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Total synthesis of Pulvomycin D

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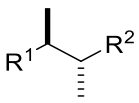
In dieser Arbeit wird von der Konvention Gebrauch gemacht, die Relativkonfiguration von Racematen durch gerade Balken (fett oder gestrichelt), die Absolut- und Relativkonfiguration enantiomerenreiner oder enantiomerenangereicherter Verbindungen in Keilform (fett oder gestrichelt) darzustellen



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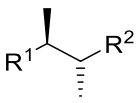

enantiomerenreine oder
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Abstract

The family of Pulvomycins consists of four polyketide natural products with interesting biological properties. No total synthesis for the macrocyclic compounds has been published so far. The construction of the 22-membered macrocycle proved to be particularly challenging. Different strategies for the ringclosure were studied, which eventually led to the successful synthesis of Pulvomycin D, one representative of the Pulvomycins. Pulvomycin D exhibits interesting cytotoxic properties against human cancer cells, making it an interesting target for new pharmaceutical compounds.

Kurzzusammenfassung

Die Familie der Pulvomycine besteht aus vier polyketiden Naturstoffen mit interessanten biologischen Eigenschaften. Bislang ist keine Totalsynthese dieser Makrolide bekannt. Der Aufbau des 22-gliedrigen Makrolactons erwies sich als besonders diffizil. Verschiedene Strategien für den Ringschluss wurden erprobt, was schließlich zur erfolgreichen Synthese von Pulvomycin D führte. Pulvomycin D zeigt vielversprechende Eigenschaften gegenüber menschlichen Krebszellen, wodurch die Verbindung ein interessantes Ziel für die Entwicklung neuer Pharmazeutika darstellt.

Table of contents

1. Introduction

"The synthesis of substances occurring in nature, perhaps in greater measure than activities in any other area of organic chemistry, provides a measure of the conditions and powers of science."

R. B. Woodward, 1956

Synthesis – from ancient Greek term *σύνθεσις* (*súnthesis*, "putting together") – describes the process of combining two or more chemical entities to form a new one.[1] Water can be synthesized from hydrogen and oxygen. Oxygen and carbon react to carbon dioxide. Carbon dioxide and water react to form carbonic acid. Step by step, synthesis leads to molecular complexity.[2]

In the early days, chemical synthesis was often the result of coincidence and curiosity. A prominent example is the discovery of European porcelain by *Böttger* and *Tschirnhaus* in 1708, while they were pursuing to "synthesize" gold.[3] It was not before the year 1800 that more scientific approaches were made and general concepts about chemical compounds were established. The synthesis of urea by Friedrich Wöhler is commonly referred to as the birth of organic synthesis.[4] For the first time, a naturally occurring substance had been synthesized from inorganic material, which broke with the generally acknowledged conventions of the time.[5] Further milestones were the first synthetic dye in 1856 (mauveine)[6], the indigo synthesis by Baeyer 1882[7], and the synthesis of glucose by E. Fischer 1889.[8] In the 20th century, synthetic targets became much more complex. Already in 1928, H. Fischer succeeded in the total synthesis of hemin.[9] New concepts like the retrosynthetic analysis allowed the systematic breakdown of complex molecules into smaller fragments.[10] Important examples probably are the total syntheses of Strychnine (1954)[11], Vitamin B12 (1973)[12], and Taxol (1994)[13] – among many others.

Total synthesis originally was the primary tool to validate the structure of isolated natural compounds. By synthesizing the putative molecule, and comparison with the natural sample, the structure could be verified or falsified. Although this approach is still relevant today and occasionally reveals misassignments in natural product characterizations, it is no longer the major motivation for total synthesis. Rather, the total synthesis acts as a practical test environment for new methods and chemical transformations, as highlighted in the above-mentioned quote.

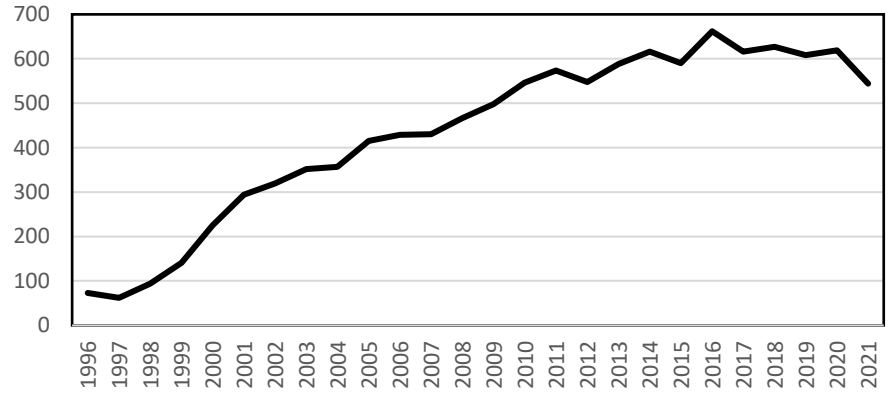


Figure 1. Scientific publications with the term "total synthesis" in the title (according to pubchem.ncbi.nlm.nih.gov).

Today, hundreds of total syntheses are published every year (Figure 1), and it is beyond doubt that the majority of these synthesized compounds do not have a direct application. In most cases, the added value is not the final product but rather the perception of which chemical transformations led to its successful synthesis – and which did not.[14] There is a point in time in probably every total synthesis project where an unexpected observation is made or an initially believed foolproof transformation turns out to be not feasible at all. These observations are probably the actual gain in knowledge and help us increase our perception of organic chemistry further. Beyond that, the total synthesis of complex natural products still emanates a profound fascination for chemists, which is again described best by a quote from Woodward and motivated us to investigate the first total synthesis of Pulvomycin:

„The structure known, but not yet accessible by synthesis, is to the chemist what the unclimbed mountain, the uncharted sea, the untilled field, the unreached planet, are to other men.“

R. B. Woodward, 1963

2. Pulvomycins A-D: Isolation, biosynthesis and biological activity

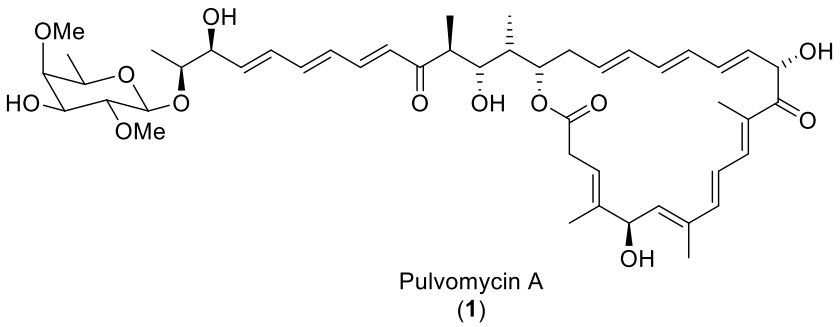


Figure 2. Structure of Pulvomycin A (**1**).

The macrolide Pulvomycin A (**1**) was first isolated in 1957 by *Zief* et al. from a not otherwise specified strain of *streptomyces*.[15] *Streptomyces* is a large genus of actinobacteria, with more than 600 known species.[16] The bacteria are gram-positive and mainly occur in soil. Similar to fungi, they grow in filamentous form and produce a mycelium as well as spores. They are also the largest producer of antimicrobial compounds.[17] Many pharmaceutically relevant antibiotics were isolated from *Streptomyces*, including Chloramphenicol from *Streptomyces venezuelae* (1947), Nystatin from *S. noursei* (1948), and Vancomycin from *S. orientalis* (1956).[16]

Over the course of the years, Pulvomycin A has been isolated from several different strains of *Streptomyces*. In 1963, *Akita* isolated the compound from *S. albosporeus*.[18] *Smith* used the strain *S. netropsis* to isolate Pulvomycin A in 1985.[19] The same strain also produces the antibiotic Netropsin. Pulvomycin A was also isolated in 1979 from *S. mobarense* by *D. Assmann*.[20] In 2020, *Moon* and co-workers used the strain *Streptomyces* sp. HRS33, which they collected from a soil sample near the Yellow Sea in South Korea.[21] The strain turned out to be similar to the known strain *S. javensis*. Due to its lability, the structure of Pulvomycin A was not fully elucidated before the year 2006. In 1985, *Smith et al.* clarified the structure by extensive NMR and MS analysis.[19] The exact assignment of all stereocenters was eventually achieved by *Parmeggiani* et al. in 2006 by cocrystallization of the compound with its biological target EF-Tu (elongation factor thermal unstable).[22]

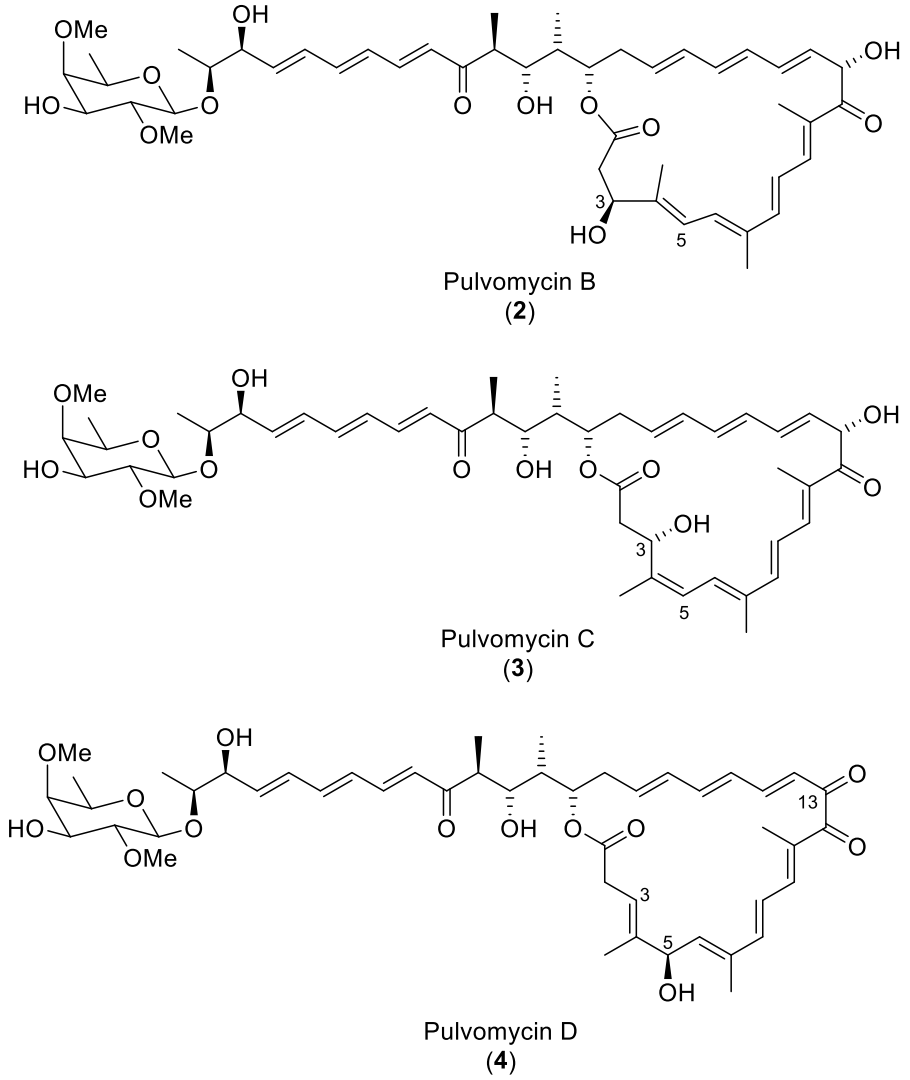
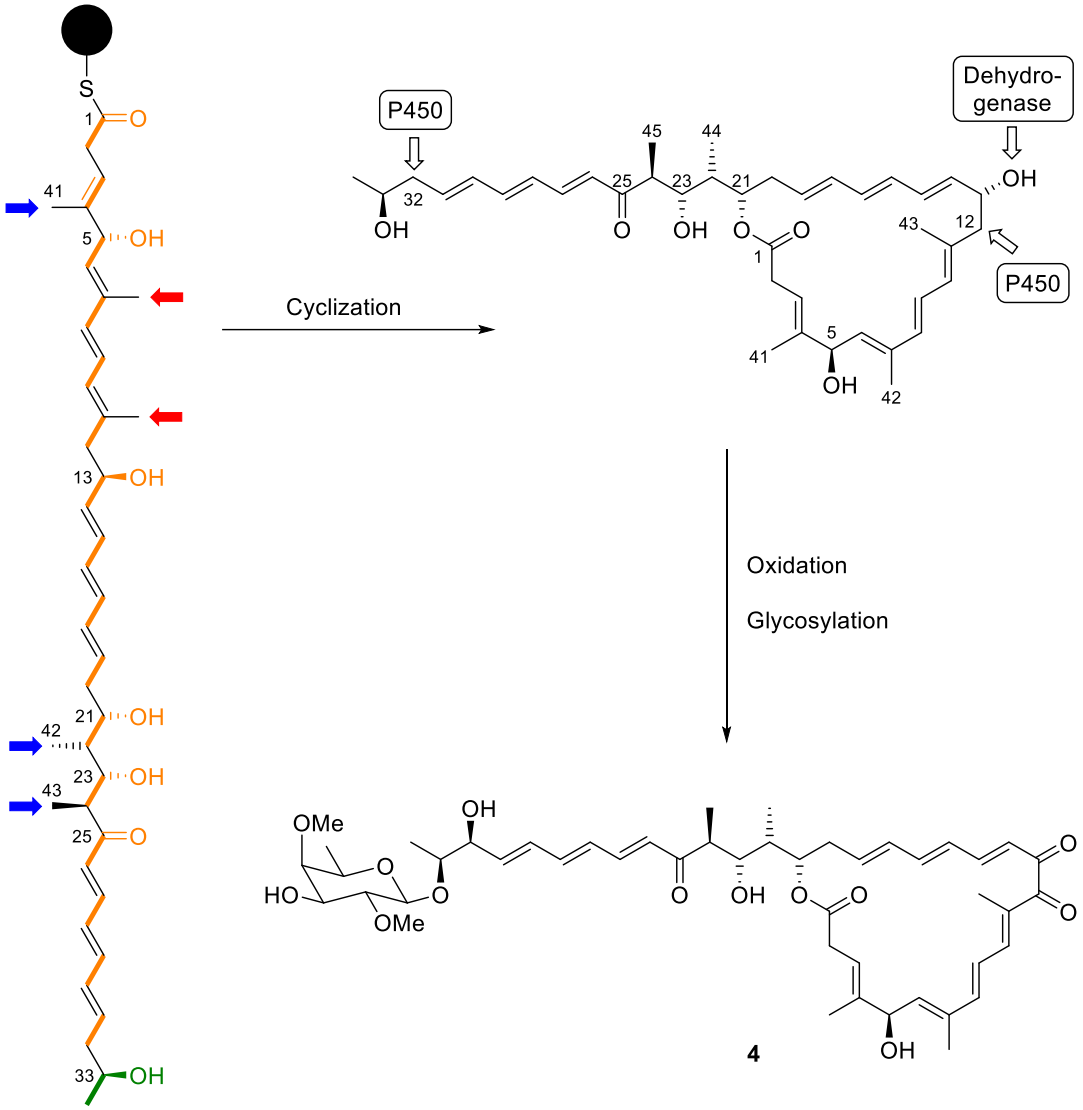


Figure 3. Structures of Pulvomycins B-D (**2**-**4**).

Besides Pulvomycin A, *Moon* et al. isolated three new compounds bearing the same carbon skeleton.[21] These new Pulvomycins B-D (**2**-**4**) are shown in figure 3. Compared to Pulvomycin A (**1**), Pulvomcins B (**2**) and C (**3**) are hydroxylated at the C3 position instead of the C5 position and differ in their C4-C5 double bond configuration. Unlike Pulvomycin A (**1**), Pulvomycin D (**4**) exhibits a carbonyl group at C13 instead of an alcohol moiety. Biosynthetically, all four Pulvomycins are derived from a polyketide pathway (Scheme 1).[23]



Scheme 1. The biosynthesis of Pulvomycin A-D (**1**-**4**) follows the well-known polyketide pathway.

Extensive feeding experiments performed by *Priestley* and *Groeger* in 1995 suggested that the backbone is derived from 16 malonyl-CoA extender units (orange) onto an acetyl-CoA starter unit (green).[24] The methyl groups C41, C44, and C45 are incorporated from methionine by methyl transfer (blue), while C42 and C43 are derived from the C2 position of an acetate (red) by aldol condensation and decarboxylation. The oxygen atoms at positions C1, C5, C13, C21, C23, C25, and C33 stem from the acetate building blocks, while C12 and C32 are probably oxygenated afterward using cytochrome P450.[21] In the case of Pulvomycin D (**4**), the ketone at C13 is probably formed by a dehydrogenase.[21] After ringclosure between C21 and C1, the fucose unit is attached by a glycosyltransferase. Pulvomycins B (**2**) and C (**3**) are most likely formed by the attack of water at the C3 position, followed by the elimination of the C5 alcohol. The antibiotic properties of Pulvomycin A (**1**) have been known since it was first isolated in 1957.[15] A new study of *Moon* from 2020 showed that only Pulvomycin A (**1**) exhibits

significant antibiotic activity, mainly against gram-positive bacteria (Table 1).[21] Pulvomycins B-D do not show any significant antibacterial characteristics.

Table 1. The activity of Pulvomycins A-D (**1**-**4**) against selected bacteria (MIC value in µg/mL).

strains	gram stain	**2**	**3**	**4**	**1**	ampicillin
S. aureus	G(+)	>128	>128	>128	1	0.13
E. faecalis	G(+)	>128	>128	>128	2	0.5
E. faecium	G(+)	>128	>128	>128	1	0.5
K. pneumoniae	G(–)	>128	>128	>128	128	64
S. enterica	G(–)	>128	>128	>128	2	0.13
E. coli	G(–)	>128	>128	>128	>128	4

The mode of action has been studied extensively and is based on inhibition of EF-Tu.[22c] Within ribosomal protein synthesis, EF-Tu forms a tertiary complex with aminoacyl-transfer-RNA (αα-tRNA) and guanosine triphosphate (GTP).[25] Only within this complex, the tRNA is activated enough to bind to the corresponding binding site within the ribosome. However, the EF-Tu GTP complex also has a strong affinity to Pulvomycin A, which blocks the active site of the cofactor. tRNA can no longer be transported to the ribosome, and the protein synthesis is stopped. Figure 4 shows a 3D model of the EF-Tu complex with Pulvomcin A and GDPNP, a GTP analog, based on the crystallographic data obtained by *Parmeggiani*.[22c]

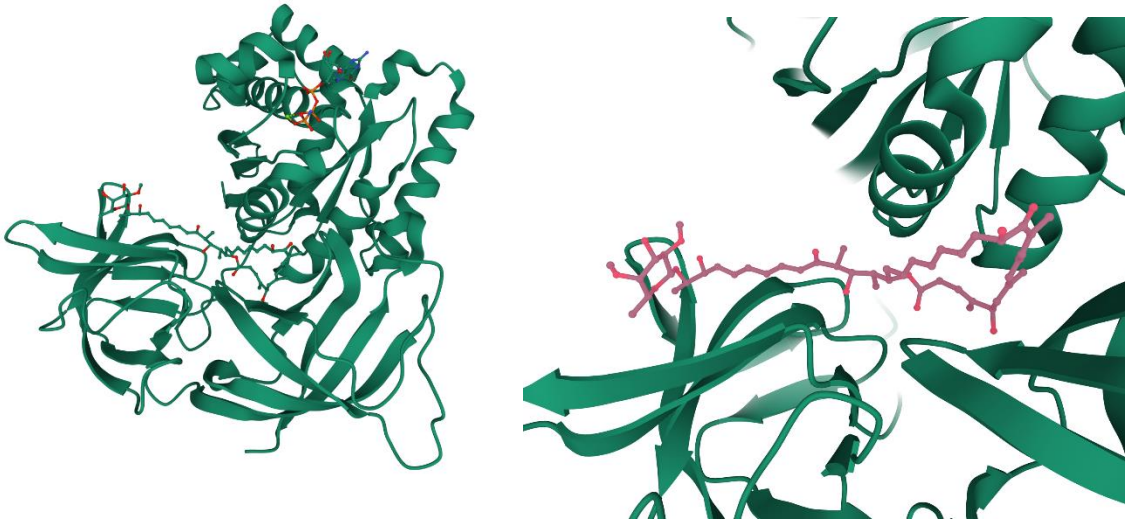


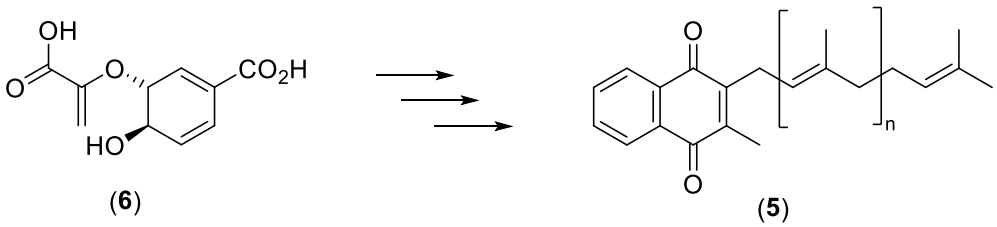
Figure 4. The tertiary complex of EF-Tu with Pulvomycin A and GDPNP (right: close up).[26]

Interestingly, the compounds also show cytotoxicity against some human cancer cell lines (Table 2). Especially Pulvomycin D (**4**) turned out to be potent against colon cancer (HCT116), stomach cancer (SNU638), liver cancer (SK-Hep-1), and breast cancer (MDA-MB-231).

