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Synthesis of the Zoanthamine ABC Ring System: Some Surprises from Intramolecular Diels−Alder Reactions

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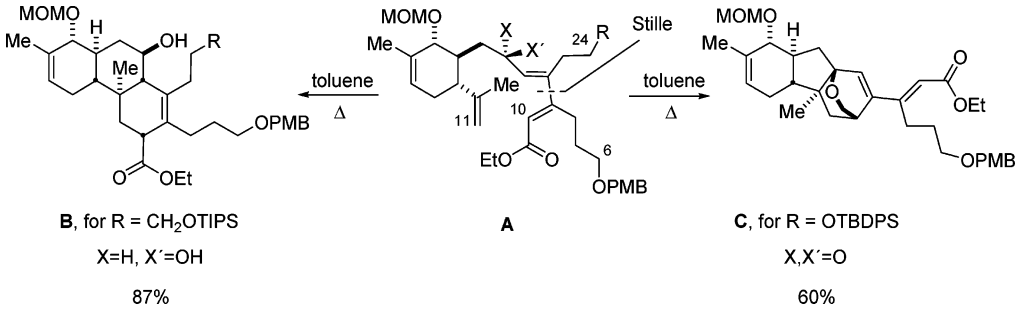

B, for R = CH_2OTIPS
X=H, X´=OH
87%

A

C, for R = OTBDPS
X,X´=O
60%

In connection with the total synthesis of the marine alkaloids zoanthamine and norzoanthamine, an elaborate model study was conducted starting from (−)-carvone. In nine steps alkenyl iodides corresponding to the C_{11}−C_{24} fragment of zoanthamine were obtained. The alkenyl iodides were coupled to various stannanes (C_6−C_{10} fragment) via the Corey modification of the Stille reaction, affording a variety of Diels−Alder precursors. An interesting and highly unexpected cascade reaction sequence was observed during the screening of an intramolecular Diels−Alder reaction, generating a novel tetracyclic framework. A slight modification in the Diels−Alder precursor allowed the desired cycloaddition to take place, giving the cycloadduct in 87% yield.

Introduction

The zoanthamine family is a structurally unique class of densely functionalized heptacyclic alkaloids (Figure 1). The parent member, zoanthamine (**1**), was isolated from the marine organism *Zoanthus* sp. found off the coast of Visakhapatnam, India and was characterized by means of X-ray crystallography and NMR spectroscopy in 1984.[1] Since that discovery, a whole family of congeners has been found around the world.[2] These marine alkaloids have been tested for biological activity, and zoanthamine itself has been found to show anti-inflammatory effects against phorbol myristate acetate (PMA) induced inflammation of the mouse ear,[3] while norzoanthamine (**2**) has been reported to be a promising drug candidate in the treatment of osteoporosis, since significant suppression of bone weight decrease and weakening in ovariectomized mice was observed when treated with the natural product.[4] Norzoanthamine has also

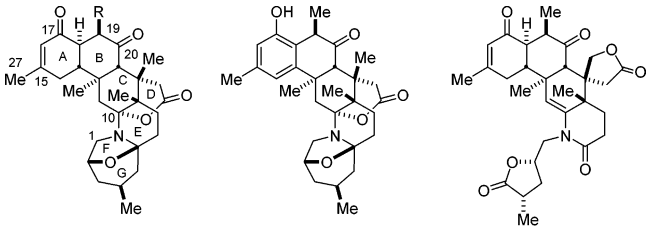

FIGURE 1. Zoanthamine alkaloids.

(1) Rao, C. B.; Anjaneyula, A. S. R.; Sarma, N. S.; Venkatateswarlu, Y.; Rosser, R. M.; Faulkner, D. J.; Chen, M. H. M.; Clardy, J. *J. Am. Chem. Soc.* **1984**, *106*, 7983.

(2) (a) Uramoto, M.; Hayashi, K.; Yamaguchi, K.; Yada, M.; Tsuji, T.; Uemura, D. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 771. (b) Atta-ur-Rahman; Alvi, K. A.; Abbas, S. A.; Choudhary, M. I.; Clardy, J. *Tetrahedron Lett.* **1989**, *30*, 6825. (c) Daranas, A. H.; Fernández, J. J.; Gavin, J. A.; Norte, M. *Tetrahedron* **1998**, *54*, 7891. (d) Daranas, A. H.; Fernández, J. J.; Gavin, J. A.; Norte, M. *Tetrahedron* **1999**, *55*, 5539. (e) Nakamura, H.; Kawase, Y.; Maruyama, K.; Murai, A. *Bull. Chem. Pharm. Bull.* **2000**, *71*, 781.

(3) (a) Rao, C. B.; Anjaneyula, A. S. R.; Sarma, N. S.; Venkatateswarlu, Y.; Rosser, R. M. Faulkner, D. J. *J. Org. Chem.* **1985**, *50*, 3757. (b) Rao, C. B.; Rao, D. V.; Raju, V. S. N.; Sulliwan, B. W.; Faulkner, D. J. *Heterocycles* **1989**, *28*, 103.

(4) Yamaguchi, K.; Yada, M.; Tsuji, T.; Kuramoto, M.; Uemura, D. *Biol. Pharm. Bull.* **1999**, *22*, 920.

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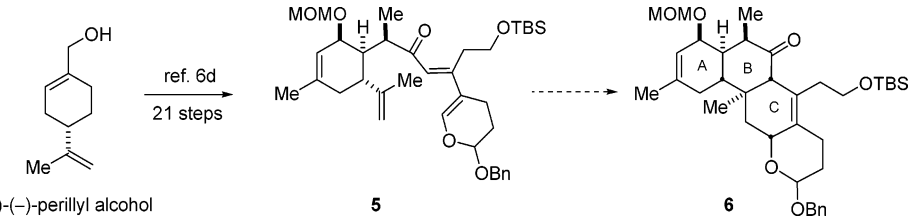
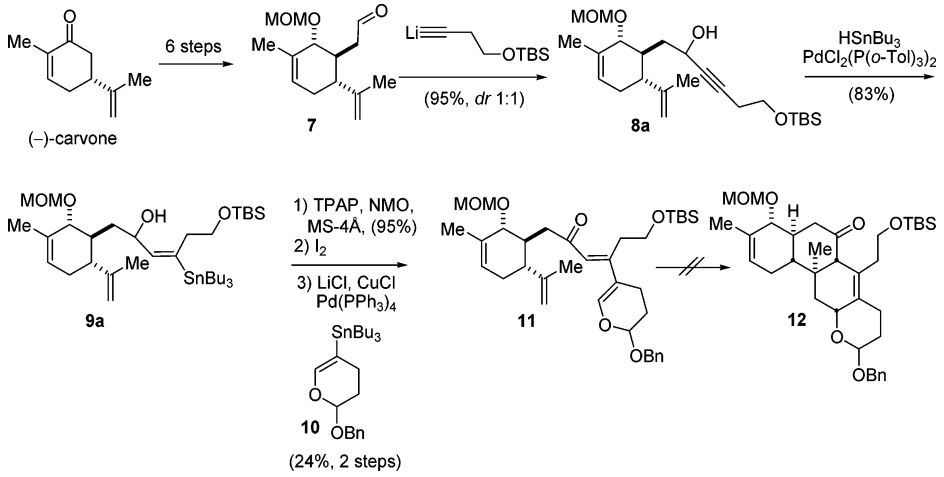
SCHEME 1



SCHEME 2



been reported to exhibit anticancer activity by inhibition of the growth of murine leukemia cells.[5]

Besides the impressively broad range of biological activities, the intriguing topology of these alkaloids has stimulated several research groups to attempt the daunting task of synthesizing these natural products, i.e., zoanthamine (**1**),[6,7] norzoanthamine (**2**),[7] zoanthenol (**3**),[8] and zoanthamide (**4**).[9] A benchmark for synthetic efforts was established in 2004, when Miyashita and co-workers reported the first total synthesis of a zoanthamine alkaloid, norzoanthamine (**2**), after 41 steps and with an impressive overall yield of 3.5%.[10] For the past few years, our own laboratory has been engaged in the development of a totally synthetic route to the zoanthamine family.[6a−d] In the present paper, we describe the development of a synthetic strategy for the stereoselective construction of the zoanthamine ABC ring system.

Results and Discussion

Previous studies in our group[6a−d] have secured a route to advanced stage conjugated dienone **5** in 21 steps from (*S*)-(−)-perillyl alcohol (Scheme 1). The key steps en route to **5** involve a Johnson−Claisen rearrangement, an iodolactonization-elimination reaction, a regioselective hydrostannation, and a Corey-modified (Cu-mediated) Stille coupling. An intramolecular Diels−Alder (IMDA) reaction was then envisaged for the transformation of **5** to the ABC ring system of the zoanthamine family.

From our initial experiments with the IMDA reaction it quickly became obvious that an optimization study would be necessary. To save the precious synthetic intermediate **5**, it was decided to work with a model system that would provide more rapid access to advanced stage intermediates. (−)-Carvone was chosen as the starting material which allowed an expeditious entry to an IMDA precursor differing mainly in the position of the C_{27} methyl group (Figure 1, Scheme 2).

Aldehyde **7** was easily obtained from (−)-carvone (6 steps, 26% yield)[11] and further transformed into the propargylic alcohol **8a** by exposure to the lithium salt of the commercial available *tert*-butyl(but-3-ynyloxy)dimethylsilane, in excellent yield (95%) as a 1:1 mixture of diastereomers. Subjecting propargylic alcohol **8a** to the regioselective Pd-catalyzed hydrostannation protocol introduced by Greeves and further developed by our group[6d,12] provided stannane **9a** in 83% yield. Stannane **9a** was oxidized using Ley's TPAP procedure[13] to the enone (95% yield, one diastereomer) and transformed into the iodide by reaction with iodine.[14] The Stille coupling between freshly prepared iodide and stannane **10**[15] was performed using the Corey modification[16]

(5) Fukuzawa, S.; Hayashi, Y.; Uemura, D.; Nagatu, A.; Yamada, K.; Ijuin, Y. *Heterocycl. Commun.* **1995**, *1*, 207.

(6) (a) Tanner, D.; Andersson, P. G.; Tedenborg, L.; Somfai, P. *Tetrahedron* **1994**, *50*, 9135. (b) Tanner, D.; Tedenborg, L.; Somfai, P. *Acta Chem. Scand.* **1997**, *51*, 1217. (c) Nielsen, T. E.; Tanner, D. *J. Org. Chem.* **2002**, *67*, 6366. (d) Nielsen, T. E.; Le Quement, S.; Juhl, M, Tanner, D. *Tetrahedron* **2005**, *61*, 8013. (e) Ghosh, S.; Rivas, F.; Fischer, D.; González, M. A.; Theodorakis, E. A. *Org. Lett.* **2004**, *6*, 941. (f) Rivas, F.; Ghosh, S.; Theodorakis, E. A. *Tetrahedron Lett.* **2005**, *46*, 5281.

(7) (a) Hikage, N.; Furukawa, H.; Takao, K.; Kobayashi, S. *Tetrahedron Lett.* **1998**, *39*, 6237. (b) Hikage, N.; Furukawa, H.; Takao, K.; Kobayashi, S. *Tetrahedron Lett.* **1998**, *39*, 6241. (c) Hikage, N.; Furukawa, H.; Takao, K.; Kobayashi, S. *Chem. Pharm. Bull.* **2000**, *48*, 1370. (d) Williams, D. R.; Brugel, T. A. *Org. Lett.* **2000**, *2*, 1023.

(8) (a) Hirai, G.; Oguri, H.; Moharram, S. M.; Koyama, K.; Hirama, M. *Tetrahedron Lett.* **2001**, *42*, 5783. (b) Hirai, G.; Koizumi, Y.; Moharram, S. M.; Oguri, H.; Hirama, M. *Org. Lett.* **2002**, *4*, 1627. (c) Hirai, G.; Oguri, H.; Hayashi, M.; Koyama, K.; Koizuma, Y.; Moharram, S. M.; Hirama, M. *Chem. Lett.* **2004**, *14*, 2647.

(9) Williams, D. R.; Cortez, G. S. *Tetrahedron Lett.* **1998**, *39*, 2675.

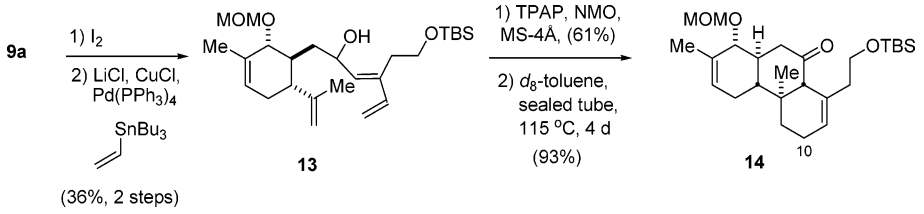
(10) Miyashita, M.; Sasaki, M.; Hattori, I.; Sakai, M.; Tanino, K. *Science* **2004**, *305*, 495.

(11) For the synthesis of aldehyde **7**, see Supporting Information.

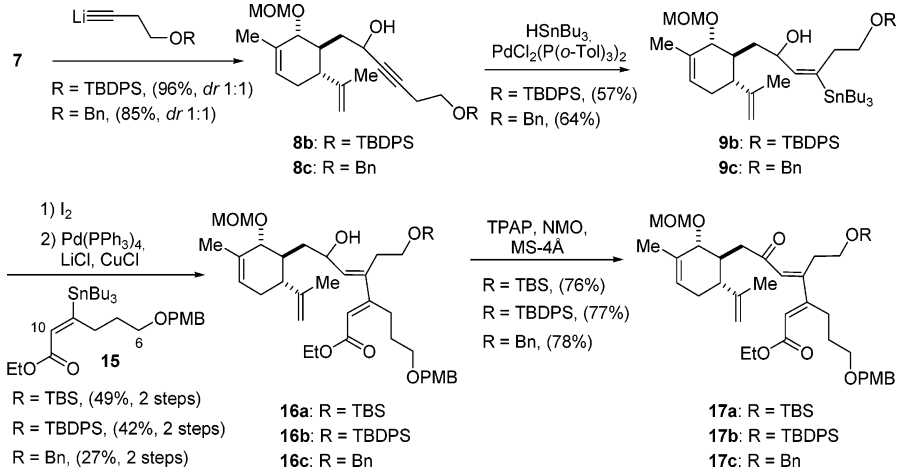
(12) Greeves, N.; Torode, J. S. *Synlett* **1994**, 537.

(13) Griffith, W. P.; Ley, S. V. *Aldrichim. Acta* **1990**, 13.

SCHEME 3



SCHEME 4



to afford diene **11** in modest yield (24%) over the two-step sequence. Unfortunately, after extensive experimentation, all attempts[17] to promote the IMDA reaction of diene **11** failed, resulting only in recovered starting material or decomposition. The complete failure of the normally reliable IMDA reaction was surprising and prompted us to investigate whether the lack of reactivity was due to steric effects, electronic effects, or a combination of the two. Therefore, the system was simplified by preparing diene **13** from stannane **9a** in a two-step procedure (Scheme 3). Performing the tin/iodide exchange on stannane **9a** instead of the corresponding enone gave a faster and cleaner reaction most likely due to the more electron rich double bond in the former. Diene **13** was oxidized and subjected to elevated temperatures in order to promote the IMDA reaction. Pleasingly, tricyclic ketone **14** was isolated as a single diastereomer in 93% yield, after heating the Diels−Alder precursor in toluene for 4 days.

This encouraging result indicated that steric effects alone were perhaps not responsible for the failure of **11** to undergo the IMDA reaction and led us to pursue a Diels−Alder precursor having an additional electron-withdrawing group positioned at the C_{10} position (zoanthamine numbering) instead of the previously installed electron-donating oxygen of the dihydropyran moiety in **11** (Scheme 2). Stannane **15** was chosen as the new C_6-C_{10} fragment,[18] having the ester functionality as the electron-withdrawing group and constitutes a suitable alternative for the previously used dihydropyran ring system. This approach would obviously entail a subsequent oxidative decarboxylation reaction[19] to access the correct oxidation state at C_{10}.

Diene **17a** was accessed through a three-step sequence from stannane **9a** (Scheme 4), in analogy to the previously used route.

To promote the thermal IMDA reaction, diene **17a** was dissolved in toluene and heated to 195 °C for 20 min in a sealed Carius tube (Scheme 5). The desired Diels−Alder product was indeed formed but to our surprise not as the main product of the reaction, which proved to be the interesting 6-5-6-6 tetracyclic diene **19**. Unfortunately, the two products were inseparable using standard chromatographic techniques. A possible mechanism for the formation of the rearrangement product **19** is shown in Scheme 6.

We then hypothesized that changing the protecting group at C_{24} to either a TBDPS or Bn group should limit or prevent the initial migration from taking place, thereby favoring the desired IMDA products **18b**−**c**. Dienes **17b** and **17c** were prepared using an analogous route to that for **17a**.[20] Surprisingly, subjecting either diene **17b** or **17c** to the previously used thermal

(14) The tin/iodide exchange was surprisingly sluggish. Furthermore the iodo derivative proved to be unstable, which prompted us to find better-suited reaction conditions for this exchange reaction (vide infra).

(15) For the synthesis of stannane **10**, see ref 6d.

(16) Han, X.; Stoltz, B. M.; Corey, E. J. *J. Am. Chem. Soc.* **1999**, *121*, 7600.

