 °C, and the resulting mixture was stirred for 1 h at −78 °C before being warmed to −10 °C. After 10 min at −10 °C, the mixture was cooled to −78 °C and diluted with 1:1 hexane−EtOAc (8.0 mL); the resulting mixture was warmed to rt. The resulting mixture was directly purified by column chromatography on silica gel (1.5 g, 7:1 hexane−EtOAc) to afford **29a** (36.1 mg, 88%: a 7:3 mixture of diastereomers) as a red syrup. The NMR chemical shifts of each isomer were determined using the spectra of a mixture of two isomers. **Major isomer of 29a**: R_f = 0.42 (3:1 hexane−EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.83 (d, J = 6.6 Hz, 3H), 1.15 (d, J = 6.6 Hz, 3H), 1.20−1.54 (m, 22H), 1.78−1.90 (m, 2H), 1.86 (s, 3H), 1.94 (m, 2H), 2.46 (d, J = 2.0 Hz, 1H), 2.98 (br, 1H), 3.58 (dd, J = 10.0, 2.0 Hz, 1H), 3.74 (m, 1H), 4.52 (dd, J = 1.8 Hz, 1H), 4.72 (br, 2H), 4.89 (br, 1H), 5.06 (br s, 1H). **Minor isomer of 29a**: R_f = 0.42 (3:1 hexane−EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.83 (d, J = 6.6 Hz, 3H), 1.12 (d, J = 6.6 Hz, 3H), 1.20−1.54 (m, 22H), 1.78−1.90 (m, 2H), 1.86 (s, 3H), 1.94 (m, 2H), 2.50 (d, J = 2.0 Hz, 1H), 3.50 (d, J = 8.4 Hz, 1H), 3.74 (m, 1H), 4.04 (dd, J = 8.2, 2.0 Hz, 1H), 4.38 (m, 1H), 4.72 (br, 2H), 4.89 (br, 1H), 5.06 (br, 1H).

Pentacarbonyl[((11*R,12*S**,13*R**,14*S**,15*R***S**)-11,13-(*O*-isopropylidenedioxy)-15-(methoxy)-12,14-dimethylheptadec-16-yn-1-oxy)(isopropenyl)carbene]chromium(0) (29c).** Red syrup (76% yield as a 7:3 mixture of diastereomers). The NMR chemical shifts of each isomer were determined using the spectra of a mixture of two isomers. **Major isomer of 29c**: R_f = 0.42 (1:1 hexane−EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.82 (d, J = 6.6 Hz, 3H), 1.04 (d, J = 7.0 Hz, 3H), 1.22−1.54 (m, 22H), 1.72−1.84 (m, 2H), 1.87 (s, 3H), 1.88−2.00 (m, 2H), 2.47 (d, J = 2.0 Hz, 1H), 3.42 (s, 3H), 3.64 (dd, J = 8.0, 2.2 Hz, 1H), 3.72 (m, 1H), 3.86 (dd, J = 9.2, 2.0 Hz, 1H), 4.72 (br, 2H), 4.89 (br, 1H), 5.06 (br, 1H). **Minor isomer of 29c**: R_f = 0.42 (1:1 hexane−EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.80 (d, J = 6.0 Hz, 3H), 1.04 (d, J = 6.6 Hz, 3H), 1.22−1.54 (m, 22H), 1.72−1.84 (m, 2H), 1.87 (s, 3H), 1.88−2.00 (m, 2H), 2.44 (d, J = 1.8 Hz, 1H), 3.42 (s, 3H), 3.62 (dd, J = 8.2, 2.0 Hz, 1H), 3.72 (m, 1H), 3.83 (dd, J = 8.4, 1.8 Hz, 1H), 4.72 (br, 2H), 4.89 (br, 1H), 5.06 (br, 1H).

Pentacarbonyl[((11*R,12*S**,13*R**,14*S**,15*R***S**)-11,13-(*O*-isopropylidenedioxy)-15-(4-methoxybenzyloxy)-12,14-dimethylheptadec-16-yn-1-oxy)(isopropenyl)carbene]chromium(0) (29d).** Red syrup (63% yield as a 7:3 mixture of diastereomers). The NMR chemical shifts of each isomer were determined using the spectra of a mixture of two isomers. **Major isomer of 29d**: R_f = 0.63 (3:1 hexane−EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.82 (d, J = 6.6 Hz, 3H), 1.06 (d, J = 6.2 Hz, 3H), 1.14−1.56 (m, 22H), 1.74−1.90 (m, 2H), 1.86 (s, 3H), 1.94 (m, 2H), 2.51 (d, J = 2.0 Hz, 1H), 3.66−3.74 (m, 1H), 3.68 (dd, J = 8.0, 2.4 Hz, 1H), 3.81 (s, 3H), 4.02 (dd, J = 8.8, 2.0 Hz, 1H), 4.42 (d, J = 11.2 Hz, 1H), 4.72 (br, 1H), 4.76 (d, J = 11.2 Hz, 1 H), 4.90 (br, 1H), 5.06 (br, 1H), 6.88 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H). **Minor isomer of 29d**: R_f = 0.63 (3:1 hexane−EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.78 (d, J = 6.0 Hz, 3H), 1.05 (d, J = 6.4 Hz, 3H), 1.14−1.56 (m, 22H), 1.74−1.90 (m, 2H), 1.86 (s, 3H), 1.94 (m, 2H), 2.48 (d, J = 2.0 Hz, 1H), 3.63 (dd, J = 8.2, 1.8 Hz, 1H), 3.66−3.74 (m, 1H), 3.80 (s, 3H), 4.02 (dd, J = 8.8, 2.0 Hz, 1H), 4.43 (d, J = 11.0 Hz, 1H), 4.72 (br, 1H), 4.73 (d, J = 11.0 Hz, 1 H), 4.90 (br, 1H), 5.06 (br, 1H), 6.86 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H).

Pentacarbonyl[((11*R,12*S**,13*S**,14*R**)-11,13-(*O*-isopropylidenedioxy)-12,14,-dimethylheptadec-15-oxo-16-yn-1-oxy)-(isopropenyl)carbene]chromium(0) (29e).** Red syrup (64% yield): R_f = 0.53 (3:1 hexane−EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.89 (d, J = 6.6 Hz, 3H), 1.21 (d, J = 6.6 Hz, 3H), 1.22−1.56 (m, 22H), 1.80−1.90 (m, 1H), 1.86 (s, 3H), 1.95 (m, 1H), 2.63 (qd, J = 6.6, 3.2 Hz, 1H), 3.26 (s, 1H), 3.74 (dt, J = 8.6, 4.0 Hz, 1H), 3.98 (dd, J = 8.0, 3.2 Hz, 1H), 4.72 (br, 2H), 4.88 (br, 1H), 5.06 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 8.9, 11.8, 19.3, 23.7, 24.7, 25.7, 26.0, 29.0, 29.3, 29.4, 29.5, 29.6, 30.6, 36.6, 50.9, 69.3, 74.2, 79.1, 79.2, 80.8, 82 (br), 100.6, 157 (br), 188.8, 219.3, 224.0.

(12*R,13*S**,14*R**,15*S**,16*R***S**)-16,18-Dihydroxy-12,14-(*O*-isopropylidenedioxy)-13,15,20-trimethyl-1-oxa[16]metacyclophane (30a).** A solution of **29a** (36.1 mg, 0.0589 mmol) in dry degassed toluene (29.5 mL) was stirred at 50 °C. After 12 h, the mixture was concentrated. The residue was purified by column chromatography on silica gel (3 g, 6:1 hexane−EtOAc) to afford **30a** (1.0 mg, 4%: a 3:2 mixture of diastereomers) as a colorless syrup. Each diastereomer as an analytical sample was partially separated by repeated column chromatography (5:1 hexane−EtOAc). **Major isomer of 30a**: R_f = 0.38 (3:1 hexane−EtOAc); IR (neat, cm^{-1}) 3376, 2930, 2858, 1502, 1459, 1415, 1381, 1221, 1196, 1103, 1000, 868; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.61 (d, J = 7.0 Hz, 3H), 0.97 (d, J = 6.9 Hz, 3H), 1.20−1.45 (m, 14H), 1.40 (s, 3H), 1.41 (s, 3H), 1.45−1.68 (m, 3H), 1.76 (m, 1H), 2.05 (m, 1H), 2.18 (s, 3H), 2.59 (m, 1H), 3.82 (dd, J = 5.5, 4.0 Hz, 1H), 3.88 (dt, J = 11.2, 6.9 Hz, 1H), 3.97 (m, 1H), 4.01 (ddd, J = 11.2, 7.2, 6.3 Hz, 1H), 4.82 (d, J = 8.3 Hz, 1H), 5.22 (s, 1 H), 6.35 (s, 1H), 6.67 (s, 1H), 7.96 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 13.1, 13.7, 16.0, 23.7, 24.6, 25.0, 27.1, 28.1, 28.2, 28.5, 28.56, 28.60, 29.3, 29.7, 32.0, 41.4, 69.2, 70.8, 78.4, 79.7, 100.8, 115.8, 119.4, 122.3, 129.1, 150.1, 150.4; LRMS (EI) m/z (M) $^+$ 448.0; HRMS (EI) m/z (M)$^+$ calcd for $C_{27}H_{44}O_5$ 448.3189, found 448.3193. **Minor isomer of 30a**: R_f = 0.38 (3:1 hexane−EtOAc); IR (neat, cm^{-1}) 3375, 2928, 2856, 1502, 1460, 1379, 1226, 1200, 1097, 1021, 871; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.83 (d, J = 7.2 Hz, 3H), 1.10 (d, J = 6.9 Hz, 3H), 1.22−1.45 (m, 14H), 1.34 (s, 3H), 1.41 (s, 3H), 1.45−1.72 (m, 3H), 1.80 (m, 1H), 1.93 (m, 1H), 2.04 (m, 1H), 2.18 (s, 3H), 2.54 (br s, 1H), 3.46 (dd, J = 7.4, 5.4 Hz, 1H), 3.85−3.97 (m, 3H), 4.89 (br d, J = 4.6 Hz, 1H), 6.39 (s, 1H), 6.67 (s, 1H), 7.65 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 9.2, 12.7, 15.9, 24.4, 25.0, 25.4, 27.6, 27.7, 28.1, 28.3, 28.7, 29.0, 29.7, 31.9, 35.3, 35.7, 70.4, 74.1, 85.0, 99.4, 112.7, 119.8, 123.1, 128.5, 148.2, 149.1; LRMS (EI) m/z (M) $^+$ 448.3; HRMS (EI) m/z (M)$^+$ calcd for $C_{27}H_{44}O_5$ 448.3189, found 448.3201.

(12*R,13*S**,14*R**,15*S**,16*R***S**)-18-Hydroxy-12,14-(*O*-isopropylidenedioxy)-16-(methoxy)-13,15,20-trimethyl-1-oxa[16]-metacyclophane (30c).** Compound **30c** was obtained as two separable diastereomers. **Major isomer of 30c** (16% yield as a colorless syrup): R_f = 0.52 (4:1 hexane−EtOAc); IR (neat, cm^{-1}) 3397, 2933, 2858, 1499, 1460, 1379, 1308, 1225, 1163, 1067, 1040, 1022, 758; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.79 (d, J = 6.6 Hz, 3H), 1.06 (d, J = 6.6 Hz, 3H), 1.20−1.66 (m, 16H), 1.33 (s, 3H), 1.41 (s, 3H), 1.70 (m, 1H), 1.81 (m, 1H), 1.86−1.98 (m, 2H), 2.18 (s, 3H), 3.38 (s, 3H), 3.40 (m, 1H), 3.82−3.98 (m, 3H), 4.22 (d, J = 6.0 Hz, 1H), 6.38 (s, 1H), 6.66 (s, 1H), 7.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 9.7, 12.4, 16.0, 24.4, 24.8, 25.5, 27.4, 27.66, 27.66, 27.8, 27.9, 28.4, 28.7, 28.9, 35.2, 44.1, 57.6, 69.4, 73.4, 85.5, 99.2, 113.8, 119.1, 121.1, 128.6, 149.2, 150.6; LRMS (EI) m/z (M$^+$) 462.3; HRMS (EI) m/z (M$^+$) calcd for $C_{28}H_{46}O_5$ 462.3345, found 462.3339. **Minor isomer of 30c** (6% yield as a colorless syrup): R_f = 0.50 (4:1 hexane−EtOAc); IR (neat, cm^{-1}) 3385, 2930, 2857, 1502, 1460, 1379, 1313, 1225, 1192, 1076, 1022, 760; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.80 (d, J = 6.4 Hz, 3H), 0.84 (d, J = 7.2 Hz, 3H), 1.16−1.80 (m, 16H), 1.40 (s, 3H), 1.43 (s, 3H), 1.65−1.82 (m, 3H), 2.19 (s, 3H), 2.55 (m, 1H), 3.34 (s, 3H), 3.54 (br dd, J = 6.0, 5.0 Hz, 1H), 3.77 (m, 1H), 3.93 (dt, J = 1.6, 6.0 Hz, 2H), 4.52 (d, J = 4.6 Hz, 1H), 6.47 (s, 1H), 6.67 (s, 1H), 7.44 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 12.2, 13.5, 16.0, 23.7, 24.0, 24.6, 26.1, 26.4, 27.2, 27.3, 27.4, 27.7, 28.5, 29.9, 33.9, 43.0, 57.1, 69.4, 70.0, 84.0, 100.5, 114.5, 119.0, 121.3, 128.8, 149.5, 150.5; LRMS (EI) m/z (M$^+$) 462.3; HRMS (EI) m/z (M$^+$) calcd for $C_{28}H_{46}O_5$ 462.3345, found 462.3325.

(12*R,13*S**,14*R**,15*S**,16*R***S**)-18-Hydroxy-12,14-(*O*-isopropylidenedioxy)-16-(4-methoxybenzyloxy)-13,15,20-trimethyl-1-oxa[16]metacyclophane (30d).** Compound **30d** was obtained as two separable diastereomers. **Major isomer of 30d** (15% yield as a colorless syrup): R_f = 0.56 (3:1 hexane−EtOAc); IR (neat, cm^{-1}) 3387, 2933, 2856, 1612, 1514, 1500, 1460, 1382, 1304, 1249, 1223, 1172, 1035, 773; ^{1}H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.73 (d, J = 6.6 Hz, 3H), 1.08 (d, J = 7.0 Hz, 3H), 1.20−1.46 (m, 14H), 1.32

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

(s, 3H), 1.39 (s, 3H), 1.62−1.78 (m, 2H), 1.78−1.96 (m, 2H), 1.96−2.08 (m, 2H), 2.21 (s, 3H), 3.41 (br t, J = 6.0 Hz, 2H), 3.78−3.98 (m, 2H), 3.81 (s, 3H), 4.30 (d, J = 10.0 Hz, 1H), 4.42 (d, J = 6.0 Hz, 1H), 4.51 (d, J = 10.0 Hz, 1H), 6.43 (s, 1H), 6.70 (s, 1H), 6.88 (d, J = 6.8 Hz, 2H), 7.24 (d, J = 6.8 Hz, 2H), 7.53 (s, 1H); LRMS (EI) m/z (M^+) 568.1; HRMS (EI) m/z (M^+) calcd for $C_{35}H_{52}O_6$ 568.3764, found 568.3783. **Minor isomer of 30d** (2% yield as a colorless syrup): R_f = 0.48 (hexane/EtOAc = 3:1); IR (neat, cm^{-1}) 3384, 2931, 2856, 1613, 1514, 1460, 1379, 1303, 1249, 1226, 1174, 1036; ^1H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.80 (d, J = 6.8 Hz, 3H), 0.83 (d, J = 7.4 Hz, 3H), 1.18−1.45 (m, 16H), 1.37 (s, 3H), 1.40 (s, 3H), 1.68−1.78 (m, 2H), 2.21 (s, 3H), 3.43−3.62 (m, 2H), 3.80 (s, 3H), 3.88−3.98 (m, 2H), 4.34 (d, J = 10.8 Hz, 1H), 4.49 (d, J = 10.8 Hz, 1H), 4.72 (d, J = 4.4 Hz, 1H), 6.46 (s, 1H), 6.70 (s, 1H), 6.86 (d, J = 8.2 Hz, 2H), 7.20−7.30 (2H, $CHCl_3$ overlapped), 7.46 (s, 1H); LRMS (EI) m/z (M^+) 568.1; HRMS (EI) m/z (M^+) calcd for $C_{35}H_{52}O_6$ 568.3764, found 568.3758.

(12*R,13*S**,14*S**,15*R**)-18-Hydroxy-12,14-(*O*-isopropylidenedioxy)-16-oxo-13,15,20-trimethyl-1-oxa[16]metacyclophane (30e).** Pale yellow needles (41% yield after air treatment): R_f = 0.67 (10:1 hexane−EtOAc); mp = 96−98 °C; IR ($CHCl_3$, cm^{-1}) 3385, 2927, 2855, 1638, 1612, 1550, 1499, 1382, 1222, 1189, 1125, 1096, 773; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.71 (d, J = 6.9 Hz, 3H), 1.16−1.44 (m, 14H), 1.30 (d, J = 6.3 Hz, 3H), 1.40 (s, 3H), 1.41 (s, 3H), 1.52−1.62 (m, 3H), 1.78−1.86 (m, 2H), 2.25 (s, 3H), 3.58 (dd, J = 9.5, 6.0 Hz, 1H), 3.68 (m, 1H), 3.90−4.08 (m, 3H), 6.82 (s, 1H), 7.18 (s, 1H), 12.34 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 12.5, 16.1, 17.0, 24.0, 24.1, 24.4, 26.1, 26.85, 26.94, 27.2, 27.3, 27.8, 27.9, 28.6, 38.7, 45.1, 67.0, 68.2, 77.7, 100.7, 110.6, 117.3, 120.5, 139.8, 149.6, 158.0, 207.8; LRMS (EI) m/z (M^+) 446.3; HRMS (EI) m/z (M^+) calcd for $C_{27}H_{42}O_5$ 446.3032, found 446.3015.

Tricarbonyl[(17,18,19,20,21,22-η)-(12*R,13*S**,14*S**,15*R**)-18-hydroxy-12,14-(*O*-isopropylidenedioxy)-16-oxo-13,15,20-trimethyl-1-oxa[16]metacyclophanyl chromium (0) ($30e_{Cr}$).** Red syrup (37% yield based on the crude ^1H NMR spectrum): R_f = 0.57 (10:1 hexane−EtOAc); IR ($CHCl_3$, cm^{-1}) 3585, 2930, 2857, 2361, 2342, 1974, 1910, 1638, 1500, 1460, 1378, 1222, 1191;^1H NMR (300 MHz, $CDCl_3$, TMS = 0.00) δ 0.73 (d, J = 6.4 Hz, 3H), 1.20−1.50 (m, 14H), 1.25 (d, J = 6.6 Hz, 3H), 1.43 (s, 3H), 1.46 (s, 3H), 1.52−1.62 (m, 3H), 1.70−1.84 (m, 2H), 2.35 (s, 3H), 3.33 (m, 1H), 3.45 (m, 1H), 3.67 (m, 1H), 3.85 (m, 1H), 3.98 (m, 1H), 5.17 (s, 1H), 5.83 (s, 1H), 11.74 (s, 1H); LRMS (EI) m/z (M^+) 582.4; HRMS (EI) m/z (M^+) calcd for $C_{30}H_{42}O_8Cr$ 582.2285, found 582.2306.