Table 2. The IC_{50} values [μM] of Pulvomycins A-D (**1**-**4**) against selected human cancer cell lines.

cell lines	**2**	**3**	**4**	**1**	etoposide
A549	24.9	1.90	2.70	4.10	0.40
HCT116	3.70	0.80	0.21	0.80	0.40
SNU638	7.30	1.10	0.34	1.60	0.40
K562	13.7	1.00	1.10	1.10	0.40
SK-Hep-1	5.10	1.30	0.40	1.10	2.40
MDA-MB-231	12.1	1.50	0.29	1.00	2.30

Very recently, Pulvomycin A (**1**) was found to be an active inhibitor of the futalosine pathway.[27] This pathway is used to produce menaquinone (**5**), an electron carrier in the respiratory chain of many bacteria, from chorismate (**6**).[28]

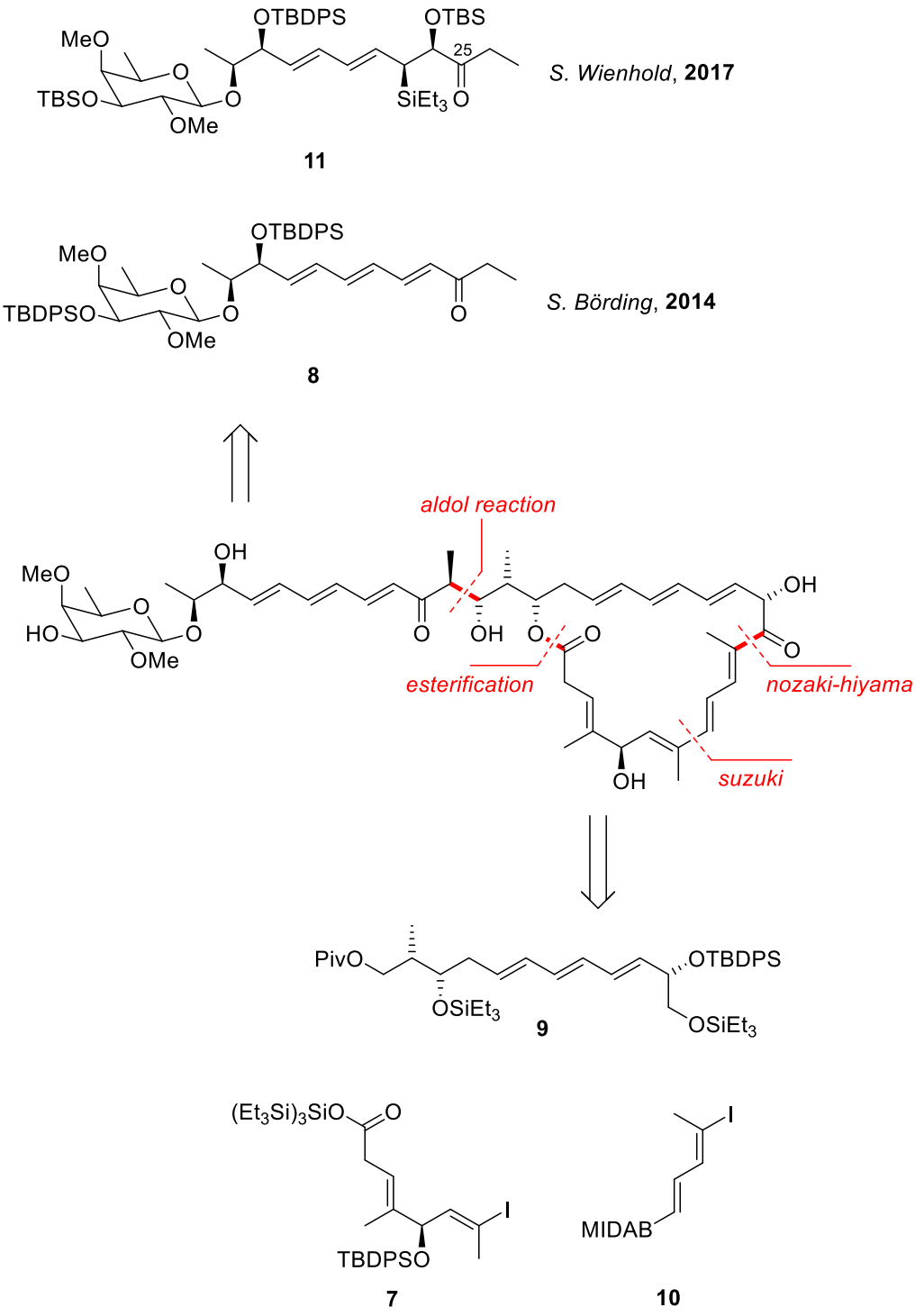


Scheme 2. Chorismate (**6**) is converted to menaquinone (**5**).

The activity of Pulvomycin A (**1**) could be determined by growth recovery experiments. Pulvomycin A showed a MIC value of 200ng/mL against *Bacillus halodurans*, which relies solely on the futalosine pathway. For the closely related species *B. subtilis*, which does not use the futalosine pathway, a much higher MIC value of 10µg/mL was determined.
In view of the promising biological activities and the challenging structure, the Pulvomycin family seemed to be an interesting synthetic target for our group.

3. Previous work and original retrosynthetic strategy

Initially, we focused our synthetic strategy solely on Pulvomycin A (**1**).[29] Three key retrosynthetic cuts led to the C1-C7 carboxylic acid fragment **7**, the C24-C40 ketone fragment **8**, and the C12-C23 triene fragment **9** (Scheme 3).[30] A silyl protection strategy was envisioned to enable a deprotection under mild conditions. The original synthetic plan involved the aldol reaction between ketone **8** and triene fragment **9**, followed by coupling with the southern fragment **7** by the linker fragment **10**. Afterward, the linear precursor should be cyclized under macrolactonization conditions.[31]

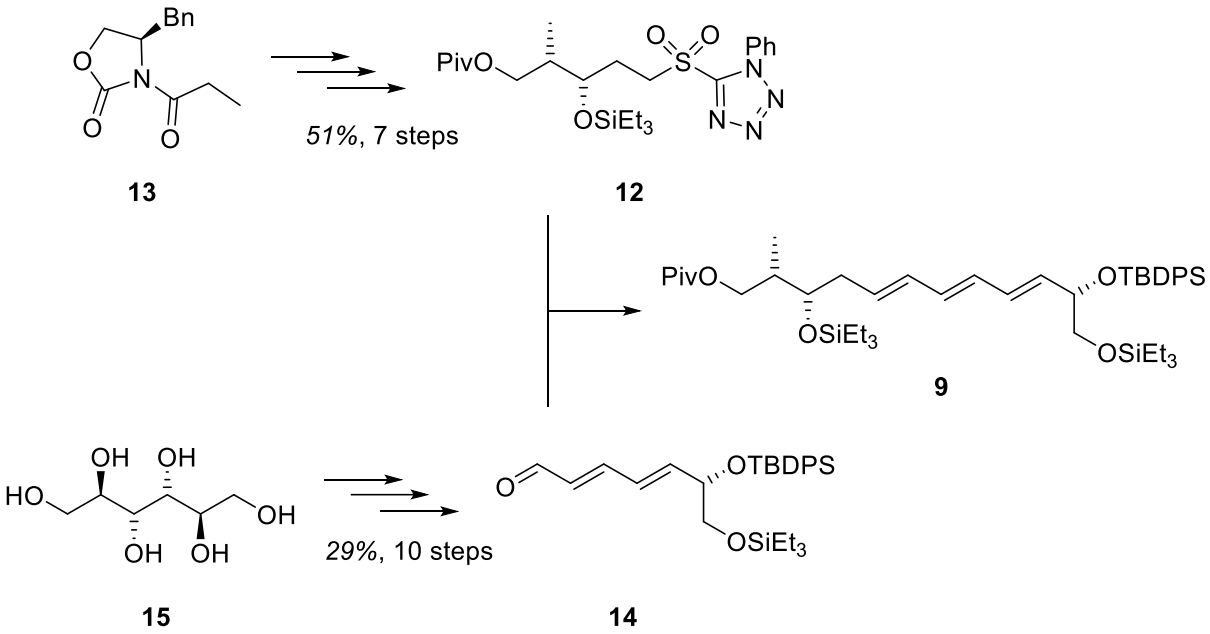


Scheme 3: Initial retrosynthetic strategy by S. Wienhold.

S. Börding initially synthesized the ketone fragment **8** in 2014.[29] However, *S. Wienhold* showed that the ketone was unreactive in an aldol reaction, probably due to the extended conjugation of the system.[30] In 2017, he refined the fragment by the installation of a *Peterson* system between C26-C27.[32] This change interrupted the conjugation, hence enabling the aldol reaction. Furthermore, he replaced the *tert*-butyldiphenylsilyl (TBDPS) protecting group at C37

with the more labile *tert*-butyldimethylsilyl (TBS) group, leading to the modified ketone fragment **11**.

The work on triene fragment **9** started with *T. Neubauer* in 2013[33] and was later modified by *T. Judt* and *S. Wienhold*.[30,34] The key step involved a *Julia-Kociensky* reaction to establish the triene (Scheme 4).[35] The sulfone **12** was accessible in 7 linear steps and 51% yield starting from literature known *Evans*-auxiliary **13** (Scheme 4).[36] The aldehyde **14** could be synthesized in 10 linear steps with 29% yield starting from *D*-Mannitol (**15**).[33,37]

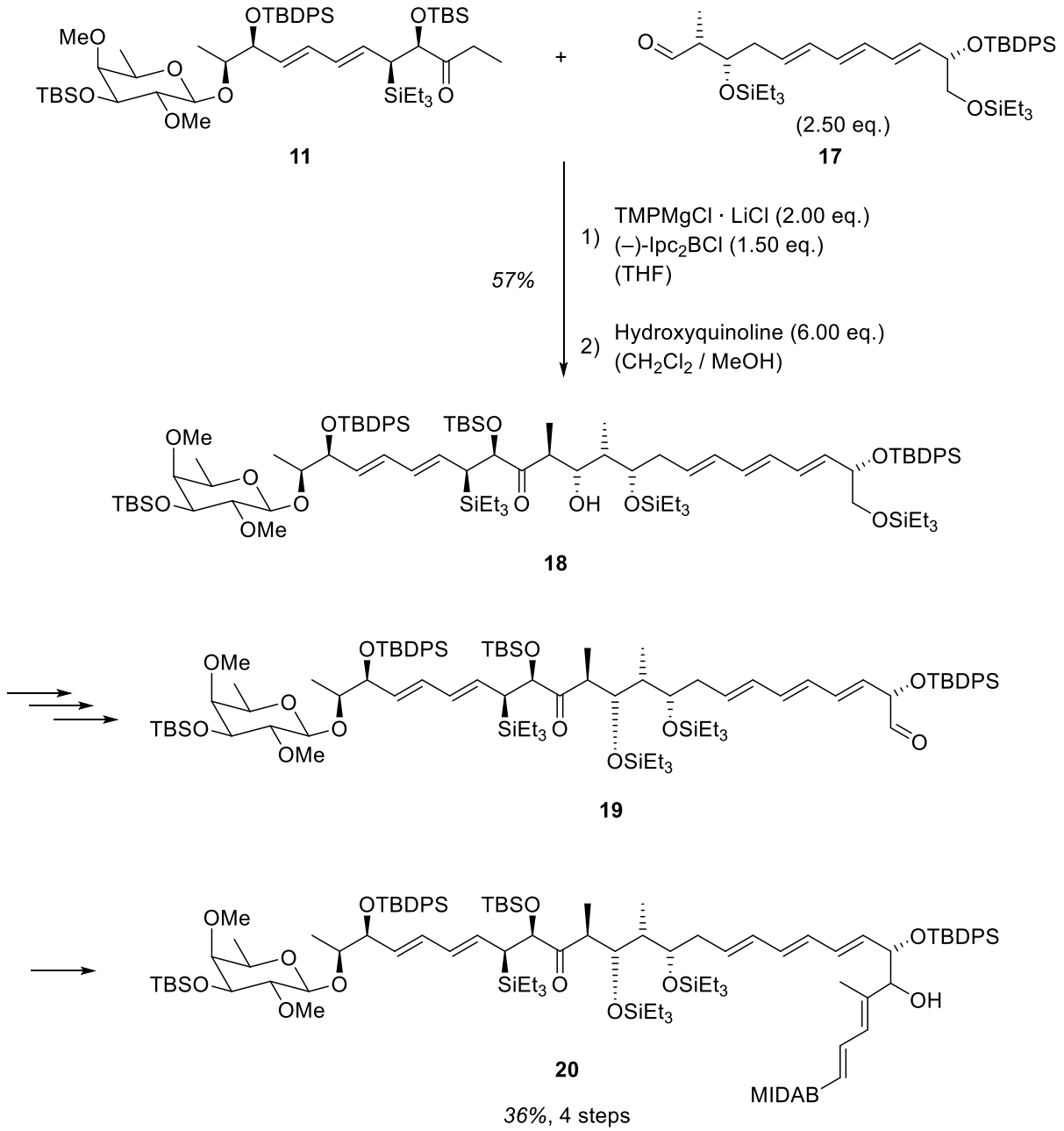


Scheme 4. Synthesis of the C12-C23 triene fragment.

The protected carboxylic acid fragment was synthesized by *S. Wienhold* starting from 1,3-propanol (**16**). In 12 linear steps, the fragment was obtained with 17% yield (Scheme 5).[30]

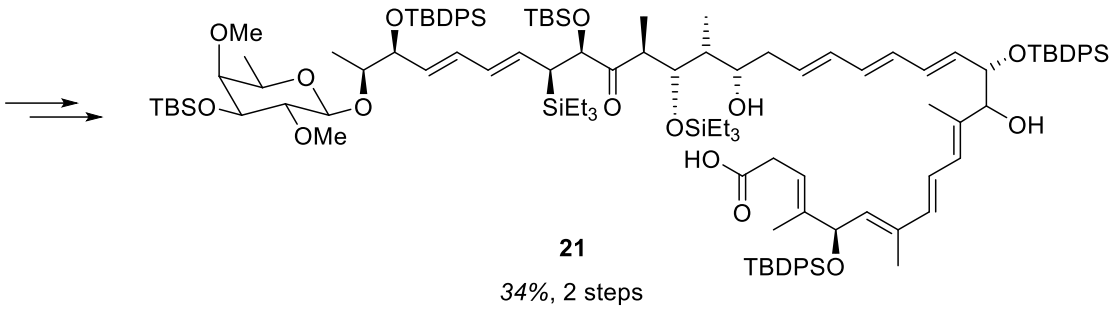
Scheme 5. Synthesis of the C1-C7 carboxylic acid fragment.

After removal of the pivaloyl group and subsequent oxidation, *S. Wienhold* was able to perform the stereoselective aldol reaction between ketone **11** and aldehyde **17** with 57% yield and perfect stereoselectivity (Scheme 6).[37,[38] The hydroxy group of aldol product **18** was protected with a triethylsilyl (TES) group. Removal of the primary TES group at C12, followed by oxidation, led to aldehyde fragment **19**. *S. Wienhold* successfully connected the literature known *N*-methyliminodiacetic acid (MIDA) protected diene[39] **11** in a *Nozaki-Hiyama* reaction leading to alcohol **20** in 36% yield over four steps.



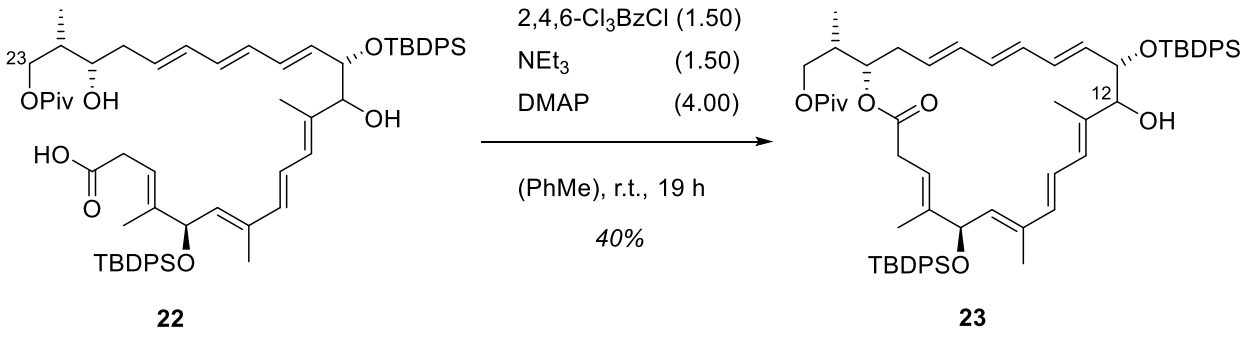
Scheme 6. Aldol reaction and elongation of the carbon skeleton.

The MIDA group was converted into the more reactive pinacol ester, which subsequently underwent *Suzuki* coupling with the southern vinyl iodide in 43% yield (Scheme 7).[40] Treatment with HF · pyridine led to the removal of the supersilyl ester and the C21 TES group in 78% yield. Unfortunately, though, no lactonization of compound **21** could be accomplished under various conditions. We concluded that the steric bulk of the neighboring TES group at C23 prevented the macrocyclization.[41] Attempts to remove this TES group in order to perform the cyclization on the unprotected 1,3-diol remained unsuccessful.



Scheme 7. *Suzuki* coupling with carboxylic acid fragment **7**, followed by deprotection.

This hypothesis was further supported by the fact that the macrocyclization proceeded with a decent yield on the truncated test substrate **22**. The absence of the sterically demanding environment at C23 enabled successful lactonization (Scheme 8).

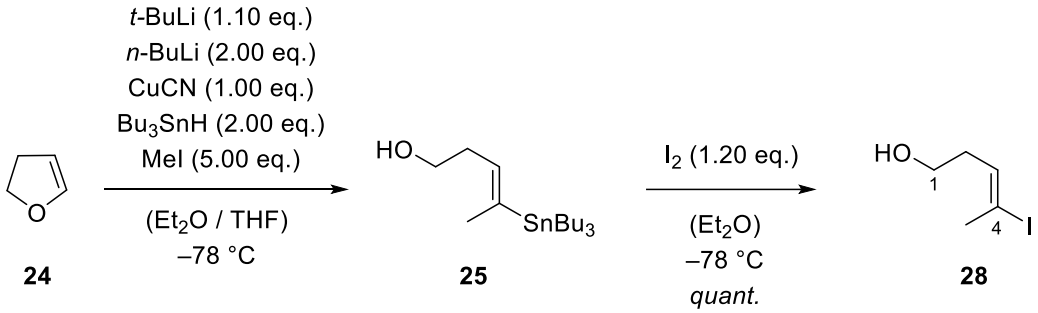


Scheme 8. Successful macrolactonization of truncated test substrate **22**.

However, despite numerous attempts, the oxidation of the alcohol group at C12 of compound **23** remained unsuccessful. Either there was no conversion, or the starting material decomposed.[30] These findings suggested that macrolactonization was not the method of choice for generating the macrocycle. Instead, a new macrocyclization strategy was to be established in the course of this work.[42]

4. Synthesis of the C1-C7 fragment

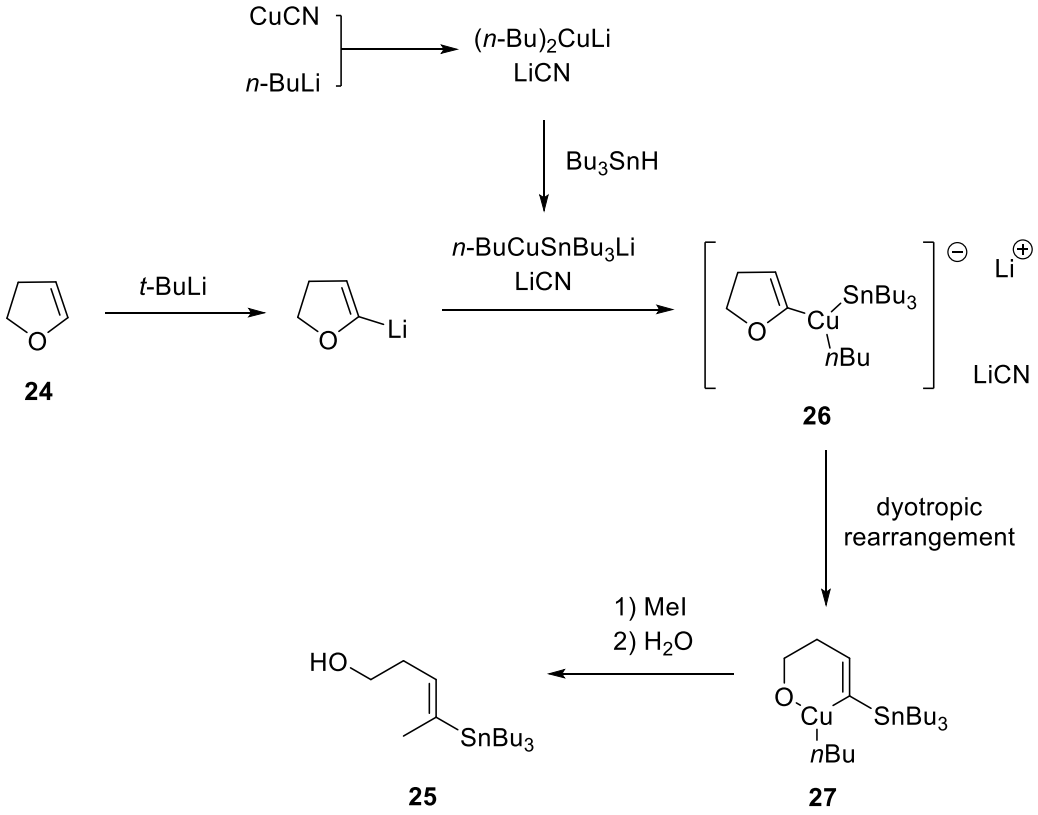
The synthesis of the C1-C7 carboxylic acid fragments commenced with a dyotropic rearrangement of 2,3-dihydrofuran (**24**, Scheme 9).[43]



Scheme 9. Synthesis of alcohol **25** by dyotropic rearrangement of 2,3-dihydrofuran (**24**).