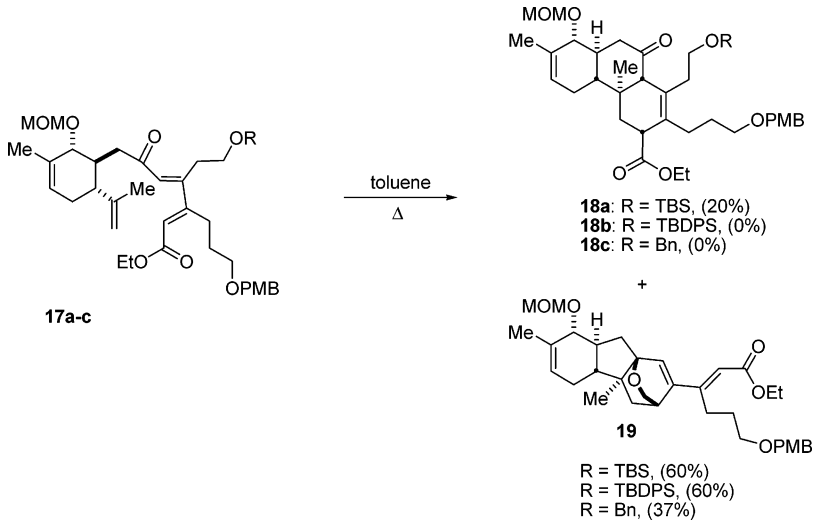
(17) Various reaction conditions, such as refluxing **11** in toluene or xylene, as well as microwave heating the D−A precursor in NMP, acetonitrile, and DMSO/H_2O ((a) Toró, A.; Deslongchamps, P. *J. Org. Chem.* **2003**, *68*, 6847) were attempted without success. Lewis acid catalysis using $LiClO_4$ (5 M in Et_2O) ((b) Braun, R.; Sauer, J. *Chem. Ber.* **1986**, *119*, 1269. (c) Grieco, P. A.; Nunes, J. J.; Gaul, M. D. *J. Am. Chem. Soc.* **1990**, *112*, 4595) and $Yb(OTf)_3$ ((d) Han, G.; Laporte, M. G.; Folmer, J. J.; Werner, K. M.; Weinreb, S. M. *J. Org. Chem.* **2000**, 6293. Review on rare-earth metal triflates in organic chemistry ((e) Kobayashi, S.; Sugiura, M.; Kitagawa, H.; Lam. W.-L. *Chem. Rev.* **2002**, 2227) did not yield any product.

(18) For the synthesis of stannane **15**, see Supporting Information.

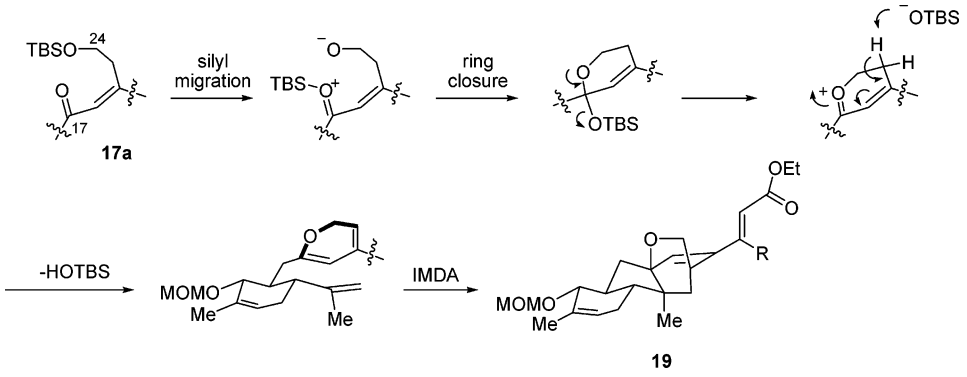
(19) Examples of oxidative decarboxylation reactions used in total synthesis: (a) Corey, E. J.; Imai, N.; Pikul, S. *Tetrahedron Lett.* **1991**, 7517. (b) Corey, E. J.; Ensley, H. E. *J. Am. Chem. Soc.* **1975**, *97*, 8. (c) Hatanaka, M.; Ueda, I. *Chem. Lett.* **1991**, *1*, 61. (d) Sebahar, P. R.; Williams, R. M. *J. Am. Chem. Soc.* **2000**, *122*, 5666. (e) Kienzle, F.; Holland, G. W.; Jernow, J. L.; Kwoh, S.; Rosen, P. *J. Org. Chem.* **1973**, *38*, 3440.

(20) Attempts to optimize the low yielding Cu-mediated Stille coupling failed, mainly due to difficulties in removing undesired homocoupling byproducts of the stannane. Reversing the stannane/iodide coupling partners did not improve the overall yield either.

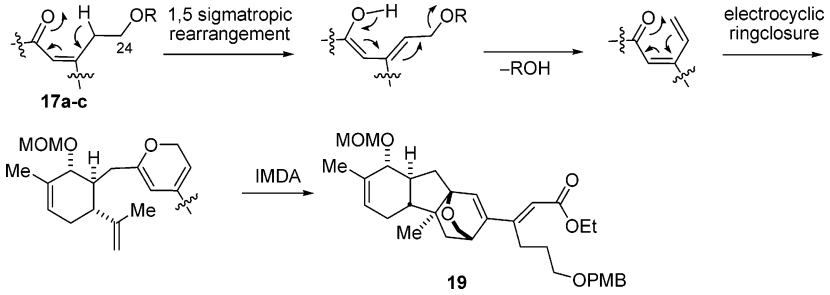
SCHEME 5



SCHEME 6



SCHEME 7

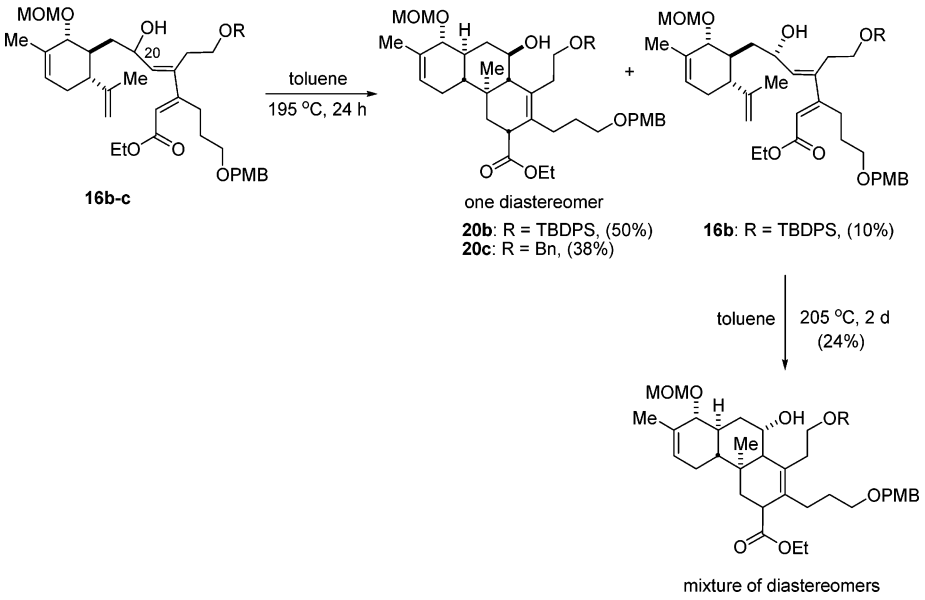


conditions resulted in exclusive formation of the *undesired* rearrangement product **19** in 60% starting from the TBDPS-protected diene and 37% yield with Bn as the protecting group. These findings made us modify the earlier proposed mechanism to one that would accommodate the elimination of the protecting group at C_{24}, regardless of the nature of that protecting group (Scheme 7). The α,β-unsaturated ketone moiety of **17a**−**c** could undergo a [1,5]-sigmatropic rearrangement, providing a highly unstable conjugated allylic enol ether. Loss of the protecting group at C_{24} would then afford a conjugated dienone, which could undergo a 6π electrocyclic ringclosure affording a pyran, which in turn is set up to participate in a hetero-IMDA, providing the tetracyclic product **19**.

In an attempt to circumvent this rearrangement, the thermal conditions were applied to the structurally related alcohols **16b**−**c** (hydroxy functionality at C_{20}, Scheme 8).

To our delight, the IMDA reaction proved viable after subjecting alcohol **16b**−**c** to elevated temperatures for extended periods of time, which provided the desired tricyclic Diels−Alder product as a single diastereomer. That only one diastereomer of the cycloaddition product was isolated presumably stems from the difference in reaction rate for the pseudoequatorial (*R*)-C_{20} vs the pseudoaxial (*S*)-C_{20} configured alcohols (Figure 2). As shown, the pseudoaxial oriented alcohol suffers from an unfavorable 1,3-diaxial interaction with the C_{28} methyl group. In the case where **16b** was heated, the desired cycloadduct product was isolated in 50% yield along with 10% unreacted starting material, both as single diastereomers. Subjecting the isolated slower reacting diastereomer **16b** to 205 °C for 2 days gave an inseparable mixture of two diastereomers, both different from **20b**. Presumably these two products arise from exo and endo TS respectively, in the IMDA reaction.

SCHEME 8



This crucial piece of evidence regarding the configuration of the alcohol at C_{20} in the IMDA reaction led us to improve the strategy by selectively constructing the desired pseudoequatorial alcohol. The configuration at C_{20} was controlled by a Carreira addition[21] of acetylene **21** to aldehyde **7**, with excellent diastereoselectivity (19:1) and good isolated yield (74%), Scheme 9. The triisopropylsilyl (TIPS) protecting group was chosen to impose more stability toward the rather vigorous thermal conditions of the IMDA reaction. The purpose of the extra methylene group in the C_{22} side chain of **24** was to further probe the mechanism of the formation of the rearrangement product **19**: on the basis of the mechanism proposed in Scheme 7, the loss of the protecting group should be prevented by the introduction of the extra methylene unit. The propargylic alcohol derived from the Carreira addition was first hydrostannylated affording stannane **22** in 61% yield (Scheme 9). In initial studies, an interesting observation was made when the subsequent tin/iodide exchange reaction was performed using 2 equiv of iodine. The product after the Stille coupling was lacking the MOM protection group as well as the isopropenyl moiety and was characterized as the 6-oxa-bicyclo[3,2,1]octane **23**, stemming from an 5-*exo*-trig iodoetherification. This observation provides

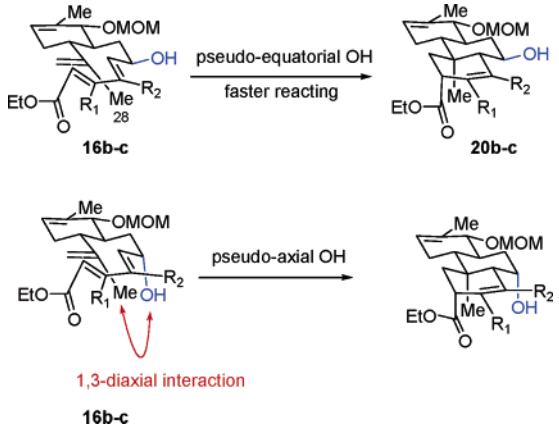
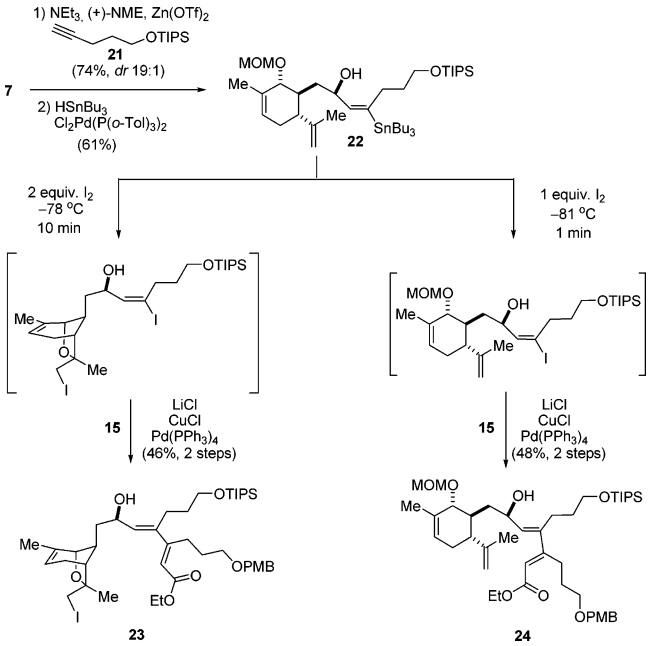


FIGURE 2. $R_1 = (CH_2)_3OPMB$, $R_2 = (CH_2)_2OTBDPS/Bn$.

SCHEME 9

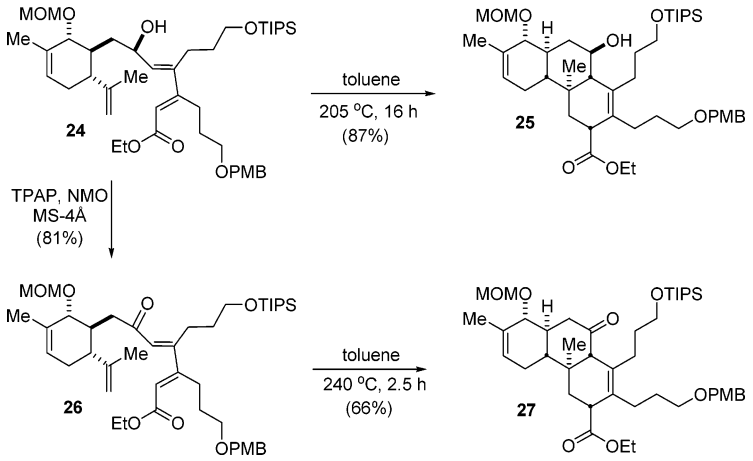


an explanation for the generally low to moderate yields of this transformation in analogous cases (vide infra). After some experimentation, improved yields of the desired mono-iodinated product could be obtained by exposing the stannane **22** to 1 equiv of iodine for 1 min at −81 °C. After the subsequent Stille coupling, diene **24** was produced in 48% yield for the two-step sequence.

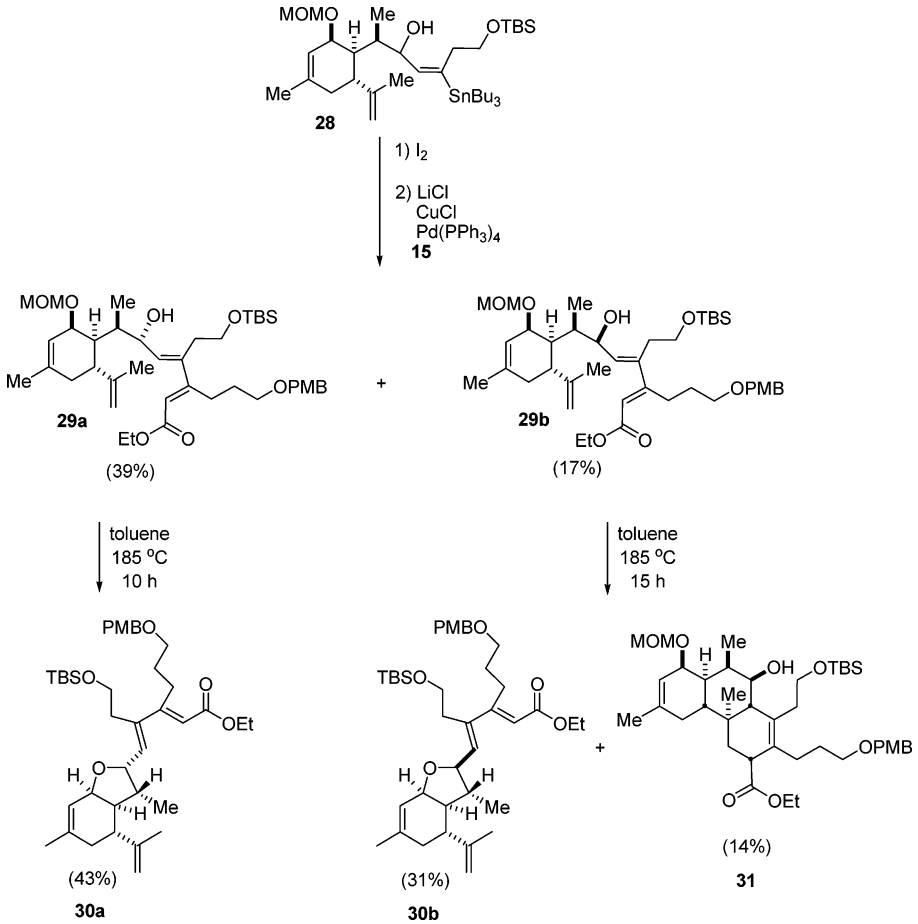
The stage was now set for the crucial IMDA reaction, and gratifyingly, the cycloaddition went smoothly to afford cycloadduct **25** in 87% yield as a single diastereomer. Oxidation of the C_{20} alcohol in **24** using the TPAP procedure gave ketone **26** in 81% yield. Heating the methylene-elongated ketone **26** to 240 °C for 2.5 h afforded the cycloadduct **27**, with *no* rearrangement

(21) Frantz, D. E.; Fässler, R.; Carreira, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 1806.

SCHEME 10



SCHEME 11



product similar to **19**, thus supporting the proposed mechanism (Scheme 7).

At this point, we decided that we had gathered enough information about the IMDA process to allow us to turn from the model systems to the substrate required for the synthesis of zoanthamine itself. Previously prepared stannane **28**[6c] was coupled with **15** to give a diastereomeric mixture of dienes **29a** (39%) and **29b** (17%), which was separated (Scheme 11). As the stereochemical configuration at C_{20} of both the major and minor diastereomer remained unknown, both were subjected to the IMDA reaction conditions. Surprisingly, the main product of *both* reactions turned out to be cyclization of the free C_{20} hydroxyl group on to C_{17}, with concomitant loss of the MOM group. The IMDA product **31** was isolated as the minor component in the reaction starting with diastereomer **29b**.