(12*R,13*R**,14*S**,15*R**,16*R**)-12,16-Epoxy-14,18-dihydroxy-13,15,20-trimethyl-1-oxa[16]metacyclophane (THP Analogue 3).** To a stirred solution of ynone **30e** (4.0 mg, 0.0090 mmol) in EtOH (0.30 mL) was added at 0 °C $NaBH_4$ (0.50 mg, 0.013 mmol). After 30 min at rt, saturated aqueous NaCl was added, and the mixture was extracted with EtOAc. The extracts were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (1 g, 2:1 hexane−EtOAc) to afford **30a** (3.9 mg, 97% as a single isomer) as a colorless syrup. To a stirred solution of the resulting alcohol (1.1 mg, 0.0022 mmol) in MeOH (0.25 mL) was added at rt (*S*)-10-camphorsulfonic acid (1.5 mg, 0.0065 mmol). After 2 h at rt, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was filtered through Celite to afford **3** (1.1 mg, 98%) as a colorless syrup: R_f = 0.28 (2:1 hexane−EtOAc); IR (neat, cm^{-1}) 3386, 2925, 2854, 1723, 1619, 1502, 1459, 1418, 1384, 1261, 1195, 1100, 1040, 771; ^1H NMR (500 MHz, $CDCl_3$, TMS = 0.00) δ 0.84 (d, J = 6.3 Hz, 3H), 1.02 (d, J = 6.9 Hz, 3H), 1.05−1.38 (m, 12H), 1.46−1.72 (m, 7H), 1.94 (m, 1H), 2.05 (br, 1H), 2.18 (s, 3H), 3.50−3.58 (m, 2H), 3.90 (br d, J = 10.1 Hz, 1H), 4.00 (dt, J = 12.3, 6.9 Hz, 1H), 4.17 (dt, J = 12.3, 6.1 Hz, 1H), 6.64 (br s, 1H), 6.67 (s, 1H); ^{13}C NMR (125 MHz, benzene-d_6, solvent residual peak =128.1) δ 6.5, 13.6, 16.3, 25.3, 26.6, 27.6, 28.75, 28.75, 28.81, 29.0, 29.4, 31.8, 37.8, 40.3, 69.3, 77.3, 80.5, 84.6, 117.3, 119.8, 124.3, 129.4, 149.3, 150.6; LRMS (EI) m/z (M^+) 390.2; HRMS (EI) m/z (M^+) calcd for $C_{24}H_{38}O_4$ 390.2770, found 390.2772. It was difficult to determine the stereochemistry of the THP ring of **3** by the J value of its ^1H NMR spectrum because the corresponding signals become broadened by atropisomerism. However, H−H COSY together with NOE experiments clearly showed the stereochemistry of **3** (see the Supporting Information).

(4*R*,5*S*,6*S*,7*R*,10*S*,11*E*,14*S*,16*S*)-17-(*tert*-Butyldimethylsilyloxymethyl)-5,7-(*O*-isopropylidenedioxy)-4,6,10,12,14,16-hexamethyloctadeca-11,17-dien-1-yn-3-one (34). To a stirred solution of **33**[10] (22.9 mg, 0.0361 mmol) in 1:22 H_2O−DMF (0.069 mL) was added at rt KF (2.1 mg, 0.036 mmol). After 12 h at rt, water was added, and the mixture was extracted with Et_2O. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (0.5 g, 3:1 hexane−EtOAc) to afford alkyne (18.3 mg, 91%, a 2:1 mixture of diastereomers) as a colorless syrup. The NMR chemical shifts of each isomer were determined using the spectra of the mixture. **Major isomer**: R_f = 0.60 (5:1 hexane−EtOAc); ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.06 (s, 6H), 0.78 (d, J = 6.6 Hz, 3H), 0.80 (d, J = 7.0 Hz, 3H), 0.91 (s, 9H), 0.92 (d, J = 7.0 Hz, 1H), 1.00 (d, J = 6.8 Hz, 3H), 1.14 (d, J = 7.0 Hz, 3H), 1.16−1.46 (m, 7H), 1.30 (s, 3H), 1.34 (s, 3H), 1.54 (s, 3H), 1.58−1.75 (m, 2H), 1.80 (m, 1H), 1.97 (dd, J = 12.0, 5.0 Hz, 1H), 2.21 (m, 1H), 2.35 (m, 1H), 2.45 (d, J = 2.2 Hz, 1H), 3.01 (br, 1H), 3.57 (dd, J = 8.0, 2.0 Hz, 1H), 3.72 (m, 1H), 4.10 (br s, 2H), 4.52 (br, 1H), 4.82 (br s, 1H), 4.86 (br d, J = 9.4 Hz, 1H), 5.03 (br d, J = 2.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.4, 7.7, 11.7, 16.1, 18.4, 19.4, 19.9, 21.3, 23.8, 24.6, 25.9, 27.1, 28.1, 32.2, 33.7, 33.8, 36.3, 41.9, 43.4, 48.2, 64.5, 66.9, 69.4, 72.9, 77.7, 83.9, 100.6, 106.9, 132.4, 132.7, 154.0. **Minor isomer**: R_f = 0.60 (5:1 hexane−EtOAc); ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.06 (s, 6H), 0.78 (d, J = 6.6 Hz, 3H), 0.80 (d, J = 7.0 Hz, 3H), 0.91 (s, 9H), 0.92 (d, J = 7.0 Hz, 1H), 1.00 (d, J = 6.8 Hz, 3H), 1.12 (d, J = 7.0 Hz, 3H), 1.16−1.46 (m, 7H), 1.30 (s, 3H), 1.40 (s, 3H), 1.54 (s, 3H), 1.56−1.75 (m, 2H), 1.80 (m, 1H), 1.97 (dd, J = 12.0, 5.0 Hz, 1H), 2.21 (m, 1H), 2.35 (m, 1H), 2.50 (d, J = 2.2 Hz, 1H), 3.53 (d, J = 9.0 Hz, 1H), 3.90 (m, 1H), 4.06 (dd, J = 8.0, 2.4 Hz, 1H), 4.10 (br s, 2H), 4.37 (m, 1H), 4.81 (br s, 1H), 4.86 (br d, J = 9.4 Hz, 1H), 5.03 (br d, J = 2.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.4, 10.7, 11.6, 16.1, 18.4, 19.4, 19.9, 21.3, 24.0, 24.8, 25.6, 27.1, 28.4, 32.2, 33.7, 33.8, 36.0, 40.0, 41.1, 41.9, 64.5, 66.6, 69.5, 73.3, 74.8, 84.6, 100.7, 106.9, 132.4, 132.7, 154.0. **Mixture of two isomers**: IR (neat, cm^{-1}) 3444, 3312, 2957, 1460, 1382, 1253, 1226, 1085, 1016, 898, 837, 776; LRMS (EI) m/z $(M)^+$ 562.4; HRMS (EI) m/z $(M)^+$ calcd for $C_{34}H_{62}O_4Si$ 562.4417, found 562.4411. To a stirred solution of this alkyne (20.0 mg, 0.0355 mmol) in dry CH_2Cl_2 (0.36 mL) was added at rt Dess-Martin periodinane (22.9 mg, 0.0544 mmol). After 1 h at rt, the resulting mixture was directly purified by column chromatography on silica gel (1 g, 5:1 hexane−EtOAc) to afford **34** (19.6 mg, 98%) as a colorless syrup: R_f = 0.70 (5:1 hexane−EtOAc); $[\alpha]^{28.0}_D$ −19.5 (c 0.56, $CHCl_3$); IR (neat, cm^{-1}) 3300, 2958, 2095, 1682, 1460, 1382, 1254, 1226, 1168, 1086, 1020, 898, 838, 761; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.07 (s, 6H), 0.78 (d, J = 6.6 Hz, 3H), 0.87 (d, J = 6.9 Hz, 3H), 0.92 (s, 9H), 0.93 (d, J = 7.0 Hz, 3H), 1.00 (d, J = 6.9 Hz, 3H), 1.17−1.50 (m, 5H), 1.20 (d, J = 6.9 Hz, 3H), 1.27 (s, 3H), 1.32 (s, 3H) 1.44 (m, 1H), 1.54 (d, J = 1.2 Hz, 3H), 1.62 (m, 1H), 1.70 (m, 1H), 1.83 (m, 1H), 1.98 (dd, J = 12.6, 5.5 Hz, 1H), 2.21 (m, 1H), 2.35 (m, 1H), 2.61 (dq, J = 3.5, 6.9 Hz, 1H), 3.23 (s, 1H), 3.72 (dt, J = 9.2, 4.6 Hz, 1H), 3.96 (dd, J = 7.7, 3.2 Hz, 1H), 4.10 (s, 2H), 4.82 (br s, 1H), 4.86 (br d, J = 9.2 Hz, 1H), 5.04 (br d, J = 2.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.4, 8.9, 11.8, 16.1, 18.4, 19.4, 19.9, 21.4, 23.7, 24.7, 25.9, 28.2, 28.5, 32.2, 33.8, 33.9, 36.6, 43.4, 48.2, 50.9, 64.6, 69.3, 74.2, 79.1, 80.9, 100.6, 106.9, 132.5, 132.7, 154.0, 188.8; LRMS (EI) m/z (M^+) 560.4; HRMS (EI) m/z (M^+) calcd for $C_{34}H_{60}O_4Si$ 560.4261, found 560.4279.

(4*R*,5*S*,6*S*,7*R*,10*S*,11*E*,14*S*,16*S*)-17-(Hydroxymethyl)-5,7-(*O*-isopropylidenedioxy)-4,6,10,12,14,16-hexamethyloctadeca-11,17-dien-1-yn-3-one (35). To a stirred solution of alcohol **34** (58.7 mg, 0.104 mmol) in THF (0.52 mL) was added at 0 °C HF−pyridine (0.036 mL). After 1 h at rt, saturated aqueous $NaHCO_3$ was added, and the organic layer of the resulting mixture was directly

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

purified by column chromatography on silica gel (3 g, 5:1 hexane−EtOAc) to afford **35** (39.3 mg, 85%) as a colorless syrup: R_f = 0.35 (5:1 hexane−EtOAc); $[\alpha]^{28.0}_D$ −4.2 (*c* 0.47, $CHCl_3$); IR (neat, cm^{-1}) 3440, 3300, 2958, 2920, 2257, 2095, 1684, 1460, 1384, 1226, 1168, 1020, 910, 738; ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.78 (d, *J* = 6.0 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 1.01 (d, *J* = 6.9 Hz, 3H), 1.19 (d, *J* = 6.9 Hz, 3H), 1.20−1.32 (m, 5H), 1.26 (s, 3H), 1.31 (s, 3H) 1.44 (m, 1H), 1.54 (d, *J* = 1.2 Hz, 3H), 1.63 (m, 1H), 1.71 (m, 1H), 1.82 (m, 1H), 1.97 (dd, *J* = 12.6, 5.0 Hz, 1H), 2.27 (m, 1H), 2.34 (m, 1H), 2.61 (dq, *J* = 3.4, 6.9 Hz, 1H), 3.24 (s, 1H), 3.72 (m, 1H), 3.96 (dd, *J* = 8.0, 3.6 Hz, 1H), 4.10 (br s, 2H), 4.86 (br d, *J* = 9.2 Hz, 1H), 4.88 (br s, 1H), 5.02 (br d, *J* = 1.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 8.9, 11.8, 16.2, 19.4, 19.8, 21.4, 23.7, 24.7, 28.2, 28.5, 32.2, 33.7, 34.4, 36.6, 43.3, 48.1, 50.9, 64.5, 69.3, 74.1, 79.1, 80.9, 100.6, 107.7, 132.3, 132.7, 154.7, 188.8; LRMS (EI) *m*/*z* (M^+) 446.3; HRMS (EI) *m*/*z* (M^+) calcd for $C_{28}H_{46}O_4$ 446.3396, found 446.3374.

Pentacarbonyl[((4*S*,6*S*,8*E*,10*S*,13*R*,14*S*,15*S*,16*R*)-13,15-(*O*-isopropylidenedioxy)-4,6,8,10,14,16-hexamethyloctadec-3-methylene-17-oxo-18-yn-1-oxy)(isopropenyl)carbene]-chromium(0) (36). To a stirred solution of **8**[24] (22.5 mg, 0.0671 mmol) in dry CH_2Cl_2 (0.80 mL) was added at −40 °C AcBr (0.0050 mL, 0.067 mmol). After 1.5 h at −78 °C, a solution of **35** (20.0 mg, 0.0448 mmol) in dry CH_2Cl_2 (0.10 mL) was added at −78 °C; the resulting mixture was warmed to 0 °C. After 10 min, the mixture was cooled to −78 °C, diluted with 5:1 hexane−EtOAc (6.4 mL), and then warmed to rt. The resulting mixture was directly purified by column chromatography on silica gel (10 g, 10:1 hexane−EtOAc) to afford **36** (27.9 mg, 90%) as a red syrup: R_f = 0.72 (5:1 hexane−EtOAc); ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.81 (d, *J* = 6.3 Hz, 3H), 0.86 (d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 1.17−1.38 (m, 5H), 1.20 (d, *J* = 6.9 Hz, 3H), 1.26 (s, 3H), 1.31 (s, 3H) 1.42 (m, 1H), 1.55 (s, 3H), 1.66 (m, 1H), 1.75 (m, 1H), 1.82 (m, 1H), 1.89 (br s, 3H), 1.97 (dd, *J* = 13.5, 5.7 Hz, 1H), 2.35 (m, 1H), 2.41 (m, 1H), 2.61 (dq, *J* = 6.9, 3.2 Hz, 1H), 3.23 (s, 1H), 3.72 (dt, *J* = 9.2, 4.3 Hz, 1H), 3.96 (dd, *J* = 7.8, 3.2 Hz, 1H), 4.83 (br, 1H), 4.87 (br d, *J* = 9.5 Hz, 1H), 5.03 (br s, 1H), 5.14 (s, 2H), 5.15 (br, 1H), 5.17 (s, 1H).

(4*S*,6*S*,8*E*,10*S*,13*R*,14*S*,15*S*,16*R*)-12,14-(*O*-Isopropylidenedioxy)-19-hydroxy-4,6,8,10,14,16,21-heptamethyl-3-methylene-17-oxo-1-oxa[17]metacyclophane (37) and (6*S*,8*S*,10*E*,12*S*,15*R*,16*S*,17*S*,18*R*)-15,17-(*O*-Isopropylidenedioxy)-2,6,8,10,12,16,18-heptamethyl-5-methylenehenicosa-1,10-dien-20-yne-3,19-dione (38). A solution of **36** (13.1 mg, 0.0189 mmol) in degassed dry toluene (9.45 mL) was stirred at 50 °C. After 3 h, the mixture was concentrated. The residue was purified by column chromatography on silica gel (3 g, 15:1 hexane−EtOAc) to afford a 3:1 mixture of **37** and $\mathbf{37}_{cr}$ (2.0 mg, 19%) as a yellow syrup together with **38** (3.6 mg, 38%) as a colorless syrup. After decomplexation of $\mathbf{37}_{Cr}$ by air treatment of the mixture, **37** was purified by column chromatography on silica gel with same solvent system as above. **37**: colorless needles; R_f = 0.70 (5:1 hexane−EtOAc); mp =93−95 °C (not recrystallized); $[\alpha]^{21.1}_D$ −24.7 (*c* 0.23, $CHCl_3$); IR (neat, cm^{-1}) 2926, 2854, 1732, 1636, 1614, 1498, 1456, 1379, 1261, 1192, 1111, 1027, 969, 872, 801, 758; ^1H NMR (500 MHz, $CDCl_3$, TMS = 0.00) δ 0.62 (d, *J* = 6.4 Hz, 3H), 0.75 (d, *J* = 7.1 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H), 1.15 (d, *J* = 7.1 Hz, 3H), 1.20−1.34 (m, 5H), 1.23 (d, *J* = 6.7 Hz, 3H), 1.38 (s, 3H), 1.39 (s, 3H), 1.47 (m, 1H), 1.69 (m, 1H), 1.70 (s, 3H), 2.00 (dd, *J* = 13.2, 4.4 Hz, 1H), 2.05 (m, 1H), 2.29 (br s, 3H), 2.30 (m, 1H), 2.45−2.52 (m, 2H), 3.45 (dq, *J* = 9.5, 6.8 Hz, 1H), 3.66 (dd, *J* = 9.5, 6.1 Hz, 1H), 3.82 (ddd, *J* = 9.8, 4.0, 3.8 Hz, 1H), 4.46 (d, *J* = 14.0 Hz, 1H), 4.57 (d, *J* = 14.0 Hz, 1H), 4.80 (br d, *J* = 10.0 Hz, 1H), 5.11 (s, 1H), 5.28 (br d, *J* = 1.2 Hz, 1H), 6.81 (s, 1H), 7.21 (s, 1H), 12.28 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 12.4, 15.9, 17.2, 18.2, 20.2, 20.4, 21.3, 24.0, 26.8, 27.2, 29.5, 30.7, 31.9, 37.2, 39.5, 42.5, 46.4, 46.8, 66.7, 71.9, 77.7, 100.6, 112.2, 112.3, 117.2, 120.4, 131.5, 132.6, 139.9, 150.2, 150.5, 158.1, 208.2; LRMS (EI) *m*/*z* (M^+) 526.3; HRMS (EI) *m*/*z* (M^+) calcd for $C_{33}H_{50}O_5$ 526.3658, found 526.3669. $\mathbf{37}_{Cr}$: The NMR chemical shifts were determined using the spectra of a mixture of **37** and $\mathbf{37}_{Cr}$: R_f = 0.65 (5:1 hexane−EtOAc); ^1H NMR (500 MHz, $CDCl_3$, TMS = 0.00, detectable peaks were listed) δ 0.73 (d, *J* = 7.2 Hz, 3H), 0.82 (d, *J* = 7.1 Hz, 3H), 0.94 (d, *J* = 7.0 Hz, 3H), 1.07 (d, *J* = 7.1 Hz, 3H), 1.20−1.34 (m, 8H), 1.36 (s, 3H), 1.39 (s, 3H), 1.70 (s, 3H), 2.38 (br s, 3H), 3.16 (m, 1H), 3.42 (m, 1H), 3.50 (dd, *J* = 9.0, 6.6 Hz, 1H), 4.17 (d, *J* = 14.0 Hz, 1H), 4.42 (d, *J* = 14.0 Hz, 1H), 4.88 (br d, *J* = 10.0 Hz, 1H), 5.13 (s, 1H), 5.16 (s, 1H), 5.24 (br s, 1H), 5.92 (s, 1H), 11.75 (s, 1H). **38**: R_f = 0.50 (5:1 hexane−EtOAc); $[\alpha]_D^{21.3}$ −29.3 (*c* 1.00, $CHCl_3$); IR (neat, cm^{-1}) 3250, 2960, 2920, 2095, 1684, 1456, 1380, 1226, 1022, 910, 755; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.77 (d, *J* = 6.6 Hz, 3H), 0.87(d, *J* = 6.9 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H), 1.17−1.42 (m, 5H), 1.20 (d, *J* = 6.9 Hz, 3H), 1.27 (s, 3H), 1.32 (s, 3H), 1.44 (m, 1H), 1.54 (br s, 3H), 1.62 (m, 1H), 1.70 (m, 1H), 1.83 (m, 1H), 1.88 (s, 3H), 1.97 (m, 1H), 2.24 (m, 1H), 2.35 (m, 1H), 2.62 (dq, *J* = 3.0, 7.0 Hz, 1H), 3.24 (s, 1H), 3.36 (d, *J* = 15.8 Hz, 1H), 3.39 (d, *J* = 15.8 Hz,1H), 3.71 (m, 1H), 3.96 (dd, *J* = 8.0, 5.2 Hz, 1H), 4.72 (br s, 1H), 4.86 (br d, *J* = 9.6 Hz, 1H), 4.94 (br s, 1H), 5.78 (br s, 1H), 5.98 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 8.9, 11.8, 16.1, 17.8, 19.3, 19.4, 21.4, 23.7, 24.8, 28.1, 28.5, 32.2, 33.8, 36.6, 37.3, 43.0, 43.1, 48.2, 50.9, 69.3, 74.2, 79.1, 80.9, 100.6, 111.9, 125.2, 132.4, 132.8, 144.5, 149.4, 188.8, 200.5; LRMS (EI) *m*/*z* (M^+) 498.4; HRMS (EI) *m*/*z* (M^+) calcd for $C_{32}H_{50}O_4$ 498.3709, found 498.3703.