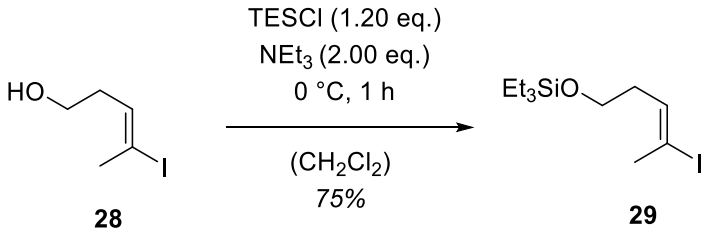
First, the furan was deprotonated using *tert*-butyllithium. In a separate flask, copper-(I)-cyanide was reacted with *n*-butyllithium to generate the corresponding cuprate. After the addition of tributyltin hydride, a mixed cuprate formed.[44] Then, the lithiated furan was added, leading to the formation of species **26** (Scheme 10). Warming the reaction to 0 °C initiated the dyotropic rearrangement leading to metallacycle **27**. The addition of methyl iodide finally led to methylation of the vinyl copper species, thereby forming the product.

Isolation of the alcohol is possible at this point, but the tin residues make chromatographic separation difficult, especially on a large scale. Therefore, the following destannylation with elemental iodine was carried out with the crude product. Aqueous workup using potassium fluoride solution resulted in the precipitation of large amounts of the tin side products, which was beneficial for purification. With this protocol, the vinyl iodide **28** was obtained in an excellent yield of 99%, starting from 2,3-dihydrofuran on a 30g scale.



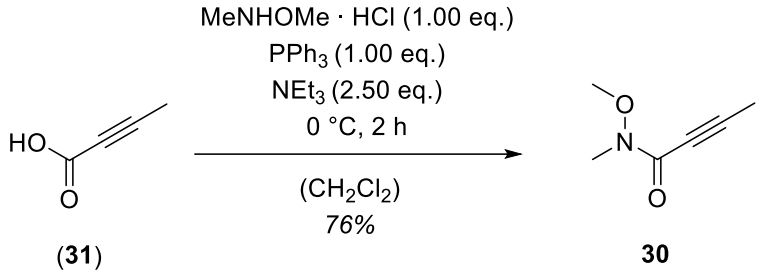
Scheme 10. A closer look at the dyotropic rearrangement sequence.[45]

TES protection of the primary alcohol **28** proceeded smoothly with 92% using triethylsilyl chloride and triethylamine as the base.[46]



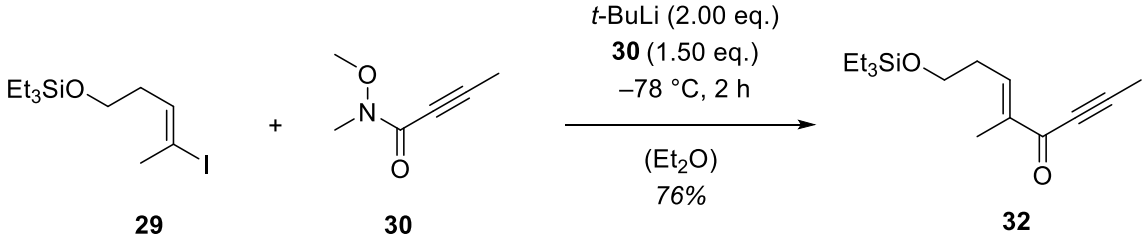
Scheme 11. TES protection of alcohol **28**.

To convert the vinyl iodide **29** into the required α-β-unsaturated carbonyl compound, we envisioned using Weinreb amide **30**. The amide was accessible by a literature-known protocol starting from commercially available tetrolic acid (**31**) and *N*,*O*-dimethylhydroxylamine (Scheme 12).[47]



Scheme 12. Preparation of Weinreb amide **30**.

The halogen metal exchange proceeded smoothly using *tert*-butyllithium in diethyl ether at –78 °C, and the addition to Weinreb amide **30** led to the desired ketone **32** in 76% yield (Scheme 13).[48]



Scheme 13. Halogen metal exchange followed by addition to Weinreb amide **30**.

With the ketone in hand, we focussed on the installation of the stereogenic center at C5 by use of the *Corey-Bakshi-Shibata* (CBS) catalyst.[49] A model for the observed stereoselectivity was suggested by *Corey* in 1987 (Figure 5).

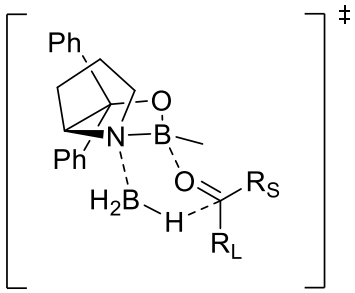


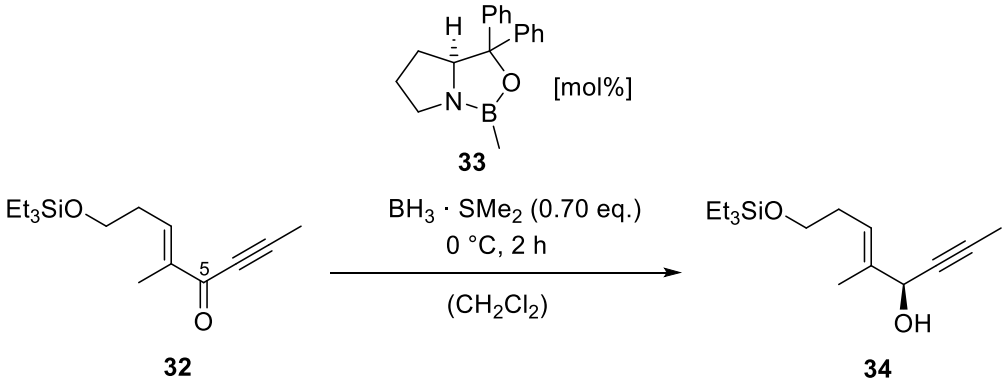
Figure 5. Transition state of the CBS reduction with the (*S*)-CBS catalyst.

The ketone is coordinated by the boron atom in such a way that the larger residue (R_L) is pointing away from the methyl group at the boron atom. The reductant is then coordinated by the nitrogen. It can be assumed that the alkynyl group of compound **32** is significantly smaller than the quaternary center at the C4 position. Therefore, we suggested that the (*S*)-CBS catalyst leads to the desired (*S*)-configured product. *T. Neubauer* and *T. Judt* already described the procedure using the (*S*)-2-methyl-CBS catalyst (**33**) and borane dimethylsulfide complex with

excellent enantiomeric excess.[33,[34] However, their experiments required stoichiometric amounts of catalyst (1.33 equivalents) and borane (1.35 equivalents). Thus, we tried to explore other reaction conditions, which would enable a more economical use of the reagent. Careful control of the reaction conversion showed that only 0.70 equivalents of borane were needed to achieve a complete reduction of the ketone.

To keep the local concentration of free borane low, thus enabling only the CBS-borane-adduct to perform the reduction, we envisioned that a very slow addition of the borane to the reaction would be beneficial. The borane was added *via* a syringe pump and a cannula that reached below the surface of the solution. With this experimental setup in hand, we tested the reduction under different catalyst loadings (Table 3). The enantiomeric excess of the reaction was monitored by chiral HPLC.

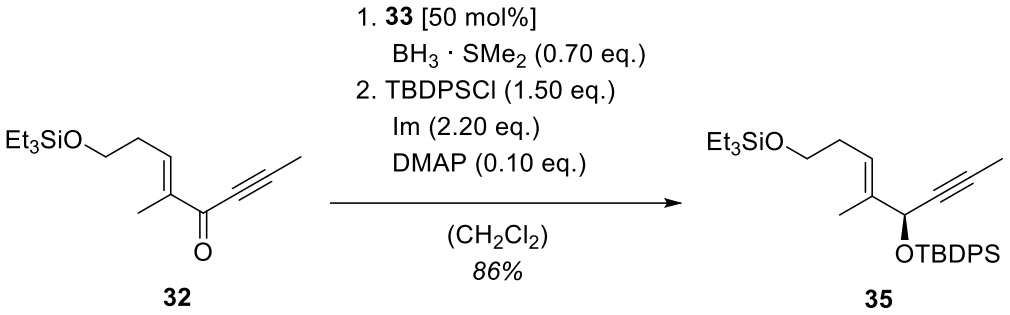
Table 3. CBS reduction of ketone **32** with different catalyst loadings.



	33 [mol%]	*ee*
1	10	66%
2	25	89%
3	50	96%

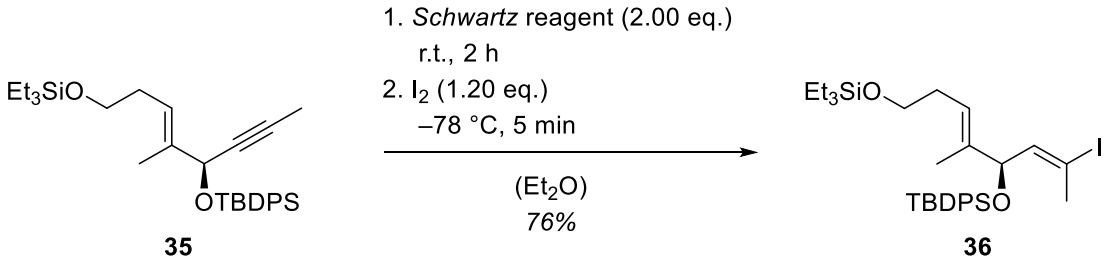
Removal of the TES group and benzyl protection of the diol was necessary to make the compound detectable and separable by chiral HPLC (see chapter 5). Lowering the catalyst loading to 10 mol% resulted in an unacceptable *ee* of only 66% (entry 1). Increasing the catalyst loading to 25 mol% already gave a decent *ee* of 89% (entry 2). To our delight, raising the catalyst loading to 50 mol% delivered the product with an excellent enantiomeric excess of 96% (entry 3).

Protection of the free hydroxy group was achieved using TBDPS chloride, imidazole, and 4-dimethylamino pyridine (DMAP).[50] On a preparative scale, it was found to be beneficial to perform the protection on the crude product of the CBS reduction, which resulted in an excellent yield of 86% over two steps (Scheme 14).



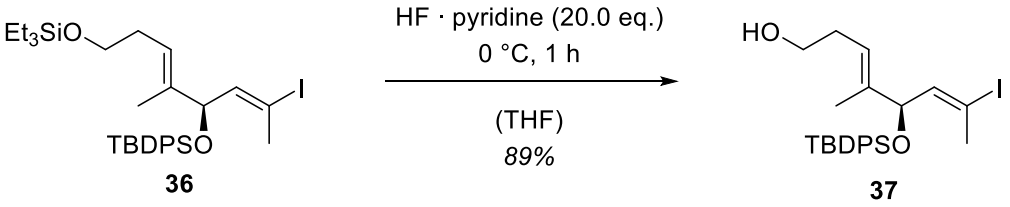
Scheme 14. Asymmetric reduction of ketone **32** followed by TBDPS protection.

Next, the alkyne was converted into vinyl iodide **36** using the *Schwartz* reagent (Scheme 15).[51] The reaction was carried out at ambient temperature until TLC showed complete conversion of the starting material.



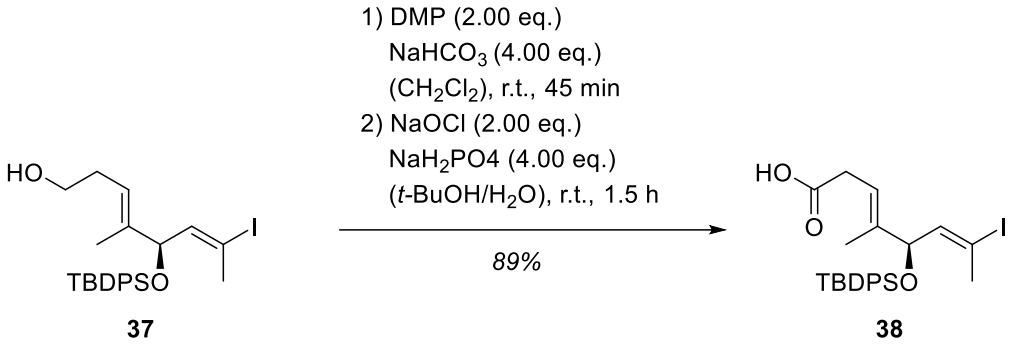
Scheme 15. Hydrozirconation iodo-de-zirconation sequence for the construction of vinyl iodide **36**.

Then, a solution of iodine in THF was added at –78 °C. The reaction was immediately quenched afterward by pouring it into a vigorously stirred mixture of sodium thiosulfate and diethyl ether. This ensured an efficient and fast quenching of the residual iodine. Even small residues of free iodine turned out to be very harmful to the molecule and decreased the yield significantly.
Removal of the TES group at C1 proceeded smoothly using HF · pyridine at 0 °C in 89% yield (Scheme 16).[52]



Scheme 16. Removal of the C1 TES group leading to alcohol **37**.

The alcohol was oxidized to the carboxylic acid in a two-step protocol (Scheme 17). First, the aldehyde was generated using *Dess-Martin* periodinane.[53] The crude aldehyde was then subjected to *Pinnick* conditions, which led to the formation of the carboxylic acid **38** in a decent yield of 89%.[54]



Scheme 17. Two-step oxidation sequence *via* a *Pinnick* protocol.

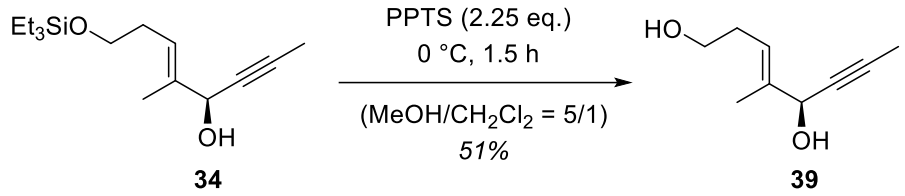
Overall, the southern C1-C7 fragment **38** could be synthesized with a yield of 20% over eight steps starting from 2,3-dihydrofuran (**24**).

5. Determination of the absolute configuration at C5

As discussed in the previous chapter, the stereogenic center at C5 was introduced by a stereoselective reduction of ketone **32** using the *Corey-Bakshi-Shibata* catalyst. We envisioned that the (*S*)-CBS catalyst should lead to the formation of the desired (*S*)-configurated product. The reaction was already carried out by *T. Neubauer* and *T. Judt*, and a high enantiomeric excess was observed with the (*S*)-2-methyl-CBS catalyst (**33**, Table 3).[33] However, no proof of the absolute configuration had been made so far.

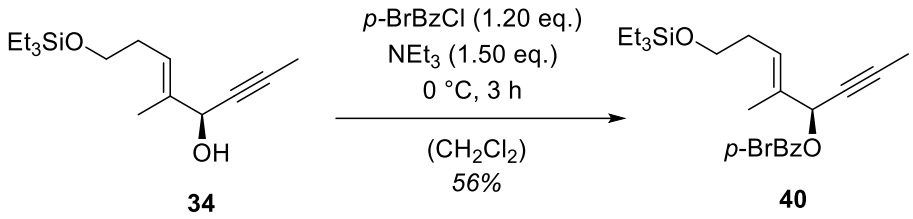
Initially, the absolute configuration should be determined by *Mosher* ester analysis of alcohol **34**.[55] Unfortunately, the esters turned out to be very unstable and rapidly decomposed, which

made a sophisticated NMR analysis impossible. Several attempts to crystallize the compound were made. Removal of the TES group at C1 using pyridinium *para*-toluenesulfonate (PPTS) led to diol **39** in 51% yield, but the substance still remained an oil (Scheme 18).



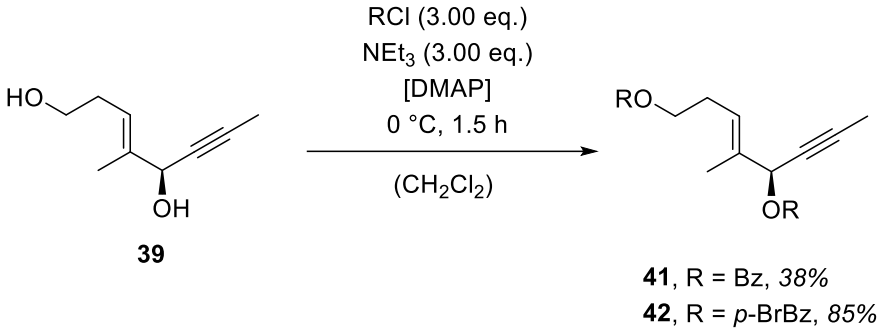
Scheme 18. Formation of diol **39**.

Attempts to increase the polarity of the compound by performing a dihydroxylation at the double bond only led to decomposition. Esterification of the alcohol with *para*-bromobenzoyl chloride led to the desired ester **40** in 56% yield (Scheme 19).



Scheme 19. Formation of the *para*-bromobenzoyl ester **40**.

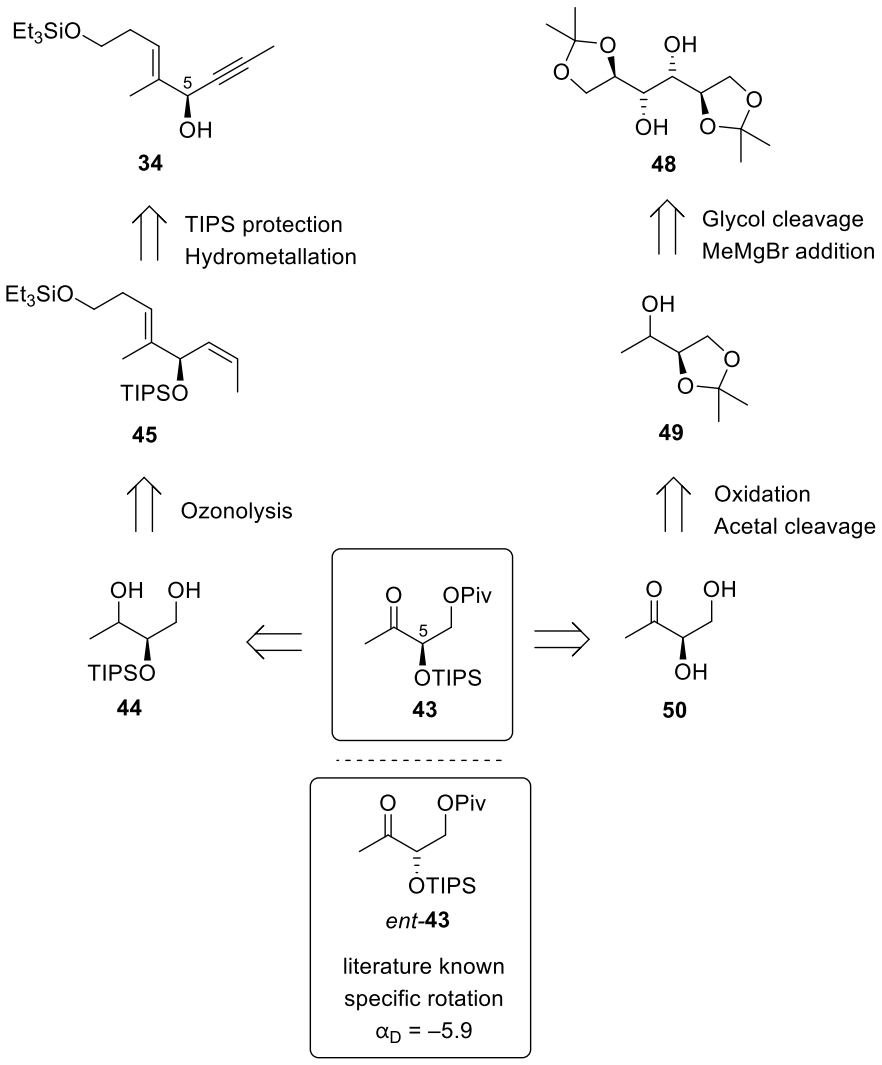
However, the product was still oily. No solid compound could be isolated when the esterification was performed with the diol **39**, either (Scheme 20). Neither the benzoyl ester **41** nor the *para*-bromo compound **42** turned out to be crystalline.



Scheme 20. Conversion of diol **39** into esters **41** and **42**. Bz: benzoyl.

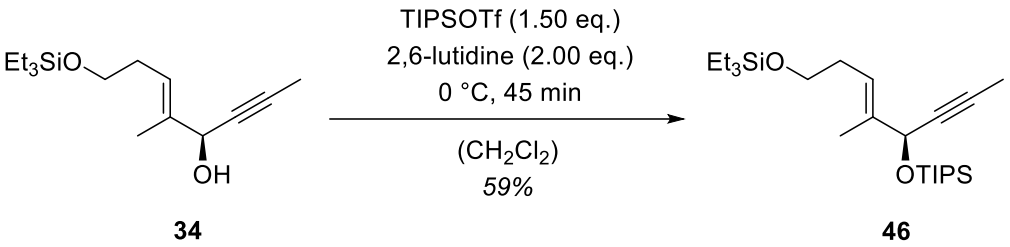
We envisioned that alcohol **34** could be converted into compound **43**, whose enantiomer *ent*-**43** is known in the literature (Scheme 21).[56] A comparison between the specific rotation of the

literature-known compound and the value of our synthetic product should then allow a statement about the configuration of the stereocenter at C5. Ketone **43** should be accessible by pivaloyl protection and oxidation of diol **44**. We imagined that the diol should be the main product of ozonolysis of diene **45**. The diene should be synthesized by the protection of alcohol **34** with the tri-*iso*-propylsilyl (TIPS) group, followed by treatment of the alkyne with the *Schwartz* reagent and subsequent quenching with water. As a reference, we also wanted to synthesize compound **43** from naturally occurring *D*-Mannitol (**15**).



Scheme 21. Determination of the absolute configuration at C5 by derivatization into literature known ketone **43**.