The reason for the occurrence of this unexpected cyclization pathway can be explained by the orientation of the MOM group in **29a** and **29b**, in comparison to the previously prepared D−A precursors **20a**−**c** and **24**. The allylic MOM groups in **29a**−**b** would be expected to be oriented in a pseudoaxial position compared to the pseudoequatorial position of **20a**−**c** and **24**. The axial orientation of the MOM groups in **29a**−**b** positions the MOM group perpendicular to the plane of the C_{15}−C_{16}

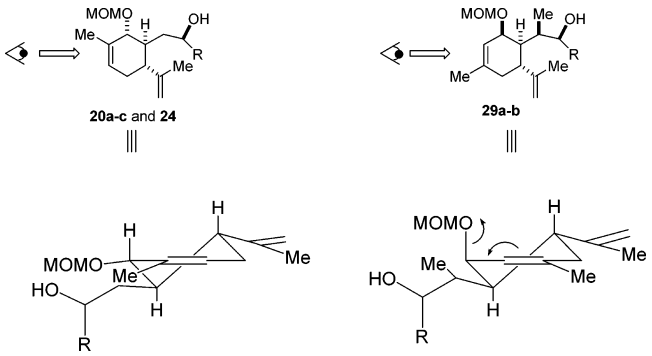


FIGURE 3. S_N1-type elimination of the MOM group in **29a**−**b**.

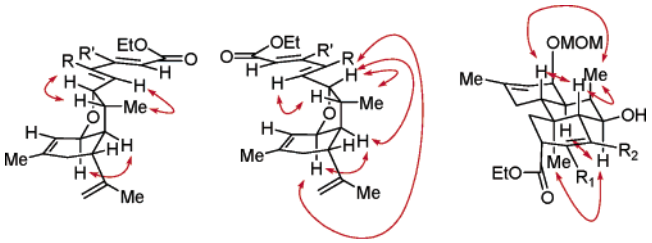


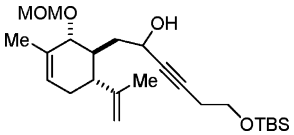
FIGURE 4. Selected nuclear Overhauser effects correlations for compounds **30a**, **30b**, and **31**.

double bond, thus making the C−O bond more prone to S_N1-type substitution.

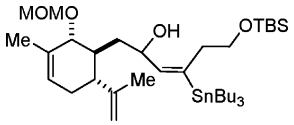
Extensive NMR analysis of **30a**, **30b**, and **31** confirmed the assumption that the diene leading to the IMDA product **31** had the C_{20} hydroxyl group in the more favorable pseudoequatorial orientation in the IMDA TS (Figure 2 and Figure 4). The obvious consequence of this result is that our original route[6d] to key intermediates of the type **29** must be modified in order to invert the stereochemistry at C_{17}.

In conclusion, we have developed a route to the ABC ring system of the zoanthamine alkaloid family based on an inverse electron demand IMDA reaction. The IMDA process explored in the present study provided some surprises as well as some important lessons relevant to our ongoing work on the total synthesis of the zoanthamine alkaloids.

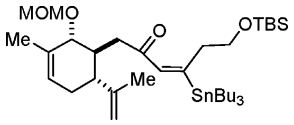
Experimental Section



(*E*)-(*R*)-6-(*tert*-Butyl-dimethyl-silanyloxy)-1-((1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)-hex-3-yne-2-ol (8a). Aldehyde **7** (1.99 g, 8.35 mmol) was dissolved in THF (20 mL), then added under argon to a mixture of *tert*-butyl-(but-3-ynyloxy)dimethylsilane (4.62 g, 25.1 mmol) and *n*-BuLi (15.6 mL, 24.2 mmol, 1.55 M in hexanes) in dry THF (20 mL) at −78 °C which had been stirred for 1 h prior to the addition, stirred for 2 h then the temperature was raised to −20 °C for 1 h, and then warmed to room temperature. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (60 mL) and diethyl ether (200 mL). The aqueous phase was extracted with diethyl ether (100 mL), and the combined organic phases were dried, filtered, and evaporated to dryness in vacuo. The residue was purified by flash column chromatography on silica gel (AcOEt:hexane, 1:2) affording **8a** (3.34 g, 95%) as a 1:1 mixture of diastereomers as well as 2.4 g (52%) of unreacted *tert*-butyl(but-3-ynyloxy)-dimethylsilane. A portion of the more polar isomer was eluted free of its epimer and characterized. In practice, the mixture was used in the subsequent step without being separated. R_f 0.45 (Et_2O:pentane, 1:4); $[\alpha]_D^{23}$ +30.0 (*c* 2.9, $CHCl_3$); IR (film) 3448, 2929, 1644, 1472, 1440, 1382, 1149, 1098, 1028, 838, 778; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.66−5.62 (m, 1H), 4.79 (bs, 2H), 4.75 (d, J = 6.6 Hz, 1H), 4.66−4.58 (m, 2H), 4.13 (d, J = 8.2 Hz, 1H), 3.76 (d, J = 7.5 Hz, 1H), 3.65 (t, J = 7.4 Hz, 2H), 3.40 (s, 3H), 2.36 (td, J = 1.9, 7.3 Hz, 2H), 2.20 (td, J = 4.8, 10.2 Hz, 1H), 2.14−2.01 (m, 1H), 2.00−1.95 (m, 1H), 1.93−1.77 (m, 2H), 1.63 (s, 6H), 1.54 (ddd, J = 3.3, 8.1, 14.6 Hz, 1H), 0.83 (s, 9H), 0.00 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 133.2, 126.5, 113.1, 95.1, 83.1, 81.1, 62.0, 60.4, 56.4, 46.6, 40.7, 37.6, 30.3, 25.9, 23.2, 20.0, 18.2, −5.3; Fast-atom bombardment mass spectroscopy (FAB-MS) calcd for [M + Na] 445.28; found 445.19; Anal. Calcd for $C_{24}H_{42}O_4Si$: C, 68.20; H, 10.02. Found: C, 67.94; H, 10.22.

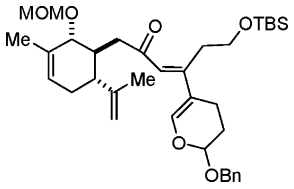


(3*E*)-4-(Tributylstannyl)-6-(*tert*-butyldimethylsilyloxy)-1-((1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)-cyclohex-3-enyl)hex-3-en-2-ol (9a). To a 1:1 mixture of epimeric alcohols **8a** (1.95 g, 4.61 mmol) and dichlorobis(tris(o-toloyl)-phosphine)palladium(II) (18 mg, 0.023 mmol) in THF (50 mL) was added dropwise tributyltin hydride (4.03 g, 13.8 mmol) over a period of 4.5 h. The reaction was stirred for an additional 1 h then directly subjected to dry column vacuum chromatography (DCVC) (AcOEt:heptane, 1:4−1:2) affording **9a** (3.83 g, 83%) as a mixture of diastereomers as well as recovered starting material **8a** (137 mg, 7%). A portion of the less polar isomer was eluted free of its epimer and characterized. In practice, the mixture was used in the subsequent step without being separated. Mixture of diastereomers: FAB-MS calcd for $[M - C_4H_{11}]^+$ 781.37; found 781.4; Anal. Calcd for $C_{46}H_{74}O_4SiSn$: C, 65.94; H, 8.90. Found: C, 65.93; H, 8.98. Less polar diastereomer: R_f 0.61 (AcOEt:heptane, 1:4); $[\alpha]_D^{23}$ + 5.9 (*c* 1.1, $CHCl_3$); IR (film) 3466, 2924, 2854, 1644, 1459, 1376, 1254, 1148, 1096, 1031, 839; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.67 (d, J = 7.6, J(Sn−H) = 68.8 Hz, 1H), 5.61 (bs, 1H), 4.79−4.70 (m, 3H), 4.67 (d, J = 6.5 Hz, 1H), 4.14 (d, J = 7.0 Hz, 1H), 3.67−3.48 (m, 2H), 3.44 (s, 3H), 3.34 (d, J = 3.9 Hz, 1H), 2.70 (dt, J = 5.7, 14.6 Hz, 1H), 2.47−2.37 (m, 1H), 2.27 (td, J = 4.9, 9.4 Hz, 1H), 2.20−1.90 (m, 3H), 2.79−1.72 (m, 3H), 1.70 (s, 3H), 1.69 (s, 3H), 1.54−1.37 (m, 6H), 1.30 (app. sextet, J = 7.4 Hz, 6H), 0.91−0.84 (m, 24H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.1, 146.8, 141.2, 133.4, 125.8, 112.3, 95.7, 82.0, 64.3, 62.9, 56.1, 46.0, 39.5, 37.8, 37.1, 30.1, 29.8, 29.1, 27.4, 26.1, 20.4, 18.9, 18.5, 13.7, 9.7.

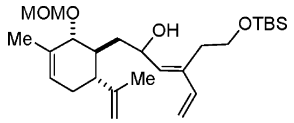


(3*E*)-4-(Tributylstannyl)-6-(*tert*-butyldimethylsilyloxy)-1-((1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)-cyclohex-3-enyl)hex-3-en-2-one (37). Alcohol **9a** (241 mg, 0.338 mmol) was dissolved in CH_2Cl_2/CH_3CN (2:3, 5 mL), then pulverized 4-Å MS followed by 4-methylmorpholine *N*-oxide (64 mg, 0.071 mmol) was added under argon and stirred for 20 min, and then tetrapropylammonium perruthenate (6.0 mg, 0.017 mmol) was added. After 0.5 h, silica gel (1 g) was added and the reaction mixture was filtered and washed with CH_2Cl_2 (2 × 5 mL) and (AcOEt:hexanes, 1:4) (2 × 5 mL) and evaporated to dryness in

vacuo. The residue was purified using flash column chromatography on silica gel (AcOEt:hexane, 1:10−1:5) affording **37** (209 mg, 87%) as a slightly yellow oil. R_f 0.62 (AcOEt:heptane, 1:3); $[\alpha]_D^{23}$ + 30.2 (*c* 1.1, $CHCl_3$); IR (film) 2956, 2926, 2855, 1686, 1572, 1464, 1376, 1253, 1095, 1030, 838, 778, 760; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.35 (s, 1H), 5.55 (bs, 1H), 4.73 (s, 1H), 4.71 (s, 1H), 4.70 (d, *J* = 6.6 Hz, 1H), 4.63 (d, *J* = 6.6 Hz, 1H), 4.02 (d, *J* = 7.4 Hz, 1H), 3.66 (t, *J* = 7.1 Hz, 2H), 3.35 (s, 3H), 3.00 (app. t, *J* = 7.0 Hz, 2H), 2.62 (dd, *J* = 5.1, 17.3 Hz, 1H), 2.56 (dd, *J* = 5.1, 17.3 Hz, 1H), 2.41 (ddd, *J* = 4.9, 10.9, 10.9 Hz, 1H), 2.35−2.30 (m, 1H), 2.18−2.11 (m, 1H), 1.95−1.90 (m, 1H), 1.71 (s, 3H), 1.63 (s, 3H), 1.52−1.46 (m, 6H), 1.32 (app. quintet, *J* = 7.3 Hz, 6H), 0.97−0.89 (m, 24H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 147.0, 138.4, 134.2, 125.0, 113.2, 97.0, 82.6, 63.0, 56.1, 54.4, 46.3, 44.5, 39.2, 39.1, 30.0, 29.0, 27.4, 26.1, 20.1, 18.6, 18.5, 13.7, 10.0, −5.2; High-resolution mass spectrometry (electrospray ionization) (HRMS (ESI)) calcd for $C_{14}H_{21}O_3$ [M − H]: 237.1491; found 237.1483.

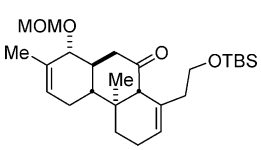


(3*E*)-4-(6-(Benzyloxy)-5,6-dihydro-4*H*-pyran-3-yl)-6-*tert*-butyldimethylsilyloxy-1-((1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)hex-3-en-2-one (11). A solution of stannane **37** (555 mg, 0.78 mmol) in CH_2Cl_2 (50 mL) was cooled to 0 °C, and a solution of iodine (201 mg, 0.79 mmol) in CH_2Cl_2 (20 mL) was added dropwise over a period of 2 min. The ice bath was removed, and the mixture was stirred under argon for 0.5 h. The reaction mixture was washed with a saturated sodium thiosulfate solution (2 × 20 mL). The organic phase was dried (Na_2SO_4), filtered, and evaporated to dryness in vacuo. The residue was subjected to flash column chromatography on silica gel (AcOEt:hexane, 1:19) affording the desired iodide (179 mg, 42%) as a colorless oil. The iodide was used immediately in the next step. A 30-mL Schlenk-tube was charged with LiCl (84 mg, 1.98 mmol) and flame dried under high vacuum. Upon cooling, tetrakis-(triphenylphosphine)palladium(0) (34 mg, 0.03 mmol) and copper-(I) chloride (163 mg, 1.65 mmol) were added, and the mixture was degassed (4×) under high vacuum with an argon purge. The iodide (179 mg, 0.33 mmol) and stannane **10** (188 mg, 0.39 mmol) were dissolved in dimethyl sulfoxide (4 mL) and added to the salts. The resulting mixture was rigorously degassed (4×) by the freeze−pump−thaw process (−78 °C to room temperature (rt), Ar). The reaction mixture was stirred at rt for 8 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with a mixture of brine and 5% ammonium hydroxide (20 mL, 1:1). The aqueous layer was further extracted with diethyl ether (2 × 10 mL), and the combined organic layers were washed with water (2 × 20 mL) and brine (20 mL), dried (Na_2SO_4), and evaporated to dryness in vacuo. The residue was purified by flash column chromatography on demetalated silica gel[22] (AcOEt:hexane, 1:19−1:3) providing **11** (115 mg, 57%) as a colorless oil. R_f 0.45 (AcOEt:heptane, 1:3); $[\alpha]_D^{23}$ +51.2 (*c* 0.7, $CDCl_3$); IR (film) 2929, 2856, 1676, 1615, 1568, 1458, 1352, 1256, 1206, 1162, 1092, 1057, 1030, 918, 893, 840, 780; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.28 (m, 5H), 7.10 (s, 1H), 6.03 (s, 1H), 5.55 (bs, 1H), 5.14 (app. t, *J* = 2.7 Hz, 1H), 4.83 (d, *J* = 12.1 Hz, 1H), 4.73−4.70 (m, 2H), 4.64−4.61 (s, 2H), 4.04 (d, *J* = 9.0 Hz, 1H), 3.76 (app. t, *J* = 6.6 Hz, 2H), 3.35 (s, 3H), 2.97 (app. t, *J* = 6.6 Hz, 2H), 2.64 (ddd, *J* = 3.5, 5.0, 17.1 Hz, 1H), 2.57 (ddd, *J* = 2.9, 4.8, 17.1 Hz, 1H), 2.46−2.31 (m, 2H), 2.19−2.11 (m, 2H), 2.04−1.99 (m, 1H), 1.96−1.90 (m 1H), 1.84 (dddd, *J* = 2.6, 6.2, 10.7, 13.4 Hz, 1H), 1.72 (s, 3H), 1.64 (s, 3H), 1.26 (dd, *J* = 2.7, 2.7 Hz, 1H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 199.1, 152.8, 147.1, 137.4, 134.2, 128.4, 127.8, 125.0, 118.9, 115.1, 113.0, 97.0, 95.7, 82.5, 69.7, 63.8, 56.1, 46.1, 45.3, 39.2, 39.1, 31.5, 30.1, 25.9, 20.1, 18.7, 18.3, 17.5, −5.3, −5.4; Anal. Calcd for $C_{36}H_{54}O_6Si$: C, 70.78; H, 8.91. Found: C, 70.69; H, 8.88.



(3*E*)-4-(2-[*tert*-Butyldimethylsilyloxy]ethyl)-1-((1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)-hexa-3,5-dien-2-ol (13). A solution of the β-stannylated allylic alcohol **9a** in CH_2Cl_2 (10 mL) was cooled to −78 °C, and a solution of iodine was added at once and stirred under argon for 5 min. The reaction mixture was washed with a saturated sodium thiosulfate solution (2 × 10 mL). The organic phase was dried (Na_2SO_4), and tetra-*n*-butylammonium diphenylphosphinate (Sn-scavenger)[23] was added and stirred for 5 min before the mixture was filtered and evaporated to dryness in vacuo. The residue was subjected to flash column chromatography on silica gel (AcOEt:hexane, 1:19) affording the desired iodide (130 mg, 84%) as a colorless oil. The iodide was used immediately in the next step. A 30-mL Schlenk tube was charged with LiCl (30.6 mg, 0.72 mmol) and flame-dried under high vacuum. Upon cooling, tetrakis-(triphenylphosphine)palladium(0) (12.5 mg, 0.010 mmol) and copper(I) chloride (59 mg, 0.60 mmol) were added, and the mixture was degassed (4×) under high vacuum with an argon purge. The iodide (66 mg, 0.12 mmol) and vinyltributylstannane (45.7 mg, 0.144 mmol) were dissolved in dimethyl sulfoxide (2 mL) and added to the salts. The resulting mixture was rigorously degassed (4×) by the freeze−pump−thaw process (−78 °C−rt, Ar). The reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with diethyl ether (10 mL) and washed with a mixture of brine and 5% ammonium hydroxide (10 mL, 1:1). The aqueous layer was further extracted with diethyl ether (2 × 5 mL), and the combined organic layers were washed with water (2 × 10 mL) and brine (10 mL), dried (Na_2SO_4), and evaporated to dryness in vacuo. The residue was purified by flash column chromatography on demetalated silica gel (AcOEt:hexane, 1:19−1:3) providing **13** (23 mg, 43%) as a colorless oil.