(4*R*,5*S*,6*S*,7*R*,10*S*,11*E*,14*S*,16*S*)-17-(*tert*-Butyldimethylsilyloxymethyl)-5,7-(*O*-isopropylidenedioxy)-4,6,10,12,14,16-hexamethyl-1-(trimethylsilyl)octadeca-11,17-dien-1-yn-3-one (39). To a stirred solution of alcohol **33** (7.2 mg, 0.011 mmol) in dry CH_2Cl_2 (0.12 mL) was added at rt Dess−Martin periodinane (7.3 mg, 0.017 mmol). After 1 h at rt, the resulting mixture was directly purified by column chromatography on silica gel (1 g, 5:1 hexane−EtOAc) to afford the known **39**[10] (7.1 mg, 98%) as a colorless syrup.

(3*S*,5*S*,7*E*,9*S*,12*R*,13*R*,14*S*,15*R*,16*R*)-12,16-Epoxy-3,5,7,9,13,15-hexamethyl-2-methylene-16-methoxy-18-(trimethylsilyl)octadec-7-en-17-yne-1,14-diol (40). A solution of **39** (7.1 mg, 0.011 mmol) and (+)-10-camphorsulfonic acid (0.8 mg, 0.003 mmol) in MeOH (0.11 mL) was stirred at rt. After 20 min, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 2:1 hexane−EtOAc) to afford **40**[10] (5.0 mg, 89%) as a colorless syrup.

(3*S*,5*S*,7*E*,9*S*,12*R*,13*R*,14*S*,15*R*,16*R*)-12,16-Epoxy-3,5,7,9,13,15-hexamethyl-2-methylene-18-(trimethylsilyl)-octadec-7-en-17-yne-1,14-diol (41). To a stirred solution of **40** (54.3 mg, 0.110 mmol) and triethylsilane (0.327 mL, 2.20 mmol) in dry acetonitrile (1.10 mL) was added at −50 °C $BF_3{\cdot}OEt_2$ (0.0124 mL, 0.132 mmol); the resulting mixture was warmed to rt. After 1 h at rt, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (2 g, hexane/EtOAc = 2:1) to afford **41**[10] (35.9 mg, 71%) as a colorless syrup.

(3*S*,5*S*,7*E*,9*S*,12*R*,13*S*,14*S*,15*S*,16*R*)-12,16-Epoxy-1,14-(*tert*-butyldimethylsilyloxy)-3,5,7,9,13,15-hexamethyl-2-methylene-18-(trimethylsilyl)octadec-7-en-17-yne (42). To a stirred solution of **41** (20.9 mg, 0.0451 mmol) in dry CH_2Cl_2 (0.450 mL) were added 2,6-lutidine (0.031 mL, 0.27 mmol) and TBSOTf (0.031 mL, 0.14 mmol) at rt. After 15 min, saturated aqueous NH_4Cl was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 5:1 hexane−EtOAc) to afford **42** (26.9 mg, 86%) as a colorless syrup: R_f = 0.95 (5:1 hexane−EtOAc); $[\alpha]^{25.6}_D$ 25.1 (*c* 0.18, $CHCl_3$); IR (neat, cm^{-1}) 3019, 2959, 2930, 2857, 1462, 1387, 1252, 1215, 1083, 1052, 1016, 844; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.07 (s, 6H), 0.17 (s, 9H), 0.78 (d, *J* = 6.3 Hz, 3H), 0.89 (d, *J* = 7.2 Hz, 3H), 0.90 (s, 9H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H), 1.16−1.38 (m, 6H), 1.53 (d, *J* = 1.5 Hz, 3H), 1.58−1.79 (m, 4H), 1.95 (dd, *J* = 12.9, 5.8 Hz, 1H), 2.21 (m, 1H), 2.32 (m, 1H), 3.24 (m, 1H), 3.33 (dd, *J* = 10.3, 4.9 Hz, 1H), 3.67 (d, *J* = 10.6 Hz, 1H), 4.10 (br s, 2H), 4.82 (br s, 1H), 4.86 (br d, *J* = 9.2 Hz, 1H), 5.03 (br d, *J* = 1.8 Hz,

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.4, −4.9, −4.2, −0.1, 5.7, 14.4, 16.1, 18.1, 18.4, 19.5, 19.9, 21.2, 25.8, 25.9, 28.2, 30.4, 32.2, 33.6, 33.9, 38.6, 39.1, 43.3, 48.3, 64.6, 73.4, 76.5, 79.6, 89.5, 103.8, 106.8, 132.3, 132.8, 154.1; LRMS (FAB) m/z (M + H$^+$) 691.0; HRMS (FAB) m/z (M + H$^+$) calcd for $C_{40}H_{79}O_3Si_3$ 691.5337, found 691.5327.

(3*S*,5*S*,7*E*,9*S*,12*R*,13*S*,14*S*,15*R*,16*R*)-14-(*tert*-Butyldimethylsilyloxymethyl)-12,16-epoxy-3,5,7,9,13,15-hexamethyl-2-methyleneoctadeca-7-en-17-yn-1-ol (43). To a stirred solution of **42** (26.9 mg, 0.0389 mmol) in THF (0.39 mL) was added at 0 °C 1.0 M TBAF in THF (0.156 mL, 0.156 mmol). After 6 h at 0 °C, saturated aqueous NH_4Cl was added, and the mixture was extracted with Et_2O. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (2 g, 10:1 hexane−EtOAc) to afford **43** (17.7 mg, 90%) a colorless syrup: R_f = 0.48 (5:1 hexane−EtOAc); $[\alpha]^{20.9}_D$ 28.7 (*c* 0.49, $CHCl_3$); IR (neat, cm^{-1}) 3379, 3313, 2957, 1461, 1384, 1256, 1085, 1049, 895, 837, 759; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.79 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 7.2 Hz, 3H), 0.90 (s, 9H), 0.92 (d, *J* = 7.2 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H), 1.16−1.35 (m, 5H), 1.53 (d, *J* = 1.2 Hz, 3H), 1.57−1.74 (m, 4H), 1.77 (m, 1H), 1.95 (dd, *J* = 13.1, 6.0 Hz, 1H), 2.27 (m, 1H), 2.32 (m, 1H), 2.45 (d, *J* = 2.0 Hz, 1H), 3.28 (ddd, *J* = 7.8, 5.5, 2.0 Hz, 1H), 3.31 (dd, *J* = 10.1, 4.6 Hz, 1H), 3.67 (dd, *J* = 10.6, 2.0 Hz, 1H), 4.11 (br s, 2H, H-1), 4.86 (d, *J* = 8.9 Hz, 1H), 4.89 (br s, 1H), 5.03 (br d, *J* = 1.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ−4.9, −4.2, 5.7, 14.2, 16.2, 18.1, 19.5, 19.7, 21.2, 25.8, 28.2, 30.5, 32.3, 33.6, 34.4, 38.4, 39.2, 43.3, 48.2, 64.6, 72.7, 73.0, 77.1, 79.7, 82.2, 107.7, 132.3, 132.8, 154.7; LRMS (EI) m/z (M$^+$) 504.5; HRMS (EI) m/z (M$^+$) calcd for $C_{31}H_{56}O_3Si$ 504.3999, found 504.3982.

(4*S*,6*S*,8*E*,10*S*,13*R*,14*S*,15*S*,16*S*,17*R*)-15-(*tert*-Butyldimethylsilyloxy)-13,17-epoxy-15,19-hydroxy-4,6,8,10,14,16,21-heptamethyl-3-methylene-1-oxa[17]metacyclophane (44). To a stirred solution of tetramethylammonium salt **8**[24] (106 mg, 0.316 mmol) in dry CH_2Cl_2 (1.98 mL) was added at −40 °C AcBr (0.022 mL, 0.30 mmol). After 1.5 h at −78 °C, a solution of **43** (100 mg, 0.198 mmol) in dry CH_2Cl_2 (0.50 mL) was added at −78 °C, and the resulting mixture was warmed to 0 °C in 1 h. After 10 min at 0 °C, the mixture was cooled to −78 °C. To the mixture was slowly added hexane/EtOAc = 1:1 (3.4 mL); the resulting mixture was warmed to rt. The resulting mixture was filtered through silica gel pad (8:1 hexane−EtOAc) to afford the crude carbene complex as a red syrup. The complex was immediately used for the next step: R_f = 0.61 (8:1 hexane−EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.80 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 7.2 Hz, 3H), 0.90 (s, 9H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.99 (d, *J* = 6.6 Hz, 3H), 1.08 (d, *J* = 6.6 Hz, 3H), 1.18−1.35 (m, 5H), 1.53 (d, *J* = 1.2 Hz, 3H), 1.57−1.70 (m, 4H), 1.75 (m, 1H), 1.89 (s, 1H), 1.95 (dd, *J* = 13.2, 6.0 Hz, 1H), 2.32 (m, 1H), 2.40 (m, 1H), 2.45 (d, *J* = 2.0 Hz, 1H), 3.28 (m, 1H), 3.31 (dd, *J* = 10.0, 4.6 Hz, 1H), 3.67 (dd, *J* = 10.9, 2.0 Hz, 1H), 4.84 (br, 1H, H-1), 4.87 (d, *J* = 8.6 Hz, 1H), 5.03 (br s, 1H), 5.14 (s, 1H), 5.15 (br s, 1H), 5.15 br, 1H), 5.17 (s, 1H). A solution of the crude carbene complex in degassed dry toluene (99.0 mL) was stirred at 50 °C. After 3 h, the mixture was concentrated. The residue was purified by column chromatography on silica gel (10 g, 15:1 hexane−EtOAc) to afford **44** (57.6 mg, 2 steps 50%) as a colorless syrup: R_f = 0.39 (8:1 hexane−EtOAc) ; $[\alpha]^{20.9}_D$ 23.1 (*c* 0.47, $CHCl_3$); IR (neat, cm^{-1}) 3417, 2958, 2857, 1513, 1458, 1413, 1378, 1256, 1193, 1082, 837, 760; ^{1}H NMR (500 MHz, 65 °C, benzene-d_6, solvent residual peak =7.16) δ 0.11 (s, 3H), 0.12 (s, 3H), 0.90 (d, *J* = 6.3 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.97−1.03 (m, 6H), 1.00 (s, 9H), 1.14 (m, 1H), 1.15 (d, *J* = 6.9 Hz, 3H), 1.16 (m, 1H), 1.25 (m, 1H), 1.32 (m, 1H), 1.46 (m, 1H), 1.58 (m, 1H), 1.63 (s, 3H), 1.64−1.84 (m, 3H), 1.70 (m, 1H), 1.89 (m, 1H), 2.14 (m, 1H), 2.18 (dd, *J* = 6.9, 3.2 Hz, 1H), 2.28 (br s, 3H), 2.29 (m, 1H), 3.39 (d, *J* = 10.3 Hz, 1H), 3.58 (dd, *J* = 10.1, 4.6 Hz, 1H), 3.98 (br, 1H), 4.43 (br d, *J* = 10.0 Hz, 1H), 4.50 (br d, *J* = 15.2 Hz, 1H), 4.58 (br d, *J* = 15.2 Hz, 1H), 4.91 (br d, *J* = 9.2 Hz, 1H), 5.00 (s, 1H), 5.27 (s, 1H), 6.15 (br s, 1H), 7.11 (br s, 1H); ^{13}C NMR (125 MHz, 65 °C, benzene-d_6, solvent peak = 128.1) δ −4.5, −3.9, 6.9, 13.9, 16.1, 18.5, 19.8, 20.1, 21.2, 22.3, 26.2, 29.9, 32.9, 33.6, 34.9, 35.5, 41.1, 41.5, 44.5, 45.6, 70.3, 78.5(br), 78.6, 78.9, 108.5, 112.2, 118.1, 126.5, 127.0, 132.1, 132.9, 146.6, 151.1, 151.7; LRMS (EI) m/z (M$^+$) 584.4; HRMS (EI) m/z (M$^+$) calcd for $C_{36}H_{60}O_4Si$ 584.4261, found 584.4272.

(*R*)-2-(1,3-Dithian-2-yl)-1-propanol (46). To a stirred solution of (*R*)-(−)-methyl 3-hydroxy-2-methylpropionate (**45**, 300 mg, 2.54 mmol) in dry CH_2Cl_2 (11.0 mL) was slowly added at −78 °C 1.02 M DIBALH in hexane (5.23 mL, 5.33 mmol). After 25 min at −78 °C, 1,3-propanedithiol (0.509 mL, 5.08 mmol) and boron trifluoride diethyl etherate (0.638 mL, 5.08 mmol) were added; the resulting mixture was warmed to rt. After 1 h at rt, EtOAc, MeOH, potassium sodium-(+)-tartrate tetrahydrate, and water were successively added at rt. After being stirred vigorously for 1 h at rt, the mixture was extracted with $CHCl_3$.The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (23 g, 10:1 $CHCl_3$−acetone) to afford the known **46**[34] (304 mg, 67%) as a colorless syrup.

(2*R*,3*S*,4*S*)-2-(1,3-Dithian-2-yl)-4-methylhex-5-en-3-ol (48). To a stirred solution of oxalyl dichloride (0.059 mL, 0.70 mmol) in dry CH_2Cl_2 (1.00 mL) was added DMSO (0.099 mL, 1.4 mmol) at −78 °C. After 15 min at −78 °C, a solution of **46** (51.9 mg, 0.291 mmol) in dry CH_2Cl_2 (0.75 mL) was added, and the resulting suspension was stirred at −78 °C for 15 min. After the addition of *N*,*N*-diisopropylethylamine (0.349 mL, 1.98 mmol), the mixture was gradually warmed to −45 °C for a period of 2 h. The resulting mixture was then recooled to −78 °C, quenched with aqueous HCl (0.5 M, 1.0 mL), and extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The resulting crude aldehyde was immediately used for the next step. To a stirred solution of the crude aldehyde in 1:1 CH_2Cl_2−H_2O (1.42 mL) were added at rt tetra-*n*-butylammonium iodide (8.6 mg, 0.233 mmol) and **47** (45.3 mg, 0.280 mmol). After 1 h at rt, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The adduct (dr 24:1) was purified by column chromatography on silica gel (2 g, 4:1 hexane−EtOAc) to afford the known **48**[33] (54.4 mg, 2 steps 80% yield) as a colorless syrup: $[\alpha]^{28.2}_D$ −5.3 (*c* 1.00, $CHCl_3$)

(2*R*,3*S*,4*S*)-2-[2-(*tert*-Butyldiphenylsilyloxymethyl)-(1,3-dithian-2-yl)]-4-methylhexen-5-en-3-ol (49). To a stirred solution of **48** (18.8 mg, 0.0807 mmol) in dry THF (0.475 mL) was added at rt 1.62 M *n*-BuLi in hexane (0.121 mL, 0.194 mmol). After 3 min at rt, paraformaldehyde (24.5 mg, 0.807 mmol) was added at rt. After 30 min at rt, saturated aqueous NH_4Cl was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 1:1 hexane−EtOAc) to afford alcohol (15.9 mg, 75%) as a colorless syrup: R_f = 0.45 (1:1 hexane−EtOAc); $[\alpha]^{17.0}_D$ 5.56 (*c* 0.47, $CHCl_3$); IR (neat, cm^{-1}) 3346, 2971, 2930, 1460, 1420, 1381, 1047, 999, 910; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.01 (d, *J* = 6.6 Hz, 3H), 1.09 (d, *J* = 7.2 Hz, 3H), 1.87 (m, 1H), 2.08 (m, 1H), 2.22−2.30 (m, 2H), 2.31−2.62 (br, 2H), 2.64−2.69 (m, 2H), 2.31−2.62 (br, 2H), 2.64−2.69 (m, 2H), 2.85−2.96 (m, 2H), 3.81 (d, *J* = 12.6 Hz, 1H), 3.93 (d, *J* = 12.6 Hz, 1H), 3.95 (d, *J* = 9.0 Hz, 1H), 5.14 (dd, *J* = 10.3, 1.7 Hz, 1H), 5.15 (dd, *J* = 16.9, 1.7 Hz, 1H), 5.74 (ddd, *J* = 17.2, 10.3, 8.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 7.2, 17.1, 25.0, 25.4, 26.3, 42.2, 42.8, 58.6, 60.7, 71.8, 116.8, 141.4; LRMS (FAB) m/z (M − H_2O + H$^+$) 245; HRMS (FAB) m/z (M$^+$) calcd for $C_{12}H_{21}OS_2$ 245.1034, found 245.1057. To a stirred solution of this alcohol (15.9 mg, 0.0606 mmol) in CH_2Cl_2 (0.200 mL) were added at rt imidazole (7.4 mg, 0.11 mmol) and TBDPSCl (0.023 mL, 0.061 mmol). After 30 min at rt, saturated aqueous NH_4Cl was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1.5 g, 15:1 hexane−acetone) to afford **49** (30.0 mg, 99%) as a colorless syrup: R_f = 0.63 (10:1 hexane−EtOAc); $[\alpha]^{21.0}_D$ 1.30 (*c* 0.50, $CHCl_3$); IR (neat, cm^{-1}) 3071, 2956, 2876, 1427, 1239, 1111, 1047, 1006, 912, 823, 739; ^{1}H

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 1.03 (d, J = 6.9 Hz, 3H), 1.10 (s, 9H), 1.11 (d, J = 6.6 Hz, 3H), 1.75 (m, 1H), 1.80 (m, 1H), 2.30 (m, 1H), 2.33−2.46 (m, 5H), 2.87 (d, J = 2.6 Hz, 1H), 3.93 (d, J = 11.2 Hz, 1H), 4.04 (d, J = 11.2 Hz, 1H), 4.19 (ddd, J = 8.9, 2.6, 1.5 Hz, 1H), 5.07 (dd, J = 10.3, 1.7 Hz, 1H), 5.11 (ddd, J = 17.2, 1.7, 1.2 Hz, 1H), 5.93 (ddd, J = 17.2, 10.3, 8.0 Hz, 1H), 7.37−7.48 (m, 6H), 7.72−7.76 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 7.3, 17.1, 19.3, 24.8, 25.6, 25.9, 26.9, 41.5, 42.3, 58.7, 63.6, 73.6, 114.4, 127.70, 127.74, 129.8, 129.9, 132.9, 133.0, 135.9, 136.0, 142.3; LRMS (EI) m/z (M^+) 500.3; HRMS (EI) m/z (M^+) calcd for $C_{28}H_{40}O_2S_2Si$ 500.2239, found 500.2249.