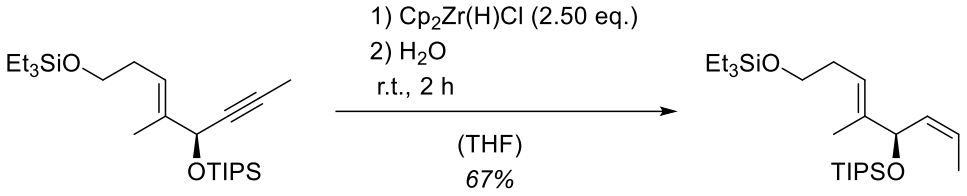
After the CBS reduction, the secondary alcohol **34** was protected using TIPS triflate and 2,6-lutidine with a yield of 59% (Scheme 22).



34 **46**

Scheme 22. TIPS protection of CBS reduction product **34**.

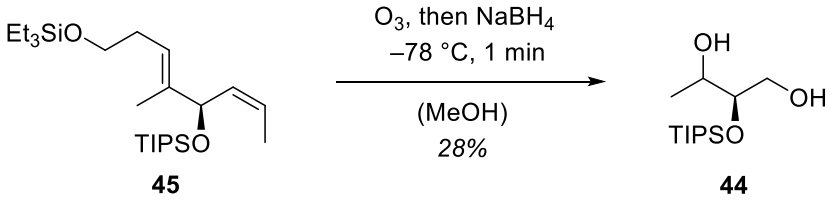
Compound **46** was treated with the *Schwartz* reagent for two hours at room temperature before the reaction was quenched by the addition of water, leading to the desired diene **45** in 67% yield (Scheme 23).



46 **45**

Scheme 23. Conversion of alkyne **46** into diene **45** using the *Schwartz* reagent.

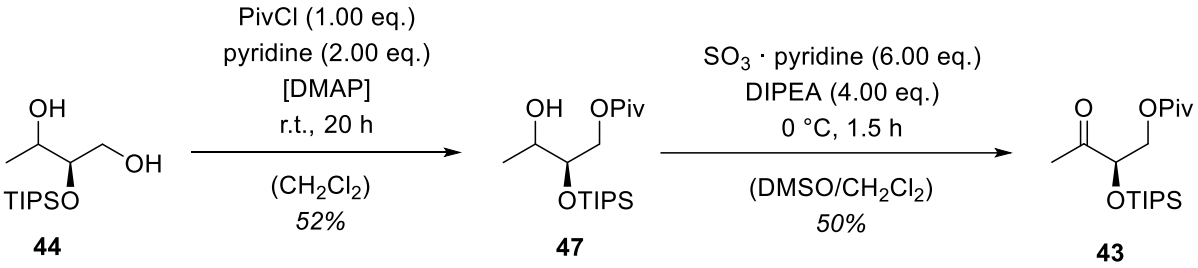
Ozonolysis of the compound turned out to be difficult due to the high reactivity of the alkenes. A very short one-minute exposure of the diene to ozone, followed by reductive sodium borohydride workup, finally delivered the desired diol **44**, although with a poor yield of only 28% (Scheme 24).



45 **44**

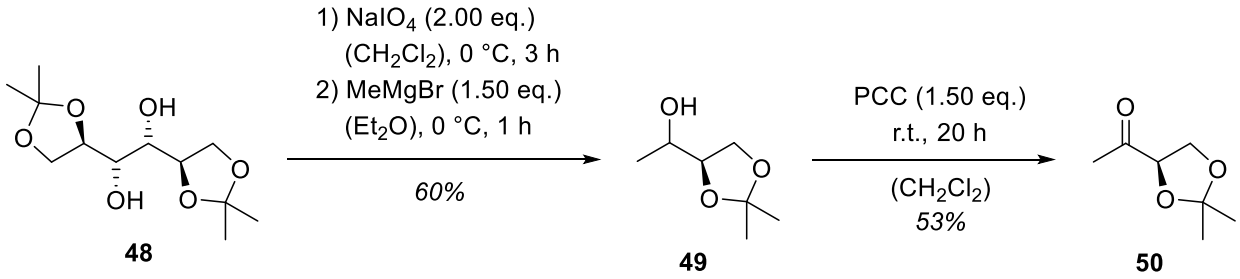
Scheme 24. Ozonolysis of diene **45** followed by a reductive workup.

The primary alcohol **44** was then converted into the pivalate **47**, and the secondary alcohol was oxidized under literature known conditions (Scheme 25).[56]



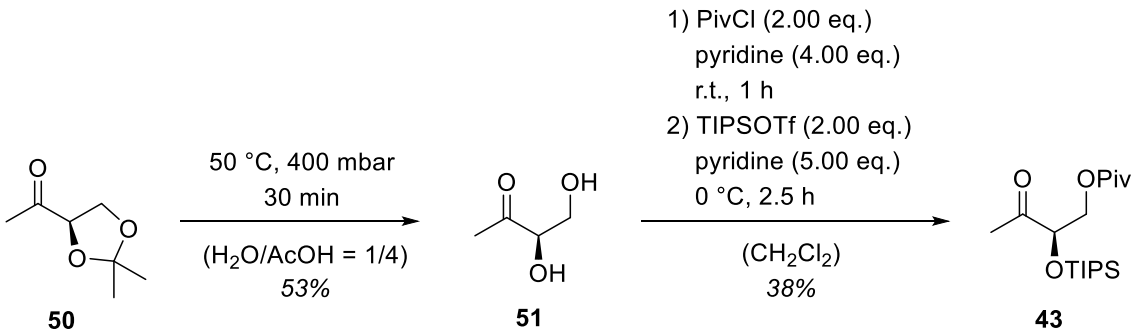
Scheme 25. Pivaloyl protection and oxidation of diol **44**.

The desired ketone **43** was isolated in a 50% yield and showed a specific rotation of +18.0. To validate this result, compound **43** was synthesized again, starting from acetal-protected D-Mannitol (**48**), which was provided by *S. Wienhold*.[30] First, a glycol cleavage with sodium periodate led to the corresponding aldehyde[57], which was directly treated with methyl magnesium bromide to deliver literature known alcohol **49** in 60% over two steps (Scheme 26).[58]



Scheme 26. Glycol cleavage of acetal protected *D*-Mannitol, followed by Grignard addition and oxidation.

The secondary alcohol was then oxidized to ketone **50** under literature known conditions.[58] Removal of the acetal group was accomplished by stirring the compound in acetic acid under reduced pressure to remove the acetone from the reaction (Scheme 27).[37]



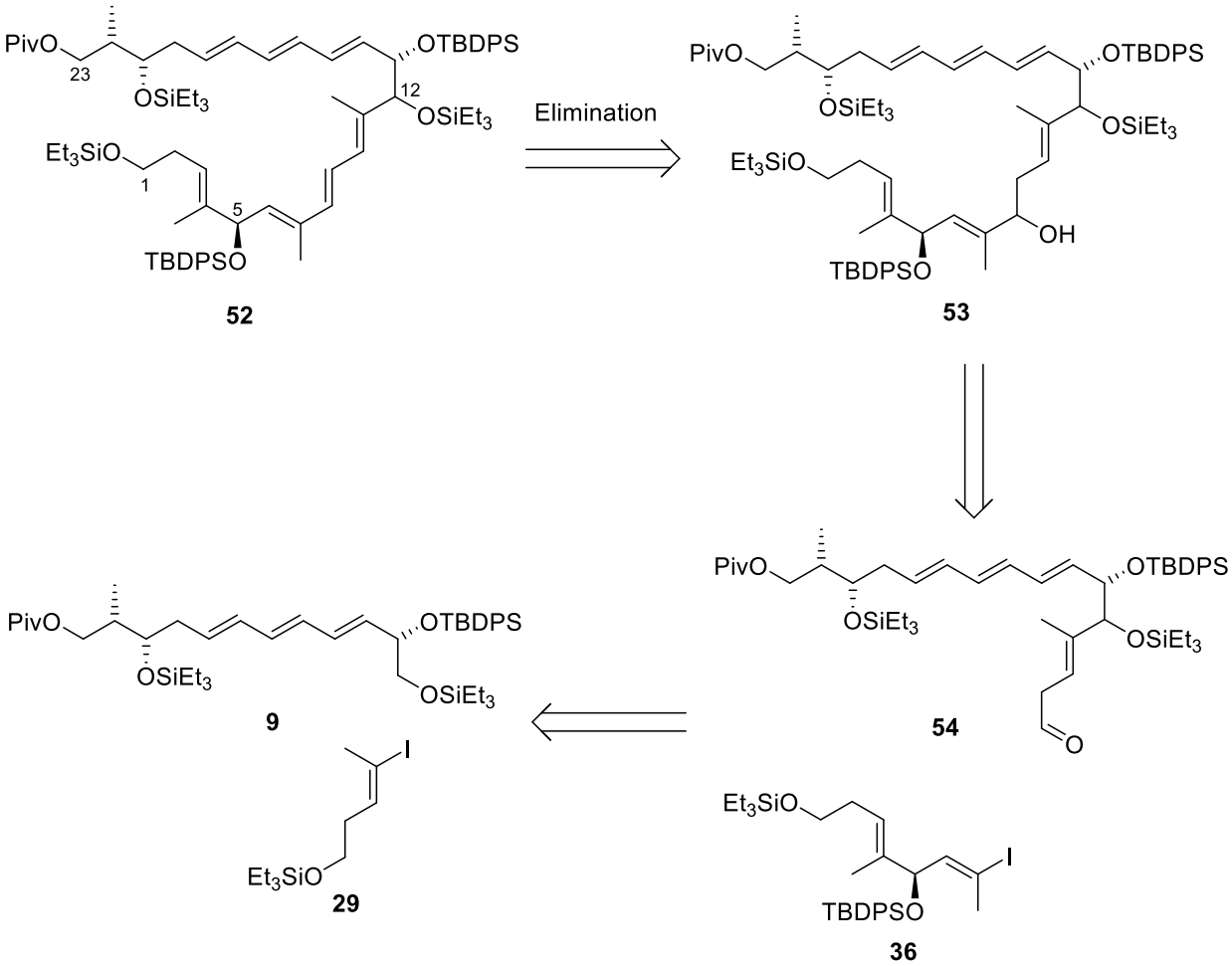
Scheme 27. Removal of the acetal and protection of the diol.

The diol **51** was obtained with 53% yield and was then successively treated with pivaloyl chloride and TIPS triflate. The protected compound **43** was isolated with 38% yield and showed a specific rotation of +11.0. This value differs from the specific rotation of +18.0, which was determined from the other route. However, this probably can be attributed to measurement error during the optical rotation measurement. In comparison, the specific rotation of the literature known enantiomer *ent*-**43** is reported to be –5.90.[56] This significant difference - especially with regards to the sign of the rotation value - strongly supports that the isolated compound **34** indeed has the expected (*S*)-configuration.

6. Construction of the C1-C23 macrolactone fragment

6.1. Triene formation by elimination

Our initial efforts focused on the formation of the C6-C11 triene unit. So far, the only successful approach involved the previously discussed Suzuki coupling with a protected dienyl iodide fragment (Scheme 7). Still, we wanted to explore other strategies for the formation of the triene aside from cross-coupling reactions. We envisioned that triene **52** could be synthesized by an elimination reaction of secondary alcohol **53** (Scheme 28).

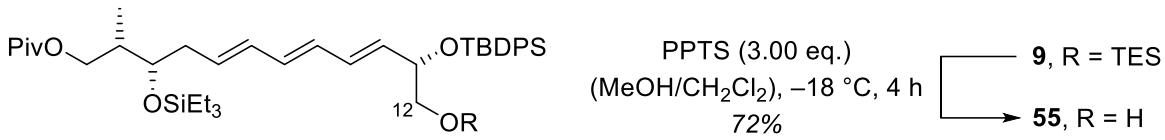


Scheme 28. Construction of triene **52** by an elimination strategy.

This alcohol could be accessed by the addition of the existing C1-C7 fragment **36** to aldehyde **54**. We assumed that a halogen metal exchange of the vinyl iodide **36** followed by addition to aldehyde **54** would be the most promising approach. Compound **54** should be obtained from known triene fragment **9** by selective removal of the C12 TES group, followed by oxidation and addition of the existing vinyl iodide fragment **29**. The dual use of fragment **29** – both for

the synthesis of the C1-C7 as well as the C8-C11 unit – would make the strategy very convergent.

Our synthesis commenced with the selective deprotection of triene fragment **9** (provided by *S. Hackl*) at the C12 position. Treatment of the compound with PPTS at –18 °C in a methanolic solution led to the desired alcohol in 72% yield (Scheme 29).

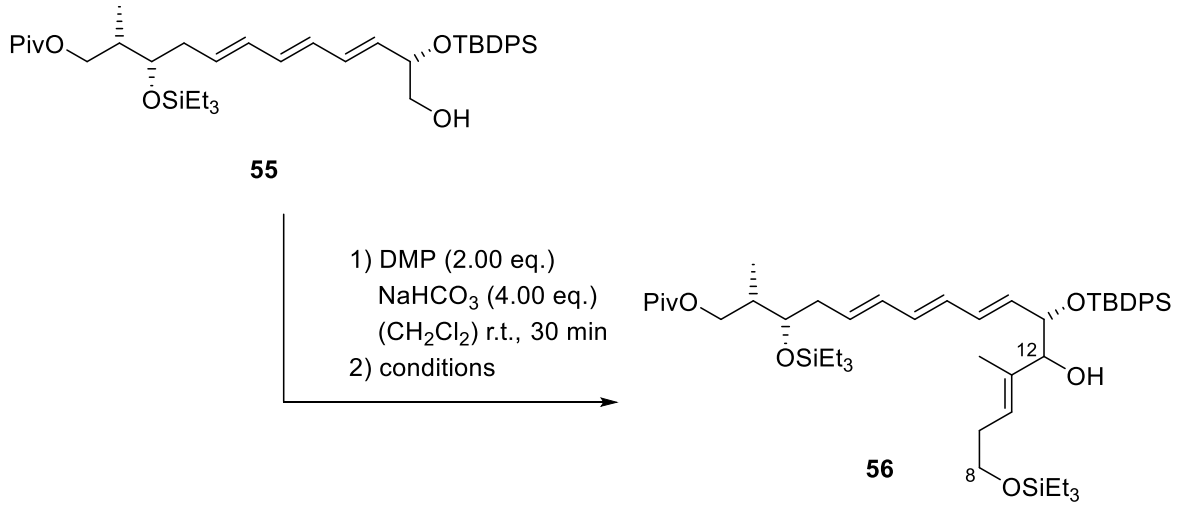


Scheme 29. Selective deprotection of the C12 TES group.

Alcohol **55** was oxidized using standard *Dess-Martin* conditions. The aldehyde turned out to be unstable on the column and was used without purification for the following experiments (Table 4).

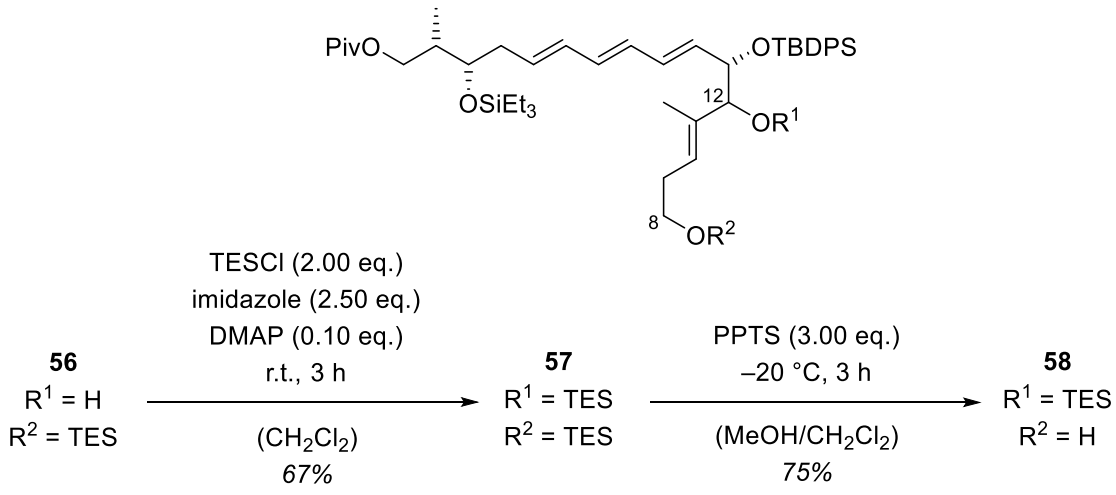
To facilitate the halogen metal exchange, vinyl iodide **29** was treated with *tert*-butyllithium at –78 °C. After stirring for ten minutes, the freshly prepared aldehyde was added. To our delight, the desired product **56** was isolated in a moderate yield of 45% as a mixture of diastereomers (entry 1). We hypothesized that the formation of the organozinc reagent would lead to a mild reaction and an increased yield. Transmetallation of the lithiated compound to zinc was facilitated by the addition of dimethyl zinc.[59] Unfortunately, the yield only marginally increased to 47%. However, the compound was isolated with an improved diastereomeric ratio of 8:1. While the diastereomeric ratio was inconsequential for further synthesis, it made NMR analysis much more convenient.

Table 4. Addition of the C5 fragment **29** *via* halogen metal exchange.



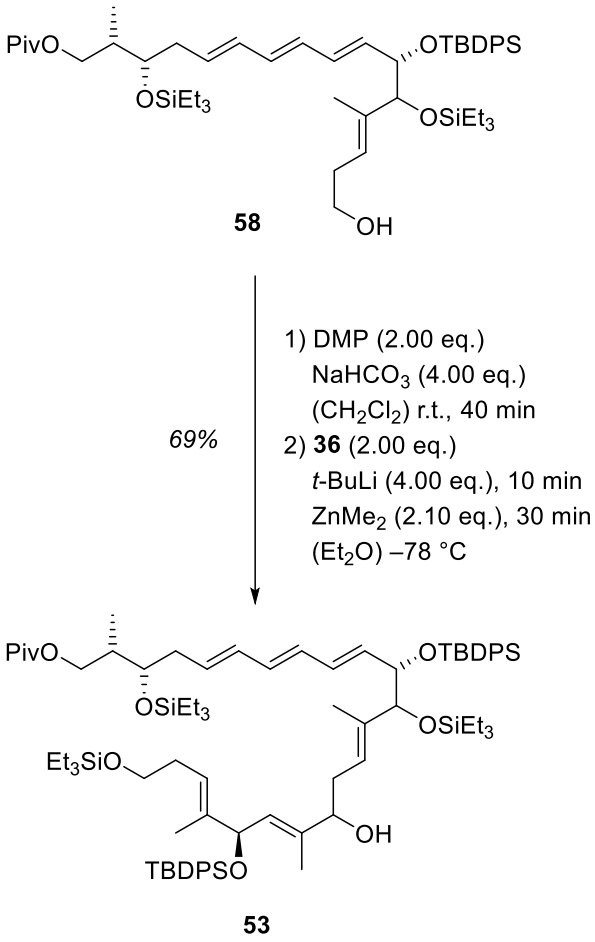
	Conditions	Solvent	T	t	Yield	d.r.
1	**29** (1.50 eq.) *t*-BuLi (3.00 eq.) then RCHO	Et_2O	–78 °C	20 min	45%	1:1
2	**29** (4.00 eq.) *t*-BuLi (8.00 eq.) $ZnMe_2$ (4.00 eq.) then RCHO	Et_2O	–78 °C	5 min 45 min	47%	8:1

TES protection of the secondary alcohol was accomplished using TESCl, imidazole, and DMAP with 67% yield (Scheme 30). The primary TES group of compound **57** was then selectively removed using PPTS at low temperature with a yield of 75%.



Scheme 30. TES protection of addition product **56** followed by removal of the C8 TES group.

The introduction of the C1-C7 **36** fragment was achieved by applying the same methodology as described above (Scheme 31). First, alcohol **58** was oxidized using *Dess-Martin* conditions. Simultaneously, vinyl iodide **36** was treated with *tert*-butyllithium and dimethyl zinc to generate the corresponding vinyl zincate. The addition of the aldehyde cleanly delivered the desired product **53** in 69% yield. Due to the lack of adjacent stereogenic centers that would allow for substrate-induced stereoselectivity, the compound was obtained as a 1:1 mixture of diastereoisomers.

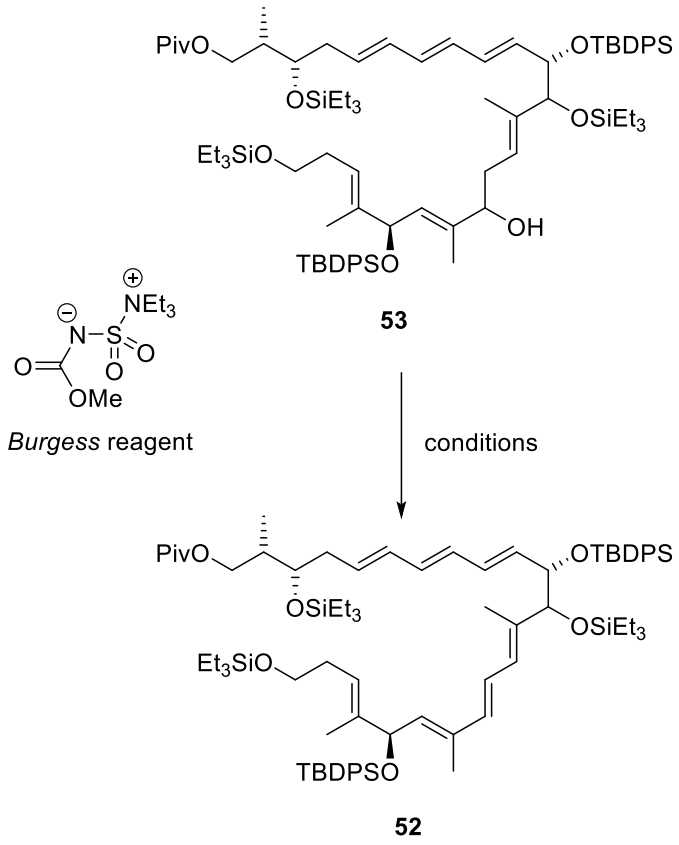


Scheme 31. Assembly of the C1-C23 fragment **53** by a metallation-addition-sequence.