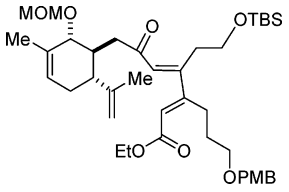
13: R_f 0.47 (AcOEt:heptane, 1:3); $[\alpha]_D^{23}$ +19.0 (*c* 1.0, $CHCl_3$); IR (film) 3440, 2927, 1643, 1471, 1430, 1375, 1140, 1094, 1028, 778; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.23 (dd, *J* = 10.8, 17.6 Hz, 1H), 6.00 (s, 1H), 5.59 (d, *J* = 8.2 Hz, 1H), 5.56 (bs, 1H), 5.14 (d, *J* = 17.6 Hz, 1H), 4.98 (d, *J* = 17.6 Hz, 1H), 4.76 (d, *J* = 6.5 Hz, 1H), 4.74 (s, 2H), 4.68−4.59 (m, 2H), 4.09 (d, *J* = 6.6 Hz, 1H), 3.71−3.58 (m, 2H), 3.49 (d, *J* = 3.4 Hz, 1H), 4.41 (s, 3H), 2.63−2.43 (m, 2H), 2.24 (td, *J* = 5.1, 9.5 Hz, 1H), 2.16−2.04 (m, 1H), 1.99 (dd, *J* = 4.0, 7.2 Hz, 1H) 1.95−1.85 (m, 1H), 1.80−1.69 (m, 2H), 1.66 (s, 3H), 1.63 (s, 3H), 1.39 (ddd, *J* = 4.3, 7.1, 14.3 Hz, 1H), 0.84 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 147.1, 139.8, 138.1, 135.8, 133.5, 128.5, 125.8, 112.5, 95.9, 82.3, 64.7, 61.8, 56.2, 46.2, 39.0, 37.8, 29.92 29.90, 26.0, 20.4, 18.7, 18.5, −5.4. HRMS (ESI) calcd for $C_{26}H_{46}O_4Si$ [M + H]$^+$: 451.3238; found 451.3231.



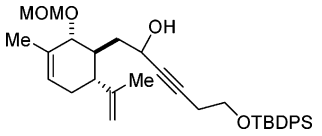
(1*R*,4a*R*,4b*S*,8a*R*,10a*S*)-4,4a,5,6,10,10a-Hexahydro-8-(2-[*tert*-butyldimethylsilyloxy]-ethyl)-1-(methoxymethoxy)-2,4b-dimethylphenanthren-9(1*H*,4b*H*,8a*H*)-one (14). Diene **13** (23 mg,

(22) Hubbard, J. S.; Harris, T. M. *J.Org. Chem.* **1981**, *46*, 2566−2570.

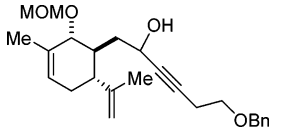
0.051 mmol) was dissolved in CH_2Cl_2 (2 mL), then pulverized 4-Å MS followed by 4-methylmorpholine *N*-oxide (10 mg, 0.071 mmol) was added under argon and stirred for 20 min, and then tetrapropylammonium perruthenate (1.0 mg, 0.026 mmol) was added. After 0.5 h, the reaction was complete based on analytical thin-layer chromatography (TLC) analysis. Silica gel (1 g) was added, and the reaction mixture was filtered and washed with CH_2Cl_2 (6 × 5 mL) and 20% AcOEt in hexanes (2 × 5 mL) affording the desired enone (14 mg, 61%) as a slightly yellow oil, which was immediately taken to the next step. The enone (14 mg, 0.031 mmol) was dissolved in d_8-toluene (0.7 mL) in a sealed NMR tube then warmed to reflux by placing the tube in a preheated oilbath at 110 °C for 4 days. The mixture was cooled to rt and purified directly using flash column chromatography on silica gel (AcOEt:hexane, 1:10) affording cycloadduct **14** (13 mg, 93%) as a colorless oil. **14**: R_f 0.40 (AcOEt:hexane, 1:3); $[\alpha]_D^{23}$ −15.0 (*c* 1.2, $CDCl_3$); IR (film) 2942, 1680, 1512, 1465, 1380, 1375, 1299, 808, 732; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.54 (bs, 1H), 4.70 (d, J = 7.0 Hz, 1H), 4.68 (d, J = 7.0 Hz, 1H), 3.91 (d, J = 7.7 Hz, 1H), 3.65−4.55 (m, 2H), 3.44 (s, 3H), 3.26 (bs, 1H), 2.76 (dd, J = 5.3, 12.3 Hz, 1H), 2.61 (dt, J = 6.2, 12.7 Hz, 1H), 2.31−2.17 (m, 4H), 2.11 (dt, J = 4.8, 17.4 Hz, 1H), 2.04−1.99 (m, 1H), 1.88−1.81 (m, 1H), 1.75−1.69 (m, 6H), 1.30 (td, J = 7.0, 11.8 Hz, 1H), 0.88 (s, 9H), 0.70 (s, 3H), 0.03 (s, 3H) 0.02 (s, 3H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 194.0, 134.6, 132.1, 124.8, 124,7, 97.6, 85.4, 63.1, 59.3, 56.4, 47.2, 46.9, 43.7, 41.1, 37.9, 33.2, 26.0, 25.7, 22.0, 19.5, 18.4, 12.8, −5.2; HRMS (ESI) calcd for $C_{26}H_{45}O_4Si$ $[M + H]^+$ 449.3082; found 449.3080.



(2*E*,4*E*)-Ethyl 4-(2-[*tert*-butyldimethylsilyloxy]-ethyl)-3-(3-(4-methoxy-benzyloxy)propyl)-7-((1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)-6-oxohepta-2,4-dienoate (17a). A 30-mL Schlenk tube was charged with LiCl and flame-dried under high vacuum. Upon cooling, tetrakis(triphenylphosphine)palladium(0) and copper(I) chloride were added, and the mixture was degassed (4×) under high vacuum with an argon purge. The freshly prepared iodide from **9a** and the stannane **15** dissolved in dimethyl sulfoxide (6 mL) were added. The resulting mixture was rigorously degassed (4×) by the freeze−pump−thaw process (−78 °C−rt, Ar). The reaction mixture was stirred at rt for 3 h. The reation mixture was diluted with diethyl ether (30 mL) and washed with a mixture of brine and 5% ammonium hydroxide (10 mL, 1:1). The aqueous layer was further extracted with diethyl ether (2 × 20 mL) and the combined organic layers were washed with water (2 × 20 mL) and brine (20 mL), dried (Na_2SO_4), and evaporated to dryness in vacuo. The residue was purified by flash column chromatography on demetalated silica gel (AcOEt:hexane, 1:4) providing diene **16a** (95 mg, 58%) as an inseparable mixture of diastereomers. Diene **16a** (95 mg, 0.136 mmol) was dissolved in CH_2Cl_2/CH_3CN ((9:1), 4 mL), then pulverized 4-Å molecular sieves (0.60 g) and 4-methylmorpholine *N*-oxide (27 mg, 0.20 mmol) was added under argon and stirred for 10 min, and then tetrapropylammonium perruthenate (4 mg, 0.011 mmol) was added. After 0.5 h, the reaction was complete according to TLC analysis. Silica gel (1 g) was added, and the reaction mixture was filtered and washed with CH_2Cl_2 (6 × 5 mL) and 20% AcOEt in hexanes (2 × 5 mL) providing **17a** (72 mg, 76%) as a colorless oil. **17a:** R_f 0.52 (AcOEt:hexane, 2:3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 6.29 (s, 1H), 5.98 (s, 1H), 5.55 (bs, 1H), 4.70 (s, 2H), 4.68 (d, J = 6.7 Hz, 1H), 4.62 (d, J = 6.7 Hz, 1H), 4.42 (s, 2H), 4.16 (q, J = 7.1 Hz, 2H), 3.99 (d, J = 8.3 Hz, 1H), 3.79 (s, 3H), 3.67 (t, J = 6.7 Hz, 2H), 3.47 (t, J = 6.4 Hz, 2H), 3.33 (s, 3H), 2.92 (t, J = 6.6 Hz, 2H), 2.89 (t, J = 7.9 Hz, 2H), 2.61 (dd, J = 2.3, 17.7 Hz, 1H), 2.58 (dd, J = 1.9, 17.7 Hz, 1H), 2.42−2.26 (m, 2H), 2.18−2.08 (m, 1H), 1.90 (app. d, J = 17.1 Hz, 1H), 1.70, (s, 3H), 1.69−1.65 (m, 2H), 1.60 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H), 0.85 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.9, 166.2, 160.9, 159.0, 154.3, 147.0, 134.2, 130.6, 129.2, 127.0, 125.1, 119.1, 113.6, 113.3, 97.0, 82.6, 72.5, 69.7, 62.6, 60.0, 56.0, 55.2, 46.4, 45.3, 39.3, 32.8, 30.0, 28.9, 26.0, 25.9, 20.0, 18.5, 18.2, 14.2, −5.5.



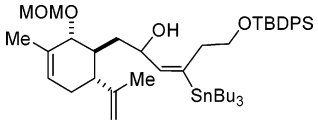
(*E*)−(*R*)-6-(*tert*-Butyl-diphenyl-silyloxy)-1-((1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)hex-3-yne-2-ol (8b). Aldehyde **7** (0.50 g, 2.1 mmol) was dissolved in THF (5 mL) and added under argon to a mixture of 1-*tert*-butyldiphenylsilanyloxy-but-3-yne (1.94 g, 6.3 mmol) and *n*-butyllithium (3.93 mL, 6.09 mmol, 1.55 M in hexanes) in dry THF (5 mL) at −78 °C, which had been stirred for 1 h prior to the addition. The reaction mixture was stirred for 2 h, then the temperature was raised to −20 °C for 1 h and then warmed to rt. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (20 mL) and diethyl ether (60 mL). The aqueous phase was extracted with diethyl ether (25 mL), and the organic phases were dried, filtered, and evaporated to dryness in vacuo. The residue was purified by flash column chromatography on silica gel (AcOEt: hexane, 1:4) affording **8b** (1.10 g, 96%) as a 1:1 mixture of diastereomers as well as 0.95 g (49%) of unreacted 1-*tert*-butyldiphenylsilanyloxy-but-3-yne. A portion of the less polar isomer was eluted free of its epimer and characterized. In practice, the mixture was used in the subsequent step without being separated. **8b:** R_f 0.46 (Et_2O:pentane, 1:4); $[\alpha]_D^{23}$ + 46.5 (*c* 0.2, $CDCl_3$); IR (film) 3440, 3071, 2925, 1671, 1644, 1428, 1378, 1360, 1210, 1149, 1113, 1030, 917, 900, 822, 736, 702, 614; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 7.0 Hz, 4H), 7.46−7.34 (m, 6H), 5.63 (bs, 1H), 4.76 (bs, 2H), 4.72 (d, J = 6.6 Hz, 1H), 4.69−4.60 (m, 2H), 4.15 (d, J = 7.8 Hz, 1H), 3.75 (t, J = 7.3 Hz, 2H), 3.73 (d, J = 7.4 Hz, 1H), 3.42 (s, 3H), 2.48 (td, J = 1.7, 7.2 Hz, 2H), 2.23 (td, J = 4.5, 10.0 Hz, 1H), 2.17−2.05 (m, 1H), 2.04−1.99 (m, 1H), 1.98−1.85 (m, 2H), 1.76−1.89 (m, 1H), 1.67 (s, 3H), 1.64 (s, 3H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.6, 135.5, 133.6, 133.2, 129.7, 127.6, 126.5, 113.0, 95.1, 83.0, 81.1, 62.5, 60.4, 56.3, 46.6, 40.7, 37.6, 30.2, 29.7, 26.8, 22.9, 20.0, 19.2, 18.3; Anal. Calcd for $C_{34}H_{46}O_4Si$: C, 74.68; H, 8.48. Found: C, 74.59; H, 8.51.



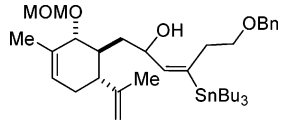
6-(Benzyloxy)-1-((1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)hex-3-yn-2-ol (8c). Aldehyde **7** (2 g, 8.39 mmol) was dissolved in THF (20 mL) and then added under argon to a mixture of *tert*-butyldimethylsilanyloxy-but-3-yne (4.03 g, 25.2 mmol) and *n*-butyllithium (15.8 mL, 25.2 mmol, 1.55 M in hexanes) in anhydrous THF (20 mL) at −78 °C, which had been stirred for 1 h prior to the addition, stirred for 2 h, and then the temperature was raised to −20 °C for 1 h and then warmed to rt. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (60 mL) and diethyl ether (200 mL). The aqueous phase was extracted with diethyl ether (100 mL), and the organic phases

(23) Srogl, J.; Allred, G. D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1997**, *119*, 12376.

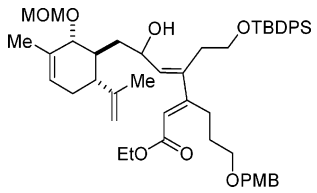
were dried, filtered, and evaporated to dryness in vacuo. The residue was purified by flash column chromatography on silica gel (AcOEt:hexane, 1:3) affording **8c** (3.84 g, 85%) as a 1:1 mixture of diastereomers as well as 1.97 g (49%) of unreacted *tert*-butyldimethylsilanyloxy-but-3-yne. A portion of both the less polar as well as the more polar isomer was eluted free of its epimer and characterized. In practice, the mixture was used in the subsequent step without being separated. **8c:** Mixture of diastereomers: FAB-MS calcd for [M + Na] 421.24; found 421.18; Anal. Calcd for $C_{25}H_{34}O_4$: C, 75.34; H, 8.60. Found: C, 75.17; H, 8.65. More polar diastereomer: R_f 0.21 (AcOEt:hexane, 1:3); $[\alpha]_D^{23}$ + 40.7 (*c* 1.2, CH_2Cl_2); IR (film) 3422, 2915, 2346, 1644, 1451, 1366, 1148, 1096, 1026, 899, 743, 700; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.26 (m, 5H), 5.60 (bs, 1H), 4.80 (bs, 2H), 4.76 (d, *J* = 6.8 Hz, 1H), 4.65 (d, *J* = 6.8 Hz, 1H), 4.54 (s, 2H), 4.52−4.44 (m, 1H), 3.96 (d, *J* = 8.1 Hz, 1H), 3.58 (t, *J* = 7.2 Hz, 2H), 3.45 (s, 3H), 3.18 (d, *J* = 5.5 Hz, 1H), 2.53 (td, *J* = 1.8, 7.2 Hz, 2H), 2.23 (td, *J* = 4.7, 10.0 Hz, 1H), 2.18−2.08 (m, 1H), 2.06−1.99 (m, 1H), 1.98−1.88 (m, 1H), 1.87−1.80 (m, 2H), 1.69 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 138.0, 133.2, 128.4, 127.7, 126.1, 113.1, 95.4, 83.1, 82.8, 80.0, 72.9, 68.4, 61.5, 56.5, 47.4, 40.6, 38.2, 30.1, 20.2, 20.1, 18.8; Less polar diastereomer: R_f 0.25 (AcOEt:hexane, 1:3); $[\alpha]_D^{23}$ + 44.8 (*c* 0.6, CH_2Cl_2); IR (film) 3447, 2922, 2238, 1643, 1438, 1359, 1148, 1094, 1030, 908, 743, 699; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.26 (m, 5H), 5.64 (bs, 1H), 4.79 (bs, 2H), 4.75 (d, *J* = 6.5 Hz, 1H), 4.72−4.68 (m, 1H) 4.67 (d, *J* = 6.5 Hz, 1H), 4.54 (s, 2H), 4.17 (d, *J* = 7.5 Hz, 1H), 3.88 (d, *J* = 7.6 Hz, 1H), 3.58 (t, *J* = 7.2 Hz, 2H), 3.45 (s, 3H), 2.53 (td, *J* = 1.9, 7.1 Hz, 2H), 2.25 (td, *J* = 4.8, 10.1 Hz, 1H), 2.13−2.02 (m, 1H), 1.96 (ddd, *J* = 2.3, 9.0, 14.3 Hz, 1H), 1.77−1.72 (m, 2H), 1.68 (s, 6H, 1.59 (ddd, *J* = 3.3, 8.1, 14.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 138.0, 133.2, 128.4, 127.6, 126.5, 113.0, 94.9, 83.0, 81.8, 80.9, 72.9, 68.4, 60.4, 56.3, 46.6, 40.6, 37.5, 30.2, 20.1, 20.0, 18.2.



(3*E*)-4-(Tributylstannyl)-6-(*tert*-butyl-diphenyl-silyloxy)-1-((1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)-cyclohex-3-enyl)hex-3-en-2-ol (9b). To a 1:1 mixture of epimeric alcohols **8b** (4.0 g, 7.3 mmol) and dichlorobis(tris(*o*-toloyl)-phosphine)palladium(II) in THF (73 mL) was added dropwise tributyltin hydride (6.9 mL, 25.6 mmol) over a period of 6 h, whereupon TLC showed complete conversion. The reaction mixture was evaporated to dryness and directly purified by flash column chromatography (AcOEt:hexane, 1:9) affording **9b** (3.5 g, 57%). A portion of the less polar isomer was eluted free of its epimer and characterized. In practice, the mixture was used in the subsequent step without being separated. **9b:** R_f 0.62 (AcOEt:heptane, 1:3); $[\alpha]_D^{23}$ + 11.1 (*c* 1.0, $CHCl_3$); IR (film) 3475, 3072, 2926, 2856, 1644, 1590, 1464, 1428, 1377, 1218, 1149, 1112, 1089, 1030, 936, 891, 823, 760, 702; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69−7.65 (m, 4H), 7.45−7.34 (m, 6H), 5.63 (bs, 1H), 5.54 (d, *J* = 7.6 Hz, *J*(Sn−H) = 68.8 Hz, 1H), 4.85−4.78 (m, 1H), 4.769 (d, *J* = 6.5 Hz, 1H), 4.766 (s, 2H), 4.69 (d, *J* = 6.5 Hz, 1H), 4.20 (d, *J* = 7.4 Hz, 1H), 3.57 (t, *J* = 7.8 Hz, 2H), 3.44 (s, 3H), 3.25 (d, *J* = 4.7 Hz, 1H), 2.72 (dt, *J* = 7.9, 13.6 Hz, 1H), 2.55 (dt, *J* = 7.9, 13.6 Hz, 1H), 2.26 (td, *J* = 5.0, 9.8 Hz, 1H), 2.19−2.08 (m, 1H), 2.06−1.90 (m, 2H), 1.79−1.71 (m, 2H) 1.70 (s, 3H), 1.67 (s, 3H), 1.43−1.31 (m, 6H), 1.23 (sextet, *J* = 7.1 Hz, 6H), 1.05 (s, 9H), 0.83 (t, *J* = 7.1 Hz, 9H) 0.78−0.72 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 146.6, 140.2, 135.5, 133.7, 133.4, 129.6, 127.6, 126.0, 112.5, 95.6, 82.4, 66.2, 64.8, 63.9, 56.2, 47.3, 46.1, 39.5, 37.8, 37.1, 30.1, 29.0, 27.3, 26.9, 20.3, 19.2, 18.6, 13.7, 9.5; FAB-MS calcd for $[M - C_4H_{11}]^+$ 781.37; found 781.4; Anal. Calcd for $C_{46}H_{74}O_4SiSn$: C, 65.94; H, 8.90. Found: C, 65.93; H, 8.98.