(3*S*,4*S*,5*R*)-5-[2-(*tert*-Butyldiphenylsilyloxymethyl)-1,3-dithian-2-yl]-3-methyl-4-(triethylsilyloxy)-1-hexene (50). To a stirred solution of **49** (169 mg, 0.337 mmol) in dry CH_2Cl_2 (3.33 mL) were added at 0 °C *N*,*N*-diisopropylethylamine (0.174 mL, 1.01 mmol) and triethylsilyl trifluoromethanesulfonate (0.198 mL, 0.876 mmol). After 30 min at 0 °C, saturated aqueous NH_4Cl was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (5 g, 4:1 hexane−EtOAc) to afford **50** (228 mg, quant) as a colorless syrup: R_f = 0.26 (10:1 hexane−EtOAc); $[\alpha]^{21.1}_D$ −0.60 (c 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.66−0.76 (m, 6H), 0.98 (d, J = 7.2 Hz, 3H), 0.99 (t, J = 8.0 Hz, 9H), 1.06 (d, J = 6.9 Hz, 3H), 1.08 (s, 9H), 1.70 (m, 1H), 1.86 (m, 1H), 2.28−2.44 (m, 5H), 2.56 (m, 1H), 3.96 (d, J = 10.9 Hz, 1H), 3.98 (d, J = 10.9 Hz, 1H), 4.50 (dd, J = 3.5, 1.8 Hz, 1H), 5.03−5.08 (m, 2H), 5.94 (ddd, J = 17.5, 9.7, 7.2 Hz, 1H), 7.34−7.47 (m, 6H), 7.70−7.78 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 5.9, 7.3, 9.3, 15.1, 19.4, 25.3, 25.4, 26.3, 26.9, 40.2, 46.9, 59.6, 64.0, 73.2, 114.4, 127.6, 127.7, 129.6, 129.7, 133.5, 133.6, 135.8, 136.1, 140.9; IR (neat, cm^{-1}) 2956, 2876, 1461, 1427, 1111, 1047, 1006, 823, 739, 703; LRMS (EI) m/z (M^+) 614.1; HRMS (EI) m/z (M^+) calcd for $C_{34}H_{54}O_2S_2Si_2$ 614.3104, found 614.3109.

(2*R*,6*S*,7*S*,8*R*)-1-(*tert*-Butyldimethylsilyloxy)-8-[2-(*tert*-butyldiphenylsilyloxymethyl)-1,3-dithian-1-oxid-2-yl]-2,6-dimethyl-7-(triethylsilyloxy)-3-nonyn-5-ol (51). A solution of **50** (105 mg, 0.171 mmol) in MeOH (5.70 mL) was cooled to −78 °C, and ozone was bubbled through the solution. After 15 min at −78 °C, oxygen was bubbled through the solution. After 10 min at −78 °C, triphenylphosphine (44.3 mg, 0.169 mmol) was added; the mixture was warmed to −40 °C. After 10 min at −40 °C, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with $CHCl_3$. The residue was purified by column chromatography on silica gel (5 g, 3:1 hexane−$CHCl_3$) to afford a 5:1 mixture of aldehyde (95.2 mg, 88%) as a colorless syrup. The aldehyde was immediately used for the next step. **Major isomer**: R_f = 0.18 (3:1 hexane−EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, TMS = 0.00) δ 0.57−0.68 (m, 6H), 0.92 (t, 9H), 1.05 (d, J = 6.7 Hz, 3H), 1.08 (s, 9H), 1.28 (d, J = 6.9 Hz, 3H), 2.06−2.19 (m, 1H), 2.30 (br q, J = 7.4 Hz, 1H), 2.48 (m, 1H), 2.56 (m, 1H), 2.87−3.10 (m, 2H), 4.34 (d, J = 11.8 Hz, 1H), 4.37 (d, J = 11.8 Hz, 1H), 4.77 (dd, J = 4.6, 1.6 Hz, 1H), 7.36−7.46 (m, 6H), 7.72−7.82 (m, 4H), 9.73 (d, J = 1.8 Hz, 1H). **Minor isomer**: R_f = 0.18 (3:1 hexane−EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, TMS = 0.00) δ 0.57−0.68 (m, 6H), 0.92 (t, 9H), 1.08 (d, J = 6.7 Hz, 3H), 1.09 (s, 9H), 1.11 (d, J = 6.9 Hz, 3H), 2.06−2.26 (m, 4H), 2.45−2.68 (m, 2H), 2.87−3.10 (m, 1H), 3.34 (m, 1H), 4.26 (d, J = 11.8 Hz, 1H), 4.50 (d, J = 11.8 Hz, 1H), 4.65 (dd, J = 4.3, 2.6 Hz, 1H), 7.36−7.46 (m, 6H), 7.72−7.82 (m, 4H), 9.75 (d, J = 2.0 Hz, 1H). To a stirred solution of **32**[10] (817 mg, 3.67 mmol) in dry Et_2O (37.0 mL) was added at 0 °C 1.57 M *n*-BuLi in hexane (2.34 mL, 4.12 mmol). After 10 min at 0 °C, HMPA (0.638 mL, 3.67 mmol) was added. After being stirred for 15 min at 0 °C, the solution of the acetylide was added via cannula to a solution of this aldehyde (931 mg, 1.47 mmol) in dry Et_2O (37 mL) at −78 °C. After 30 min at −78 °C, saturated aqueous NH_4Cl was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (50 g, 3:1 hexane−$CHCl_3$) to afford **51** (990 mg, 81%, a mixture of four diastereomers) as a colorless syrup. **Major isomer of 51**: R_f = 0.35 (3:1 hexane−EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.06 (s, 6H), 0.42−0.53 (m, 6H), 0.81 (t, J = 8.0 Hz, 9H), 0.89 (s, 9H), 0.98 (d, J = 7.2 Hz, 3H), 1.06 (s, 9H), 1.15 (d, J = 7.2 Hz, 3H), 1.20 (d, J = 6.9 Hz, 3H), 1.70 (m, 1H), 2.14−2.32 (m, 3H), 2.61 (m, 1H), 2.73 (m, 1H), 2.97 (m, 1H), 3.04 (m, 1H), 3.41 (m, 1H), 3.44 (dd, J = 9.8, 8.9 Hz, 1H), 3.74 (dd, J = 9.8, 5.2 Hz, 1H), 4.32 (d, J = 12.1 Hz, 1H), 4.44 (br s, 1H), 4.52 (m, 1H), 4.56 (d, J = 12.1 Hz), 7.39−7.48 (m, 6H), 7.78−7.85 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.34, −5.30, 5.4, 7.0, 10.9, 11.4, 17.3, 18.3, 19.1, 25.9, 26.8, 26.9, 28.7, 29.2, 42.8, 46.7, 47.3, 60.3, 63.6, 67.1, 68.8, 71.6, 81.2, 88.1, 127.9, 128.0, 129.96, 129.99, 132.2, 132.3, 135.7, 135.8; **Mixture of four isomers of 51:** IR (neat, cm^{-1}) 3357, 2956, 1463, 1415, 1252, 1113, 1057, 1007, 838, 757; LRMS (EI) m/z ($M - H_2O)^+$ 812.6; HRMS (EI) m/z (M^+) calcd for $C_{44}H_{74}O_5S_2Si_3$ 830.4286, found 830.4291.

(2*S*,5*S*,6*R*,7*S*,8*R*,9*R*)-10-(*tert*-Butyldiphenylsilyloxy)-5,9-epoxy-2,6,8-trimethyl-3-decyne-1,7,9-triol (52) and (2*S*,5*R*,6*R*,7*S*,8*R*,9*S*)-10-(*tert*-Butyldiphenylsilyloxy)-5,9-epoxy-2,6,8-trimethyl-3-decyne-1,7,9-triol (Diastereomer of 52). A solution of **51** (85.4 mg, 0.103 mmol) and *N*-bromosuccinimide (110 mg, 0.617 mmol) in 97:3 acetone−H_2O (5.00 mL) was stirred at 0 °C. After 1.5 h, saturated aqueous Na_2SO_3 was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (4 g, 2:1 hexane−EtOAc) to afford **52** (36.6 mg, 79%) and **diastereomer of 52** (6.7 mg, 14%) as a colorless syrup. **52**: R_f = 0.25 (1:1 hexane−EtOAc); $[\alpha]^{21.2}_D$ 21.6 (c 0.50, $CHCl_3$); IR (neat, cm^{-1}) 3387, 2933, 1428, 1113, 1041, 822, 758, 705; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.98 (d, J = 6.6 Hz, 3H), 1.06 (d, J = 7.2 Hz, 3H), 1.08 (s, 9H), 1.21 (d, J = 6.9 Hz, 3H), 1.48 (br s, 1H), 1.62 (m, 1H), 1.80 (br s, 1H), 2.07 (m, 1H), 2.76 (m, 1H), 3.28 (d, J = 1.5 Hz, 1H), 3.50−3.63 (m, 2H), 3.59 (d, J = 10.3 Hz, 1H), 3.65 (d, J = 10.3 Hz, 1H), 3.87 (br, 1H), 4.86 (dd, J = 2.2, 2.0 Hz, 1H), 7.36−7.46 (m, 6H), 7.69−7.76 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 6.2, 12.0, 17.0, 19.3, 26.8, 29.6, 35.9, 39.6, 63.0, 66.8, 67.5, 72.2, 80.5, 86.5, 98.8, 127.65, 127.72, 129.81, 129.81, 132.7, 133.1, 135.6, 135.9; LRMS (EI) m/z ($M - H_2O)^+$ 478.2; HRMS (EI) m/z ($M - H_2O)^+$ calcd for $C_{29}H_{38}O_4Si$ 478.2539, found 478.2536. **Diastereomer of 52**: R_f = 0.50 (1:1 hexane−EtOAc); $[\alpha]^{21.2}_D$ −31.73 (c 0.50, $CHCl_3$); IR (neat, cm^{-1}) 3386, 2934, 1460, 1113, 1044, 825, 740, 703; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.88 (d, J = 7.2 Hz, 3H), 1.07 (s, 9H), 1.08 (d, 3H), 1.20 (d, J = 6.9 Hz, 3H), 1.76 (br s, 1H), 1.91 (ddq, J = 13.7, 2.6, 6.9 Hz, 1H), 2.13 (dq, J = 2.0, 7.2 Hz, 1H), 2.74 (m, 1H), 3.48−3.60 (m, 3H), 3.55 (d, J = 10.3 Hz, 1H), 3.59 (d, J = 10.3 Hz, 1H), 4.29 (s, 1H), 4.61 (d, J = 11.2 Hz, 1H), 7.36−7.47 (m, 6H), 7.65−7.75 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 12.7, 13.8, 17.0, 19.4, 26.8, 30.0, 35.4, 39.1, 62.4, 66.8, 68.0, 75.1, 80.8, 86.6, 98.8, 127.7, 127.8, 129.85, 129.89, 132.6, 133.0, 135.5, 135.8; LRMS (EI) m/z ($M - H_2O)^+$ 478.3; HRMS (EI) m/z ($M - H_2O)^+$ calcd for $C_{29}H_{38}O_4Si$ 478.2539, found 478.2534.

(2*S*,5*S*,6*R*,7*S*,8*R*,9*R*)-10-(*tert*-Butyldiphenylsilyloxy)-5,9-epoxy-2,6,8-trimethyl-3-decyne-1,7-diol (53). To a stirred solution of **52** (24.6 mg, 0.0500 mmol) in dry CH_2Cl_2 (0.70 mL) was added at −78 °C triethylsilane (0.011 mL, 0.075 mmol). After 10 min at −78 °C, boron trifluoride diethyl etherate (0.007 mL, 0.075 mmol) was added at −78 °C; the resulting mixture was warmed to rt. After 30 min at rt, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 3:1 hexane−EtOAc) to afford **53** (23.8 mg, 87%) as a colorless syrup: R_f = 0.23 (3:1 hexane−EtOAc); $[\alpha]^{21.4}_D$ −26.1 (c 0.50, $CHCl_3$); IR (neat, cm^{-1}) 3408, 2933, 2858, 1472, 1428, 1266, 1113, 1042, 1010, 823, 739, 704; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.89 (d, J = 6.6 Hz, 3H), 1.06 (s, 9H), 1.13 (d, J = 6.9 Hz, 3H), 1.21 (d, J = 6.9 Hz, 3H), 1.65 (br, 1H), 1.84 (br s, 1H), 1.91 (m, 1H), 2.04 (m, 1H), 2.77 (dq, J = 7.2, 7.2 Hz, 1H), 3.01 (ddd, J = 10.1, 2.6, 2.6 Hz, 1H), 3.43 (m, 1H), 3.53−3.64 (m, 2H), 3.77 (dd, J = 11.5, 3.7 Hz, 1H), 3.84 (dd, J = 11.5, 2.0 Hz, 1H), 4.21 (s, 1H), 7.35−7.44 (m, 6H), 7.67−7.78 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 6.9,

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

12.8, 17.0, 19.3, 26.8, 29.6, 32.9, 39.9, 64.6, 66.8, 70.0, 76.8, 80.1, 82.6, 87.1, 127.5, 127.6, 129.5, 129.6, 133.6, 133.7, 135.7, 135.8; LRMS (EI) m/z (M − tBu)$^+$ 423.3; HRMS (EI) m/z (M − tBu)$^+$ calcd for $C_{25}H_{31}O_4Si$ 423.1992, found 423.1999. The stereochemistry of THP ring was determined by irradiation of H-5; NOE were observed at H-6, H-7, and H-9 that was consistent with the desired stereochemistry.

(2*S*,5*R*,6*S*,7*S*,8*R*,9*R*)-10-(*tert*-Butyldiphenylsilyloxy)-5,9-epoxy-2,6,8-trimethyldecane-1,7-diol (54). To a stirred solution of **53** (23.5 mg, 0.0489 mmol) and hydrazine monohydrate (0.20 mL) in EtOH (0.40 mL) was slowly added at 80 °C 30 wt % aqueous hydrogen peroxide (0.40 mL). After 2 h at 80 °C, saturated aqueous HCl was added, and the mixture was extracted with Et_2O. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 1:1 hexane−EtOAc) to afford **54** (21.1 mg, 89%) as a colorless syrup: R_f = 0.24 (2:3 hexane−EtOAc); $[\alpha]^{21.2}_D$ 2.64 (c 0.50, $CHCl_3$); IR (neat, cm^{-1}) 3386, 2931, 2858, 1462, 1428, 1112, 1010, 758, 703; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.87 (d, J = 6.6 Hz, 3H), 0.91 (d, J = 6.9 Hz, 3H), 0.95 (d, J = 6.6 Hz, 3H), 1.05 (s, 9H), 1.46 (m, 1H), 1.55−1.68 (m, 4H), 1.81 (m, 1H), 1.86 (m, 1H), 2.97 (ddd, J = 9.8, 4.6, 2.1 Hz, 1H), 3.29 (ddd, J = 7.5, 4.9, 1.5 Hz, 1H), 3.40 (dd, J = 6.3, 4.9 Hz, 1H), 3.44 (dd, J = 10.6, 6.3 Hz, 1H), 3.52 (dd, J = 10.6, 5.7 Hz, 1H), 3.75 (dd, J = 11.5, 4.6 Hz, 1H), 3.81 (dd, J = 11.5, 2.1 Hz, 1H), 7.33−7.44 (m, 6H), 7.63−7.78 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 5.5, 13.0, 16.6, 19.3, 26.7, 29.6, 30.1, 33.2, 35.9, 38.5, 64.8, 68.3, 77.1, 78.8, 82.6, 127.5, 127.6, 129.49, 129.52, 133.7, 133.9, 135.6, 135.8; LRMS (EI) m/z (M − tBu)$^+$ 427.2; HRMS (EI) m/z (M − tBu)$^+$ calcd for $C_{25}H_{35}O_4Si$ 427.2305, found 427.2308.

(2*S*,3*R*,4*S*,5*S*,6*R*,9*S*)-1-(*tert*-Butyldiphenylsilyloxy)-2,6-epoxy-3,5,9-trimethyl-10-undecyn-4-ol (56). To a stirred solution of **54** (22.0 mg, 0.0454 mmol) in CH_2Cl_2 (4.5 mL) were added at 0 °C TEMPO (1.4 mg, 0.090 mmol), KBr (1.1 mg, 0.075 mmol), saturated aqueous $NaHCO_3$ (1.8 mL), and 0.25 M aqueous NaOCl (1.8 mL, 0.55 mmol). After 1.5 h at 0 °C, saturated aqueous Na_2SO_3 was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 4:1 hexane−EtOAc) to afford aldehyde (20.2 mg, 92%) as a colorless syrup: R_f = 0.77 (2:1 hexane−EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.89 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.9 Hz, 3H), 1.05 (s, 9H), 1.11 (d, J = 6.9 Hz, 3H), 1.34−1.46 (m, 2H), 1.64 (m, 1H), 1.77−1.88 (m, 2H), 1.94 (m, 1H), 2.39 (ddq, J = 2.0, 2.0, 6.9 Hz, 1H), 2.98 (ddd, J = 10.1, 4.3, 2.0 Hz, 1H), 3.31 (ddd, J = 8.9, 4.0, 1.7 Hz, 1H), 3.42 (m, 1H), 3.76 (dd, J = 11.2, 4.3 Hz, 1H), 3.81 (dd, J = 11.2, 2.0 Hz, 1H), 7.34−7.44 (m, 6H), 7.68−7.76 (m, 4H), 9.60 (d, J = 2.0 Hz, 1H). This aldehyde was immediately used for the next step. To a stirred solution of **55** (19.8 mg, 0.103 mmol) in dry THF (0.14 mL) was added at −78 °C 1.0 M NaOMe in MeOH (0.104 mL, 0.104 mmol). After 10 min at −78 °C, a solution of **54** (20.2 mg, 0.0418 mmol) in dry THF (0.104 mL) was added at −78 °C; the resulting mixture was warmed to rt. After 30 min at rt, saturated aqueous NH_4Cl was added and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 5:1 hexane−EtOAc) to afford **56** (19.3 mg, 97%) as a colorless syrup: R_f = 0.52 (2:1 hexane−EtOAc); $[\alpha]^{20.9}_D$ 19.3 (c 0.46, $CHCl_3$); IR (neat, cm^{-1}) 3423, 3308, 2932, 2858, 1428, 1217, 1112, 1009, 75, 704;^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.90 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H), 1.05 (s, 9H), 1.20 (d, J = 7.2 Hz, 3H), 1.40−1.54 (m, 2H), 1.65 (m, 1H), 1.78−1.89 (m, 3H), 2.06 (dd, J = 2.6, 0.9 Hz, 1H), 2.48 (m, 1H), 2.98 (ddd, J = 9.8, 4.0, 1.7 Hz, 1H), 3.34 (ddd, J = 8.9, 4.0, 1.7 Hz, 1H), 3.42 (m, 1H), 3.76 (dd, J = 11.5, 4.0 Hz, 1H), 3.82 (dd, J = 11.5, 1.7 Hz, 1H), 7.30−7.44 (m, 6H), 7.64−7.78 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 5.6, 13.0, 19.3, 20.9, 25.4, 26.7, 30.3, 33.1, 33.2, 38.8, 64.7, 68.5, 77.1, 77.3, 82.6, 88.9, 127.5, 127.6, 129.47, 129.51, 133.7, 134.0, 135.6, 135.8; LRMS (EI) m/z (M − tBu)$^+$ 421.3; HRMS (EI) m/z (M − tBu)$^+$ calcd for $C_{26}H_{33}O_3Si$ 421.2199, found 421.2209.