With alcohol **53** in hand, the stage was set for the envisioned elimination reaction towards the desired triene fragment **52**. Literature reports suggested the formation of the mesylate, followed by treatment with base.[60] Indeed, treatment of the compound with mesyl chloride and a large excess of triethylamine led to the direct formation of the triene **52**, albeit in a low yield of only 23% (Table 5, entry 1). Furthermore, the reaction was not reproducible and often led to the decomposition of the starting material.

Gratifyingly, treatment of compound **53** with an excess of the *Burgess* reagent at 50 °C reproducibly led to the formation of the product in an acceptable yield of 55% (entry 2).[61]

Table 5. Elimination of alcohol **53** to triene **52**.

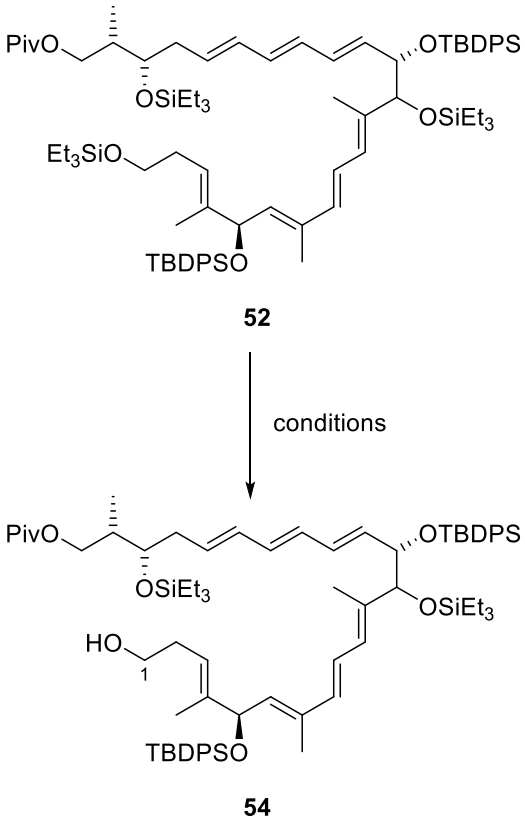


	Conditions	Solvent	T	t	Yield
1	MsCl (4.00 eq.) NEt_3 (100 eq.)	CH_2Cl_2	–78 °C ⟶ r.t.	24 h	23%
2	*Burgess* reagent (8.75 eq.)	toluene	50 °C	2 h	45%

The NMR showed two major diastereoisomers in a ratio of 3.6:1. These are probably caused by an E/Z mixture of the newly formed alkene, while the minor isomers, which stem from the C12 position, could not be detected anymore. A separation of the isomers was not possible at this point. Instead, the E/Z mixture was used for the next steps.

Deprotection of the primary TES group using PPTS only led to the decomposition of the material (Table 6, entry 1). To our delight, an excess of HF · pyridine delivered the desired primary alcohol **54** with a moderate yield of 62% (entry 2).

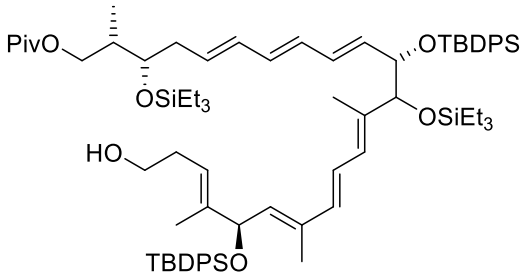
Table 6. Conditions for the deprotection of the C1 alcohol.



	Conditions	Solvent	T	t	Yield
1	PPTS (3.00 eq.)	MeOH/CH_2Cl_2	–20 °C	2 h	decomp.
2	HF · pyridine (84.0 eq.)	THF/Et_2O	0 °C	4 h	45%

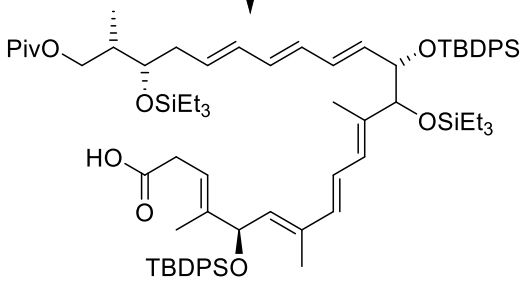
An oxidation sequence was intended to deliver carboxylic acid **55**.[62] While the oxidation under *Dess-Martin* conditions cleanly formed the aldehyde (according to TLC) within 40 minutes, the application of the *Pinnick* conditions only led to rapid decomposition of the material (Table 7, entry 1). Literature-known conditions for aerial oxidation using TEMPO also led to decomposition (entry 2).[63] Pyridinium dichromate (PDC) did not show conversion of the starting material (entry 3).[64]

Table 7. Attempts for the oxidation of alcohol **54** to carboxylic acid **55**.



54

conditions



55

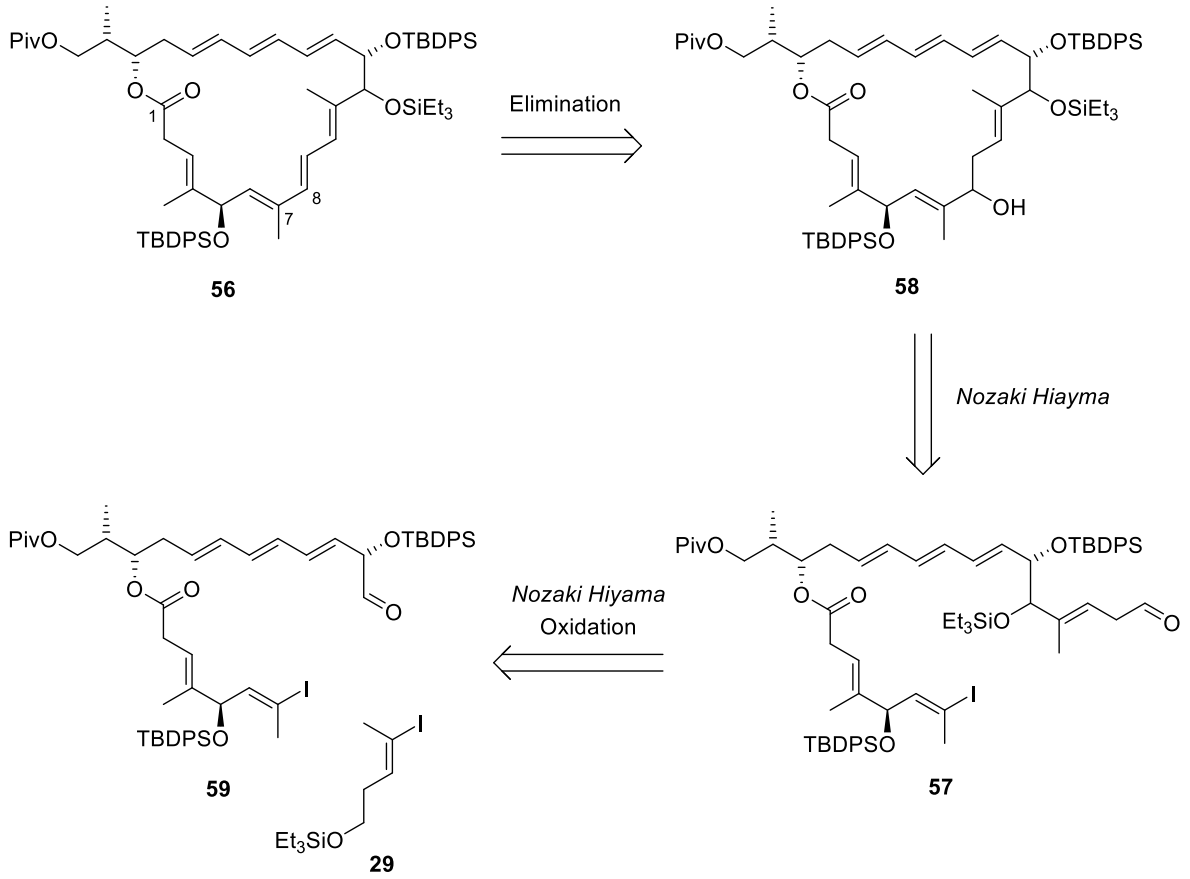
	Conditions	Solvent	T	t	Result
1	DMP (2.00 eq.) $NaHCO_3$ (4.00 eq.) then: NaOCl (3.00 eq.) NaH_2PO_4 (5.00 eq.) 2-methyl-2-buten (11.0 eq.)	1) CH_2Cl_2 2) *t*BuOH/H_2O	r.t.	1) 40 min 2) 30 min	decomp.
2	TEMPO (0.10 eq.) $Fe(NO_3)_3$ (0.10 eq.) KCl (0.10 eq.) O_2	DCE	r.t.	40 min	decomp.
3	PDC (3.50 eq.)	DMF	r.t.	24 h	n.c.

Around the time of these results, *S. Wienhold* discovered that the macrolactonization was not applicable to the C1-C40 fragment of Pulvomycin (see chapter 3). These new findings, along with the non-satisfying yield of the sequence (4.0% over seven steps from triene fragment **9** to

the primary alcohol **54**), made an application in the late stage of the total synthesis not feasible. Instead, we focused on macrocyclization strategies aside from lactonization approaches.

6.2. Macrocyclization approach by *Nozaki Hiyama* reaction

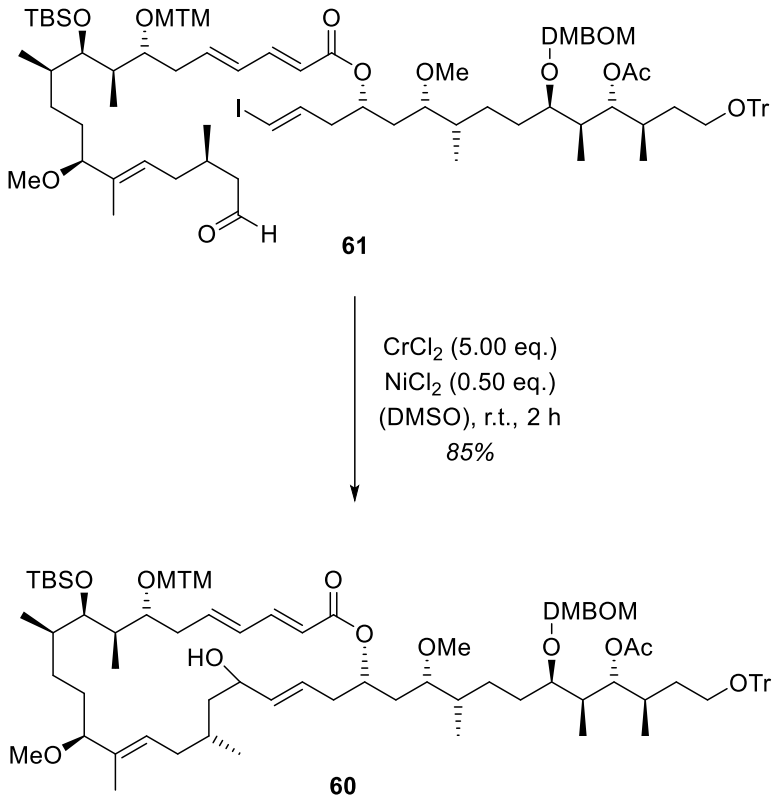
We envisioned that the macrocycle **56** could be accessible by ringclosure between C7 and C8. An intramolecular *Nozaki-Hiyama* reaction[65] of compound **57**, followed by the elimination of alcohol **58**, was intended to form the carbon bond (Scheme 32). The cyclization precursor **57** should be synthesized from aldehyde **59** and known C_5 unit **29**. Aldehyde **59** could be accessible from literature known triene fragment **9** after deprotection and selective esterification of the secondary alcohol with the previously described carboxylic acid **38**.



Scheme 32. Retrosynthesis of macrocycle **56** *via* intramolecular *Nozaki-Hiyama* reaction.

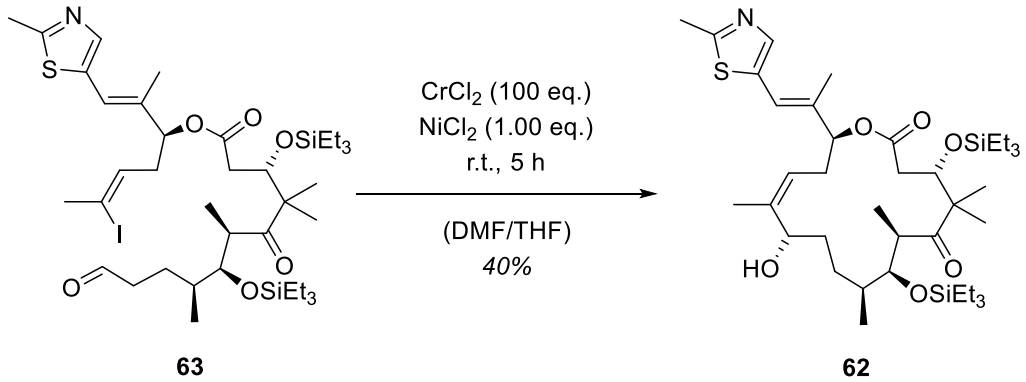
In recent years, the *Nozaki-Hiyama* reaction has become a widely used method for performing macrocyclizations.[66] The mild reaction conditions paired with a very high functional group tolerance render this method very applicable for use in late-stage total synthesis.[67] An outstanding example of a *Nozaki-Hiyama* cyclization is depicted in scheme 33. On the way

towards Aplyronine A, compound **61** was cyclized with an excellent yield using a slight excess of chromium-(II)-chloride and 10 mol% nickel-(II)-chloride in DMSO.[68]



Scheme 33. Macrocyclization *via Nozaki-Hiyama* coupling in the synthesis of Aplyronine A. DMBOM: [3,4-(dimethoxybenzyl)oxy]methyl, Tr: trityl, MTM: methylthiomethyl.

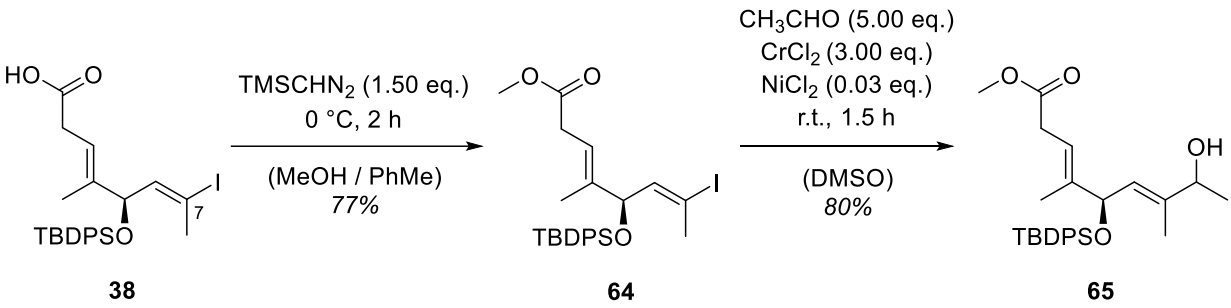
Similar conditions were used in the synthesis of protected Epothilone analog **62** by *Danishefsky* and co-workers (Scheme 34).[69]



Scheme 34. *Nozaki-Hiyama* approach towards protected Epothilone analog **62**.

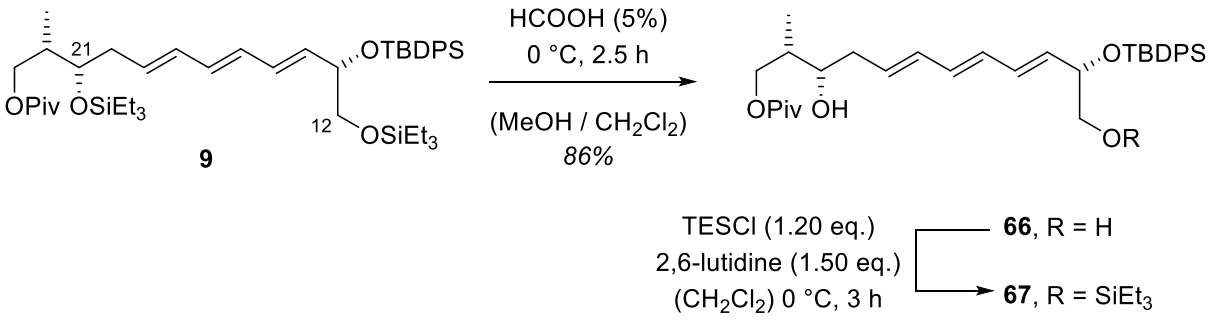
A larger excess of chromium chloride was employed (100 eq.), whereas the relative amount of nickel chloride was reduced to 1 mol% compared to the previous example. Compound **63** was converted into the desired macrocycle, although with a moderate yield of 40%.

Before synthesizing the actual cyclization precursor **57**, we wanted to verify if the vinyl iodide at C7 would undergo a *Nozaki-Hiyama* reaction in general. Therefore, carboxylic acid **38** was converted into the corresponding methyl ester **64** by treatment with TMS-diazomethane in 77% yield (Scheme 35).[70] Then, a *Nozaki-Hiyama* reaction using acetaldehyde was performed. Using three equivalents of chromium-(II)-chloride, 1 mol% nickel-(II)-chloride, and an excess of acetaldehyde, the desired product **65** was obtained in 80% yield.



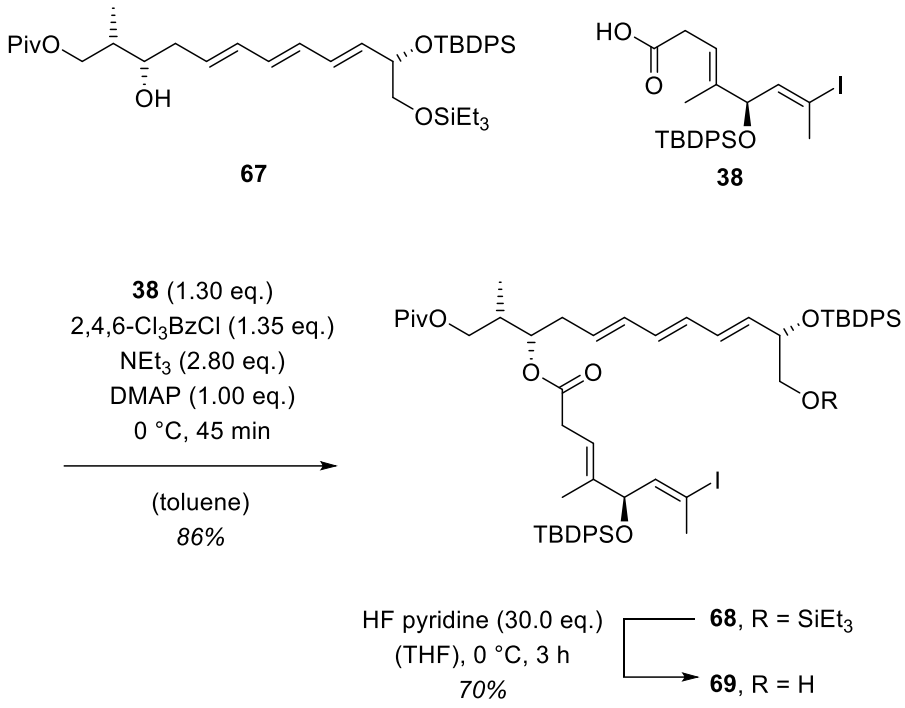
Scheme 35. Test reaction to analyze the reactivity of the vinyl iodide at C7.

With these promising results in hand, we proceeded with the synthesis of the macrocyclization precursor. The literature known triene fragment **9** was synthesized and provided by *S. Hackl*. In the first step, both TES groups were removed by treating the compound with 5% formic acid in dichloromethane and methanol (Scheme 36).[71] The diol **66** was then selectively TES protected at the primary position in 86% yield. This was accomplished by using 2,6-lutidine as a sterically demanding base.[72]



Scheme 36. Deprotection of the C12 and C21 TES groups using formic acid.

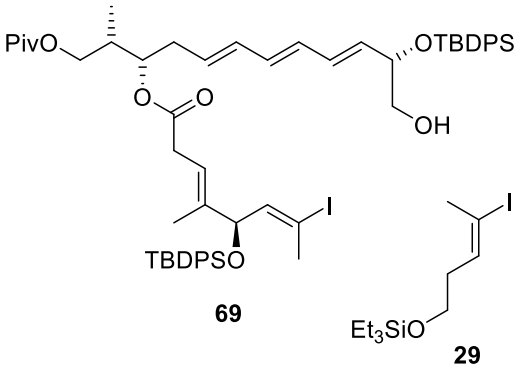
Next, the secondary alcohol **67** was esterified with the carboxylic acid fragment **38** (Scheme 37). A *Yamaguchi* protocol was used to generate the ester bond.[73] After the formation of the mixed anhydride using 2,4,6-trichlorobenzoyl chloride and triethylamine, the alcohol was added. The addition of DMAP initiated the reaction.

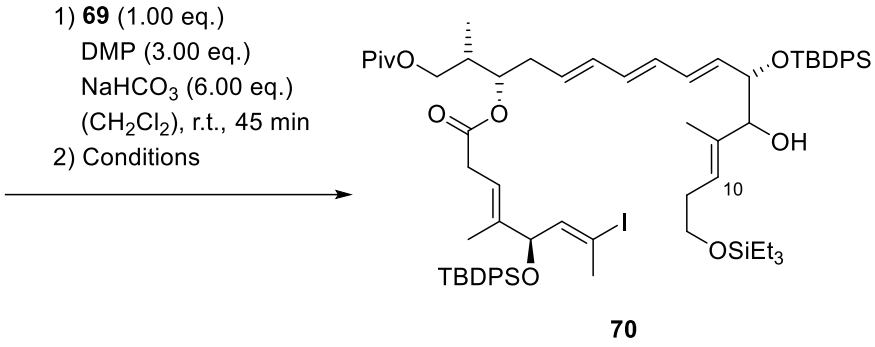


Scheme 37. Formation of the ester **68** followed by removal of the C12 TES group.