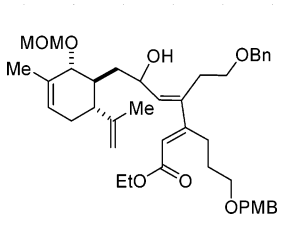


(3*E*)-4-(Tributylstannyl)-6-(benzyloxy)-1-((1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)hex-3-en-2-ol (9c). To a 1:1 mixture of epimeric alcohols **8c** (2.7 g, 6.77 mmol) and dichlorobis(tris(*o*-toloyl)phosphine)palladium(II) (53 mg, 0.067 mmol) in THF (68 mL) was added dropwise tributyltin hydride (6.4 mL, 23.7 mmol) over a period of 6 h, resulting in 80% conversion based on analytical TLC analysis. Additional tributyltin hydride (1.3 mL, 4.83 mmol) was added over the next 2 h, which resulted in complete conversion. The reaction mixture was evaporated to dryness and subsequently purified by flash column chromatography (AcOEt:heptane, 1:9) affording **9c** (2.98 g, 64%) as a colorless oil. A portion of both the less polar as well as the more polar isomer was eluted free of its epimer and characterized. In practice, the mixture was used in the subsequent step without being separated. **9c:** Less polar diastereomer: R_f 0.44 (AcOEt:heptane, 1:3); $[\alpha]_D^{23}$ + 3.6 (*c* 3.4, $CHCl_3$); IR (film) 3466, 2916, 1644, 1455, 1376, 1360, 1210, 1149, 1096, 1030, 909, 735, 698, 666; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.24 (m, 5H), 5.68 (d, *J* = 7.8 Hz, *J*(Sn−H) = 34.3 Hz, 1H), 5.61 (bs, 1H), 4.78 (d, *J* = 6.7 Hz, 1H), 4.76 (s, 2H), 4.75−4.68 (m, 1H), 4.67 (d, *J* = 6.7 Hz, 1H) 4.49 (s, 2H), 4.11 (d, *J* = 7.1 Hz, 1H), 3.43 (s, 3H), 3.41−3.35 (m, 2H), 2.80 (dt, *J* = 7.0, 13.8 Hz, 1H), 2.47 (dt, *J* = 5.8, 13.8 Hz, 1H), 2.23 (td, *J* = 4.9, 9.1 Hz, 1H), 2.19−1.89 (m, 3H), 1.78−1.72 (m, 1H), 1.70 (s, 3H), 1.68 (s, 3H), 1.50−1.39 (m, 6H), 1.28 (app. sextet, *J* = 7.1 Hz, 6H), 0.90−0.81 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2, 146.6, 141.5, 137.9, 133.3, 128.4, 127.9, 127.7, 125.8, 112.2, 95.7, 82.0, 73.2, 69.4, 64.1, 56.2, 45.9, 39.3, 37.7, 33.9, 29.7, 29.1, 27.4, 20.5, 18.9, 13.7, 9.6; FAB-MS calcd for $[M]^+$ 689.37; found 689.25; Anal. Calcd for $C_{37}H_{62}O_4Sn$: C, 64.44; H, 9.06. Found: C, 64.55; H, 9.21. More polar diastereomer: R_f 0.41 (AcOEt:hexane, 1:3); $[\alpha]_D^{23}$ + 17.3 (*c* 3.5, $CHCl_3$); IR (film) 3474, 2925, 1644, 1376, 1359, 1210, 1149, 1092, 1029, 890, 735, 697; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.25 (m, 5H), 5.68 (d, *J* = 7.9 Hz, *J*(Sn−H) = 34.7 Hz, 1H), 5.61 (bs, 1H), 4.79 (s, 1H), 4.76 (s, 1H), 4.73 (d, *J* = 6.8 Hz, 1H), 4.63 (d, *J* = 6.8 Hz, 1H), 4.59−4.52 (m, 1H), 4.49 (s, 2H), 3.87 (d, *J* = 6.1 Hz, 1H), 3.52−3.45 (m, 1H), 3.43 (s, 3H), 3.39−3.30 (m, 1H), 3.28 (d, *J* = 3.0 Hz, 1H), 2.84 (dt, *J* = 8.2, 13.6 Hz, 1H), 2.42 (dt, *J* = 5.0, 13.6 Hz, 1H), 2.21−2.11 (m, 2H), 2.05−1.93 (m, 2H), 1.72 (s, 3H), 1.71 (s, 3H), 1.67−1.54 (m, 2H), 1.50−1.39 (m, 6H), 1.29 (app. sextet, *J* = 7.1 Hz, 6H), 0.90−0.81 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2, 146.9, 142.2, 137.8, 133.1, 128.4, 127.9, 127.7, 125.7, 112.2, 95.2, 81.6, 73.2, 69.4, 65.1, 56.3, 46.8, 39.6, 37.8, 34.0, 29.3, 29.1, 27.4, 20.5, 19.5, 13.7, 9.6.

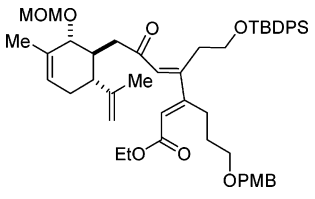


(2*E*,4*E*)-Ethyl 4-(2-(*tert*-butyl-diphenyl-silyloxy)-ethyl)-6-hydroxy-3-(3-(4-methoxy-benzyloxy)propyl)-7-[(1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl]-hepta-2,4-dienoate (16b). A solution of the β-stannylated allylic alcohol **9b** (1.8 g, 2.15 mmol) in CH_2Cl_2 (100 mL) was cooled to −78 °C, and a solution of iodine was added at once and stirred under argon for 5 min. The reaction mixture was washed with a saturated sodium thiosulfate solution (2 × 20 mL). The organic phase was dried (Na_2SO_4), and tetra-*n*-butylammonium diphenylphosphinate (Sn-scavenger)[23] was added and stirred for 5 min before the mixture was filtered and evaporated to dryness in vacuo. The residue was

subjected to flash column chromatography on silica gel (AcOEt:hexane, 1:20) affording the desired iodide (1.04 g, 71%) as a transparent oil. The iodide was immediately taken to the next step. A 100-mL Schlenk tube was charged with LiCl (391 mg, 9.21 mmol) and flame-dried under high vacuum. Upon cooling, tetrakis-(triphenylphosphine)palladium(0) (178 mg, 0.154 mmol) and copper(I) chloride (762 mg, 7.70 mmol) were added, and the mixture was degassed (4×) under high vacuum with an argon purge. The iodide (1.04 g, 1.54 mmol) and stannane **15** (961 mg, 1.69 mmol) were dissolved in dimethyl sulfoxide (50 mL) and degassed then added to the reaction mixture. The resulting mixture was rigorously degassed (2×) by the freeze−pump−thaw process (−78 °C−rt, Ar). The reaction mixture was stirred at room temperature for 20 h. The reaction mixture was diluted with diethyl ether (200 mL) and washed with a mixture of brine and 5% aqueous ammonium hydroxide (120 mL, 1:1). The aqueous layer was further extracted with diethyl ether (2 × 150 mL), and the combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), dried (Na_2SO_4), and evaporated to dryness in vacuo. The residue was purified by flash column chromatography on demetalated silica gel (AcOEt:hexane, 1:9) providing **16b** (751 mg, 59%) as a colorless oil. A portion of both the less polar as well as the more polar isomer was eluted free of its epimer and characterized. In practice, the mixture was used in the subsequent step without being separated. Less polar diastereomer: R_f 0.46 (AcOEt:heptane, 2:3); $[\alpha]_D^{23}$ + 9.5 (*c* 1.1, $CDCl_3$); IR (film) 3448, 2933, 1714, 1609, 1512, 1466, 1430, 1376, 1298, 1245, 1174, 1112, 1032, 882, 822, 743, 708; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (td, J = 1.6, 7.6 Hz, 4H), 7.41−7.32 (m, 6H), 7.24 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 5.80 (s, 1H), 5.79 (d, J = 7.5 Hz, 1H), 5.63 (bs, 1H), 4.80−4.72 (m, 4H), 4.67 (d, J = 6.5 Hz, 1H), 4.40 (s, 2H), 4.19 (d, J = 8.5 Hz, 1H), 4.13 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 3.61 (td, J = 2.3, 6.5 Hz, 2H), 3.44 (t, J = 6.7 Hz, 2H), 3.41 (s, 3H), 2.77 (td, J = 4.0, 7.8 Hz, 2H), 2.68−2.51 (m, 2H), 2.24 (td, J = 4.6, 10.1 Hz, 1H), 2.17−2.09 (m, 1H), 2.06−1.99 (m, 1H), 1.92 (dt, J = 3.4, 17.5 Hz, 1H), 1.79 (ddd, J = 3.0, 10.4, 14.3, 1H), 1.68 (s, 3H), 1.65 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H), 1.03 (s, 9H), 0.94−0.86 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 161.1, 159.0, 146.9, 138.0, 136.6, 135.5, 133.4, 130.8, 129.6, 129.2, 127.7, 126.2, 116.5, 113.7, 112.8, 95.6, 82.9, 72.4, 69.9, 68.1, 65.4, 62.7, 59.6, 56.2, 55.2, 46.5, 39.5, 37.7, 31.5, 30.4, 29.2, 26.8, 25.7, 20.2, 19.1, 18.3, 14.3; HRMS (ESI) calcd for $C_{50}H_{68}O_8SiNa$ $[M + Na]^+$ 847.4581; found 847.4569. More polar diastereomer: R_f 0.43 (AcOEt:heptane, 2:3); $[\alpha]_D^{23}$ + 11.0 (*c* 0.7, $CDCl_3$); IR (film) 3449, 2934, 2855, 1715, 1610, 1513, 1466, 1430, 1368, 1298, 1246, 1175, 1096, 1033, 918, 822, 744, 702; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (td, J = 1.7, 7.6 Hz, 4H), 7.41−7.32 (m, 6H), 7.25 (d, J = 7.8 Hz, 2H), 6.85 (d, J = 7.8 Hz, 2H), 5.77 (d, J = 8.1 Hz, 1H) 5.76 (s, 1H), 5.61 (bs, 1H), 4.78 (s, 1H), 4.76 (s, 1H), 4.74 (d, J = 6.8 Hz, 1H), 4.63 (d, J = 6.8 Hz, 1H), 4.50−4.42 (m, 1H), 4.40 (s, 2H), 4.13 (q, J = 7.1 Hz, 2H), 3.86 (d, J = 7.1 Hz, 1H), 3.79 (s, 3H), 3.61−3.55 (m, 2H), 3.43 (t, J = 7.0 Hz, 2H), 3.42 (s, 3H), 3.31 (d, J = 3.9 Hz, 1H), 2.75 (t, J = 6.7 Hz, 2H), 2.68−2.59 (m, 1H), 2.54−2.45 (m, 1H), 2.18 (d, J = 8.7 Hz, 1H), 2.05−1.85 (m, 2H), 1.71 (s, 3H), 1.70 (s, 3H), 1.67−1.58 (m, 1H), 1.36 (dd, J = 7.2, 14.9 Hz, 1H), 1.26 (t, J = 7.1 Hz, 3H), 1.03 (s, 9H), 0.92 (t, J = 7.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 160.9, 159.0, 146.9, 137.8, 137.1, 135.5, 133.3, 130.8, 129.7, 129.2, 127.7, 126.0, 116.4, 113.7, 113.0, 95.3, 82.8, 72.4, 69.9, 67.2, 62.8, 59.7, 56.4, 55.2, 47.7, 39.5, 38.0, 31.5, 30.0, 29.2, 26.8, 25.6, 20.2, 19.1, 19.0, 14.3.

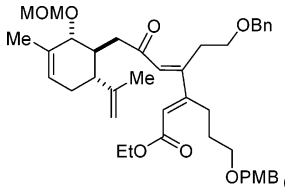


(2*E*,4*E*)-Ethyl 4-(2-[benzyloxy]-ethyl)-6-hydroxy-3-(3-(4-methoxy-benzyloxy)propyl)-7-((1*S*,2 *R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)-hepta-2,4-dienoate (16c). A solution of the β-stannylated allylic alcohol **9c** (2.98 g, 4.30 mmol) in CH_2Cl_2 (80 mL) was cooled to −78 °C, and a solution of iodine (1.31 g, 5.16 mmol) in CH_2Cl_2 (80 mL) was added in one portion and stirred under argon for 10 min. The reaction mixture was washed with a saturated sodium thiosulfate solution (2 × 20 mL). Tetrabutylammonium diphenylphosphinate (Sn-scavenger) was added and stirred for 5 min, then *n*-hexane (150 mL) and Na_2SO_4 were added and cooled to 0 °C then stirred for 10 min before the mixture was filtered and evaporated to dryness in vacuo. The residue was subjected to flash column chromatography on silica gel (AcOEt:heptane, 1:10−1:5) affording the desired iodide (1.2 g, 53%) as a cloudy white oil. The iodide was immediately taken on to the next step. A 100-mL Schlenk tube was charged with LiCl (580 mg, 13.7 mmol) and flame-dried under high vacuum. Upon cooling, tetrakis-(triphenylphosphine)palladium(0) (264 mg, 0.23 mmol) and copper(I) chloride (1.13 g, 11.4 mmol) were added, and the mixture was degassed (4×) under high vacuum with an argon purge. The iodide (1.20 g, 2.28 mmol) and stannane **15** (1.30 g, 2.28 mmol) were dissolved in dimethyl sulfoxide (50 mL) and degassed and then added to the reaction mixture. The resulting mixture was rigorously degassed (3×) by the freeze−pump−thaw process (−78 °C−rt, Ar). The reaction mixture was stirred at room temperature for 14 h before being diluted with diethyl ether (200 mL) and washed with a mixture of brine and 5% aqueous ammonium hydroxide (120 mL, 1:1). The aqueous layer was further extracted with diethyl ether (2 × 150 mL), and the combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), dried (Na_2SO_4), and evaporated to dryness in vacuo. The residue was purified by flash column chromatography on demetalated silica gel (AcOEt:heptane, 2:3) affording **16c** (788 mg, 51%) as a colorless oil and a mixture of diastereomers. A portion of the less polar isomer was eluted free of its epimer and characterized. In practice, the mixture was used in the subsequent step without being separated. Less polar diastereomer: R_f 0.29 (AcOEt:heptane, 2:3); $[\alpha]_D^{23}$ + 2.0 (*c* 0.5, CH_2Cl_2); IR (film) 3448, 2924, 1714, 1614, 1609, 1512, 1456, 1376, 1367, 1298, 1245, 1174, 1093, 1031, 882, 821, 743, 699; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.23 (m, 7H), 6.86 (d, J = 8.6 Hz, 2H), 5.83 (d, J = 8.4 Hz, 1H), 5.81 (s, 1H), 5.61 (bs, 1H), 4.77 (d, J = 6.5 Hz, 1H), 4.76 (s, 2H), 4.75−4.69 (m, 1H), 4.66 (d, J = 6.5 Hz, 1H), 4.46 (s, 2H), 4.41 (s, 2H), 4.15 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 3.54 (d, J = 3.6 Hz, 1H), 3.47 (t, J = 6.5 Hz, 1H), 3.42 (s, 3H), 2.99−2.89 (m, 1H), 2.80−2.69 (m, 2H), 2.53 (dt, J = 5.5, 14.2 Hz, 1H), 2.23 (td, J = 4.7, 9.6 Hz, 1H), 2.13−1.99 (m, 2H), 1.97−1.87 (m, 1H), 1.82−1.73 (m, 1H), 1.69 (s, 3H), 1.66 (s, 3H), 1.37 (ddd, J = 3.5, 7.9, 14.4 Hz, 1H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 160.7, 159.0, 147.0, 138.0, 137.7, 136.8, 133.4, 130.7, 129.2, 128.4, 127.8, 127.7, 126.0, 116.5, 113.6, 112.5, 95.6, 82.3, 72.4, 69.9, 68.1, 65.0, 59.7, 56.2, 55.2, 46.3, 39.2, 37.6, 29.9, 29.2, 28.8, 25.7, 20.3, 18.6, 14.3; HRMS (ESI) calcd for $C_{41}H_{56}O_8Na$ [M + Na] 699.3873; found 699.3888.