(3*S*,6*R*,7*S*,8*S*,9*R*,10*R*)-8-(*tert*-Butyldimethylsilyloxy)-11-(*tert*-butyldiphenylsilyloxy)-6,10-epoxy-3,7,9-trimethyl-1-undecyne (57). To a stirred solution of **56** (19.3 mg, 0.0403 mmol) in dry CH_2Cl_2 (1.40 mL) were added at 0 °C 2,6-lutidine (0.014 mL, 0.081 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.014 mL, 0.060 mmol). After 30 min at 0 °C, saturated aqueous NH_4Cl was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 10:1 hexane−EtOAc) to afford **57** (23.3 mg, 97%) as a colorless syrup: R_f = 0.84 (2:1 hexane−EtOAc); $[\alpha]^{21.0}_D$ 22.8 (c 0.53, $CHCl_3$); IR (neat, cm^{-1}) 3311, 2931, 2858, 1472, 1255, 1112, 1012, 836, 704; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.06 (s, 3H), 0.06 (s, 3H), 0.79 (d, J = 6.6 Hz), 0.92 (s, 9H), 0.93 (d, 3H), 1.05 (s, 9H), 1.21 (d, J = 6.9 Hz, 3H), 1.39−1.53 (m, 2H), 1.61−1.74 (m, 2H), 1.74−1.87 (m, 2H), 2.06 (d, J = 2.3 Hz, 1H), 2.49 (m, 1H), 2.97 (ddd, J = 10.1, 4.6, 2.3 Hz, 1H), 3.31 (ddd, J = 8.9, 3.8, 1.7 Hz, 1H), 3.36 (dd, J = 10.3, 4.9 Hz, 1H), 3.74 (dd, J = 11.2, 4.6 Hz, 1H), 3.80 (dd, J = 11.2, 2.3 Hz, 1H), 7.31−7.44 (m, 6H), 7.65−7.78 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.8, −4.1, 5.9, 13.5, 18.2, 19.3, 20.9, 25.4, 25.9, 26.8, 30.4, 33.1, 33.6, 39.7, 65.1, 68.4, 77.8, 77.9, 82.7, 89.1, 127.48, 127.54, 129.42, 129.42, 133.9, 134.1, 135.7, 135.8; LRMS (EI) m/z (M − tBu)$^+$ 535.4; HRMS (EI) m/z (M − tBu)$^+$ calcd for $C_{32}H_{47}O_3Si_2$ 535.3064, found 535.3088.

(4*S*,7*R*,8*S*,9*S*,10*R*,11*R*)-9-(*tert*-Butyldimethylsilyloxy)-12-(*tert*-butyldiphenylsilyloxy)-7,11-epoxy-4,8,10-trimethyldodec-2-yne (58). To a stirred solution of **57** (188 mg, 0.317 mmol) in dry THF (3.17 mL) were added at −78 °C 1.62 M *n*-BuLi in hexane (0.24 mL, 0.38 mmol) and MeI (0.032 mL, 0.51 mmol); the mixture was warmed to rt. After 1 h at rt, saturated aqueous NH_4Cl was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (10 g, 10:1 hexane−EtOAc) to afford **58** (191 mg, 99%) as a colorless syrup: R_f = 0.54 (10:1 hexane−EtOAc); $[\alpha]^{21.0}_D$ 26.8 (c 0.50, $CHCl_3$); IR (neat, cm^{-1}) 2931, 2857, 1472, 1388, 1255, 1112, 1012, 836, 703; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.06 (s, 3H), 0.07 (s, 3H), 0.79 (d, J = 6.3 Hz, 3H), 0.92 (s, 9H), 0.93 (d, 3H), 1.06 (s, 9H), 1.16 (d, J = 6.9 Hz, 3H), 1.37−1.48 (m, 2H), 1.62 (m, 1H), 1.72 (m, 1H), 1.76−1.85 (m, 2H), 1.81 (d, J = 2.6 Hz, 3H), 2.43 (m, 1H), 2.97 (ddd, J = 10.3, 4.6, 2.3 Hz, 1H), 3.31 (ddd, J = 8.5, 4.3, 1.8 Hz, 1H), 3.36 (dd, J = 10.3, 4.9 Hz, 1H), 3.75 (dd, J = 11.2, 4.6 Hz, 1H), 3.81 (dd, J = 11.2, 2.3 Hz, 1H), 7.35−7.44 (m, 6H), 7.71−7.79 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.8, −4.1, 3.6, 5.9, 13.5, 18.2, 19.3, 21.4, 25.8, 25.9, 26.7, 30.6, 33.6, 33.7, 39.6, 65.1, 75.7, 77.9, 78.1, 82.6, 83.8, 127.45, 127.53, 129.42, 129.44, 133.9, 134.1, 135.7, 135.9; LRMS (EI) m/z (M − tBu)$^+$ 549.5; HRMS (EI) m/z (M − tBu)$^+$ calcd for $C_{33}H_{49}O_3Si_2$ 549.3220, found 549.3213.

(2*E*,4*S*,7*R*,8*S*,9*S*,10*R*,11*R*)-12-(*tert*-Butyldimethylsilyloxy)-9-(*tert*-butyldiphenylsilyloxy)-7,11-epoxy-2-iodo-4,8,10-trimethyldodec-2-ene (59). To a stirred solution of **58** (13.4 mg, 0.0221 mmol) in dry benzene (0.22 mL) was added at 50 °C zirconocene hydride chloride (14.2 mg, 0.055 mmol). After 10 min at 50 °C, a saturated solution of iodine in CH_2Cl_2 was rapidly added via cannula at −18 °C until a purple color was observed. After 10 min at rt, saturated aqueous $Na_2S_2O_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 10:1 hexane−EtOAc) to afford **59** (16.0 mg, 99%) as a colorless syrup: R_f = 0.56 (10:1 hexane−EtOAc); $[\alpha]^{20.9}_D$ 25.2 (c 0.49, $CHCl_3$); IR (neat, cm^{-1}) 2930, 2857, 1472, 1388, 1254, 1112, 1012, 836, 774, 703; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.05 (s, 3H), 0.06 (s, 3H), 0.78 (d, J = 6.3 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H), 0.92 (s, 9H), 0.98 (d, J = 6.6 Hz, 3H), 1.06 (s, 9H), 1.23−1.35 (m, 2H), 1.46 (m, 1H), 1.62 (m, 1H), 1.68 (m, 1H), 1.75 (m, 1H), 2.38 (d, J = 1.5 Hz, 3H), 2.40 (m, 1H), 2.96 (ddd, J = 10.3, 4.9, 2.3 Hz, 1H), 3.25 (ddd, J = 8.3, 4.6, 1.8 Hz, 1H), 3.34 (dd, J = 10.0, 4.6 Hz, 1H), 3.74 (dd, J = 11.2, 4.9 Hz, 1H), 3.80 (dd, J = 11.2, 2.3 Hz, 1H), 5.98 (dd, J = 9.8, 1.5 Hz, 1H), 7.35−7.45 (m, 6H), 7.70−7.78 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$,

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

$CDCl_3$ = 77.0) δ −4.8, −4.1, 5.8, 13.5, 18.1, 19.3, 20.3, 25.9, 26.8, 27.8, 30.6, 33.3, 33.7, 35.7, 39.5, 65.2, 77.8, 78.3, 82.7, 92.5, 127.46, 127.54, 129.48, 129.48, 133.9, 134.0, 135.7, 135.8, 147.3; LRMS (EI) m/z (M^+) 734.8; HRMS (EI) m/z (M^+) calcd for $C_{37}H_{59}O_3Si_2I$ 734.3048, found 734.3058.

(2*R*,3*R*,4*S*,5*S*,6*R*,9*S*,10*E*)-4-(*tert*-Butyldimethylsilyloxy)-2,6-epoxy-11-iodo-3,5,9-trimethyldodec-10-en-1-ol (60). To a stirred solution of **59** (70.0 mg, 0.0952 mmol) in DMF (1.90 mL) were added at rt 1.0 M TBAF in THF (0.095 mL, 0.095 mmol) and AcOH (0.005 mL, 0.01 mmol). After 48 h at 40 °C, saturated aqueous NH_4Cl was added, and the mixture was extracted with Et_2O. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 20:1 hexane−EtOAc) to afford **60** (38.9 mg, 82%) as a colorless syrup: R_f = 0.14 (10:1 hexane−EtOAc); $[\alpha]^{20.8}_D$ 39.4 (c 0.55, $CHCl_3$); IR (neat, cm^{-1}) 3457, 2957, 2856, 1461, 1387, 1253, 1086, 836, 774; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.05 (s, 3H), 0.06 (s, 3H), 0.83 (d, J = 6.3 Hz, 3H), 0.86 (d, J = 6.9 Hz, 3H), 0.91 (s, 9H), 0.97 (d, J = 6.9 Hz, 3H), 1.21−1.40 (m, 3H), 1.52−1.62 (m, 2H), 1.71 (m, 1H), 2.12 (dd, J = 8.3, 4.3 Hz, 1H), 2.37 (d, J = 1.7 Hz, 3H), 2.38 (m, 1H), 3.05 (ddd, J = 10.3, 7.2, 2.9 Hz, 1H), 3.31 (ddd, J = 8.1, 5.2, 2.0 Hz, 1H), 3.37 (dd, J = 10.1, 4.6 Hz, 1H), 3.53 (ddd, J = 11.5, 7.2, 4.3 Hz, 1H), 3.75 (ddd, J = 11.5, 8.3, 2.9 Hz, 1H), 5.95 (dq, J = 10.0, 1.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.8, −4.1, 5.7, 13.3, 18.1, 20.3, 25.8, 27.7, 30.4, 33.2, 34.0, 35.7, 39.3, 64.0, 77.3, 78.5, 81.8, 92.7, 147.0; LRMS (EI) m/z (M^+) 496.3; HRMS (EI) m/z (M^+) calcd for $C_{21}H_{41}O_3SiI$ 496.1870, found 496.1867.

(2*R*,3*R*,4*S*,5*S*,6*R*,9*S*,10*E*,13*S*,15*S*)-4,16-Bis(*tert*-butyldimethylsilyloxymethyl)-2,6-epoxy-3,5,9,11,13,15-hexamethylheptadeca-10,16-diene-1-ol (62). To a stirred solution of **61**[10] (25.2 mg, 0.0667 mmol) in dry Et_2O (0.20 mL) were rapidly added at −78 °C 1.59 M *t*-BuLi in pentane (0.083 mL, 0.13 mmol), 1.0 M *B*-MeO-9-BBN in THF (0.158 mL, 0.158 mmol), and dry THF (0.20 mL). After 10 min at −78 °C, the resulting suspension was warmed to rt in 1 h. A solution of **60** (13.1 mg, 0.0264 mmol) and $PdCl_2$(dppf) (1.1 mg, 0.0013 mmol) in DMF (0.26 mL) was added at rt. After 1 h at rt, saturated aqueous NH_4Cl was added, and the mixture was extracted with Et_2O. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 30:1 hexane−EtOAc) to afford **62** (16.2 mg, 98%) as a colorless syrup: R_f = 0.51 (5:1 hexane−EtOAc); $[\alpha]^{21.0}_D$ 19.2 (c 0.41, $CHCl_3$); IR (neat, cm^{-1}) 3475, 2957, 2857, 1472, 1254, 1085, 836, 775; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.07 (s, 6H), 0.78 (d, J = 6.3 Hz, 3H), 0.82 (d, J = 6.3 Hz, 3H), 0.85 (d, J = 6.9 Hz, 3H), 0.90 (s, 9H), 0.92 (s, 9H), 0.93 (d, 3H), 1.00 (d, J = 6.9 Hz, 3H), 1.20−1.66 (m, 6H), 1.54 (s, 3H), 1.66−1.73 (m, 2H), 1.98 (dd, J = 12.9, 5.7 Hz, 1H), 2.16 (dd, J = 8.6, 4.3 Hz, 1H), 2.21 (m, 1H), 2.33 (m, 1H), 3.05 (ddd, J = 10.3, 7.5, 2.6 Hz, 1H), 3.32 (m, 1H), 3.36 (dd, J = 10.0, 4.6 Hz, 1H), 3.52 (ddd, J = 11.5, 7.5, 4.3 Hz, 1H), 3.74 (ddd, J = 11.5, 8.6, 2.6 Hz, 1H), 4.10 (s, 2H), 4.82 (br s, 1H), 4.86 (d, J = 9.2 Hz, 1H), 5.04 (dt, J = 1.8, 1.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.4, −4.9, −4.1, 5.7, 13.3, 16.1, 18.1, 18.4, 19.5, 19.9, 21.3, 25.8, 26.0, 28.3, 30.7, 32.3, 33.9, 34.0, 34.1, 40.0, 43.4, 48.2, 64.1, 64.6, 77.5, 78.7, 81.7, 106.9, 132.5, 132.8, 154.1; LRMS (EI) m/z (M^+) 624.5; HRMS (EI) m/z (M^+) calcd for $C_{36}H_{72}O_4Si_2$ 624.4969, found 624.4976.

(3*R*,4*R*,5*S*,6*S*,7*R*,10*S*,11*E*,14*S*,16*S*)-5,17-bis(*tert*-Butyldimethylsilyloxymethyl)-3,7-epoxy-4,6,10,12,14,16-hexamethyloctadeca-11,17-dien-1-yne (63). To a stirred solution of alcohol **62** (3.7 mg, 0.0056 mmol) in dry CH_2Cl_2 (0.3 mL) were added at 0 °C tetra-*n*-propylammonium perruthenate (0.2 mg, 0.0006 mmol), NMO (5.0 mg, 0.0043 mmol), and MS4A (1.8 mg). After 1.5 h at rt, the resulting mixture was filtered through silica gel pad and concentrated to afford the crude aldehyde (3.1 mg). To a stirred solution of **55** (4.3 mg, 0.022 mmol) in dry THF (0.15 mL) was added at −78 °C 1.0 M NaOMe in MeOH (0.022 mL, 0.022 mmol). After 10 min at −78 °C, a solution of the crude aldehyde (3.1 mg) in dry THF (0.05 mL) was added at −78 °C; the resulting mixture was warmed to rt. After 30 min at rt, saturated aqueous NH_4Cl was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 20:1 hexane−EtOAc) to afford **63** (2.8 mg, two steps 77%) as a colorless syrup: R_f = 0.76 (5:1 hexane−EtOAc); $[\alpha]^{20.8}_D$ 31.4 (c 0.55, $CHCl_3$); IR (neat, cm^{-1}) 3314, 2957, 1461, 1385, 1254, 1085, 1006, 837, 775; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.07 (s, 6H), 0.77 (d, J = 6.6 Hz, 3H), 0.89 (d, J = 7.2 Hz, 3H), 0.90 (s, 9H), 0.92 (s, 9H), 0.92 (d, J = 6.3 Hz, 3H), 0.99 (d, J = 6.3 Hz, 3H), 1.00 (d, J = 6.9 Hz, 3H), 1.17−1.35 (m, 5H), 1.53 (d, J = 1.2 Hz, 1H), 1.57−1.72 (m, 4H), 1.77 (m, 1H), 1.95 (dd, J = 12.6, 5.5 Hz, 1H), 2.20 (m, 1H), 2.32 (m, 1H), 2.45 (d, J = 2.0 Hz, 1H), 3.28 (ddd, J = 7.2, 4.9, 1.5 Hz, 1H), 3.31 (dd, J = 10.1, 4.6 Hz, 1H), 3.67 (dd, J = 10.6, 2.0 Hz, 1H), 4.10 (s, 2H), 4.82 (br s, 1H), 4.86 (d, J = 9.5 Hz, 1H), 5.03 (dt, J = 1.8, 1.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.4, −4.9, −4.2, 5.7, 14.2, 16.1, 18.1, 18.4, 19.5, 19.9, 21.2, 25.8, 25.9, 28.1, 30.5, 32.2, 33.6, 33.8, 38.4, 39.2, 43.3, 48.2, 64.6, 72.7, 73.0, 77.1, 79.6, 82.2, 106.8, 132.3, 132.8, 154.1; LRMS (EI) m/z (M^+) 618.4; HRMS (EI) m/z (M^+) calcd for $C_{37}H_{70}O_3Si_2$ 618.4864, found 618.4844.

(3*S*,5*S*,7*E*,9*S*,12*R*,13*S*,14*S*,15*R*,16*R*)-14-(*tert*-Butyldimethylsilyloxymethyl)-12,16-epoxy-3,5,7,9,13,15-hexamethyl-2-methyleneoctadeca-7-en-17-yn-1-ol (43). A solution of **63** (4.0 mg, 0.0065 mmol) and pyridinium *p*-toluenesulfonate (0.4 mg, 0.0016 mmol) in 1:1 EtOH−H_2O (0.065 mL) was stirred at rt. After 10 h, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 10:1 hexane−EtOAc) to afford **43** (3.0 mg, 92%) as a colorless syrup. The resulting alcohol was identical with previously obtained **43**.

(4*S*,6*S*,8*E*,10*S*,13*R*,14*S*,15*S*,16*S*,17*R*,)-15,19-Bis(*tert*-butyldimethylsilyloxy)-13,17-epoxy-4,6,8,10,14,16,21-heptamethyl-3-methylene-1-oxa[17]metacyclophane (64). To a stirred solution of **44** (133.0 mg, 0.227 mmol) in dry CH_2Cl_2 (2.27 mL) were added 2,6-lutidine (0.158 mL, 1.36 mmol) and TBSOTf (0.157 mL, 0.682 mmol) at rt. After 30 min, saturated aqueous NH_4Cl was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (5 g, 10:1 hexane−EtOAc) to afford **64** (151.0 mg, 98%) as a colorless syrup: R_f = 0.67 (8:1 hexane−EtOAc); $[\alpha]^{16.8}_D$ 24.2 (c 0.49, $CHCl_3$); IR (neat, cm^{-1}) 2957, 2929, 2858, 1502, 1460, 1403, 1254, 1197, 1080, 1005, 898, 865, 837, 777; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.05 (s, 3H), 0.06 (s, 3H), 0.16 (s, 3H), 0.21 (s, 3H), 0.70 (d, J = 6.6 Hz, 3H, Me), 0.79 (d, J = 6.3 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.90 (s, 9H), 0.95 (d, J = 6.9 Hz, 3H), 1.02 (s, 9H), 1.09 (d, J = 6.6 Hz, 3H), 1.17 (m, 1H), 1.21−1.33 (m, 3H), 1.47−1.58 (m, 3H), 1.63 (s, 3H), 1.67−1.75 (m, 3H), 2.21 (s, 3H), 2.16−2.27 (m, 3H), 3.33 (d, J = 10.9 Hz, 1H), 3.47 (dd, J = 10.0, 4.6 Hz, 1H), 4.23 (d, J = 10.0 Hz, 1H), 4.54 (d, J = 14.1 Hz, 1H), 4.59 (d, J = 14.1 Hz, 1H), 4.75 (d, J = 8.9 Hz, 1H), 4.96 (s, 1H), 5.06 (s, 1H), 6.52 (s, 1H), 6.91 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.8, −4.4, −4.2, −4.0, 6.5, 13.3, 16.2, 18.2, 19.2, 20.2, 20.7, 22.1, 25.9, 26.0, 29.3, 32.3, 33.0, 34.7, 34.9, 40.75, 40.80, 43.9, 45.2, 69.9, 76.9, 78.1, 78.2, 108.2, 111.3, 120.3, 125.4, 130.9, 131.7, 132.3, 145.3, 150.6, 151.3; LRMS (EI) m/z (M^+) 697.9; HRMS (EI) m//z (M^+) calcd for $C_{42}H_{74}O_4Si_2$ 698.5126, found 698.5123;.