An excess of carboxylic acid was required to ensure complete conversion of the starting material, delivering the desired product **68** in an excellent yield of 86%. Subsequently, the primary TES group was removed using HF · pyridine, and the alcohol was oxidized to the aldehyde under *Dess-Martin* conditions. Initially, the vinyl iodide fragment **29** should be added after halogen metal exchange (Table 8, entry 1). While the reaction looked clean on TLC, the proton spectrum lacked the additional signal for the C10 alkene proton. Furthermore, ESI MS showed that the isolated compound had a mass of +16 compared to the desired product. While a sophisticated characterization of the isolated compound was not possible, the analytical data suggests oxygen incorporation to the molecule.

Table 8. Installation of the C8-C11 linker fragment.



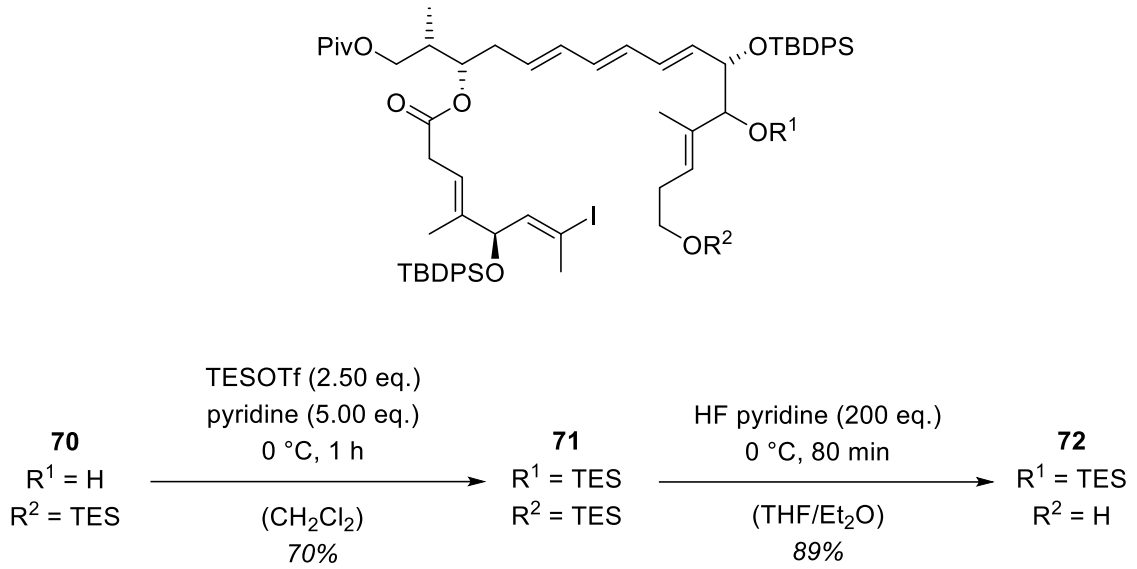


	Conditions	Solvent	T	t	Result
1	**29** (3.00 eq.) *t*-BuLi (5.00 eq.) $ZnMe_2$ (2.60 eq.) then RCHO	Et_2O	–78 °C	3 h	oxidated product
2	**29** (15.0 eq.) $CrCl_2$ (6.40 eq.) $NiCl_2$ (6.1 mol%) then RCHOCHO	DMSO	r.t.	2 h	42%

As an alternative, an intermolecular *Nozaki-Hiyama* coupling was considered to couple the two fragments. Vinyl iodide **29** was used in significant excess (15.0 equivalents) and stirred with $CrCl_2$ and $NiCl_2$ separately for ten minutes before adding the aldehyde. We hoped that this would minimize the chance of an undesired intramolecular *Nozaki-Hiyama* reaction at the C7 position. After the addition of the aldehyde at ambient temperature, full conversion was observed after two hours.

To our delight, the desired addition product **70** could now be obtained in a moderate yield of 42%. No reaction at the C7 iodide was observed.

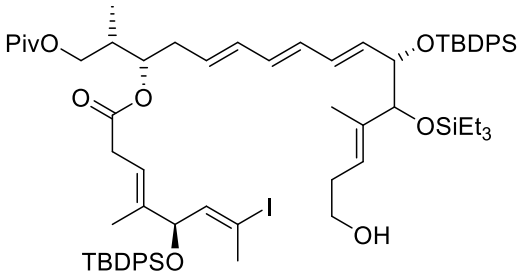
TES protection of the secondary alcohol using TES triflate and subsequent removal of the primary TES group with HF · pyridine proceeded with 70% and 89%, respectively (Scheme 38).



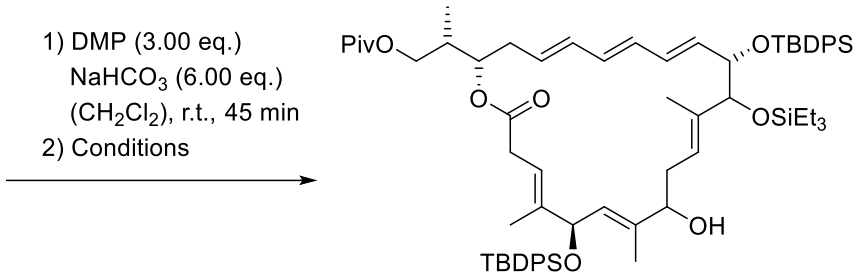
Scheme 38. TES-protection of the secondary alcohol **70** and removal of the primary TES group.

Oxidation of the primary alcohol **72** to the aldehyde worked well under *Dess-Martin* conditions. However, the aldehyde turned out to be very sensitive and could not be purified by column chromatography. Therefore, the aldehyde was used without purification in the following cyclization experiments (Table 9). Using six equivalents of a mixture of $CrCl_2$ and $NiCl_2$ (100:1), no conversion was observed after three hours (entry 1). Stirring for 24 hours only led to the decomposition of the starting material (entry 2). Increasing the excess of chromium-(II)-chloride to 100 equivalents only resulted in decomposition, too (entry 3). The product could be detected by ESI-MS when five equivalents of a 10:1 mixture of $CrCl_2$ and $NiCl_2$ in DMSO were used (entry 4). However, TLC analysis showed only very weak spots and mainly decomposition. We eventually concluded that the aldehyde is too sensitive and decomposes under the reaction conditions.

Table 9. Experiments for the *Nozaki-Hiyama* cyclization.



72

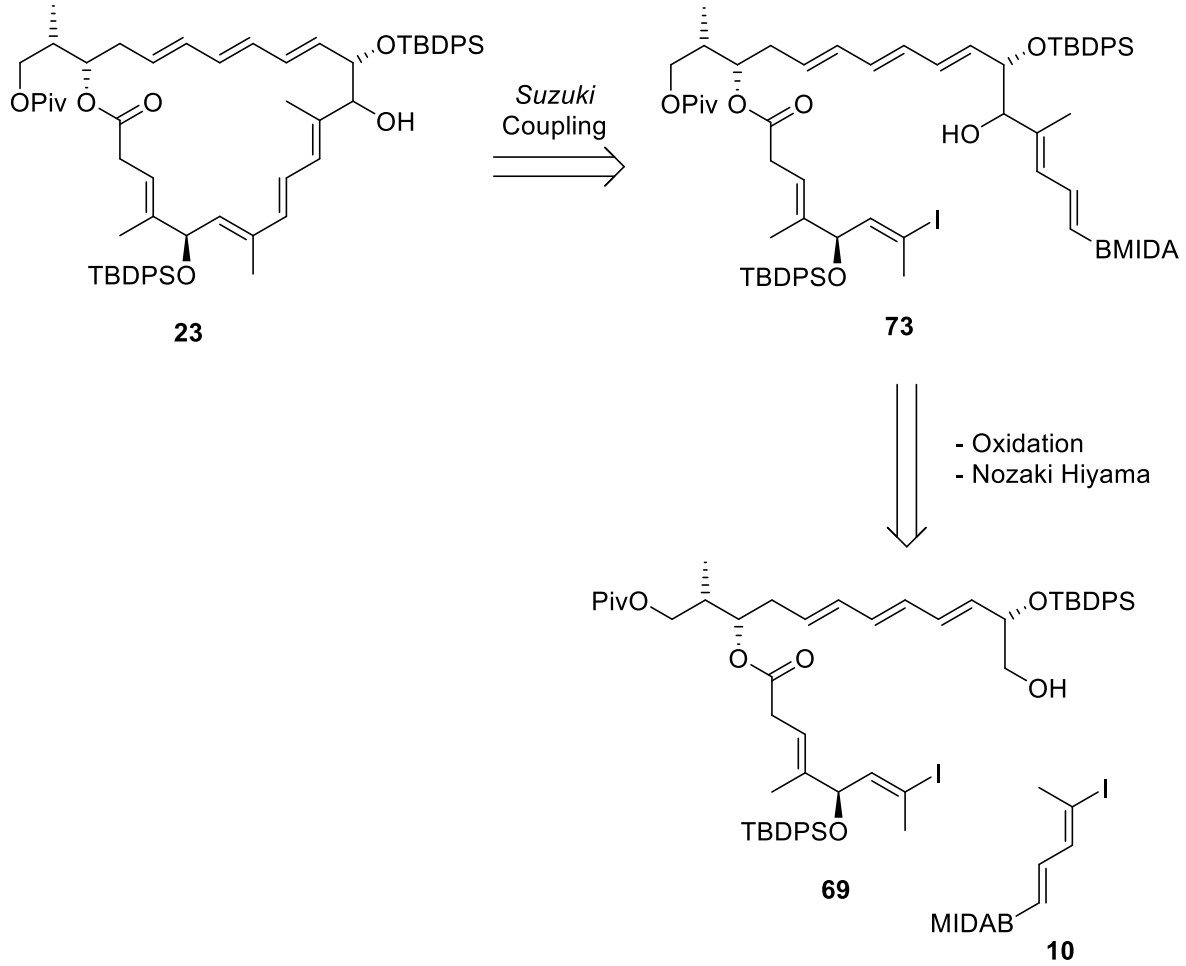


58

	$CrCl_2$ [eq.]	$NiCl_2$ [eq.]	Solvent	T	t	Result
1	6.00	0.06	DMSO	r.t.	3 h	n.c.
2	6.00	0.06	DMSO	r.t.	24 h	decom.
3	100	1.00	DMSO	r.t.	1 h	decom.
4	5.00	0.50	DMSO	r.t.	2.5 h	traces

6.3. Macrocyclization approach by *Suzuki* coupling

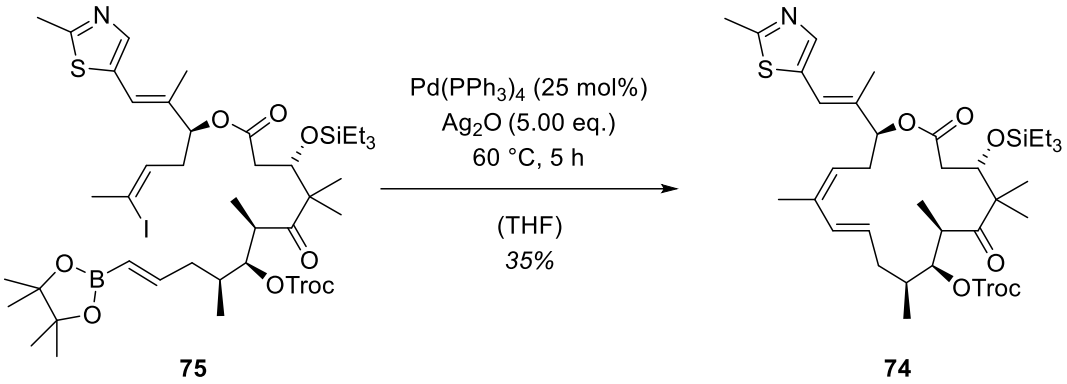
Eventually, we decided not to investigate the *Nozaki Hiyama* strategy further. Instead, we turned our attention towards a macrocyclization by an intramolecular *Suzuki* coupling.[74] As pointed out in chapter 3, *S. Wienhold* successfully connected the northern aldehyde fragment **19** to the southern fragment **7** using the dienyl iodide **10**.[30] We envisioned that the same principle should be possible in an intramolecular fashion. The corresponding cyclization precursor **73** could be synthesized by coupling diene **10** to the previously described alcohol **69** (Scheme 39).



Scheme 39. Putative synthesis of macrocycle **56** by intramolecular *Suzuki* coupling.

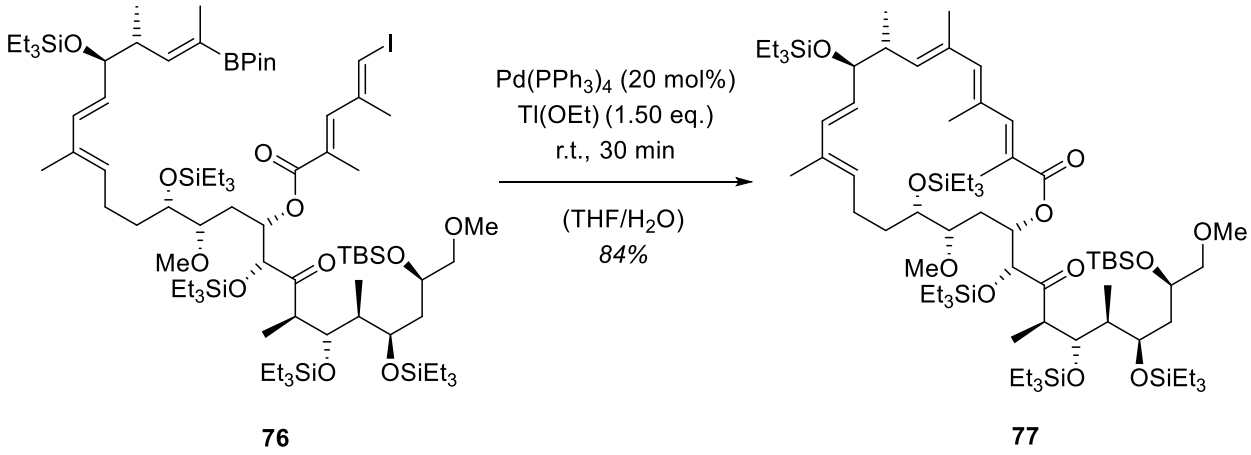
As with the *Nozaki-Hiyama* coupling, intramolecular *Suzuki* reactions are widely used for constructing macrocyclic molecules.[75] An example can again be found in the synthesis of Epothilone derivative **74** from *Danishefsky* and co-workers (Scheme 40).[69] Instead of the previously mentioned aldehyde **63**, the authors were also able to synthesize compound **75**,

which underwent intramolecular *Suzuki* cyclization upon treatment with a palladium(0) catalyst.



Scheme 40. Intramolecular *Suzuki* coupling for the construction of Epothilone core **74**.

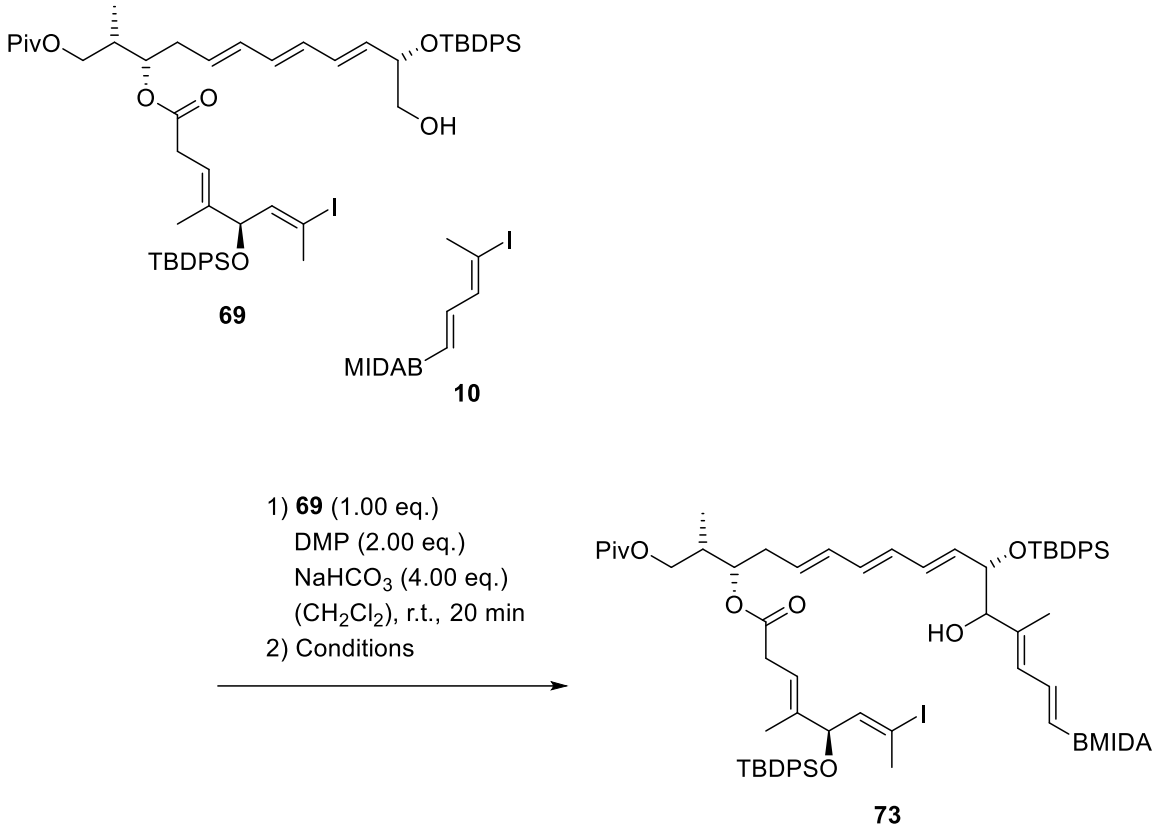
Another example can be found in the synthesis of Apoptolidinones A and D (Scheme 41).[76] Here, a triene unit was constructed by cyclization of compound **76** using $Pd(PPh_3)_4$ and thallium ethoxide as the base. The 20-membered macrolactone **77** was obtained in 84% yield while the sensitive TES ethers remained untouched.



Scheme 41. *Suzuki* cyclization leading to triene **77**.

In an initial experiment, the same reaction conditions as for the previously described *Nozaki-Hiyama* precursor **72** were applied (Table 10). Dienyl iodide **10** was stirred together with chromium-(II)-chloride and nickel-(II)-chloride for ten minutes before the aldehyde was added (entry 1).

Table 10. Synthesis of the *Suzuki* cyclization precursor **73**.



	$CrCl_2$ / $NiCl_2$ * [eq.]	**10** [eq.]	Solvent	T	t	Result
1	5.00	10.0	DMSO	r.t.	10 min / 1 h	traces
2	20.0	4.00	DMF	r.t.	1 h	23 %
3	20.0	4.00	DMF	r.t.	22 h	22 %
4	4.00	2.00	DMF	r.t.	2 h	-
5	50.0	4.00	DMF	r.t.	2 h	14 %
6	20.0	4.00	DMSO	r.t.	4 h	13 %

*100/1 mixture

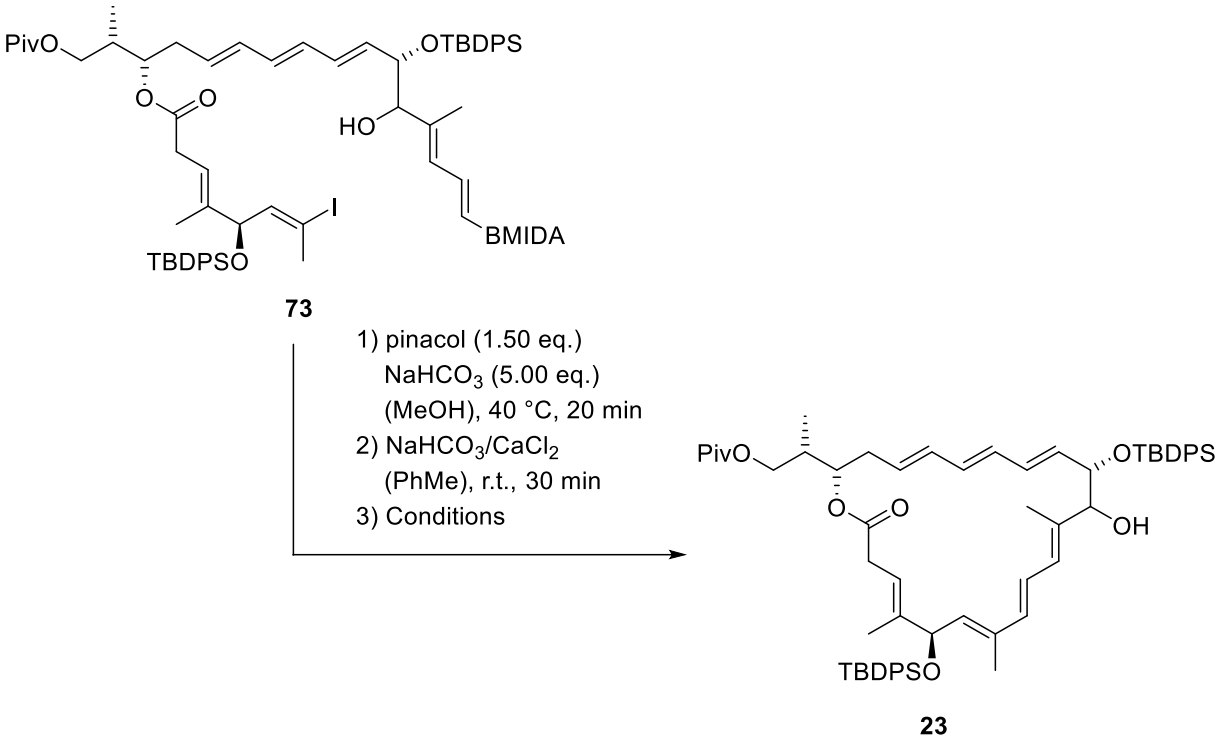
Unfortunately, this procedure only resulted in the formation of traces of the product. When dienyl iodide **10** and aldehyde were combined and then added to a suspension of the metal salts in DMF, the desired product could be isolated, albeit in a low yield of 23% (entry 2). Increasing the reaction time to 22 hours only marginally improved the yield (entry 3). A larger excess of chromium chloride decreased the yield to 14% (entry 5), while a lower amount of chromium-(II)-chloride resulted in sluggish conversion (entry 4). Switching to DMSO made no difference

(entry 6). In most experiments, the product was contaminated with varying amounts of the proto-deiodinated compound, suggesting an undesired reaction at the C7 position. Probably iodide **10** is less reactive than previously used iodide **29**, which leads to a competing reaction at C7. The two products have the same R_f value and cannot be separated. Although the BMIDA compounds are known to be bench-stable, addition product **73** turned out to be rather labile in our case.