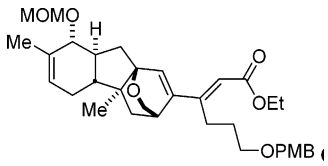
(2*E*,4*E*)-Ethyl 4-(2-(*tert*-butyl-diphenyl-silyloxy)-ethyl)-3-(3-(4-methoxy-benzyloxy)propyl)-7-[(1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl]-6-oxo-hepta-2,4-dienoate (17b). 16b (95 mg, 0.12 mmol) was dissolved in CH_2Cl_2/CH_3CN ((9:1), 4 mL), then pulverized 4-Å MS (0.6 g) followed

by 4-methylmorpholine *N*-oxide (23 mg, 0.17 mmol) were added under argon. The reaction mixture was stirred for 10 min, then tetrapropylammoniumperruthenate (4 mg, 0.011 mmol) was added. After 0.5 h, the reaction was complete according to TLC analysis. Silica gel (1 g) was added, and the reaction mixture was filtered and washed with CH_2Cl_2 (6 × 5 mL) and 20% AcOEt in *n*-hexane (2 × 5 mL) affording **17b** (73 mg, 77%) as a colorless oil. **17b:** R_f 0.48 (AcOEt:heptane, 1:4); $[\alpha]_D^{23}$ +25.0 (*c* 2.1, $CHCl_3$); IR (film) 3074, 2936, 2364, 1713, 1686, 1616, 1590, 1512, 1467, 1428, 1366, 1304, 1252, 1174, 1121, 925, 821, 743, 708; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, J = 7.4 Hz, 4H), 7.41−7.33 (m, 6H) 7.25 (d, J = 8.5 Hz, 2H) 6.87 (d, J = 8.5 Hz, 2H), 6.28 (s, 1H), 5.95 (s, 1H), 5.56 (bs, 1H), 4.66 (app. d, J = 6.6 Hz, 3H) 4.59 (d, J = 6.6 Hz, 1H), 4.40, (s, 2H), 4.16 (q, J = 7.1 Hz, 2H), 3.99 (d, J = 8.5 Hz, 1H), 3.80 (s, 3H), 3.71 (t, J = 6.6 Hz, 2H), 3.45 (t, J = 6.4 Hz, 2H), 3.29 (s, 3H), 3.01 (t, J = 6.6 Hz, 2H), 2.84 (t, J = 7.8 Hz, 2H), 2.61 (dd, J = 4.8, 17.5 Hz, 1H), 2.56 (dd, J = 4.8, 17.5 Hz, 1H), 2.36 (dt, J = 4.6, 10.7 Hz, 1H), 2.33−2.26 (m, 1H), 2.17−2.09 (m, 1H), 1.90 (app. d, J = 17.4 Hz, 1H), 1.71, (s, 3H), 1.70−1.64 (m, 2H), 1.57 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.0, 166.2, 161.1, 159.2, 154.3, 147.6, 135.8, 134.5, 133.6, 130.6, 129.5, 129.2, 129.0, 128.2, 127.6, 127.2, 125.3, 125.1, 119.4, 114.3, 113.6, 96.9, 82.7, 72.6, 69.7, 63.4, 60.1, 56.0, 55.2, 46.3, 45.2, 39.3, 32.4, 30.1, 28.9, 26.8, 25.9, 20.0, 19.1, 18.4, 14.4; HRMS (ESI) calcd for $C_{50}H_{67}O_8Si$ [M + H] 823.4605; found 823.4633.

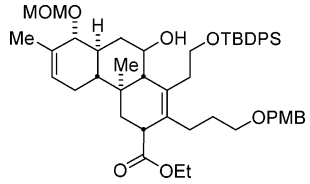


(2*E*,4*E*)-Ethyl-4-(2-(benzyloxy)-ethyl)-3-(3-(4-methoxy-benzyloxy)propyl)-7-[(1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl]-6-oxo-hepta-2,4-dienoate (17c). **16b** (389 mg, 0.575 mmol) was dissolved in CH_2Cl_2/CH_3CN ((9:1), 15 mL), then pulverized 4-Å MS (3 g) and 4-methylmorpholine-*N*-oxide (109 mg, 0.805 mmol) were added under argon and stirred for 10 min, and then tetrapropylammonium perruthenate (20 mg, 0.058 mmol) was added. After 0.5, h the reaction was complete according to TLC analysis. Silica gel (30 g) was added, and the reaction mixture was filtered and washed with CH_2Cl_2 (2 × 20 mL) and AcOEt (6 × 20 mL) and then evaporated to dryness. The residue was purified by flash column chromatography (AcOEt:heptane, 1:4) affording **17c** (304 mg, 78% and 20 mg contaminated with small amount of unidentified byproduct) as a colorless oil. R_f 0.35 (AcOEt:heptane, 1:3) $[\alpha]_D^{23}$ + 16.6 (*c* 2.0, $CHCl_3$); IR (film) 3406, 2935, 1716, 1688, 1610, 1513, 1451, 1368, 1298, 1246, 1175, 1096, 1033, 918, 883, 822, 744; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28−7.25 (m, 5H), 7.21 (d, J = 8.3 Hz, 2H), 6.82 (d, J = 8.3 Hz, 2H), 6.26 (s, 1H), 5.90 (s, 1H), 5.51 (bs, 1H), 4.66−4.63 (m, 3H), 4.57 (d, J = 6.7 Hz, 1H), 4.44 (s, 2H), 4.37 (s, 2H), 4.13 (q, J = 7.2 Hz, 2H), 3.96 (d, J = 7.8 Hz, 1H), 3.75 (s, 3H), 3.50 (t, J = 7.0 Hz, 2H), 3.42 (t, J = 6.4 Hz, 2H), 3.27 (s, 3H), 3.01 (t, J = 6.9 Hz, 2H), 2.88−2.82 (m, 2H), 2.59 (dd, J = 2.7, 17.3 Hz, 1H), 2.54 (dd, J = 2.3, 17.5 Hz, 1H), 2.39−2.22 (m, 2H), 2.15−2.02 (m, 1H), 1.86 (dt, J = 4.6, 17.3 Hz, 1H), 1.74−1.61 (m, 5H), 1.55 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.0, 166.1, 160.7, 159.1, 153.5, 147.0, 138.4, 134.2, 130.6, 129.3, 128.3, 127.5, 127.4, 127.3, 125.1, 118.9, 113.7, 113.4, 97.1, 82.7, 72.7, 72.5, 69.7, 69.1, 60.1, 56.0, 55.2, 46.4, 45.3, 39.3, 30.1, 29.8, 28.9, 26.0, 20.0, 18.5, 14.2; HRMS (ESI) calcd for $C_{41}H_{54}O_8$ [M+H] 675.3897; found 675.3861.

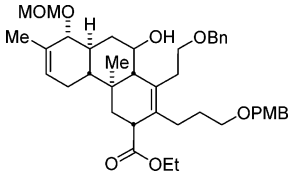
Compound 19. Ketone **17b** (20 mg, 0.024 mmol) was dissolved in anhydrous toluene (5 mL) in an oven-dried Carius tube and



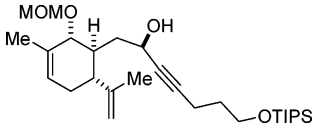
degassed by bubbling argon through for 1 min. The Carius tube was then lowered into a preheated saltbath at 195 °C, and the reaction mixture was stirred for 30 min before cooling to rt. The reaction mixture was evaporated to dryness and purified by flash column chromatography (Et_2O:hexane, 2:5) providing 12 mg (60%) of **19** as a colorless oil. **19:** R_f 0.41 (AcOEt:heptane, 1:4); $[\alpha]_D^{23}$ +7.5 (*c* 1.1, $CHCl_3$); IR (film) 2934, 2856, 1715, 1610, 1514, 1456, 1298, 1246, 1175, 1096, 1032, 918, 822; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 6.79 (s, 1H), 5.91 (s, 1H), 5.61 (bs, 1H), 4.76 (d, J = 6.8 Hz, 1H) 4.71 (d, J = 6.8 Hz, 1H), 4.44 (s, 2H), 4.18 (q, J = 7.1 Hz, 2H), 4.06 (d, J = 6.5 Hz, 1H), 3.80 (s, 3H), 3.69 (dd, J = 1.8, 6.9 Hz, 1H), 3.53 (t, J = 6.4 Hz, 2H), 3.40 (s, 3H), 3.15 (d, J = 7.0 Hz, 1H), 3.03−2.96 (m, 2H), 2.89 (ddd, J = 6.0, 9.9, 12.3 Hz, 1H),2.22 (dd, J = 9.7, 14.2 Hz, 1H), 2.11−2.05 (m, 2H), 1.98 (dd, J = 4.9, 14.3 Hz, 1H), 1.95−1.90 (m, 2H), 1.86−1.77 (m, 2H), 1.73 (s, 3H), 1.48 (d, J = 12.6 Hz, 1H), 1.29 (t, J = 7.1 Hz, 3H), 1.26 (s, 1H), 1.07 (ddd, J = 3.1, 3.6, 12.4 Hz, 1H), 0.56 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 155.2, 142.7, 136.7, 135.0, 130.7, 129.1, 126.3, 114.7, 113.7, 96.5, 84.9, 84.0, 72.5, 70.0, 68.1, 59.9, 55.6, 55.3, 50.1, 46.9, 45.7, 35.0, 33.9, 33.6, 30.1, 26.7, 25.2, 20.8, 19.6, 14.3; HRMS (ESI) calcd for $C_{34}H_{47}O_7$ [M + H] 567.3322; found 567.3308.



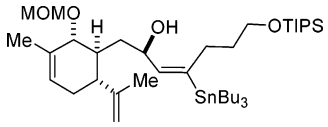
(3*R*,4a*S*,4b*R*,8*R*,8a*S*,10a*S*)-Ethyl 1-(2-(*tert*-butyl-diphenyl-silyloxy)-ethyl)-2-(3-(4-methoxybenzyloxy)propyl)-3,4,4a,4b,5,8,-8a,9,10,10a-decahydro-10-hydroxy-8-(methoxymethoxy)-4a,7-dimethylphenanthrene-3-carboxylate (20b). A diastereomeric mixture (ratio not determined) of **16b** (18 mg, 0.022 mmol) was dissolved in anhydrous toluene in a Carius tube and degassed by bubbling argon through for 2 min. The mixture of diastereomers was then heated to 195 °C for 24 h. The mixture was evaporated to dryness and purified by flash column chromatography (AcOEt:heptane, 2:3) affording **20b** (9 mg, 50%) as one diastereomer. **20b:** R_f 0.26 (AcOEt:heptane, 2:3); $[\alpha]_D^{23}$ −23.9 (*c* 0.8, $CDCl_3$); IR (film) 3440, 3049, 2934, 1724, 1611, 1513, 1465, 1428, 1368, 1299, 1246, 1175, 1094, 1032, 918, 822, 736, 703, 613; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (dd, J = 6.4, 14.0 Hz, 4H), 7.43−737 (m, 6H), 7.17 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.4 Hz, 2H), 5.53 (bs, 1H), 4.75 (d, J = 6.8 Hz, 1H), 4.72 (d, J = 6.8 Hz, 1H), 4.32 (s, 2H), 4.18−4.08 (m, 2H), 3.94 (app. td, J = 4.7, 10.5 Hz, 1H), 3.79 (s, 3H), 3.81−3.78 (m, 5H), 3.67 (d, J = 7.7 Hz, 1H), 3.46 (s, 3H), 3.41 (app. td, J = 3.4, 13.4 Hz, 1H), 3.32 (d, J = 3.6 Hz, 1H), 3.26 (td, J = 2.9, 6.3 Hz, 2H), 3.12 (t, J = 7.4 Hz, 1H), 2.80−2.68 (m, 2H), 2.51 (dt, J = 4.4, 12.8 Hz, 1H), 2.19−2.08 (m, 2H), 1.98 (dt, J = 5.0, 17.0 Hz, 1H), 1.85−1.64 (m, 6H), 1.59−1.45 (m, 2H), 1.24 (t, J = 7.2 Hz, 3H), 1.05 (s, 9H), 0.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 158.9, 147.2, 135.7, 133.8, 133.0, 132.6, 130.6, 129.8, 129.1, 127.7, 125.1, 113.6, 97.8, 85.3, 72.3, 69.8, 67.0, 65.2, 60.5, 56.3, 55.2, 55.0, 46.6, 43.4, 41.6, 39.5, 38.9, 38.7, 31.4, 28.6, 27.2, 26.8, 25.4, 19.9, 19.0, 17.1, 14.7, 14.2; HRMS calcd for $C_{50}H_{69}O_8$ [M + H] 825.4762; found 825.4720.



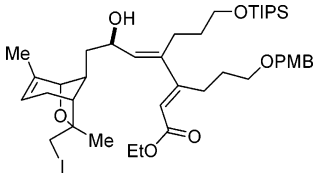
(3*R*,4a*S*,4b*R*,8*R*,8a*S*,10a*S*)-Ethyl 1-(2-benzyloxy-ethyl)-2-(3-(4-methoxybenzyloxy)propyl)-3,4,4a,4b,5,8,8a,9,10, 10a-decahydro-10-hydroxy-8-(methoxymethoxy)-4a,7-dimethylphenanthrene-3-carboxylate (20c). A diastereomeric mixture of **16c** (10 mg, 0.0148 mmol) was dissolved in toluene (5 mL) in a Carius tube and degassed by bubbling argon through for 2 min. The mixture was then heated to 195 °C for 24 h. The mixture was evaporated to dryness and purified by flash column chromatography (AcOEt:heptane, 2:3) providing a single diastereomer **20c** (3.8 mg, 38%) as a colorless film. **20c:** R_f 0.28 (AcOEt:heptane, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.31 (m, 3H), 7.26 (s, 2H), 7.23 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 5.51 (bs, 1H), 4.70 (d, J = 6.8 Hz, 1H), 4.66 (d, J = 6.8 Hz, 1H), 4.51 (d, J = 12.0 Hz, 1H), 4.48 (d, J = 12.0 Hz, 1H), 4.40 (s, 2H), 4.30−4.27 (m, 1H), 4.12−4.00 (m, 2H), 3.79 (s, 3H), 3.65 (d, J = 8.4 Hz, 1H), 3.56 (dd, J = 5.5, 8.9 Hz, 1H), 3.47 (dd, J = 8.1, 9.8 Hz, 1H), 3.43 (s, 3H), 3.38 (t, J = 6.4 Hz, 1H), 3.05−3.02 (m, 1H), (ddd, J = 7.1, 8.5, 14.5 Hz, 1H), 2.48−2.36 (m, 2H), 2.08 (dt, J = 4.7, 13.8 Hz, 1H), 2.02 (d, J = 4.5 Hz, 1H), 1.99−1.91 (m, 4H), 1.88−1.83 (m, 2H), 1.67−1.61 (m, 5H), 1.55−1.52 (m, 2H), 1.47 (td, J = 5.4, 11.9 Hz, 1H), (ddd, J = 3.9, 11.0, 14.5 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H), 0.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.9, 137.6, 134.0, 133.8, 132.7, 130.6, 129.2, 129.1, 128.4, 127.8, 127.7, 125.1, 113.7, 97.9, 85.3, 73.2, 72.4, 71.0, 69.9, 66.7, 60.5, 56.3, 55.2, 55.0, 54.4, 46.5, 43.4, 41.3, 39.6, 39.0, 38.8, 29.4, 28.8, 27.3, 25.4, 19.9, 17.2, 14.2; HRMS calcd for $C_{41}H_{56}O_8Na$ [M + Na] 699.3873; found 699.3871.



(*R*)-1-(Triisopropyl-silyloxy)-7-[(1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl]hept-4-yne-6-ol (38). A 100-mL Schlenk flask was charged with $Zn(OTf)_2$ (26.5 g, 72.9 mmol) and heated to 120 °C under vacuum for 24 h. After cooling to rt (+)-*N*-methylephedrine ((+)-NME) (13.3 g, 74.1 mmol) was added under Ar, purging with Ar (2×) and kept under vacuum for 15 min. Anhydrous toluene (16.5 mL) followed by Et_3N (10.3 mL) was added, and after 2 h triisopropyl(pent-4-ynyloxy)silane (**21**) (16.8 g, 69.82 mmol) was added in one portion. After 1 h, aldehyde **7** (5.89 g, 24.7 mmol) was added in one portion at rt and stirred under argon. The reaction mixture was stirred for 25 h upon which the reaction mixture had turned yellow. The mixture was diluted with AcOEt (180 mL), washed with saturated aqueous NH_4Cl (2 × 50 mL). The combined aqueous phases were back extracted with AcOEt (3 × 15 mL) and the combined organic phases were dried (Na_2SO_4) filtered and evaporated to dryness in vacuo. The residue was purified by flash column chromatography (Et_2O:*n*-hexane, 1:2) (3×) providing the alcohol **38** (8.49 g, 74%) as a colorless oil and as a single diastereomer. TIPS−butanol (8.6 g, 51%) was recovered from the column chromatography procedure and (+)-NME (12.0 g, 90%) was recovered from the combined aqueous phases by the addition of concentrated NaOH and subsequent collection of the precipitate. **38:** R_f 0.18 (Et_2O:hexane, 1:3); $[\alpha]_D^{23}$ +34.2 (*c* 2.3, $CHCl_3$); IR (film) 3441, 2944, 2866, 1644, 1472, 1463, 1381, 1149, 1105, 1028, 883, 682; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (bs, 1H), 4.80 (bs, 2H), 4.77 (d, J = 7.3 Hz, 1H), 4.66 (d, J = 7.3 Hz, 1H), 4.51−4.43 (m, 1H), 3.96 (d, J = 7.7 Hz, 1H), 3.74 (t, J = 6.1 Hz, 2H), 3.46 (s, 3H), 3.08 (d, J = 5.5 Hz, 1H), 2.32 (td, J = 1.9, 7.2 Hz, 2H), 2.21 (dd, J = 4.4, 10.3 Hz, 1H), 2.16−1.99 (m, 2H), 1.98−1.88 (m, 1H), 1.86−1.79 (m, 2H), 1.73−1.68 (m, 9H), 1.05 (s, 18H), 1.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.8, 133.4, 126.0, 113.0, 95.5, 84.3, 82.7, 82.0, 61.9, 61.5, 56.5, 47.4, 40.8, 38.2, 31.9, 30.1, 20.2, 18.0, 15.2, 11.9; FAB-MS calcd for [M + Na] 501.34; found 501.33; Anal. Calcd for $C_{27}H_{48}O_4Si$: C, 70.20; H, 10.53. Found: C, 69.96; H, 10.61.