(5*R*,6*S*,7*S*,8*S*,9*R*,12*S*,16*S*,18*S*,*E*)-4,7-Bis(*tert*-butyldimethylsilyloxy)-5,9-epoxy-2,6,8,12,14,16,18-heptamethyl-19-methylene-5,6,7,8,9,10,11,12,15,16,17,18,19,20-tetradecahydrobenzo[18]annulen-1-ol (65a). A solution of **64** (648 mg, 0.972 mmol), DMAP (11.9 mg, 0.0972 mmol), and Ac_2O (8.1 mL) in degassed *N*,*N*-dimethylaniline (32.4 mL) was stirred at 155 °C. After 5 h, 1.0 M aqueous HCl was added at rt, and the mixture was extracted with Et_2O. The extracts were washed with 1.0 M aqueous HCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (20 g, 10:1 hexane−EtOAc) to afford acetate (638 mg, 93%) as a colorless syrup: R_f = 0.53 (8:1 hexane−

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

EtOAc); $[\alpha]^{20.8}_D$ +27.0 (*c* 0.46, $CHCl_3$); IR (neat, cm^{-1}) 2957, 2858, 1759, 1470, 1367, 1256, 1192, 1082, 895, 836, 760; ^1H NMR (500 MHz, 65 °C, benzene-d_6, solvent residual peak =7.16) δ 0.13 (s, 3H), 0.14 (s, 3H), 0.17 (s, 3H), 0.19 (s, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3He), 1.00 (s, 9H), 1.01 (shoulder, 3H), 1.07 (shoulder, 3H), 1.08 (s, 9H), 1.19 (d, *J* = 6.9 Hz, 3H), 1.25−1.37 (m, 2H), 1.48−1.66 (m, 4H), 1.68 (s, 3H), 1.83−1.97 (m, 3H), 1.95 (s, 3H), 2.06 (s. 3H), 2.08−2.24 (m, 2H), 2.29 (m, 1H), 3.42 (br d, *J* = 16.3 Hz, 1H), 3.53 (d, *J* = 10.6 Hz, 1H), 3.67 (dd, *J* = 10.0, 4.9 Hz, 1H), 4.12 (br d, *J* = 16.3 Hz, 1H), 4.50 (br s, 1H), 4.86 (s, 1H), 4.88 (d, *J* = 12.8 Hz, 1H), 4.98 (d, *J* = 10.6 Hz, 1H), 6.66 (s, 1H); ^{13}C NMR (125 MHz, 65 °C, benzene-d_6, solvent peak =128.1) δ −4.6, −4.5, −4.04, −3.97, 8.0, 13.5, 16.8, 18.5, 18.6, 19.0, 19.5, 20.4, 20.6, 22.1, 26.2, 26.3, 29.4, 33.6, 34.0, 35.5, 36.3, 37.7, 38.9, 42.2, 44.3, 46.7, 79.0, 79.4, 80.7, 108.8, 119.6, 128.5, 130.5, 130.8, 133.5, 134.3, 145.1, 151.3, 155.9, 167.8; LRMS (EI) *m*/*z* (M^+) 741.1; HRMS (EI) *m*/*z* (M^+) calcd for $C_{44}H_{76}O_5Si_2$ 740.5231, found 740.5259. To a stirred solution of this acetate (150 mg, 0.215 mmol) in CH_2Cl_2 (2.15 mL) was added at −78 °C 1.0 M DIBALH in hexane (0.472 mL, 0.472 mmol). After 15 min at −78 °C, EtOAc, MeOH, potassium sodium (+)-tartrate tetrahydrate, and water were successively added at −78 °C and the mixture was warmed to rt. After being stirred vigorously for 4 h at rt, the mixture was extracted with $CHCl_3$.The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (20 g, 3:1 hexane−$CHCl_3$) to afford **65a** (136 mg, 95%) as a colorless syrup: R_f = 0.42 (3:1 hexane−$CHCl_3$); $[\alpha]^{20.8}_D$ 0.05 (*c* 0.47, $CHCl_3$); IR (neat, cm^{-1}) 3460, 2958, 2930, 2858, 1471, 1255, 1216, 1083, 1037, 898, 837, 761; ^1H NMR (500 MHz, 65 °C, benzene-d_6, solvent residual peak =7.16) δ 0.15 (s, 6H), 0.20 (s, 3H), 0.21 (s, 3H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 1.01 (m, 1H), 1.02 (s, 9H), 1.03 (d, *J* = 6.6 Hz, 3H), 1.10 (s, 9H), 1.16 (d, *J* = 7.2 Hz, 3H), 1.38 (m, 1H), 1.54 (m, 1H), 1.61 (s. 3H), 1.65 (m, 1H), 1.79−1.89 (m, 4H), 2.08−2.17 (m, 2H), 2.32 (s, 3H), 2.27−2.41 (m, 3H), 3.39 (d, *J* = 15.8 Hz, 1H), 3.54 (d, *J* = 11.2 Hz, 1H), 3.68 (dd, *J* = 9.8, 4.9 Hz, 1H), 4.66 (d, *J* = 15.8 Hz, 1H), 4.87 (d, *J* = 9.8 Hz, 1H), 4.90 (br s, 1H), 4.92 (s, 1H), 5.00 (d, *J* = 10.6 Hz, 1H), 6.40 (br s, 1H), 6.69 (s, 1H); ^{13}C NMR (125 MHz, 65 °C, benzene-d_6, solvent peak =128.1) δ −4.6, −4.4, −4.0, −3.9, 7.7, 13.7, 16.6, 17.7, 18.6, 19.9, 20.3, 22.1, 26.2, 26.4, 28.3, 33.1, 33.5, 34.9, 36.1, 38.3, 39.5, 42.0, 44.9, 46.1, 78.9, 79.5, 80.3, 113.0, 120.2, 125.1, 125.8, 127.2, 131.3, 131.8, 146.9, 151.1, 158.7; LRMS (EI) *m*/*z* (M^+) 698.3; HRMS (EI) *m*/*z* (M^+) calcd for $C_{42}H_{74}O_4Si_2$ 698.5126, found 698.5123.

((7*S*,9*S*,13*S*,16*R*,17*S*,18*S*,19*S*,20*R*,*E*)-1,18-Bis((*tert*-butyldimethylsilyl)oxy)-4,6:16,20-diepoxy-3,7,9,11,13,17,19-heptamethyl-5,6,7,8,9,10,13,14,15,16,17,18,19,20-tetradecahydrobenzo[18]annulen-6-yl)methanol (66). To a stirred solution of **65a** (2.3 mg, 0.0033 mmol) in dry CH_2Cl_2 (0.11 mL) were added $VO(acac)_2$ (0.2 mg, 0.0007 mmol), 0.786 M TBHP (0.042 mL, 0.033 mmol), and AcOH (0.0098 mL, 0.17 mmol) at 0 °C. After 1 h, saturated aqueous $Na_2S_2O_3$ was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 20:1 hexane−EtOAc) to afford **66** (1.3 mg, 55%) as a colorless syrup: R_f = 0.42 (10:1 hexane−EtOAc); $[\alpha]^{16.2}_D$ 10.11 (*c* 0.40, $CHCl_3$); IR (neat, cm^{-1}) 2957, 2930, 2858, 1461, 1383, 1255, 1217, 1082, 1004, 837, 759; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.05 (s, 6H), 0.12 (s, 3H), 0.19 (s, 3H), 0.64 (d, *J* = 6.6 Hz, 3H), 0.72 (d, *J* = 7.0 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.0 Hz, 3H), 0.89 (s, 9H), 0.92 (d, *J* = 7.8 Hz, 3H), 0.99 (s, 9H), 1.10−1.38 (m, 6H), 1.48−1.66 (m, 3H), 1.55 (s, 3H), 1.70 (m, 1H), 1.95 (m, 1H), 2.02 (m, 1H), 2.12 (s. 3H), 2.28 (m, 1H), 2.92 (d, *J* = 16.5 Hz, 1H), 3.37 (br d, *J* = 10.9 Hz, 1H), 3.45 (dd, *J* = 10.3, 4.6 Hz, 1H), 3.72 (dd, *J* = 11.5, 3.4 Hz, 1H), 3.75 (d, *J* = 16.5 Hz), 3.77 (m, 1H), 4.33 (d, *J* = 10.6 Hz, 1H), 4.66 (d, *J* = 10.1 Hz, 1H), 6.32 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.9, −4.5, −4.3, −4.1, 6.8, 12.8, 13.4, 15.5, 18.1, 18.4, 19.4, 20.6, 22.5, 25.6, 25.9, 26.1, 30.6, 32.7, 33.0, 34.9, 36.7, 36.8, 37.0, 40.8, 45.5, 66.8, 77.2, 77.6, 77.9, 94.2, 117.1, 118.5, 125.6, 127.5, 129.2, 131.4, 146.2, 153.0; LRMS (EI) *m*/*z* (M^+) 714.0; HRMS (EI) *m*/*z* (M^+) calcd for $C_{42}H_{74}O_5Si_2$ 714.5075, found 714.5070.

(7*S*,9*S*,13*S*,16*R*,17*S*,18*S*,19*S*,20*R*,*E*)-1,18-Bis((*tert*-butyldimethylsilyl)oxy)-4,6:16,20-diepoxy-3,7,9,11,13,17,19-heptamethyl-5,6,7,8,9,10,13,14,15,16,17,18,19,20-tetradecahydrobenzo[18]annulene-6-carboxylic acid (67). To a stirred solution of alcohol **66** (52.0 mg, 0.0727 mmol) in dry CH_2Cl_2 (2.4 mL) were added at 0 °C tetra-*n*-propylammonium perruthenate (2.6 mg, 0.0073 mmol), NMO (21.3 mg, 0.182 mmol), and MS4A (52.0 mg). After 2 h at 0 °C, the resulting mixture was filtered through silica gel and concentrated. To the residue in *t*-BuOH (2.04 mL) and H_2O (0.4 mL) were added at rt 2-methyl-2-butene (0.061 mL, 0.73 mmol), NaH_2PO_4 (21.0 mg, 0.175 mmol), and $NaClO_2$ (17.2 mg, 0.190 mmol). After 2 h at rt, H_2O was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (3 g, 10:1 hexane−EtOAc) to afford **67** (48.4 mg, 2 steps 91%) as a colorless syrup: R_f = 0.61 (1:1 hexane−EtOAc); $[\alpha]^{20.8}_D$ 19.4 (*c* 0.36, $CHCl_3$); IR (neat, cm^{-1}) 2957, 2930, 2858, 1716, 1462, 1383, 1257, 1213, 1082, 837, 760; ^1H NMR (500 MHz, benzene-d_6, solvent residual peak =7.16) δ 0.13 (s, 6H), 0.15 (s, 3H), 0.169 (s, 3H), 0.174 (s, 3H), 0.81 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 1.02 (s, 9H), 1.06 (s, 9H), 1.10 (d, *J* = 6.6 Hz, 3H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.18 (m, 1H), 1.22−1.35 (m, 2H), 1.43−1.55 (m, 2H), 1.58 (s, 3H), 1.70 (m, 1H), 1.73−1.89 (m, 3H), 1.95(m, 1H), 2.07 (m, 1H), 2.22 (s. 3H), 2.33 (m, 1H), 2.66 (m, 1H), 3.49 (d, *J* = 10.4 Hz, 1H), 3.70 (dd, *J* = 10.0, 4.6 Hz, 1H), 3.79 (d, *J* = 16.4 Hz, 1H), 4.23 (d, *J* = 16.4 Hz, 1H), 4.68 (d, *J* = 10.6 Hz, 1H), 4.79 (d, *J* = 9.8 Hz, 1H), 6.53 (s, 1H); ^{13}C NMR (125 MHz, benzene-d_6, solvent peak =128.1) δ −4.6, −4.4, −4.0, −3.9, 7.2, 13.1, 13.9, 15.6, 18.5, 18.6, 19.6, 20.5, 22.9, 26.1, 26.2, 26.3, 32.6, 33.1, 33.5, 35.6, 36.4, 37.5, 38.2, 41.5, 45.4, 77.7, 78.4, 78.8, 93.8, 118.3, 119.4, 125.9, 126.8, 129.7, 132.0, 147.1, 153.0, 178.1; LRMS (EI) *m*/*z* (M^+) 728.0; HRMS (EI) *m*/*z* (M^+) calcd for $C_{42}H_{72}O_6Si_2$ 728.4868, found 728.4856.

(7*S*,9*S*,13*S*,16*R*,17*S*,18*S*,19*S*,20*R*,*E*)-18-(*tert*-Butyldimethylsilyloxy)-1-hydroxy-4,6:16,20-diepoxy-3,7,9,11,13,17,19-heptamethyl-5,6,7,8,9,10,13,14,15,16,17,18,19,20-tetradecahydrobenzo[18]annulene-6-carboxylic Acid (68). To a stirred solution of **67** (10.0 mg, 0.0137 mmol) in THF (0.914 mL) were added at rt 1.0 M TBAF in THF (0.069 mL, 0.069 mmol) and AcOH (0.008 mL). After 9 h at rt, saturated aqueous NH_4Cl was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 2:1 hexane−acetone) to afford **68** (5.8 mg, 69%) as a colorless syrup: R_f = 0.28 (2:1 hexane−acetone); $[\alpha]^{20.9}_D$ 7.52 (*c* 0.49, $CHCl_3$); IR (neat, cm^{-1}) 3241, 2959, 2858, 1718, 1460, 1383, 1255, 1225, 1081, 837, 759; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.06 (s, 3H), 0.07 (s, 3H), 0.77 (d, *J* = 6.3 Hz, 3H), 0.78 (d, *J* = 6.6 Hz, 3H), 0.86 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.90 (s, 9H), 0.96 (d, *J* = 6.9 Hz, 3H), 1.06−1.40 (m, 4H), 1.51−1.76 (m, 5H), 1.58 (s, 3H), 1.93 (m, 1H), 2.06 (m, 1H), 2.17 (s, 3H), 2.25−2.34 (m, 2H), 3.37 (d, *J* = 16.9 Hz, 1H), 3.45 (d, *J* = 11.2 Hz, 1H), 3.52 (dd, *J* = 10.0, 4.6 Hz, 1H), 4.04 (d, *J* = 16.9 Hz, 1H), 4.21 (br s, 1H), 4.36 (d, *J* = 10.6 Hz, 1H), 4.66 (d, *J* = 9.7 Hz, 1H), 6.34 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.8, −4.2, 6.8, 12.5, 13.4, 15.2, 18.2, 19.4, 20.2, 22.5, 25.8, 25.9, 32.6, 32.8, 33.1, 35.3, 35.5, 37.1, 37.8, 40.8, 45.2, 76.6, 77.6, 77.8, 93.2, 115.7, 118.1, 122.2, 126.1, 129.5, 131.7, 146.6, 151.5, 176.4; LRMS (EI) *m*/*z* (M^+) 614.4, ($M - CO_2^+$) 570.5; HRMS (EI) *m*/*z* (M^+) calcd for $C_{36}H_{58}O_6Si$ 614.4003, found 614.3993.

Kendomycin (1). To a stirred solution of **68** (36.9 mg, 0.0600 mmol) in EtOH (4.0 mL) was added at rt IBX (50.5 mg, 0.180 mmol). After 30 min at rt, the mixture was filtered through silica gel (1 g, 3:1 hexane−EtOAc) to give a red *o*-quinone solution: R_f = 0.85 (2:1 hexane−acetone); UV (2:1 hexane−acetone) λ_{max} 541 nm. After concentration to tenth volume, to the mixture were successively added at 0 °C MeCN (0.23 mL) and 46 wt % aqueous HF solution (0.12 mL). After 2 h at rt, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with 1:1 hexane−EtOAc. The extracts were

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

purified by column chromatography on silica gel (3 g, 1:1 hexane−EtOAc) to afford kendomycin (**1**) (9.4 mg, two steps 32%) as yellow crystals: R_f = 0.46 (1:1 hexane−EtOAc); mp 236−240 °C (not recrystallized); $[\alpha]^{21.1}_D$ −79.0 (*c* 0.13, $CHCl_3$), $[\alpha]^{28.0}_D$ −79 (*c* 0.12, MeOH); UV (MeCN) λ_{max} nm (log ε); 308 (4.13); IR (neat, cm^{-1}) 3346, 2927, 1612, 1577, 1457, 1380, 1329, 1261, 1216, 1099, 1045, 914, 758; ^{1}H NMR (500 MHz, acetone-d_6, solvent residual peak =2.04) δ 0.71 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 7.1 Hz, 3H), 1.21−1.37 (m, 2H), 1.45 (ddd, *J* = 13.2, 11.2, 3.2 Hz, 1H), 1.57 (m, 2H), 1.61 (s, 3H), 1.63 (m, 1H), 1.67 (m, 1H), 1.71 (m, 1H), 1.84 (s, 3H), 1.88 (m, 1H), 1.96 (m, 1H), 2.12 (br d, *J* = 17.2 Hz, 1H), 2.36 (m, 1H), 2.41 (m, 1H), 3.53 (br ddd, *J* = 11.0, 2.3, 1.2 Hz, 1H), 3.57 (td, *J* = 10.3, 4.6 Hz, 1H), 3.90 (d, *J* = 4.6 Hz, 1H), 4.36 (d, *J* = 10.4 Hz, 1H), 4.64 (br d, *J* = 9.8 Hz, 1H), 6.50 (br s, 1H), 7.19 (s, 1H), 8.08 (s, 1H); ^{13}C NMR (125 MHz, acetone-d_6, solvent peak =29.8) δ 7.2, 7.6, 12.7, 13.3, 19.7, 19.9, 22.7, 26.5, 33.4, 33.6, 35.9, 38.2, 39.8, 40.8, 41.5, 46.1, 76.3, 77.7, 78.7, 104.3, 111.0, 119.1, 129.9, 130.2, 132.1, 141.3, 146.8, 168.6, 182.1; LRMS (EI) *m*/*z* (M^+) 486.3; HRMS (EI) *m*/*z* (M^+) calcd for $C_{29}H_{42}O_6$ 486.2981, found 486.2994.

(2*R*,3*S*,4*R*)-3-(*tert*-Butyldimethylsilyloxy)-4-(1,3-dithian-1-oxide-2-yl)-2-methyl-1-pentanal (69). Compound **69** was prepared as a 7:3 mixture of diastereomers resulting from sulfoxide center from **48** by ozone oxidation as the same manner as the previous synthesis of racemate,[33] and the spectral data of **69** were identical with those of the previously prepared racemates.