Despite the low yield and the side reaction, the intramolecular *Suzuki* coupling was attempted. The conditions previously optimized by *S. Wienhold* were applied (Table 11).[30] First, the BMIDA ester was treated with methanol, sodium bicarbonate, and pinacole, followed by stirring with calcium chloride. Due to the high reactivity of the compound, purification turned out to be not feasible. Instead, the crude material was directly subjected to the Suzuki conditions. Using 30 mol% of $Pd_2(dba)_3$, 2.20 equivalents of triphenylarsane and five equivalents of silver oxide, the desired product was observed by ESI-MS (entry 1). When the calcium chloride step was omitted, the product (identified by ESI-MS) could be isolated in 10% yield (entry 2). However, the small quantities of material precluded detailed characterization. Using literature known conditions for *Suzuki* macrocyclization employing thallium ethoxide (entry 3) led to decomposition of the starting material.[76,[77]

A main problem for the unsuccessful results probably is the unclear reaction environment. Due to the reactivity and instability of the cyclization precursor, no statement about the purity of the compound could be made. The variety of different reagents used in the MIDA hydrolysis and the subsequent *Suzuki* coupling made a sophisticated optimization of the conditions difficult. Furthermore, residues of the reagent used for the hydrolysis of the MIDA ester might have an influence on the cyclization reaction.

Table 11. Conditions for the intramolecular *Suzuki* reaction.

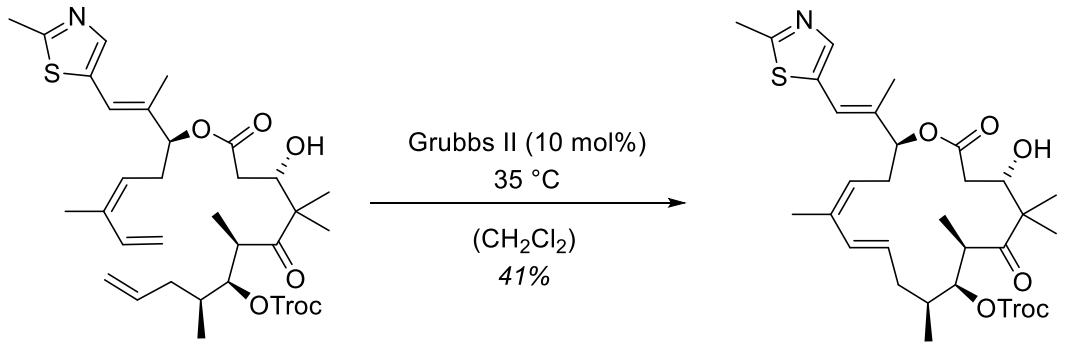


	Conditions	Solvent	T	t	Result
1	Pd_2dba_3 (30 mol%) $AsPh_3$ (2.20 eq.) Ag_2O (5.00 eq.)	THF/H_2O 10/1	r.t.	30 min	traces
2	*skip step 2* Pd_2dba_3 (30 mol%) $AsPh_3$ (2.20 eq.) Ag_2O (5.00 eq.)	THF/H_2O 10/1	r.t.	1 h	10 %
3	$Pd(PPh_3)_4$ (30 mol%) TlOEt (2.00 eq.)	THF/H_2O 3/1	r.t.	20 min	decompositon

The low yields for the intermolecular *Nozaki-Hiyama* reaction further limited the applicability in a late stage of the total synthesis. Furthermore, the uncontrollable contamination of the *Nozaki-Hiyama* cyclization precursor with hydro-de-iodinated product made the experiments even more difficult.

6.4. Macrocyclization approach by ring-closing metathesis

A widely used method for generating macrocycles is the ring-closing metathesis.[78] Advantages are the high functional group tolerance and the availability of highly advanced catalytic systems like the *Grubbs* catalysts.[79] One example can again be found in the Epothilone synthesis by *Danishefsky* (Scheme 42).

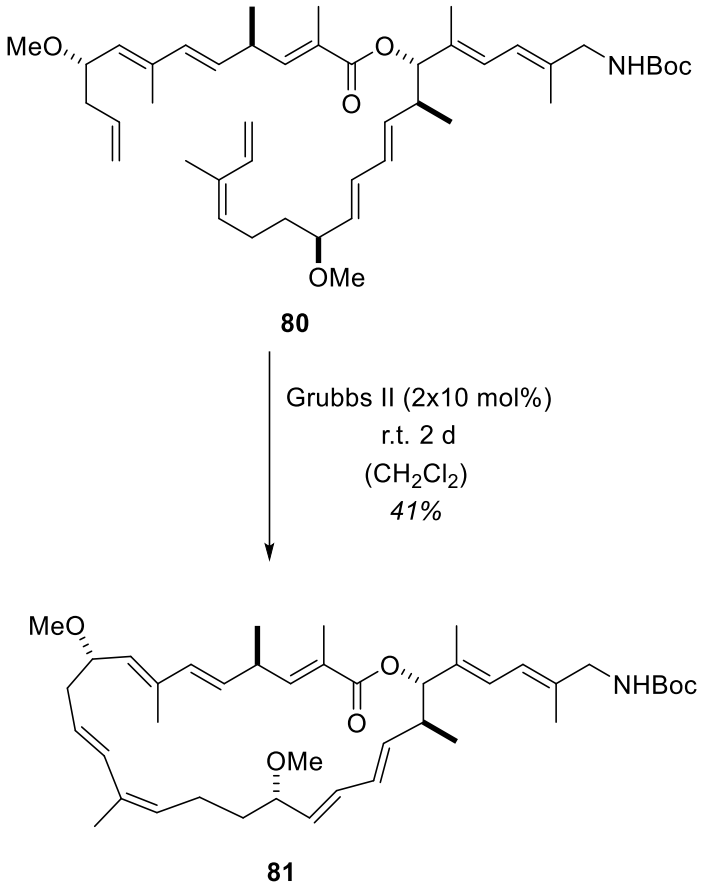


79 **78**

Scheme 42. Ring-closing metathesis in the synthesis of Epothilone analog **78**.

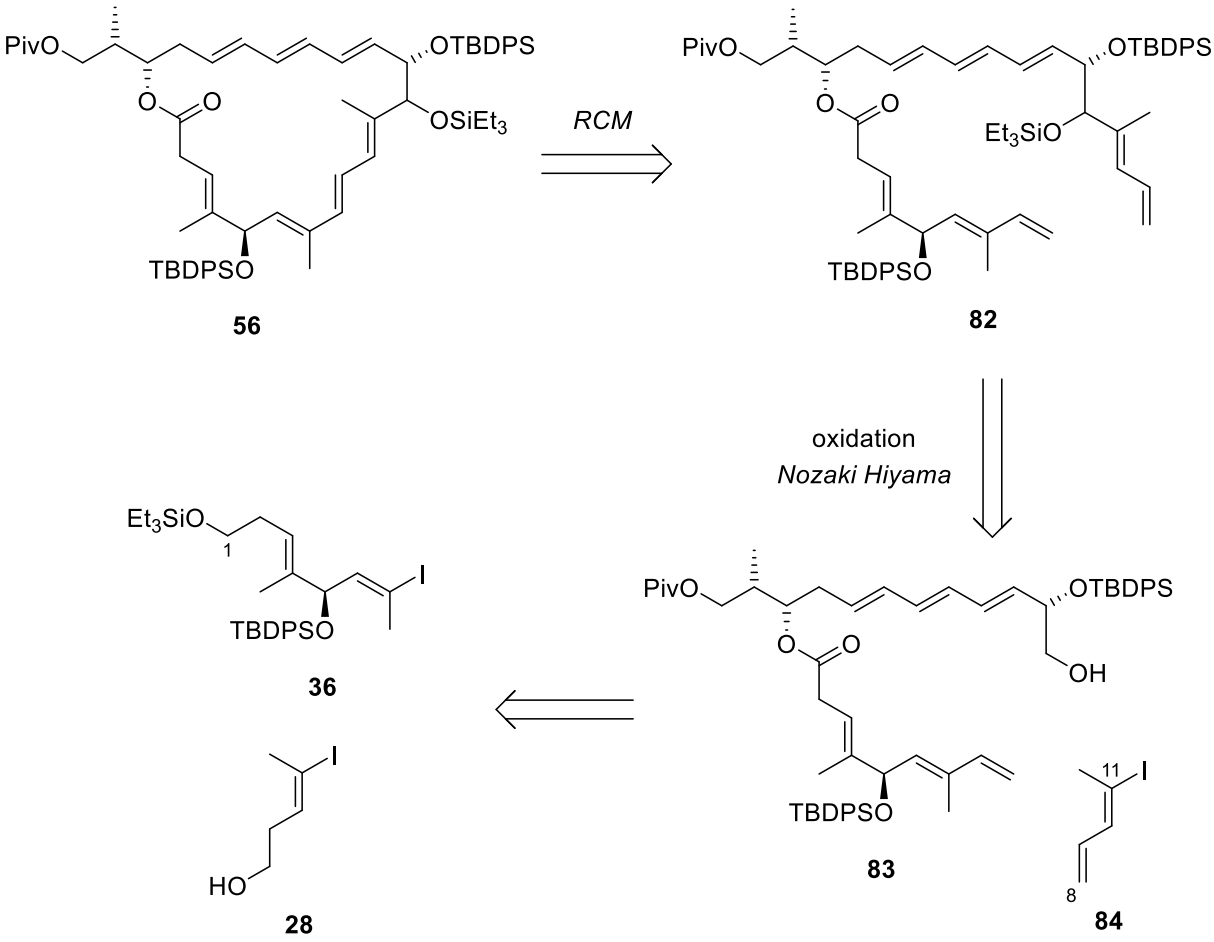
Even with the unprotected alcohol **79**, the desired product was obtained in 41% yield employing the second generation *Grubbs* catalyst.[80]

Fürstner et al. accomplished a very impressive application of the ring-closing metathesis for their synthesis of Iejimalide B (Scheme 43).[81] Starting from precursor **80**, the very sensitive macrocycle **81** could be constructed in an excellent yield of 96%. This result is particularly interesting because the reaction takes place exclusively at the two terminal double bonds. Despite the reaction time of two days, no interference with the internal double bonds was observed. This result encouraged us that a similar strategy would also work in our case.



Scheme 43. Cyclization of the complex macrolactone **81** using the second generation *Grubbs* catalyst.

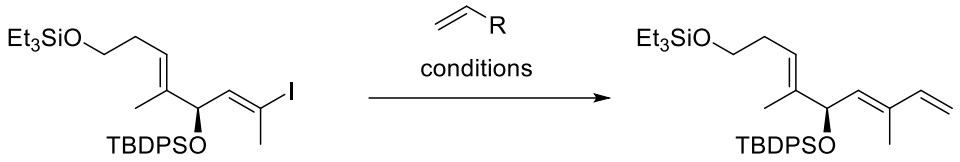
A possible precursor for the ring-closing metathesis is given in scheme 44. Due to the lack of reactive functional groups, we envisioned compound **82** to be much more stable compared to the previous cyclization precursors, and we hoped that this would lead to much better control over the reaction. As with the previous strategies, the C8-C11 linker should be installed by a *Nozaki-Hiyama* reaction starting from alcohol **83** and the dienyl iodide **84**. We envisioned that the dienyl iodide could be prepared from known alcohol **28** by an elimination reaction. Fragment **83** should be accessible by coupling iodide **36** with an appropriate C2 unit, followed by oxidation of the C1 alcohol and esterification with known alcohol **67**.



Scheme 44. Retrosynthetic analysis for the metathesis approach.

Starting from vinyl iodide **36**, the desired diene **85** could be synthesized by a *Stille* coupling[82] using tributyl vinyl tin and $Pd_2(dba)_3$, albeit in a very low yield of only 12% (Table 12, entry 1). Gratifyingly, the vinyl residue could also be attached by a *Suzuki* reaction using commercially available vinylboronic acid pinacol ester (entry 2) or potassium vinyltrifluoroborate (entry 3) with much better yields.[83]

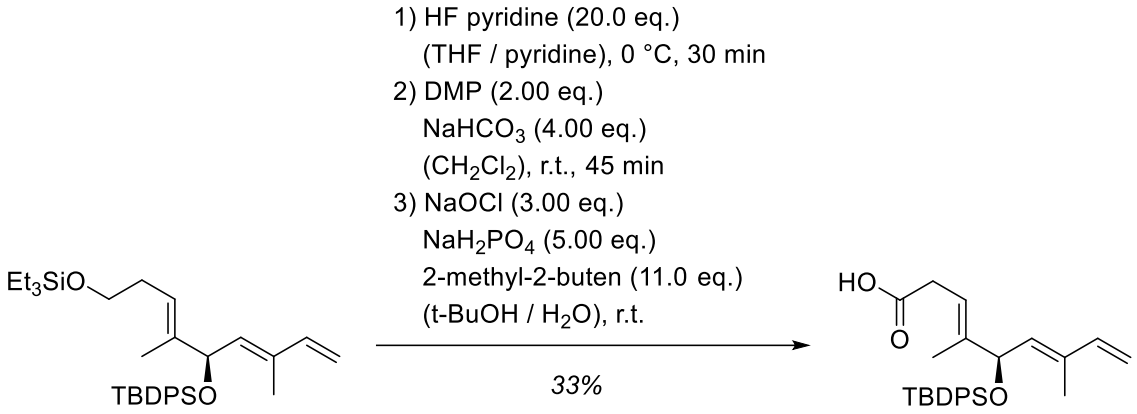
Table 12. Installation of the vinyl group by different cross-coupling experiments.



36 **85**

	Conditions	T	t	Result
1	R = $SnBu_3$ (3.00) Pd_2dba_3 (0.20) PPh_3 (0.40)	50 °C	30 min	12%
2	R = BPin (3.00) Pd_2dba_3 (0.15) $AsPh_3$ (1.20) Ag_2O (5.00)	r.t.	30 min	85%
3	R = BF_3K (3.00) Pd_2dba_3 (0.15) $AsPh_3$ (1.20) Ag_2O (5.00)	r.t.	2 h	77%

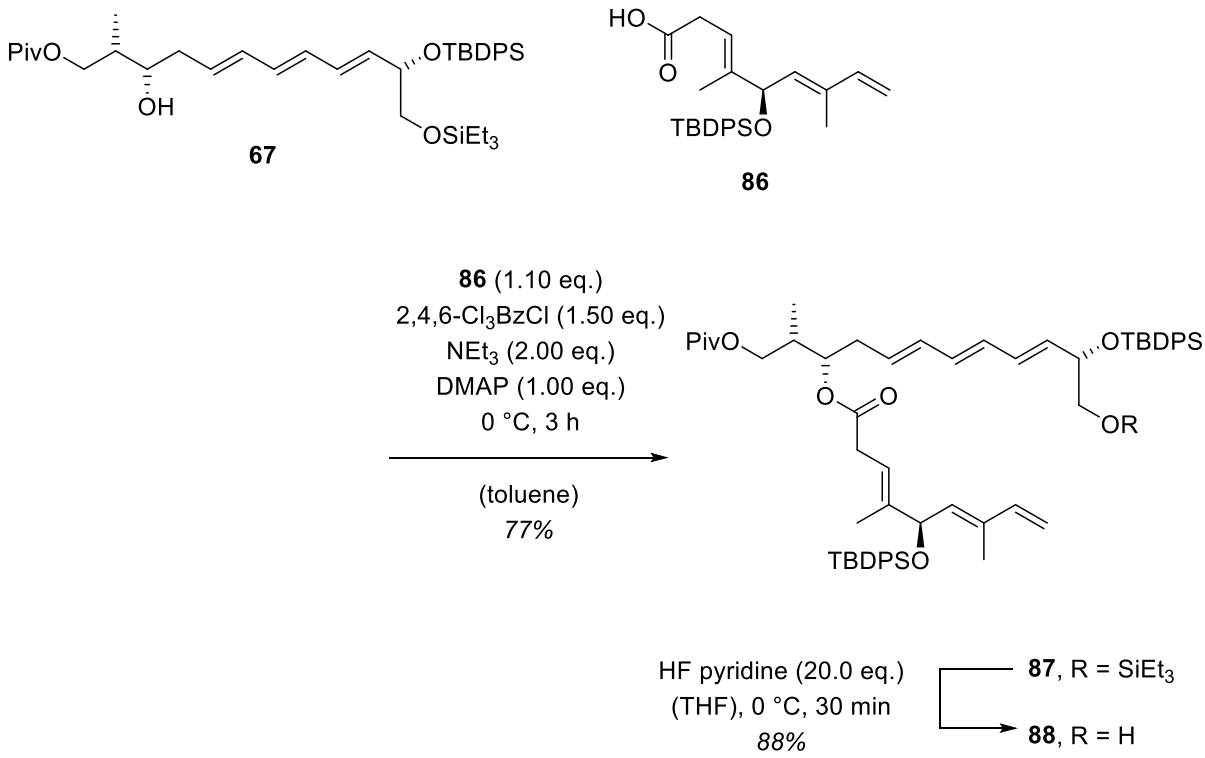
In analogy to the synthesis of carboxylic acid **38**, the TES group was removed with HF · pyridine, and the alcohol was oxidized in a two-step protocol, delivering the carboxylic acid **86** in 33% yield over three steps (Scheme 45).



85 **86**

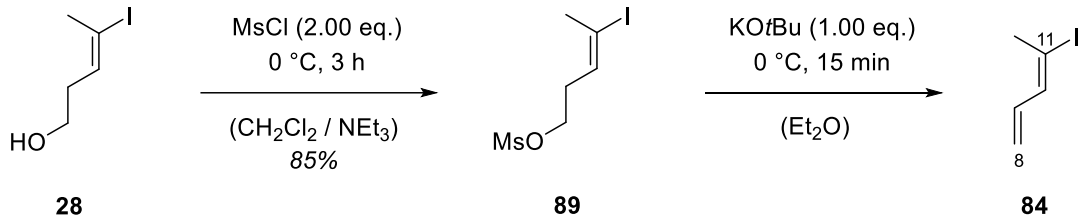
Scheme 45. Cleavage of the TES group followed by two-step oxidation to the carboxylic acid **86**.

Esterification with the secondary alcohol **67** proceeded smoothly under known *Yamaguchi* conditions, and the primary TES group could be removed in 88% yield using HF · pyridine (Scheme 46).



Scheme 46. Esterification of acid **86** with known alcohol **67**.

For the synthesis of the C8-C11 linker, alcohol **28** was converted into the mesylate **89** by reaction with mesyl chloride (Scheme 47).[84] Then, the mesylate was treated with potassium *tert*-butoxide, which cleanly furnished the desired elimination product **84**.[85]



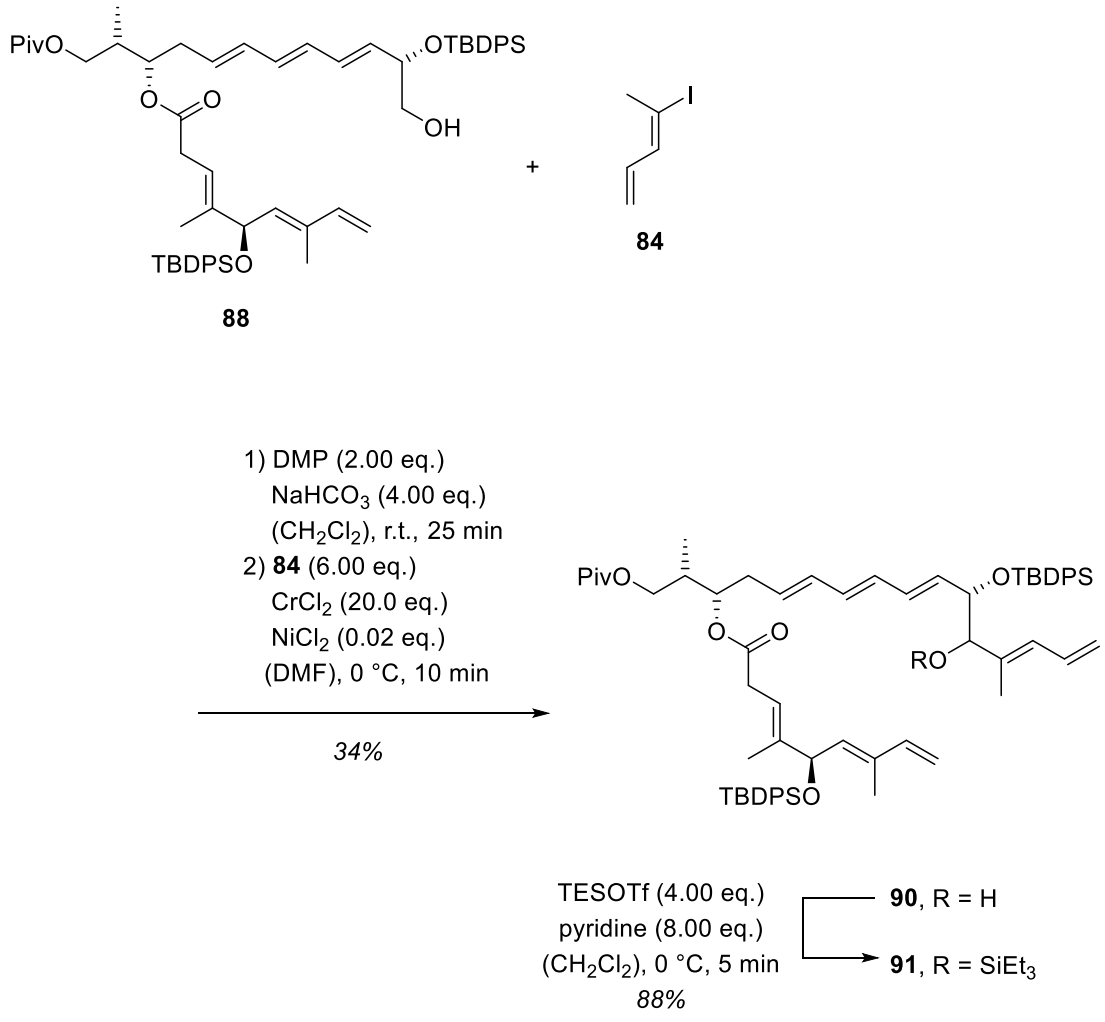
28 **89** **84**

Scheme 47. Preparation of sensitive dienyl iodide **84** by elimination of known alcohol **28**.