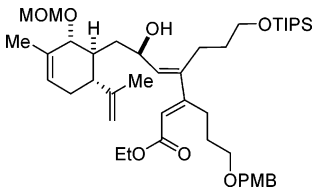


(*R*,4*E*)-4-(Tributylstannyl)-1-(tri-isopropyl-silyloxy)-7-((1S,-2R,6R)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)hept-4-ene-6-ol (22). To alcohol **38** (9.89 g, 20.7 mmol) and dichlorobis(tris(*o*-toloyl)phosphine)palladium(II) (168 mg, 63.9 mg, 0.21 mmol) in THF (200 mL) was added dropwise tributyltin hydride (18.6 g, 63.9 mmol) during 6 h. Full conversion was achieved after additional tributyltinhydride was added (24.8 g, 85.2 mmol) as indicated by TLC analysis. The reaction mixture was evaporated to a volume of 50 mL and purified by directly subjecting the reaction mixture to flash column chromatography (AcOEt: heptane, 1:9) and (AcOEt:heptane, 1:10) affording **22** (9.64 g, 61%) as a colorless oil. **22:** R_f 0.68 (AcOEt:heptane, 1:3); $[\alpha]_D^{23}$ + 23.8 (*c* 1.5, $CHCl_3$); IR (film) 3465, 2925, 1643, 1464, 1377, 1149, 1096, 1016, 882, 683; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (bs, 1H), 5.54 (d, J = 7.9 Hz, 1H), 4.78 (bs, 2H), 4.76 (d, J = 6.9 Hz, 1H), 4.65 (d, J = 6.9 Hz, 1H), 4.58−4.49 (m, 1H), 3.89 (d, J = 7.6 Hz, 1H), 3.68 (t, J = 6.3 Hz, 2H), 3.46 (s, 3H), 3.17 (d, J = 3.9 Hz, 1H), 2.49−2.37 (m, 2H), 2.30−2.11 (m, 3H), 2.08−1.90 (m, 2H), 1.76−1.68 (m, 10H), 1.64−1.41 (m, 12H), 1.30 (sextet, J = 7.0 Hz, 6H), 1.07 (s, 18H), 1.05 (s, 3H), 0.88 (t, J = 7.0 Hz, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2, 145.1, 144.7, 133.4, 125.9, 112.5, 95.3, 82.6, 66.1, 63.1, 56.4, 47.3, 40.0, 38.2, 33.9, 30.1, 29.8, 29.1, 27.4, 20.4, 19.2, 18.0, 13.7, 12.0, 9.7; MS (FAB) calcd for [M + Na] 793.46; found 793.46; Anal. Calcd for $C_{39}H_{76}O_4SiSn$: C, 62.41; H, 10.21. Found: C, 62.09; H, 10.36.

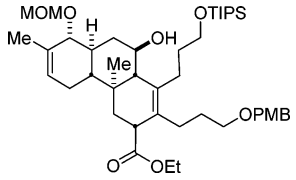


(*R*,2*E*,4*E*)-Ethyl 3-(3-(4-methoxybenzyloxy)propyl)-6-hydroxy-4-(3-(tri-isopropylsilyloxy)propy l)-7-(7-(iodomethyl)-4,7-dimethyl-6-oxa-bicyclo[3.2.1]oct-3-en-8-yl)hepta-2,4-dienoate (23). A solution of the β-stannylated allylic alcohol **22** (100 mg, 0.13 mmol) in CH_2Cl_2 (5 mL) was cooled to −78 °C and a solution of I_2 in CH_2Cl_2 (73 mg, 0.29 mmol, 5 mL, 1.1 equiv) was added in one portion and stirred under argon for 10 min. This was followed by the addition of another solution of I_2 in CH_2Cl_2 (73 mg, 0.29 mmol, 5 mL, 1.1 equiv), and the reaction mixture was stirred for 10 min. The reaction mixture was washed with a saturated sodium thiosulfate solution (10 mL), the aqueous phase was back extracted with CH_2Cl_2 (10 mL), and the combined organic phases were evaporated to dryness and subjected to flash column chromatography on silica gel (AcOEt:heptane, 1:10) affording the di-iodinated product (59 mg, 66%) as a transparent oil. The reaction was also tried with ICl providing the di-iodinated product in 60% yield (53 mg). The products from both reactions were immediately taken on to the next step. A 100-mL Schlenk tube was charged with LiCl and flame-dried under high vacuum. Upon cooling, tetrakis-(triphenylphosphine)palladium(0) and copper(I) chloride were added, and the mixture was degassed (4×) under high vacuum with an argon purge. The iodide (99 mg, 0.144 mmol) and the stannane

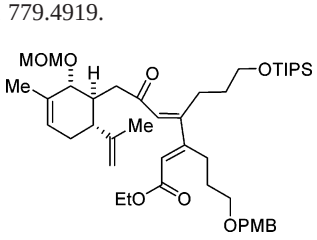
15 (108 mg, 0.19 mmol) were dissolved in dimethyl sulfoxide (2 mL) and were degassed and added to the Schlenk flask containing the salts. The flask was washed with DMSO (1 mL) and the washings were added to the reaction mixture. The resulting mixture was rigorously degassed (4×) by the freeze−pump−thaw process (−78 °C−rt, Ar). The reaction mixture was stirred at room temperature for 20 h. The reaction mixture was diluted with diethyl ether (20 mL) and washed with a mixture of brine and 5% ammonium hydroxide (12 mL, 1:1). The aqueous layer was further extracted with diethyl ether (2 × 15 mL), and the combined organic layers were washed with water (2 × 10 mL) and brine (10 mL), dried (Na_2SO_4), and evaporated to dryness in vacuo. The residue was purified by flash column chromatography on demetalated silica gel (AcOEt:heptane, 2:5) affording **23** (84 mg, 70%) as a colorless oil. **23:** R_f 0.21 (AcOEt:heptane, 1:2); $[\alpha]_D^{23}$ +1.4 (*c* 0.9, CH_2Cl_2); IR (film) 3442, 2933, 2864, 1713, 1612, 1514, 1464, 1368, 1302, 1248, 1178, 1099, 1037, 882, 819, 689; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 5.85 (s, 1H), 5.76 (d, J = 8.6 Hz, 1H), 5.32 (bs, 1H), 4.49−4.43 (m, 1H), 4.42 (s, 2H), 4.14 (q, J = 7.1 Hz, 2H), 4.03 (d, J = 4.5 Hz, 1H), 3.80 (s, 3H), 3.72−3.60 (m, 2H), 3.47 (t, J = 6.5 Hz, 2H), 3.34−3.27 (m, 2H), 3.02 (ddd, J = 6.4, 9.7, 13.0 Hz, 1H), 2.72−2.61 (m, 4H), 2.47−2.29 (m, 2H), 2.21−2.13 (m, 2H), 1.74−1.61 (m, 9H), 1.47 (m, 3H), 1.27 (t, J = 7.1 Hz, 3H), 1.07 (s, 18H), 1.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 160.8, 159.0, 141.7, 136.8, 134.6, 130.6, 129.2, 121.0, 116.9, 113.7, 83.7, 79.9, 72.5, 69.8, 67.1, 61.4, 59.8, 55.2, 42.8, 39.8, 34.2, 31.1, 29.2, 28.0, 25.5, 25.3, 23.5, 21.8, 18.01, 17.98, 14.3, 11.9.



(*R*,2*E*,4*E*)-Ethyl 3-(3-(4-methoxybenzyloxy)propyl)-6-hydroxy-4-(3-(tri-isopropylsilyloxy)-propyl)-7-((1*S*,2*R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)hepta-2,4-dienoate (24). A solution of the β-stannylated allylic alcohol **22** (490 mg, 0.64 mmol) in CH_2Cl_2 (30 mL) was cooled to −81 °C (Et_2O/CO_2) and a solution of I_2 in CH_2Cl_2 (178 mg, 0.70 mmol, 1.1 equiv, 20 mL) precooled to −81 °C was transferred using cannula to the reaction flask in one portion. The reaction mixture was stirred under argon for 1 min, then poured into a saturated sodium thiosulfate solution (10 mL), the aqueous phase was back extracted with CH_2Cl_2 (10 mL), and the combined organic phases were evaporated to dryness and subjected to flash column chromatography on demetalated silica gel (AcOEt:heptane, 1:10) affording the desired iodide (270 mg, 70%) as a slightly yellow oil and was immediately taken on to the Stille coupling. A 100-mL Schlenk tube was charged with LiCl (110 mg, 2.59 mmol) and flame-dried under high vacuum. Upon cooling, tetrakis(triphenylphosphine)palladium(0) (50 mg, 0.046 mmol) and copper(I) chloride (214 mg, 2.16 mmol) were added, and the mixture was degassed (4×) under high vacuum with an argon purge. The iodide (256 mg, 0.432 mmol) and stannane **15** (294 mg, 0.52 mmol) were dissolved in DMSO (1 mL) and were degassed and added to the Schlenk flask containing the salts. The flask that contained the iodide and the stannane **15** was washed with DMSO (1 mL) and the washings were added to the reaction mixture. The resulting mixture was rigorously degassed (3×) by the freeze−pump−thaw process (−78 °C−rt, Ar). The reaction mixture was stirred at rt overnight, then diluted with diethyl ether (30 mL) and washed with a mixture of brine and 5% aqueous ammonium hydroxide (30 mL, 1:1). The aqueous layer was further extracted with diethyl ether (2 × 30 mL), and the combined organic layers were dried (Na_2SO_4) and evaporated to dryness in vacuo. The residue was purified by flash column chromatography on demetalated silica gel (AcOEt:heptane, 1:3) and subsequently further purified on regular silica gel twice with (MeOH:CH_2Cl_2, 1:49) and once with (AcOEt:CH_2Cl_2, 1:9) affording **24** (202 mg, 63%) as a colorless oil. **24:** R_f 0.36 (MeOH:CH_2Cl_2, 3:97); $[\alpha]_D^{23}$ +6.0 (*c* 3.4, $CHCl_3$); IR (film) 3450, 2944, 2965, 1714, 1609, 1512, 1459, 1368, 1245, 1174, 1096, 1034, 882, 821, 683; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 5.85 (s, 1H), 5.68 (d, J = 8.3 Hz, 1H), 5.60 (bs, 1H), 4.78 (s, 2H), 4.74 (d, J = 6.8 Hz, 1H), 4.63 (d, J = 6.8 Hz, 1H), 4.49−4.42 (m, 1H), 4.41 (s, 2H), 4.13 (q, J = 7.1 Hz, 2H), 3.87 (d, J = 7.5 Hz, 1H), 3.78 (s, 3H), 3.65 (td, J = 1.6, 5.9 Hz, 2H), 3.46 (t, J = 6.7 Hz, 2H), 3.45−3.43 (m, 1H), 3.43 (s, 3H), 2.93−2.76 (m, 2H), 2.44−2.26 (m, 2H), 2.25−1.88 (m, 4H), 1.72 (s, 3H), 1.76−1.64 (m, 8H), 1.59−1.50 (m, 3H), 1.27 (t, J = 7.1 Hz, 3H), 1.05 (s, 18H), 1.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 161.0, 159.0, 147.0, 140.6, 135.3, 133.3, 130.7, 129.1, 126.0, 116.3, 113.6, 112.8, 95.3, 82.9, 72.4, 69.9, 67.1, 62.7, 59.6, 56.4, 55.2, 47.7, 39.6, 38.1, 32.1, 30.1, 29.2, 25.5, 24.5, 20.2, 19.0, 18.0, 14.2, 11.9; HRMS calcd for [M − C_3H_7] 713.4451; found 713.4356.

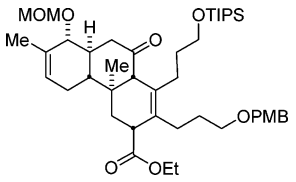


(3*R*,4a*S*,4b*R*,8*R*,8a*S*,10*R*,10a*S*)-Ethyl 2-(3-(4-methoxybenzyloxy)propyl)-3,4,4a,4b,5,8,8a,9,10,10a-decahydro-10-hydroxy-1-(3-(tri-isopropylsilyloxy)-propyl)-8-(methoxymethoxy)-4a,7-dimethylphenanthrene-3-carboxylate (25). The diastereomerically pure alcohol **24** (117 mg, 0.155 mmol) was dissolved in anhydrous toluene (10 mL) and transferred to a Carius tube and warmed to 205−210 °C in a saltbath and stirred overnight. At this point, NMR analysis ($CDCl_3$) indicated that no starting material was left. The reaction mixture was evaporated to dryness in vacuo and purified by flash column chromatography (AcOEt:CH_2Cl_2, 1:9−1:8) providing (101 mg, 87%) **25** as a colorless oil. **25:** R_f 0.36 (AcOEt:CH_2Cl_2, 1:4); $[\alpha]_D^{23}$ −32.01 (*c* 1.8, $CHCl_3$); IR (film) 3482, 2942, 1740, 1732, 1715, 1609, 1514, 1464, 1385, 1359, 1298, 1253, 1174, 1148, 1096, 1030, 917, 882, 821, 804, 735, 683; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 5.53 (bs, 1H), 4.74 (d, J = 6.9 Hz, 1H), 4.71 (d, J = 6.9 Hz, 1H), 4.40 (s, 2H), 4.19−4.03 (m, 2H), 3.94 (td, J = 4.7, 10.5 Hz), 3.79 (s, 3H) 3.73−3.67 (m, 2H), 3.62 (td, J = 3.7, 9.1 Hz), 3.44 (s, 3H), 3.39 (t, J = 6.4 Hz, 2H), 3.21 (bs, 1H), 3.09 (t, J = 7.6 Hz, 1H), 2.57 (td, J = 6.0, 12.9 Hz, 1H), 2.51 (dt, J = 4.4, 17.2 Hz, 1H), 2.36−2.25 (m, 2H), 2.13 (td, J = 5.5, 10.6 Hz, 1H), 1.97 (dt, J = 4.3, 17.3 Hz, 1H), 1.87−1.77 (m, 3H, H-5), 1.73−1.56 (m, 9H), 1.28−1.21 (app. t, J = 7.1 Hz, 4H), 1.11 (td, J = 7.2, 14.7 Hz, 1H), 1.08−1.05 (m, 21H), 0.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2, 159.0, 136.6, 133.6, 130.7, 130.5, 129.1, 125.3, 113.6, 97.6, 85.3, 72.4, 70.0, 66.8, 63.2, 60.4, 56.2, 55.2, 54.8, 46.5, 43.2, 41.3, 39.9, 39.1, 38.6, 32.2, 29.7, 29.4, 26.9, 25.4, 19.8, 18.0, 17.3, 14.2, 11.9; HRMS (ESI) calcd for $C_{44}H_{72}O_8SiNa$ [M + Na] 779.4894; found 779.4919.

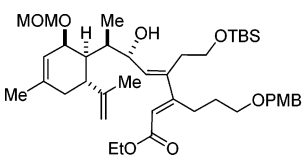


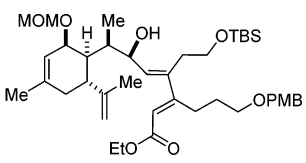
(2*E*,4*E*)-Ethyl 3-(3-(4-methoxybenzyloxy)propyl)-4-(3-(tri-isopropylsilyloxy)-propyl)-7-((1*S*,2 *R*,6*R*)-2-(methoxymethoxy)-3-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)-6-oxohepta-2,4-di-

enoate (26). Alcohol **24** (30 mg, 0.040 mmol) was dissolved in CH_2Cl_2/CH_3CN ((9:1), 2 mL), then pulverized 4-Å MS (0.5 g) and 4-methylmorpholine-*N*-oxide (7.6 mg, 0.056 mmol) was added under argon. The mixture was stirred for 10 min, then tetrapropylammonium perruthenate (1.4 mg, 0.004 mmol) was added. After 1 h, the reaction was complete according to TLC analysis. The reaction mixture was filtered through a plug of Celite and washed with 0.25% MeOH in CH_2Cl_2 (6 × 5 mL) and evaporated to dryness. The residue was purified by flash column chromatography (AcOEt:heptane, 1:4) affording **26** (24.5 mg, 81%) as a colorless oil. **26:** R_f: 0.48 (AcOEt:heptane, 1:3); $[\alpha]_D^{23}$ + 35.9 (*c* 1.1, $CHCl_3$); IR (film) 2942, 2865, 1716, 1688, 1609, 1513, 1460, 1367, 1246, 1175, 1096, 1034, 883, 822, 735, 683; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.3 Hz, 2H), 6.86 (d, J = 8.3 Hz, 2H), 6.24 (s, 1H), 5.94 (s, 1H), 5.54 (bs, 1H), 4.70 (s, 2H), 4.68 (d, J = 6.8 Hz, 1H), 4.61 (d, J = 6.8 Hz, 1H), 4.41 (s, 2H), 4.16 (q, J = 7.07 Hz, 2H), 3.99 (d, J = 7.7 Hz, 1H), 3.79 (s, 3H), 3.70 (t, J = 6.1 Hz, 2H), 3.47 (t, J = 6.4 Hz, 2H), 3.32 (s, 3H), 2.90−2.85 (m, 2H), 2.79−2.74 (m, 2H), 2.61 (dd, J = 4.1, 17.5 Hz, 1H), 2.57 (dd, J = 3.3, 17.5 Hz, 1H), 2.42−2.25 (m, 2H), 2.19−2.07 (m, 1H), 1.90 (dt, J = 4.4, 17.5 Hz, 1H), 1.75−1.65 (m, 5H), 1.62−1.54 (m, 6H), 1.28 (t, J = 7.1 Hz, 3H), 1.07−1.00 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.1, 166.2, 160.4, 159.1, 156.7, 147.0, 134.2, 130.6, 129.2, 126.1, 125.1, 118.7, 113.7, 113.3, 97.1, 82.7, 72.5, 72.5, 69.7, 63.1, 60.0, 56.0, 55.2, 46.4, 45.2, 39.3, 32.2, 30.1, 29.0, 25.68, 25, 59, 20.0, 18.4, 18.0, 14.2; HRMS (ESI) calcd for $C_{44}H_{70}O_8SiNa$ [M + Na] 777.4738; found 777.4767.