(2′*R*,3′*S*,4′*S*,5′*R*)-2[3,5,15-Tris(*tert*-butyldimethylsilyloxy)-4-methylpentadecan-2-yl]-1,3-dithiane 1-Oxide (71a). To a stirred solution of 1-(*tert*-butyldimethylsiloxy)-9-decyne (**70**)[43] (806 mg, 3.00 mmol) in dry THF (13.4 mL) was added at −10 °C 1.65 M *n*-BuLi in hexane (1.63 mL, 2.68 mmol). After 10 min at −10 °C, HMPA (0.466 mL, 2.68 mmol) was added. After being stirred for 10 min at −10 °C, the solution of the acetylide was cooled to −78 °C, and to this was added a solution of **69** (391 mg, 1.07 mmol) in dry Et_2O (3.25 mL) via cannula. The resulting solution was warmed to 0 °C in 1 h, and then saturated aqueous NH_4Cl was added and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (35 g, 2:1 $CHCl_3$−EtOAc) to afford the adducts (480 mg) as a 5:1 mixture of C5 diastereomers of a colorless syrup. A major isomer for an analytical sample was purified by repeated column chromatography: R_f = 0.43 (2:1 $CHCl_3$−EtOAc); $[\alpha]^{27.4}_D$ +8.70 (*c* 1.55, $CHCl_3$); IR (neat, cm^{-1}) 3356, 2931, 2857, 1734, 1471, 1463, 1427, 1388, 1253, 1216, 1094, 1020, 837, 758; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 6H), 0.14 (s, 6H), 0.89 (s, 9H), 0.92 (s, 9H), 1.09 (d, *J* = 7.2 Hz, 3H), 1.17 (d, *J* = 7.2 Hz, 3H), 1.25−1.33 (m, 6H), 1.38 (m, 2H), 1.45−1.56 (m, 4H), 2.02 (m, 1H), 2.17−2.30 (m, 3H), 2.43 (m, 1H), 2.58−2.68 (m, 3H), 2.98 (m, 1H), 3.46 (m, 1H), 3.59 (t, *J* = 6.6 Hz, 2H), 3.70 (d, *J* = 3.5 Hz, 1H), 4.06 (dd, *J* = 6.3, 3.2 Hz, 1H), 4.71 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ−5.3, −3.9, −3.8, 12.2, 12.4, 18.3, 18.4, 18.8, 25.8, 26.0, 26.1, 28.7, 28.9, 29.2, 29.3, 29.7, 30.1, 32.9, 34.4, 42.8, 54.5, 63.3, 63.6, 70.3, 76.8, 80.2, 86.2, LRMS (EI) *m*/*z* (M − *t*-Bu)$^+$ 575.4; HRMS (EI) *m*/*z* (M^+) calcd for $C_{28}H_{55}O_4Si_2S_2$ 575.3080, found 575.3093. To a stirred solution of a mixture of the adducts (606 mg, 0.957 mmol) and hydrazine monohydrate (3.48 mL, 71.8 mmol) in EtOH (12.0 mL) was slowly added at 90 °C 30 wt % aqueous hydrogen peroxide (9.19 mL, 90.0 mmol). After 1 h at 90 °C, saturated aqueous NH_4Cl was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (31 g, 2:1 $CHCl_3$−EtOAc) to afford the saturated alcohol (341 mg, 2 steps 40%) as a colorless syrup: R_f = 0.24 (2:1 $CHCl_3$−EtOAc); $[\alpha]^{26.9}_D$ −2.1 (*c* 1.02, $CHCl_3$); IR (neat, cm^{-1}) 3409, 2929, 2856, 1463, 1427, 1388, 1254, 1097, 1024, 836, 775, 757; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 6H), 0.14 (s, 3H), 0.15 (s, 3H), 0.88 (s, 9H), 0.92 (s, 9H), 1.06 (d, *J* = 7.2 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.23−1.35 (m, 14H), 1.41−1.58 (m, 4H), 1.78 (m, 1H), 2.24 (m, 1H), 2.43 (m, 1H), 2.54−2.64 (m, 3H), 2.99 (dqd, *J* = 8.0, 7.2, 2.6 Hz, 1H), 3.50 (m, 1H), 3.58 (t, *J* = 6.6 Hz, 2H), 3.60 (d, *J* = 2.6 Hz, 1H), 3.82 (dd, *J* = 8.0, 1.7 Hz, 1H), 4.11 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.3, −3.8, −3.3, 12.1, 12.9, 18.3, 18.4, 25.8, 26.0, 26.2, 26.4, 29.4, 29.58, 29.64, 29.64, 29.64, 29.9, 30.0, 32.9, 34.4, 35.1, 37.9, 54.6, 63.3, 70.2, 70.5, 80.6; LRMS (EI) *m*/*z* (M − *t*Bu)$^+$ 579.5; HRMS (EI) *m*/*z* (M − *t*Bu)$^+$ calcd for $C_{28}H_{59}O_4Si_2S_2$ 579.3393, found 579.3372. To a stirred solution of the resulting alcohol (358 mg, 0.562 mmol) in dry CH_2Cl_2 (5.62 mL) were added at 0 °C *N*,*N*-diisopropylethylamine (0.192 mL, 1.12 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.194 mL, 0.843 mmol). After 1 h at 0 °C, saturated aqueous NH_4Cl was added and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (15 g, 3:1 hexane−EtOAc) to afford **71a** (313 mg, 74%) as a colorless syrup: R_f = 0.35 (3:1 hexane−EtOAc); $[\alpha]^{25.7}_D$ −0.5 (*c* 1.20, $CHCl_3$); IR (neat, cm^{-1}) 2930, 2857, 1471, 1427, 1389, 1361, 1255, 1216, 1061, 1030, 837, 759; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.04 (s, 6H), 0.05 (s, 3H), 0.07 (s, 3H), 0.09 (s, 3H), 0.11 (s, 3H), 0.88 (s, 9H), 0.89 (s, 9H), 0.90 (s, 9H), 0.96 (d, *J* = 7.2 Hz, 3H), 1.05 (d, *J* = 7.2 Hz, 3H), 1.24−1.44 (m, 14H), 1.46−1.60 (m, 4H), 1.86 (m, 1H), 2.22 (m, 1H), 2.43 (m, 1H), 2.54−2.64 (m, 3H), 2.83 (m, 1H), 3.44 (m, 1H), 3.56 (d, *J* = 3.5 Hz, 1H), 3.59 (t, *J* = 6.6 Hz, 2H), 3.68 (m, 1H), 3.92 (dd, *J* = 4.0, 4.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.3, −4.3, −4.1, −3.7, −3.5, 11.67, 11.73, 18.2, 18.3, 18.4, 23.9, 25.6, 25.98, 26.04, 26.1, 29.3, 29.5, 29.6, 29.66, 29.66, 29.8, 30.1, 32.9, 33.4, 35.3, 44.5, 54.2, 63.3, 72.3, 73.3, 74.4; LRMS (EI) *m*/*z* (M − *t*Bu)$^+$ 694.1; HRMS (EI) *m*/*z* (M − *t*Bu)$^+$ calcd for $C_{34}H_{73}O_4Si_3S_2$ 693.4258, found 693.4244.

(4*R*,5*S*,6*S*,7*R*)-4,6-Dimethyl-5,7,17-tris(*tert*-butyldimethylsilyloxy)pentadec-1-yn-3-one (72a). To a stirred solution of **71a** (13.4 mg, 0.0178 mmol) in 97:3 acetone−H_2O (0.356 mL) were added at 0 °C $NaHCO_3$ (29.9 mg, 0.356 mmol) and *N*-bromosuccinimide (19.0 mg, 0.107 mmol). After 10 min at 0 °C, saturated aqueous $Na_2S_2O_3$ was added and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (0.7 g, 10:1 hexane−EtOAc) to afford the aldehyde (9.9 mg, 86%) as a colorless syrup: R_f = 0.77 (10:1 hexane−EtOAc); $[\alpha]^{25.7}_D$ −21.1 (*c* 0.32, $CHCl_3$); IR (neat, cm^{-1}) 2929, 2857, 2708, 1730, 1471, 1463, 1387, 1361, 1255, 1099, 1033, 939, 909, 836, 775; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ −0.03 (s, 3H), 0.05 (s, 6H), 0.06 (s, 3H), 0.07 (s, 3H), 0.08 (s, 3H), 0.84 (d, *J* = 6.9 Hz, 3H), 0.85 (s, 9H), 0.887 (s, 9H), 0.893 (s, 9H), 1.13 (d, *J* = 6.9 Hz, 3H), 1.25−1.32 (m, 14H), 1.47−1.62 (m, 4H), 1.73 (m, 1H), 2.47 (m, 1H), 3.60 (t, *J* = 6.6 Hz, 2H), 3.82 (m, 1H), 4.30 (dd, *J* = 6.9, 1.8 Hz, 1H), 9.69 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.3, −4.1, −3.94, −3.86, −3.2, 7.5, 9.9, 18.26, 18.30, 18.4, 25.2, 25.8, 25.9, 25.98, 26.00, 29.4, 29.5, 29.59, 29.61, 29.8, 32.9, 35.5, 42.3, 50.0, 63.3, 71.9, 72.7, 205.4; LRMS (EI) *m*/*z* (M − *t*Bu)$^+$ 587.4; HRMS (EI) *m*/*z* (M − *t*Bu)$^+$ calcd for $C_{31}H_{67}O_4Si_3$ 587.4347, found 587.4353. To a stirred solution of the resulting aldehyde (34.4 mg, 0.0534 mmol) in dry Et_2O (1.07 mL) was added at −78 °C 0.5 M ethynylmagnesium bromide in Et_2O (0.320 mL, 0.160 mmol). After 30 min at −78 °C, the resulting mixture was warmed to −10 °C and then quenched with saturated aqueous NH_4Cl. The mixture was extracted with EtOAc, and the extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (3 g, 40:1 hexane−EtOAc) to afford the ethynyl adducts (34.5 mg, 96%: a 1.5:1 mixture of diastereomers) as a colorless syrup. The mixture was used for the next step withnout further purification. To a stirred solution of the mixture of the alcohol (14.3 mg, 0.0213 mmol) in dry CH_2Cl_2 (0.213 mL) was added at rt Dess−Martin periodinane (11.8 mg, 0.0280 mmol). After 40 min at rt, the resulting mixture was directly purified by column chromatography on silica gel (1 g, 10:1 hexane−EtOAc) to afford **72a** (13.9 mg, 97%) as a colorless syrup: R_f = 0.65 (10:1 hexane−EtOAc); $[\alpha]^{24.9}_D$ −17.4 (*c* 0.28, $CHCl_3$); IR (neat, cm^{-1}) 3299, 3020, 2930, 2857, 2094, 1734, 1682, 1471, 1374, 1254, 1216, 1095, 1046, 836, 756; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ −0.02 (s, 3H), 0.05 (s, 6H), 0.079 (s, 3H), 0.081 (s,

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

3H), 0.10 (s, 3H), 0.85 (s, 9H), 0.85 (d, J = 7.2 Hz, 3H), 0.893 (s, 9H), 0.895 (s, 9H), 1.14 (d, J = 6.6 Hz, 3H), 1.22−1.35 (m, 14H), 1.47−1.56 (m, 4H), 1.70 (ddq, J = 7.2, 3.2 7.2 Hz, 1H), 2.72 (dq, J = 1.7, 6.9 Hz, 1H), 3.21 (s, 1H), 3.60 (t, 2H, J = 6.9 Hz), 3.84 (m, 1H), 4.52 (dd, 1H, J = 6.9, 1.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −5.23, −4.0, −3.8, −3.1, 8.2, 10.0, 18.32, 18.33, 18.4, 25.2, 25.8, 26.0, 26.1, 29.4, 29.5, 29.59, 29.61, 29.9, 32.9, 35.6, 42.7, 51.8, 63.3, 72.5, 72.6, 79.1, 81.4, 190.0; LRMS (EI) m/z (M)$^+$ 668.5, (M − tBu)$^+$ 611.4; HRMS (EI) m/z (M − tBu)$^+$ calcd for $C_{33}H_{67}O_4Si_3$ 611.4347, found 611.4327.

(2*S*,5*S*,6*R*,7*S*,8*R*,9*R*)-11,15-Epoxy-12,14-dimethyl-16-heptadecyne-1,13-diol (73a). To a stirred solution of **72a** (10.4 mg, 0.0155 mmol) and triethylsilane (0.023 mL, 0.14 mmol) in dry acetonitrile (0.12 mL) was added at −40 °C $BF_3{\cdot}OEt_2$ (0.015 mL, 0.12 mmol). After 50 min at −40 °C, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (0.3 g, 2:3 hexane−EtOAc) to afford **73a** (3.7 mg, 77%) as a colorless syrup: R_f = 0.48 (2:3 hexane−EtOAc); $[\alpha]^{25.0}_D$ 37.8 (c 0.40, $CHCl_3$); IR (neat, cm^{-1}) 3384, 3311, 2927, 2854, 2122, 1461, 1388, 1342, 1308, 1262, 1097, 1060, 1005; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.92 (d, J = 6.9 Hz, 3H), 1.09 (d, J = 6.6 Hz, 3H), 1.24−1.42 (m, 14H), 1.47−1.59 (m, 4H), 1.76 (ddq, J = 10.6, 10.4, 6.6 Hz, 1H), 1.87 (ddq, J = 4.9, 2.0, 6.9 Hz, 1H), 2.48 (d, 1H, J = 2.3 Hz), 3.34 (ddd, J = 7.8, 5.8, 2.0 Hz, 1H), 3.40 (dd, J = 10.6, 4.9 Hz, 1H), 3.64 (br t, J = 6.6 Hz, 2H), 3.70 (dd, J = 10.4, 2.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 5.4, 13.6, 25.7, 25.8, 29.4, 29.45, 29.47, 29.52, 29.52, 32.5, 32.8, 38.1, 38.3, 63.1, 72.6, 73.2, 76.4, 79.7, 81.9; LRMS (EI) m/z (M − H_2O+H)$^+$ 293.2; HRMS (EI) m/z (M − H_2O+H)$^+$ calcd for $C_{19}H_{33}O_2$ 293.2481, found 293.2482.

(12*R*,13*R*,14*S*,15*R*,16*R*)-12,16-Epoxy-14,18-dihydroxy-13,15,20-trimethyl-1-oxa[16]metacyclophane (Optically Pure THP Analogue 3). To a stirred solution of tetramethylammonium salt **8**[24] (29.1 mg, 0.0868 mmol) in dry CH_2Cl_2 (0.943 mL) was added at −40 °C AcBr (0.0061 mL, 0.082 mmol). After 1.5 h at −78 °C, a solution of **73a** (13.3 mg, 0.0410 mmol) in dry CH_2Cl_2 (0.20 mL) was added at −78 °C, and the resulting mixture was gradually warmed to 0 °C. After 10 min at 0 °C, the mixture was cooled to −78 °C and diluted with 1:1 hexane−EtOAc (4.9 mL). The resulting mixture was warmed to rt and then was concentrated at 0 °C. A solution of the chromium carbene complex in degassed dry toluene (20.5 mL) was stirred at 50 °C. After 4 h, the mixture was concentrated. The residue was purified by column chromatography on silica gel (1 g, 2:1 hexane−EtOAc) to afford (+)-**3** (6.0 mg, 2 steps 38%) as colorless solids. Its spectral data were identical with those of the racemate: $[\alpha]^{26.0}_D$ 57.4 (c 0.98, $CHCl_3$)

(2′*R*,3′*S*,4′*S*,5′*R*)-2-[(3,5-Bis(*tert*-butyldimethylsilyloxy)-4-methylhex)-2-yl-1,3-dithiane 1-Oxide (71b). To a stirred solution of **69** (339 mg, 0.930 mmol) in dry Et_2O (9.30 mL) was added at 0 °C 3 M methylmagnesium bromide in Et_2O (0.372 mL, 1.12 mmol). After 10 min at 0 °C, saturated aqueous NH_4Cl was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (10 g, 1:1 acetone−EtOAc) to afford a 1.4:1 inseparable mixture of the adduct and its diastereomer (231 mg, 65%) as colorless syrups. The NMR chemical shifts of each isomer were determined using the spectra of the mixture. **Major isomer**: R_f = 0.35 (1:1 acetone−EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.08 (s, 3H), 0.11 (s, 3H), 0.88 (d, J = 6.9 Hz, 3H), 0.89 (s, 9H), 1.11 (d, J = 7.2 Hz, 3H), 1.18 (d, J = 6.3 Hz, 3H), 1.76 (m, 1H), 2.21 (m, 1H), 2.38 (m, 1H), 2.55−2.68 (m, 3H), 2.83 (m, 1H), 3.09 (br s, 1H), 3.46 (m, 1H), 3.71 (dq, J = 9.0, 6.3 Hz, 1H), 3.87 (d, J = 3.5 Hz, 1H), 4.13 (dd, J = 4.9, 3.7 Hz, 1H). **Minor isomer:** R_f = 0.35 (1:1 acetone−EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.12 (s, 3H), 0.13 (s, 3H), 0.90 (s, 9H), 1.06 (d, J = 7.2 Hz, 3H), 1.09 (d, J = 6.9 Hz, 3H), 1.14 (d, J = 6.3 Hz, 3H), 1.72 (m, 1H), 2.18 (m, 1H), 2.40 (m, 1H), 2.55−2.68 (m, 3H), 2.97 (m, 1H), 3.46 (m, 1H), 3.58 (d, J = 2.6 Hz, 1H), 3.82 (dd, J = 8.1, 1.8 Hz, 1H),.4.32 (dq, J = 1.7, 6.3 Hz, 1H). The major adduct was separated after next silylation and the stereochemistry of the major isomer was determined after construction of THP ring (**74**). To a stirred solution of the mixture of the adducts (145 mg, 0.381 mmol) in dry CH_2Cl_2 (3.80 mL) were added at 0 °C *N*,*N*-diisopropylethylamine (0.133 mL, 0.762 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.131 mL, 0.572 mmol). After 1 h at 0 °C, saturated aqueous NH_4Cl was added and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (5 g, 2:3 hexane−EtOAc) to afford a mixture of **71b** and its diastereomer (177 mg, 94%). The hardly separable diastereomer was repeatedly removed by exhaust column chromatography. **71b**: as a colorless syrup; R_f = 0.43 (2:3 hexane−EtOAc); $[\alpha]^{21.7}_D$ −13.5 (c 1.14, $CHCl_3$); IR (neat, cm^{-1}) 2957, 2930, 2857, 1472, 1463, 1372, 1254, 1039, 962, 837, 774; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.06 (s, 6H), 0.09 (s, 6H), 0.890 (s, 9H), 0.893 (s, 9H), 1.00 (d, J = 7.2 Hz, 3H), 1.03 (d, J = 7.2 Hz, 3H), 1.26 (d, J = 6.3 Hz, 3H), 1.75 (ddq, J = 8.3, 3.0, 7.2 Hz, 1H), 2.22 (m, 1H), 2.41 (m, 1H), 2.55−2.64 (m, 3H), 2.84 (m, 1H), 3.45 (m, 1H), 3.61 (d, J = 2.9 Hz, 1H), 3.72 (dq, J = 8.6, 6.3 Hz, 1H), 3.91 (dd, J = 5.5, 3.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.5, −4.3, −4.0, −3.6, 12.0, 13.0, 18.1, 18.3, 23.1, 25.9, 26.0, 29.4, 29.8, 33.8, 47.9, 54.3, 70.3, 71.7, 74.5; LRMS (EI) m/z (M − tBu)$^+$ 437.3; HRMS (EI) m/z (M − tBu)$^+$ calcd for $C_{19}H_{41}O_3Si_2S_2$ 437.2036, found 437.2036.

(4*R*,5*S*,6*S*,7*R*)-3,5-Bis(*tert*-butyldimethylsilyloxy)-4,6-dimethyloct-1-yn-3-one (72b). A solution of **71b** (50.2 mg, 0.101 mmol) and *N*-bromosuccinimide (155 mg, 0.871 mmol) in 32:1 acetone−H_2O (2.17 mL) was stirred at 0 °C. After 5 min, saturated aqueous $Na_2S_2O_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 4:1 hexane−acetone) to afford the aldehyde (35.1 mg, 89%) as a colorless syrup: R_f = 0.75 (4:1 hexane−acetone); ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ −0.02 (s, 3H), 0.06 (s, 3H), 0.07 (s, 3H), 0.08 (s, 3H), 0.85 (s, 9H), 0.89 (s, 9H), 0.89 (d, J = 7.2 Hz, 3H), 1.13 (d, J = 6.9 Hz, 3H), 1.18 (d, J = 6.3 Hz, 3H), 1.59 (ddq, J = 6.6, 4.0, 6.9 Hz, 1H), 2.46 (dq, J = 2.3, 7.2 Hz, 1H), 3.94 (dq, J = 4.0, 6.3 Hz, 1H), 4.29 (dd, J = 6.6, 2.3 Hz, 1H), 9.68 (s, 1H). The resulting aldehyde was immediately used for the next step. To a stirred solution of the resulting aldehyde (35.1 mg, 0.0903 mmol) in dry Et_2O (1.80 mL) was added at −78 °C 0.5 M ethynylmagnesium bromide in THF (0.542 mL, 0.271 mmol). After 1 h at −78 °C, saturated aqueous NH_4Cl solution was added at −10 °C and the resulting mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 4:1 hexane−acetone) to afford a mixture of the adducts (35.2 mg, 94%: a 2:1 mixture of diastereomers) as a colorless syrup. To a stirred solution of a mixture of the adducts (52.8 mg, 0.127 mmol) in dry CH_2Cl_2 (1.27 mL) was added at rt Dess−Martin periodinane (70.0 mg, 0.381 mmol). After 1 h at rt, the resulting mixture was directly purified by column chromatography on silica gel (2 g, 10:1 hexane−EtOAc) to afford **72b** (46.5 mg, 89%) as a colorless syrup: R_f = 0.73 (10:1 hexane−EtOAc); $[\alpha]^{19.0}_D$ −25.4 (c 0.70, $CHCl_3$); IR (neat, cm^{-1}) 3299, 3020, 2931, 2858, 2095, 1680, 1525, 1473, 1387, 1253, 1216, 1046, 929, 837, 770; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ −0.01 (s, 3H), 0.07 (s, 6H), 0.08 (s, 3H), 0.85 (s, 9H), 0.89 (s, 9H), 0.90 (d, J = 6.0 Hz, 3H), 1.14 (d, J = 6.6 Hz, 3H), 1.20 (d, J = 6.3 Hz, 3H), 1.55 (ddq, J = 6.6, 4.0, 6.6 Hz, 1H), 2.72 (dq, J = 2.3, 6.9 Hz, 1H), 3.22 (s, 1H), 3.95 (dq, J = 4.0, 6.0 Hz, 1H), 4.51 (dd, J = 6.6, 2.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.4, −4.3, −3.9, −3.3, 8.8, 10.3, 18.2, 18.3, 22.8, 25.9, 26.0, 47.1, 51.6, 68.7, 72.5, 79.2, 81.3, 190.0; LRMS (EI) m/z (M − tBu)$^+$ 355; HRMS (EI) m/z (M − tBu)$^+$ calcd for $C_{18}H_{35}O_3Si_2$ 355.2125, found 355.2120.