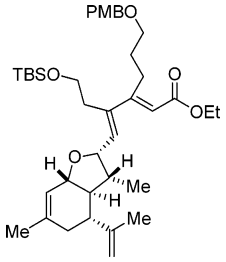


(3*R*,4a*S*,4b*R*,8*R*,8a*S*,10a*S*)-Ethyl 2-(3-(4-methoxybenzyloxy)-propyl)-3,4,4a,4b,5,8,8a,9,10,10a-decahydro-1-(3-(tri-isopropylsilyloxy)-propyl)-8-(methoxymethoxy)-4a,7-dimethyl-10-oxophenanthrene-3-carboxylate (27). The keto-ester **26** (50 mg, 0.066 mmol) was dissolved in anhydrous toluene (5 mL) and transferred to a Carius tube. The solution was degassed by bubbling argon through and lowered into a preheated 240 °C saltbath and stirred for 2.5 h. The reaction mixture was evaporated to dryness in vacuo and purified by flash column chromatography (AcOEt:pentane, 1:5−1:3) providing **26** (33 mg, 66%) as a colorless oil. **26:** R_f 0.34 (AcOEt:pentane, 1:2); $[\alpha]_D^{23}$ +42.0 (*c* 0.7, $CDCl_3$); IR (film) 2943, 2864, 1716, 1610, 1512, 1467, 1386, 1368, 1351, 1298, 1246, 1175, 1148, 1096, 1033, 918, 882, 822, 683; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 5.54 (bs, 1H), 4.69 (d, J = 7.0 Hz, 1H), 4.66 (d, J = 7.0 Hz, 1H), 4.39 (s, 2H), 4.20−4.01 (m, 2H), 3.90 (d, J = 8.8 Hz, 1H), 3.80 (s, 3H) 3.62 (td, J = 1.5, 6.4 Hz, 2H), 3.42 (s, 3H), 3.39 (td, J = 1.3, 6.4 Hz, 2H), 3.20 (bs, 1H), 3.06 (d, J = 6.8 Hz, 1H), 2.73 (dd, J = 5.5, 12.1 Hz, 1H), 2.55−2.25 (m, 5H), 2.22−2.07 (m, 3H), 2.00 (dd, J = 7.5, 14.7 Hz, 2H), 1.83 (app. d, J = 14.3 Hz, 1H), 1.74−1.64 (m, 6H), 1.55−1.40 (m, 3H) 1.22 (t, J = 7.2 Hz, 3H), 1.05 (s, 18H), 1.04 (s, 3H), 0.61 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.3, 174.5, 159.0, 134.6, 130.9, 130.6, 129.5, 129.2, 124.6, 113.7, 97.6, 85.2, 72.5, 70.0, 63.6, 60.7, 59.4, 56.5, 55.2, 54.4, 47.3, 46.8, 43.6, 42.6, 40.7, 32.2, 29.2, 28.9, 25.9, 25.6, 19.5, 18.0, 14.1, 13.4, 11.9; HRMS (ESI) calcd for $C_{44}H_{70}O_8Si$ [M + H] 755.4918; found 755.4921.

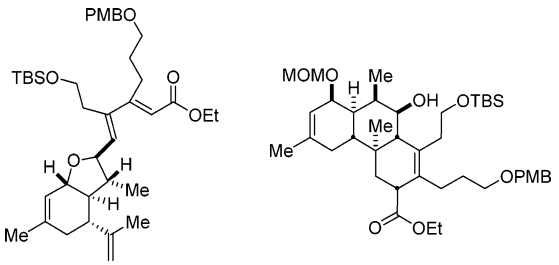




(2*E*,4*E*,6*R*,7*R*)-Ethyl 3-(3-(4-methoxybenzyloxy)propyl)-6-hydroxy-4-(2-(*tert*-butyldimethylsilyloxy)-ethyl)-7-((1*R*,2*S*,6*R*)-2-(methoxymethoxy)-4-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)-octa-2,4-dienoate (29a) and (2*E*,4*E*,6*S*,7*R*)-Ethyl 3-(3-(4-methoxybenzyloxy)propyl)-6-hydroxy-4-(2-(*tert*-butyldimethylsilyloxy)-ethyl)-7-((1*R*,2*S*,6*R*)-2-(methoxymethoxy)-4-methyl-6-(prop-1-en-2-yl)cyclohex-3-enyl)octa-2,4-dienoate (29b). A 30-mL Schlenk tube was charged with LiCl (37 mg, 1.07 mmol) and flame-dried under high vacuum. Upon cooling, tetrakis(triphenylphosphine)-palladium(0) (21 mg, 0.018 mmol) and copper(I) chloride (89 mg, 0.90 mmol) were added, and the mixture was degassed (4×) under high vacuum with an argon purge. The iodide (prepared from stannane **28**) (101 mg, 0.179 mmol) and stannane **15** (122 mg, 0.21 mmol) was dissolved in dimethyl sulfoxide (6 mL), degassed by bubbling argon through for 2 min, and then added to the solids under vacuum at −78 °C. The resulting mixture was rigorously degassed (3×) by the freeze−pump−thaw process (−78 °C−rt, Ar). The reaction mixture was stirred at room temperature for 18 h. The reaction mixture was diluted with diethyl ether (10 mL) and washed with a mixture of brine and 5% aqueous ammonium hydroxide (10 mL, 1:1). The aqueous layer was further extracted with diethyl ether (10 mL), and the combined organic layers were washed with water (10 mL), dried (Na_2SO_4), and evaporated to dryness in vacuo. The residue was purified by flash column chromatography on demetalated silica gel (AcOEt:pentane, 1:20−1:5) followed by flash column chromatography on silica gel (Et_2O:CH_2Cl_2, 1:20−1:10) providing the two separated diastereomers of the title compound (major diastereomer **29a**, 50 mg, 39%; minor diastereomer **29b**, 22 mg, 17%, total yield 56%) each as colorless oils**.** Major diastereomer **29a**: R_f 0.42 (Et_2O:CH_2Cl_2, 1:4); $[\alpha]_D^{23}$ − 23.7 (*c* 2.4, $CDCl_3$); IR (film) 3406, 2935, 1715, 1610, 1513, 1466, 1368, 1246, 1166, 1096, 1032, 831, 778; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 7.2 Hz, 2H), 6.86 (d, J = 7.2 Hz, 2H), 5.83 (s, 1H), 5.82 (d, J = 7.2 Hz, 1H), 5.68 (bs, 1H), 4.90−4.86 (m, 3H), 4.76 (s, 1H), 4.68 (d, J = 7.3 Hz, 1H), 4.61 (d, J = 6.7 Hz, 1H), 4.41 (s, 2H), 4.25 (bs, 1H), 4.14 (q, J = 7.2 Hz, 2H), 3.80 (s, 3H), 3.54 (t, J = 6.8 Hz, 2H), 3.47 (t, J = 6.7 Hz, 2H), 3.42 (s, 3H), 2.88−2.78 (m, 3H), 2.63−2.54 (m, 1H), 2.53−2.43 (m, 1H), 2.12 (dd, J = 6.2, 12.3 Hz, 1H), 2.03−1.87 (m, 1H), 1.82−1.75 (m, 1H), 1.72 (s, 3H), 1.71−1.67 (m, 5H), 1.26 (t, J = 7.2 Hz, 3H), 1.05 (d, J = 6.9 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 161.8, 157.2, 146.8, 139.9, 136.1, 130.8, 129.2, 119.9, 116.0, 113.9, 113.6, 93.9, 72.4, 69.9, 68.6, 66.4, 62.1, 59.6, 56.3, 55.2, 52.2, 44.8, 40.1, 39.6, 37.3, 31.8, 29.1, 25.9, 23.0, 18.9, 18.3, 14.3, 11.9, −5.4; HRMS (ESI) calcd for $C_{41}H_{66}O_8SiNa$ [M+Na]: 737.4420; found 737.4416. Minor diastereomer **29b**: R_f: 0.34 (Et_2O:CH_2Cl_2, 1:4); $[\alpha]_D^{23}$ −11.0 (*c* 1.0, $CDCl_3$); IR (film) 3442, 2934, 1715, 1610, 1513, 1468, 1368, 1298, 1246, 1174, 1096, 1035, 830, 778; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 5.81 (s, 1H), 5.75 (d, J = 8.6 Hz, 1H), 5.63 (bs, 1H), 4.86 (bs, 2H), 4.76 (d, J = 6.6 Hz, 1H), 4.64 (d, J = 6.6 Hz, 1H), 4.41 (s, 2H), 4.28 (t, J = 9.4 Hz, 1H), 4.15 (q, J = 7.1 Hz, 2H), 4.08 (d, J = 4.3 Hz, 1H) 3.80 (s, 3H), 3.68−3.61 (m, 1H), 3.56−3.49 (m, 1H), 3.47 (t, J = 6.4 Hz, 2H), 3.38 (s, 3H), 3.16 (d, J = 2.3 Hz, 1H), 2.98 (ddd, J = 6.5, 9.8, 12.7 Hz, 1H), 2.84−2.67 (m, 2H), 2.61 (app. q, J = 7.2 Hz, 1H), 2.43 (dt, J = 5.6, 14.1 Hz, 1H), 2.14 (dt, J = 2.8, 11.0 Hz, 1H), 2.01 (app. d, J = 7.6 Hz, 2H), 1.87 (t, J = 7.2 Hz, 1H), 1.77 (s, 3H), 1.74−1.66 (m, 5H), 1.27 (t, J = 7.1 Hz, 3H), 0.95 (d, J = 6.9 Hz, 3H), 0.87 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 161.1, 159.0, 148.3, 139.7, 138.2, 136.4, 130.7, 129.2, 121.5, 116.6, 113.7, 113.0, 95.4, 74.2, 72.4, 69.9, 69.8, 61.5, 59.8, 55.7, 55.2, 52.2, 40.8, 40.7, 40.4, 36.9, 30.2, 29.1, 26.0, 23.2, 19.5, 18.4, 14.5, 14.3, −5.4; HRMS (ESI) calcd for $C_{41}H_{66}O_8SiNa$ [M + Na] 737.4420; found 737.4389.



(2*E*,4*E*)-Ethyl 6-(*tert*-butyldimethyl-silyloxy)-hex-3-(3-(4-methoxybenzyloxy)propyl)-4-(((2*S*, 3*R*,3a*R*,4*R*,7a*R*)-2,3,3a,4,5,-7a-hexahydro-3,6-dimethyl-4-(prop-1-en-2-yl)benzofuran-2-yl)-methylene)-2-enoate (30a). The diastereomerically pure alcohol **29a** (18 mg, 0.025 mmol) was dissolved in anhydrous toluene (10 mL) and transferred to a Carius tube and warmed to 185 °C in a saltbath with stirring for 10 h. The reaction mixture was evaporated to dryness in vacuo and purified by flash column chromatography (AcOEt:CH_2Cl_2, 1:10−1:6) providing **30a** (7 mg, 43%) as a colorless oil. **30a:** R_f 0.73 (AcOEt:CH_2Cl_2, 1:4); IR (film) 2929, 1712, 1611, 1514, 1464, 1378, 1249, 1171, 1096, 1036, 836, 776; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 5.85 (d, J = 6.1 Hz, 1H), 5.84 (s, 1H), 5.59 (bs, 1H), 4.86 (dd, J = 6.3, 7.9 Hz, 1H), 4.84 (s, 1H), 4.81 (s, 1H), 4.48 (bs, 1H), 4.41 (s, 2H), 4.14 (q, J = 7.1 Hz, 2H), 3.80 (s, 3H), 3.58−3.49 (m, 2H), 3.47 (t, J = 6.5 Hz, 2H), 2.94−2.88 (m, 1H), 2.85−2.79 (m, 1H), 2.52−2.40 (m, 2H), 2.31−2.22 (m, 2H), 1.94−1.92 (m, 2H), 1.87 (dd, J = 5.9, 11.8 Hz, 1H), 1.74 (s, 3H), 1.73−1.69 (m, 5H), 1.27 (t, J = 7.1 Hz, 3H), 0.94 (d, J = 7.3 Hz, 3H), 0.86 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 160.9, 158.9, 146.9, 138.60, 138.59, 132.1, 130.8, 129.1, 120.0, 116.1, 113.6, 112.3, 76.2, 73.6, 72.4, 69.9, 62.0, 59.7, 55.2, 47.7, 43.3, 41.3, 35.0, 32.1, 29.2, 25.9, 25.7, 23.6, 19.2, 18.2, 15.8, 14.2, −5.4; HRMS (ESI) calcd for $C_{39}H_{61}O_6Si$ [M + H] 653.4232; found 653.4239.



(2*E*,4*E*)-Ethyl 6-(*tert*-butyldimethyl-silyloxy)-3-(3-(4-methoxybenzyloxy)propyl)-4-(((2*R*,3*R*,3a*R*,4*R*,7a*R*)-2,3,3a,4,5,7a-hexahydro-3,6-dimethyl-4-(prop-1-en-2-yl)benzofuran-2-yl)methylene)-hex-2-enoate (30b) and (3*R*,4a*S*,4b*R*,8*S*,8a*R*,9*R*,10*R*,10a*S*)-Ethyl 2-(3-(4-methoxybenzyloxy)propyl)-3,4,4a,4b,5,8,8a,9,10,10a-decahydro-10-hydroxy-1-(2-(*tert*-butyldimethyl-silyloxy)-ethyl)-8-(methoxymethoxy)-4a,6,9-trimethylphenanthrene-3-carboxylate (31). The diastereomerically pure alcohol **29b** (7 mg, 0.0098 mmol) was dissolved in anhydrous toluene (5 mL) and transferred to a Carius tube and warmed to 185 °C in a saltbath with stirring for 15 h. The reaction mixture was evaporated to dryness in vacuo and purified by flash column chromatography (AcOEt:CH_2Cl_2, 1:10−1:6) providing **30b** (2 mg, 31%), cycloadduct 31 (1 mg, 14%), and starting material **29b** (1 mg) all as colorless films. **30b**: R_f 0.73 (AcOEt:CH_2Cl_2, 1:4); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 8.5 Hz, 2H), 5.84 (s, 1H), 5.73 (d, J = 8.7 Hz, 1H), 5.62 (bs, 1H), 4.81 (s, 1H), 4.78 (s, 1H), 4.41 (s, 2H), 4.21 (bs, 1H), 4.16−4.11 (m, 3H), 3.80 (s, 3H), 3.62−3.53 (m, 2H), 3.46 (t, J = 6.6 Hz, 2H), 2.92−2.86 (m, 1H), 2.83−2.77 (m, 1H), 2.57 (app. q, J = 7.4 Hz, 2H), 2.15 (td, J = 4.3, 11.1 Hz, 1H), 1.97 (app. q, J = 11.6 Hz, 1H), 1.87 (dd, J = 4.3, 16.6 Hz, 1H), 1.74 (s, 3H), 1.73−1.69 (m, 5H), 1.27 (t, J = 7.1 Hz, 3H), 1.04(d, J = 6.7 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H); HRMS (ESI) calcd for $C_{39}H_{61}O_6Si$ [M + H] 653.4206; found 653.4207. **31**: R_f 0.23 (AcOEt:CH_2Cl_2, 1:4); $[\alpha]_D^{23}$ −74.0 (*c* 0.1, $CDCl_3$); IR (film) 3450, 2930, 1731, 1625, 1512, 1459, 1253, 1241, 1174, 1087, 1034, 821; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 5.70 (d, J = 4.1 Hz, 1H), 4.78 (d, J = 6.7 Hz, 1H), 4.63 (d, J = 6.7 Hz, 1H), 4.41 (s, 2H), 4.26 (d, J = 7.0 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 4.03 (dd, J = 2.9, 4.8 Hz, 1H), 3.93 (ddd, J = 4.7, 5.9, 7.0 Hz, 1H), 3.80 (s, 3H), 3.74 (dt, J = 7.3, 9.7 Hz, 1H), 3.64 (dt, J = 6.1, 9.7 Hz, 1H), 3.40 (t, J = 6.2 Hz, 2H), 3.15 (dd, J = 3.9, 8.3 Hz, 1H), 2.64−2.54 (m, 2H), 2.40−2.27 (m, 2H), 2.18 (d, J = 5.9 Hz, 1H), 2.11 (td, J = 5.6, 11.0 Hz, 1H), 2.07 (dd, J = 3.9, 16.1 Hz, 1H), 1.88−1.82 (m, 2H), 1.80−1.73 (m, 2H), 1.71 (s, 3H), 1.69−1.65 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H), 1.14 (d, J = 7.1 Hz, 3H), 0.89 (s, 9H), 0.76 (s, 3H), 0.06 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.3, 161.0, 139.9, 132.9, 130.6, 129.1, 121.5, 113.6, 112.9, 95.0, 72.4, 71.8, 70.3, 69.8, 63.3, 60.4, 55.9, 55.2, 54.7, 42.7, 40.9, 40.1, 38.4, 36.2, 35.6, 31.8, 28.7, 27.7, 25.9, 23.6, 16.2, 14.1, 11.9, −5.4; HRMS (ESI) calcd for $C_{41}H_{66}O_8SiNa$ [M + Na] 737.4419; found 737.4399.

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Supporting Information Available: Experimental details for the synthesis of stannane **15** and aldehyde **7**. Copies of ^{1}H NMR and ^{13}C NMR spectra of **7, 37, 13, 14, 17a, 16b-**α, **16b-**β, **17b**, **19**, **16c-**α, **17c**, **20c**, **20b**, **23**, **24**, **25**, **26**, **27**, **29b**, **29a**, **30a**, **30b**, **31**. This material is available free of charge via the Internet at http://pubs.acs.org.

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