(3*R*,4*R*,5*S*,6*S*,7*R*)-4,6-Dimethyl-3,7-epoxyoct-1-yn-5-ol (73b). To a stirred solution of **72b** (46.5 mg, 0.113 mmol) and triethylsilane (0.180 mL, 1.13 mmol) in dry acetonitrile (0.870 mL) was added at −40 °C $BF_3{\cdot}OEt_2$ (0.139 mL, 1.13 mmol). After 1 h at −40 °C, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl,

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (2 g, 2:1 hexane−EtOAc) to afford **73b** (14.3 mg, 75%) as colorless needles: R_f = 0.43 (2:1 hexane−EtOAc); $[\alpha]^{18.3}_D$ 49.7 (*c* 0.60, $CHCl_3$); mp 64−65 °C (not recrystallized); IR (neat, cm^{-1}) 3410, 3254, 2973, 2917, 2117, 1630, 1457, 1389, 1337, 1315, 1253, 1180, 1099, 1061, 1024, 904, 878; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.95 (d, *J* = 7.2 Hz, 3H), 1.09 (d, *J* = 6.6 Hz, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.75 (ddq, *J* = 10.6, 10.6, 6.6 Hz, 1H), 1.83 (ddq, *J* = 4.9, 2.0, 7.2 Hz, 1H), 2.48 (d, *J* = 2.3 Hz, 1H), 3.42 (dd, *J* = 10.6, 4.9 Hz, 1H), 3.59 (dq, *J* = 2.0, 6.6 Hz, 1H), 3.72 (dd, *J* = 10.6, 2.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 5.2, 13.5, 18.6, 37.8, 39.6, 72.5, 73.3, 75.2, 76.3, 81.7; LRMS (EI) *m*/*z* $(M)^+$ 168.0; HRMS (EI) *m*/*z* $(M)^+$ calcd for $C_{10}H_{16}O_2$ 168.1150, found 168.1144.

2-[(2*R*,3*R*,4*S*,5*S*,6*R*)-4-Hydroxy-3,5,6-trimethyltetrahydropyran-2-yl]-5-methyl-4-nonanyloxyphenol (74). To a stirred solution of tetramethylammonium salt **8**[24] (42.6 mg, 0.127 mmol) in dry CH_2Cl_2 (3.00 mL) was added at −78 °C AcBr (0.0089 mL, 0.12 mmol). After 1.5 h at −78 °C, 1-nonyl alcohol (0.021 mL, 0.12 mmol) was added, and the resulting mixture was gradually warmed to 0 °C and then concentrated to afford a carbene complex: ^1H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.95 (br, 3H), 1.10−1.76 (m, 12H), 1.82−2.05 (m, 2H), 1.92 (br s, 3H). 4.67 (br s, 2H), 4.90 (br s, 1H), 5.07 (br s, 1H); The resulting carbene complex was mixed with **73b** (14.3 mg, 0.0851 mmol) in CH_2Cl_2 (0.5 mL) and then concentrated to dryness. The mixture was dissolved in degassed dry toluene (1.70 mL) and this was stirred at 50 °C. After 2 h, the mixture was concentrated. The residue was purified by column chromatography on silica gel (1 g, 2:1 hexane−EtOAc) to afford (+)-**74** (19.0 mg, two steps 57%) as a colorless syrup: R_f = 0.49 (2:1 hexane−EtOAc); $[\alpha]^{21.2}_D$ 62.9 (*c* 1.00, $CHCl_3$); IR (neat, cm^{-1}) 3390, 2927, 2856, 1504, 1459, 1367, 1207, 1099, 1043, 1020, 928, 872, 757; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.85 (d, *J* = 6.3 Hz, 3H), 0.88 (t, *J* = 6.9 Hz, 3H), 1.03 (d, *J* = 7.2 Hz, 3H), 1.23−1.38 (m, 10H), 1.25 (d, *J* = 6.6 Hz, 3H), 1.41−1.47 (m, 2H), 1.92−1.99 (m, 2H), 2.16 (s, 3H), 3.55 (br d, *J* = 9.7 Hz, 1H), 3.79 (dq, *J* = 2.0, 6.3 Hz, 1H), 3.84 (br t, *J* = 6.6 Hz, 2H), 4.02 (d, *J* = 10.3 Hz, 1H), 6.39 (s, 1H), 6.69 (s, 1H), 7.39 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 5.6, 13.8, 14.1, 15.9, 18.6, 22.7, 26.1, 29.3, 29.4, 29.51, 29.54, 31.9, 36.3, 39.6, 69.2, 75.9, 76.6, 86.1, 112.9, 119.5, 121.4, 128.2 148.7, 150.1; LRMS (EI) *m*/*z* $(M)^+$ 392.1; HRMS (EI) *m*/*z* $(M)^+$ calcd for $C_{24}H_{40}O_4$ 392.2927, found 392.2931. Coupling constants in ^1H NMR spectrum ($J_{2,3}$ = 10.3 Hz, $J_{3,4}$ = 9.7 Hz, $J_{4,5}$: br, $J_{5,6}$ = 2.0 Hz) indicate that the THP ring has a chair conformation with the desired configration.

(2′*R*,3′*S*,4′*S*,5′*R*)-2-[(3,5-Bis(*tert*-butyldimethylsilyloxy)-4-methylnon)-2-yl-1,3-dithiane 1-Oxide (71c). To a stirred suspension of magnesium turnings (52.5 mg, 2.16 mmol) in dry Et_2O (1.00 mL) was added dropwise at rt iodobutane (0.0956 mL, 0.864 mmol) in dry Et_2O (5.00 mL) via drip funnel. The resulting suspension was cooled to −78 °C, and to this was added **69** (78.8 mg, 0.216 mmol) in dry Et_2O (1.00 mL). The mixture was gradually warmed to 0 °C in 1 h. After 15 min at 0 °C, saturated aqueous NH_4Cl and was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was partially purified by column chromatography on silica gel (3 g, 1:1 $CHCl_3$−EtOAc) to afford a mixture of products which contains a mixture of adducts (a 1.5:1 diastereomers) along with sulfoxide isomers. The mixture was subjected to the next step without further purification. To a stirred solution of the mixture of the adducts (88.3 mg, 0.209 mmol) in dry CH_2Cl_2 (2.10 mL) were added at 0 °C *N*,*N*-diisopropylethylamine (0.073 mL, 0.419 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.072 mL, 0.314 mmol). After 2 h at 0 °C, saturated aqueous NH_4Cl was added, and the mixture was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (5 g, 2:3 hexane−EtOAc) to afford **71c** as a single isomer (31.2 mg, 2 steps 28%). **71c**: colorless syrup; R_f = 0.61 (2:3 hexane−EtOAc); $[\alpha]^{21.9}_D$ −4.2 (*c* 0.53, $CHCl_3$); IR (neat, cm^{-1}) 2956, 2931, 2858, 1471, 1463, 1387, 1254, 1050, 938, 836, 774; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.05 (s, 3H), 0.06 (s, 3H), 0.09 (s, 3H), 0.10 (s, 3H), 0.89 (s, 9H), 0.90 (s, 9H), 0.91 (t, *J* = 7.2 Hz, 3H), 0.96 (d, *J* = 7.2 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 1.27−1.41 (m, 4H), 1.51−1.61 (m, 2H), 1.86 (ddq, *J* = 7.5, 4.0, 7.2 Hz, 1H), 2.21 (m, 1H), 2.42 (m, 1H), 2.54−2.61 (m, 3H), 2.82 (m, 1H), 3.44 (m, 1H), 3.56 (d, *J* = 3.5 Hz, 1H), 3.68 (ddd, *J* = 8.6, 4.6, 3.9 Hz, 1H), 3.92 (dd, *J* = 4.3, 4.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.3, −4.1, −3.8, −3.5, 11.7, 11.9, 14.1, 18.2, 18.3, 23.1, 26.0, 26.05, 26.07, 29.3, 29.8, 33.4, 34.9, 44.3, 54.2, 72.2, 73.2, 74.4; LRMS (EI) *m*/*z* $(M - t\text{Bu})^+$ 479.3; HRMS (EI) *m*/*z* $(M - t\text{Bu})^+$ calcd for $C_{22}H_{47}O_3Si_2S_2$ 479.2505, found 479.2507. The stereochemistry of the newly formed hydroxy group by the reaction of **69** with *n*-BuMgI was determined after construction of THP ring (**75**).

(4*R*,5*S*,6*S*,7*R*)-3,5-Bis(*tert*-butyldimethylsilyloxy)-4,6-dimethylundec-1-yn-3-one (72c). A solution of **71c** (60.0 mg, 0.112 mmol) and *N*-bromosuccinimide (120 mg, 0.672 mmol) in 32:1 acetone−H_2O (2.30 mL) was stirred at 0 °C. After 5 min, saturated aqueous $Na_2S_2O_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (2 g, 3:1 hexane−acetone) to afford the aldehyde (44.5 mg, 92%) as a colorless syrup. The resulting aldehyde was immediately used for the next step: R_f = 0.85 (10:1 hexane−acetone); ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ −0.03 (s, 3H), 0.06 (s, 3H), 0.07 (s, 3H), 0.08 (s, 3H), 0.84 (shoulder, 3H), 0.85 (s, 9H), 0.89 (s, 9H), 0.90 (t, *J* = 7.2 Hz, 3H), 1.12 (d, *J* = 7.2 Hz, 3H), 1.18−1.35 (m, 4H), 1.47−1.53 (m, 2H), 1.73 (ddq, *J* = 7.2, 3.2, 6.9 Hz, 1H), 2.47 (dq, *J* = 1.7, 7.2 Hz, 1H), 3.82 (ddd, *J* = 7.5, 4.9, 3.2 Hz, 1H), 4.29 (dd, *J* = 6.9, 2.1 Hz, 1H), 9.69 (s, 1H). To a stirred solution of the resulting aldehyde (44.5 mg, 0.103 mmol) in dry Et_2O (2.10 mL) was added at −78 °C 0.5 M ethynylmagnesium bromide in THF (0.620 mL, 0.310 mmol). After 15 min at −78 °C, saturated aqueous NH_4Cl solution was added at −10 °C, and the resulting mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 4:1 hexane−acetone) to afford ethynyl adducts (42.4 mg, 90%: a 2:1 mixture of diastereomers) as a colorless syrup. To a stirred solution of the mixture of the adducts (42.3 mg, 0.0928 mmol) in dry CH_2Cl_2 (1.27 mL) was added at rt Dess−Martin periodinane (51.2 mg, 0.279 mmol). After 1 h at rt, the resulting mixture was directly purified by column chromatography on silica gel (1.5 g, 10:1 hexane−EtOAc) to afford **72c** (28.7 mg, 70%) as a colorless syrup: R_f = 0.73 (10:1 hexane−EtOAc); $[\alpha]^{18.6}_D$ −38.2 (*c* 1.17, $CHCl_3$); IR (neat, cm^{-1}) 3300, 3012, 2928, 2856, 2094, 1736, 1679, 1464, 1376, 1254, 1218, 1047, 910, 837, 771; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ −0.02 (s, 3H), 0.076 (s, 3H), 0.080 (s, 3H), 0.082 (s, 3H), 0.85 (s, 9H), 0.86 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.90 (t, *J* = 6.9 Hz, 3H), 1.14 (d, *J* = 6.6 Hz, 3H), 1.18−1.35 (m, 4H), 1.48−1.57 (m, 2H), 1.70 (ddq, *J* = 7.2, 3.5, 6.9 Hz, 1H), 2.72 (dq, *J* = 1.8, 6.9 Hz, 1H), 3.21 (s, 1H), 3.85 (m, 1H), 4.52 (dd, *J* = 7.2, 1.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ −4.0, −3.8, −3.1, 8.2, 10.0, 14.1, 18.32, 18.32, 23.0, 26.0, 26.1, 27.3, 42.7, 51.8, 72.5, 72.6, 79.1, 81.4, 190.0; LRMS (EI) *m*/*z* $(M - t\text{Bu})^+$ 397; HRMS (EI) *m*/*z* $(M - t\text{Bu})^+$ calcd for $C_{21}H_{41}O_3Si_2$ 397.2594, found 397.2594.

(3*R*,4*R*,5*S*,6*S*,7*R*)-4,6-Dimethyl-3,7-epoxyundec-1-yn-5-ol (73c). To a stirred solution of **72c** (28.7 mg, 0.0631 mmol) and triethylsilane (0.094 mL, 0.63 mmol) in dry acetonitrile (0.450 mL) was added at −40 °C $BF_3{\cdot}OEt_2$ (0.059 mL, 0.63 mmol). After 1 h at −40 °C, saturated aqueous $NaHCO_3$ was added, and the mixture was extracted with EtOAc. The extracts were washed with saturated aqueous NaCl, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1 g, 2:1 hexane−EtOAc) to afford **73c** (7.5 mg, 57%) as colorless needles: R_f = 0.52 (2:1 hexane−EtOAc); $[\alpha]^{18.9}_D$ 55.5 (*c* 0.75, $CHCl_3$); mp 86−88 °C (not recrystallized); IR (neat, cm^{-1}) 3413, 3285, 2958, 2936, 2872, 2122, 1631, 1459, 1389, 1343, 1310, 1159, 1100, 1063, 1004, 946; ^1H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.95 (d, *J* = 6.9 Hz, 3H), 1.09 (d, *J* = 6.6 Hz, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.75 (ddq, *J* = 10.6, 10.6, 6.6 Hz, 1H), 1.83 (ddq, *J* = 6.9, 2.0, 6.9 Hz, 1H), 2.48 (d, *J* = 2.3

dx.doi.org/10.1021/jo5015273 | J. Org. Chem. 2014, 79, 9922−9947

Hz, 1H), 3.42 (dd, J = 10.6, 4.9 Hz, 1H), 3.59 (dq, J = 2.0, 6.6 Hz, 1H), 3.72 (dd, J = 10.6, 2.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 5.2, 13.5, 18.6, 37.8, 39.6, 72.5, 73.3, 75.2, 76.3, 81.7; LRMS (EI) m/z $(M)^+$ 210.2; HRMS (EI) m/z $(M)^+$ calcd for $C_{13}H_{22}O_2$ 210.1620, found 210.1617.

2-[(2*R*,3*R*,4*S*,5*S*,6*R*)-4-Hydroxy-3,5,6-trimethyltetrahydropyran-2-yl]-5-methyl-4-(nonanyloxy)phenol (75). To a stirred solution of tetramethylammonium salt **8**^{24} (107 mg, 0.301 mmol) in dry CH_2Cl_2 (7.50 mL) was added at −78 °C AcBr (0.022 mL, 0.30 mmol). After 1 h at −78 °C, 1-hexanol (0.038 mL, 0.12 mmol) was added, and the resulting mixture was gradually warmed to 0 °C and then concentrated to afford a carbene complex: ^{1}H NMR (300 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.91 (br, 3H), 1.25−1.40 (m, 4H), 1.50 (m, 2H), 1.87 (s, 3H), 1.95 (m, 2H), 4.72 (br s, 2H), 4.89 (br s, 1H), 5.06 (br s, 1H). The resulting carbene complex was mixed with **73c** (37.2 mg, 0.177 mmol) in CH_2Cl_2 (1.0 mL) and then concentrated to dryness. The mixture was dissolved in degassed dry toluene (3.54 mL) and this was stirred at 50 °C. After 2 h, the mixture was concentrated. The residue was purified by column chromatography on silica gel (1.5 g, 5:1 $CHCl_3$−EtOAc) to afford (+)-**75** (41.9 mg, two steps 60%) as a colorless syrup: R_f = 0.57 (5:1 $CHCl_3$−EtOAc); $[\alpha]^{21.7}_D$ +62.7 (c 0.79, $CHCl_3$); IR (neat, cm^{-1}) 3380, 3019, 2931, 2861, 1501, 1459, 1383, 1218, 1094, 1041, 772; ^{1}H NMR (500 MHz, $CDCl_3$, $CHCl_3$ = 7.26) δ 0.86 (d, J = 6.6 Hz, 3H), 0.88 (t, J = 6.9 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H),1.01 (d, J = 7.2 Hz, 3H), 1.23−1.37 (m, 8H), 1.41−1.49 (m, 3H), 1.65 (m, 1H), 1.75 (m, 2H), 1.95 (m, 1H), 1.99 (m, 1H), 2.17 (s, 3H), 3.53 (br d, J = 9.0 Hz, 1H), 3.54 (dt, J = 2.0, 6.6 Hz, 1H), 3.85 (t, J = 6.6 Hz, 2H), 4.00 (d, J = 10.6 Hz, 1H), 6.38 (s, 1H), 6.69 (s, 1H), 7.50 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, $CDCl_3$ = 77.0) δ 5.8, 13.8, 13.96, 14.01, 15.9, 22.6, 25.8, 27.9, 29.5, 31.6, 32.3, 36.8, 38.3, 69.2, 76.6, 80.2, 86.2, 112.8, 119.5, 121.5, 128.0, 148.8, 150.0; LRMS (EI) m/z $(M)^+$ 392.3; HRMS (EI) m/z $(M)^+$ calcd for $C_{24}H_{40}O_4$ 392.2927, found 392.2928. Coupling constants in ^{1}H NMR spectrum ($J_{2,3}$ = 10.6 Hz, $J_{3,4}$ 9.0 Hz, $J_{4,5}$: br, $J_{5,6}$ = 2.0 Hz) indicate that the THP ring has a chair conformation with the desired configration.

Antibacterial Activity. Minimum inhibitory concentrations of **1**, **2**, **3**, **74**, and **75** were determined by the standard agar dilution method recommended by the Clinical Laboratory Standards Institute (CLSI) guidelines.[44] Bacteria were incubated on Mueller−Hinton agar (Becton Dickinson) at 37 °C for 18 h.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of new compounds and the natural kendomycin (**1**). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Takeda Pharmaceutical Co. Ltd. for providing us natural kendomycin (TAN 2162) and Drs. Masayuki Igarashi and Kunio Inoue (Microbial Chemistry Research Foundation) for the antimicrobial test. This research was partially supported by JGC-S scholarship foundation (JGC corporation to Y.S.), Amano Foundation (Amano National Industrial Research Institute to Y.S.), and a MEXT-Supported Program for the Strategic Research Foundation at Private Universities 2012-2016 (to M.N.).

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