Dienyl iodide **84** turned out to be very volatile and not stable on the column, which made isolation and purification difficult. Therefore, diethyl ether was chosen as the solvent for the elimination step to make the removal of the solvent easier. Additionally, extraction after

aqueous workup was done with pentane instead of diethyl ether to exclude polar side products. By employing this protocol, the desired dienyl iodide **84** could be isolated in reasonably pure form without the need for further purification. Due to the volatility of the compound, it was routinely obtained in varying concentrations with diethyl ether (20-30%). Attempts to isolate the compound in a pure form usually led to a high loss of material. Furthermore, the compound rapidly decomposed if the solvent was removed completely. The residual solvent proved to have no significant impact on the subsequent *Nozaki-Hiyama* reaction, though.

The quality of the potassium *tert*-butanolate turned out to be of great importance for the reaction outcome. Older batches of the base resulted in sluggish conversion and required 1.5 – 2.0 equivalents to achieve complete elimination.



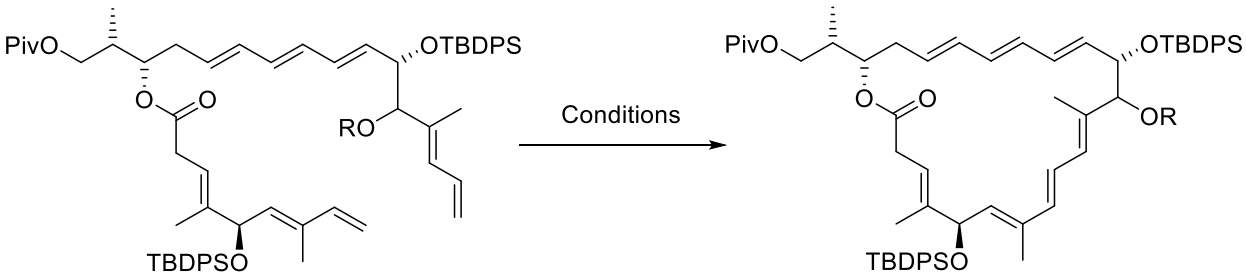
Scheme 48. Preparation of the metathesis precursors **90** and **91**.

On the contrary, when employing fresh potassium *tert*-butanolate, even slight excess of reagent immediately led to decomposition of the product.

With the dienyl iodide in hand, we proceeded towards the *Nozaki-Hiyama* reaction with alcohol **88** (Scheme 48). After oxidation to the aldehyde, the standard conditions for the *Nozaki-Hiyama* reaction were applied. Using six equivalents of iodide **84** and 20.0 equivalents of chromium-(II)-chloride, the product was obtained with an acceptable yield of 34%.

For the subsequent cyclization experiments, both the free alcohol **90** and the TES-protected derivative **91** were employed. The TES group was installed using TES triflate in 88% yield.[86] The experiments of the ring-closing metathesis are depicted in Table 13. Surprisingly, treatment of the TES-protected compound **91** with several catalysts (Figure 6) in dichloromethane led to no conversion, even at elevated temperatures (entries 1-3). When toluene was used as the solvent, traces of product could be observed by ESI-MS when the catalyst was used stoichiometrically at 60 °C (entry 4). However, the material decomposed with prolonged reaction time. Employing the third generation Grubbs catalyst led to no conversion at ambient temperature and decomposition at 50 °C (entries 5-6).

Table 13. Attempts for the ring-closing metathesis.



	Conditions	Solvent	R	T	t	Result
1	Grubbs I (0.10 eq.)	CH_2Cl_2	TES	r.t. ⟶ 40 °C	24 h	n.c.
2	Grubbs II (0.10 eq.)	CH_2Cl_2	TES	r.t. ⟶ 40 °C	24 h	n.c.
3	Grubbs II Hoveyda (0.10 eq.)	CH_2Cl_2	TES	r.t. ⟶ 40 °C	24 h	n.c.
4	Grubbs II (1.00 eq.)	PhMe	TES	r.t. ⟶ 45 °C	24 h	traces decomp.
5	Grubbs III (0.10 eq.)	PhMe	TES	r.t.	15 h	n.c.
6	Grubbs III (0.10 eq.)	PhMe	TES	50 °C	1.5 h	decomp.
7	Grubbs II (0.10 eq.)	PhMe	H	60 °C	1.5 h	traces

8	Grubbs II (0.60 eq.)	PhMe	H	r.t.	6 h	traces decomp.
9	Grubbs I (0.50 eq.)	PhMe	H	r.t. ⟶ 65 °C	3 h	traces decomp.

With the unprotected substrate **90**, traces of product were observed by ESI-MS with the Grubbs II catalyst at 60 °C (entry 7). Increasing the amount of catalyst led to product formation at room temperature (entry 8) - however, decomposition set in with prolonged reaction time. The same observation could be made with the first-generation Grubbs catalyst (entry 9).

Although product formation was observed *via* ESI-MS in some of the experiments, no material could be isolated. No significant change on TLC was observed, indicating that the product probably has a very similar retention value as the starting material. Hence, isolation of the desired product was not possible using standard chromatographic methods. With prolonged reaction time, the formation of a baseline spot on TLC was observed for most experiments. Probably, the terminal double bonds are not reactive enough, or the macrocycle is too strained. With a longer reaction time, the internal double bonds might begin to react with the catalyst, leading to the decomposition of the material.

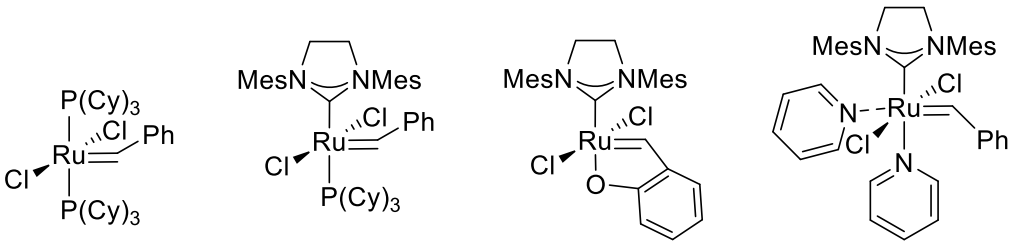
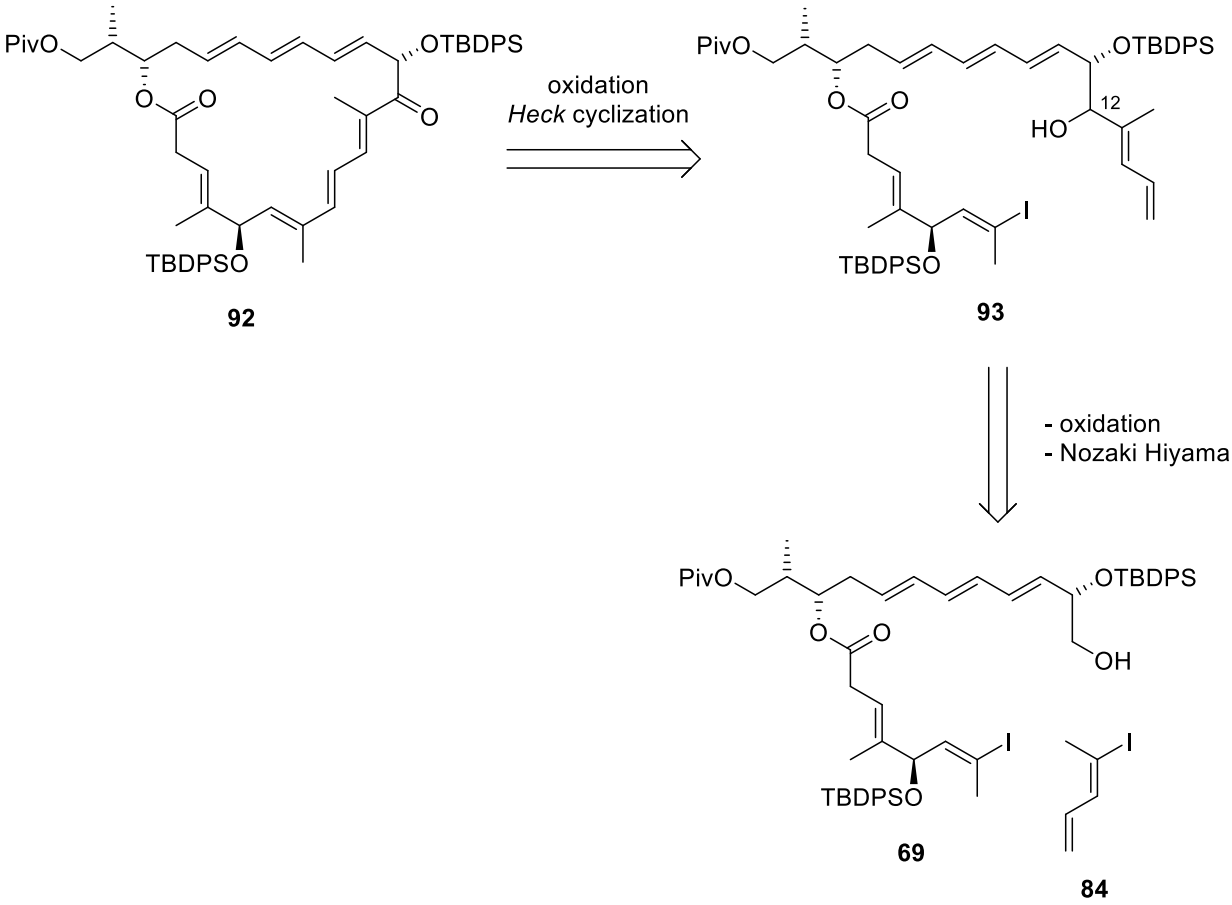


Figure 6. Overview of the different Grubbs catalysts.

6.5. Macrocyclization approach by *Heck* reaction

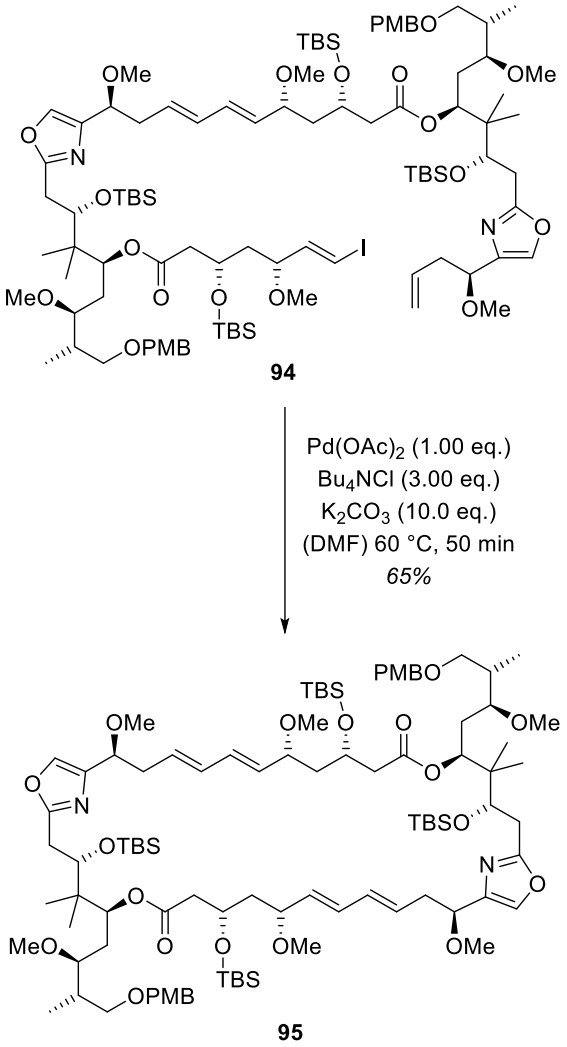
Looking at the failed ring-closing metathesis, we envisioned that we could attempt a *Heck* reaction to generate macrocycle **92** by replacing the vinyl group of compound **90** with a vinyl iodide moiety (Scheme 49). We imagined that oxidation of alcohol **93** to the ketone prior to the cyclization would be possible because *Heck* reactions with enone substrates are widely known.[87] . Hence, we would also circumvent the problem of the late-stage oxidation at C12, as discussed in chapter 3.



Scheme 49. Formation of macrocycle **92** by an intramolecular *Heck* reaction.

Cyclization precursor **93** should be accessible from the known alcohol **69** and previously described dienyl iodide **84** by applying the already established *Nozaki-Hiyama* protocol.

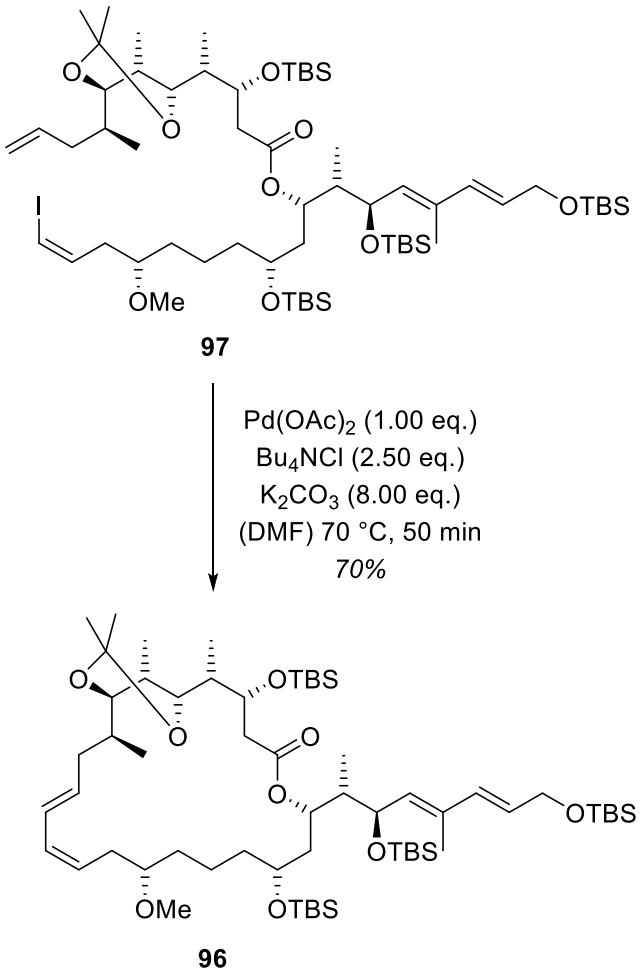
Macrocyclization strategies using an intramolecular *Heck* reaction are known in the literature, even for complex natural products. A prominent example is the total synthesis of Rhizopodin by *Menche* and co-workers (Scheme 50).[88]



Scheme 50. Heck cyclization in the total synthesis of Rhizopodin.

Starting from compound **94**, macrocycle **95** was obtained with 77% yield by applying palladium-(II)-acetate in combination with potassium carbonate and tetrabutylammonium chloride. Application of more advanced catalysts like $Pd_2(dba)_3$ or the addition of phosphane ligands only led to decomposition of the starting material **94**.

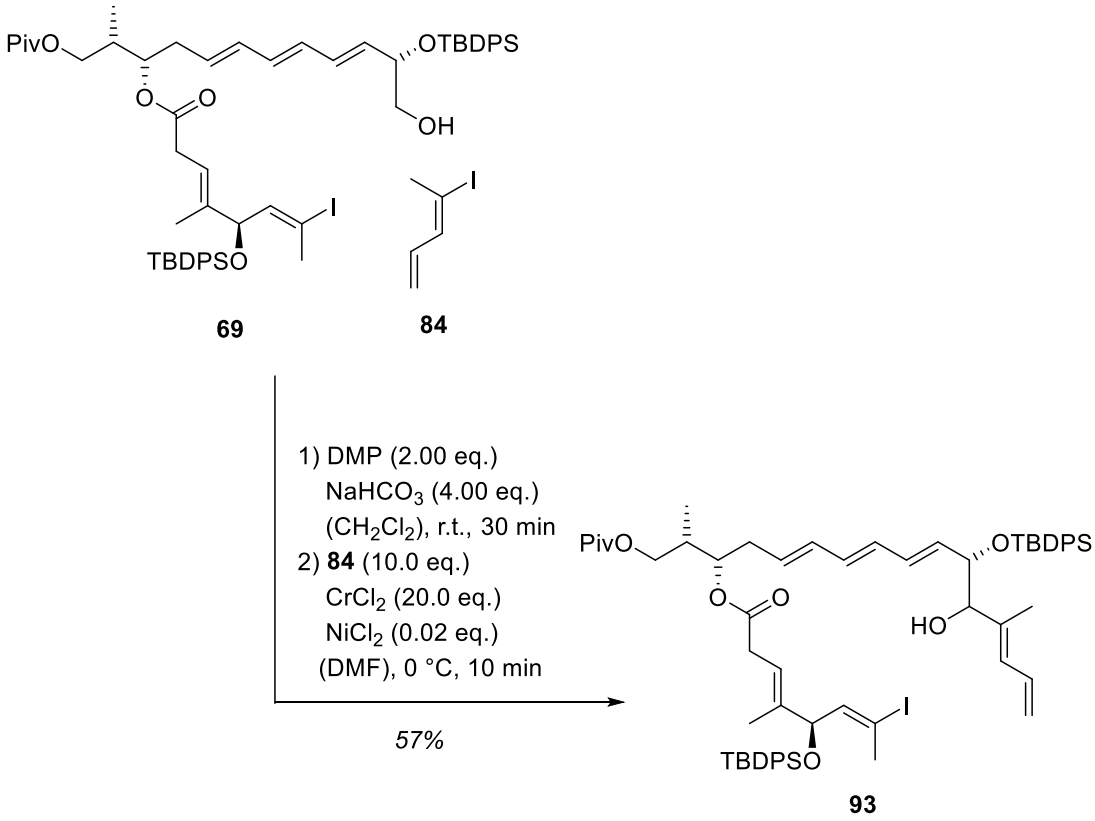
Similar conditions were applied in the synthesis of Etnangien, also by the *Menche* group.[70] Ringclosure of the 22-membered macrocycle **96** was achieved with 70% yield, again employing a stoichiometric amount of palladium-(II)-acetate (Scheme 51).



Scheme 51. Cyclization of compound **97** using *Jefferey* conditions.

These conditions are commonly referred to as *Jefferey* conditions and, in many cases, provide an enhanced reaction rate compared to ligand stabilized palladium(0) sources.[89] It is believed that palladium nanoclusters are formed, stabilized by a monolayer of the tetraalkylammonium salts.[90] However, ligandless conditions without the use of such tetraalkylammonium salts have been reported, too.[91]

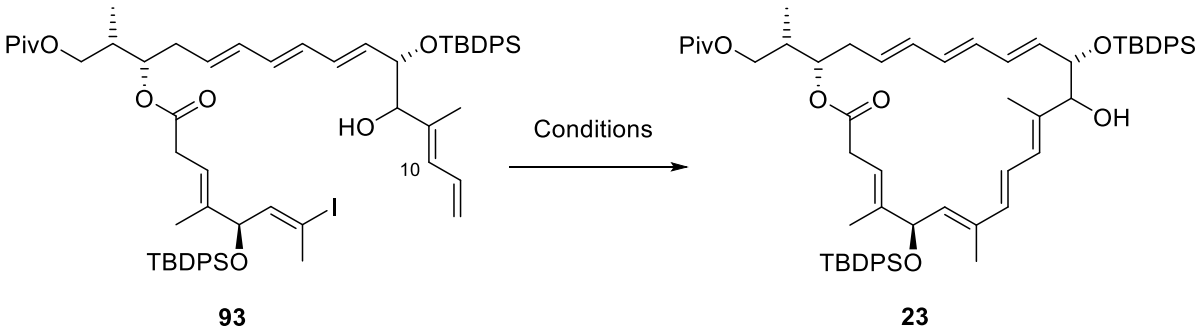
Our synthesis commenced with the preparation of the cyclization precursor **93**. Using the same reaction conditions as for the metathesis precursor **90**, the *Nozaki Hiyama* coupling with dienyl iodide **84** led to the desired product **93** in a moderate yield of 57% (Scheme 52).



Scheme 52. Preparation of the *Heck* cyclization precursor **93**.

Heck reactions with unprotected allyl alcohols leading to trienols are known in the literature.[92] Thus, we commenced our cyclization experiments using free alcohol **93** (Table 14).

Table 14. Attempts for the cyclization of unprotected alcohol **93**.



	Conditions	T	Solvent	t	Result
1	$Pd(OAc)_2$ (0.50 eq.) K_2CO_3 (2.00 eq.) TBACl (1.00 eq.)	r.t.	DMF	1 h	correct mass observed

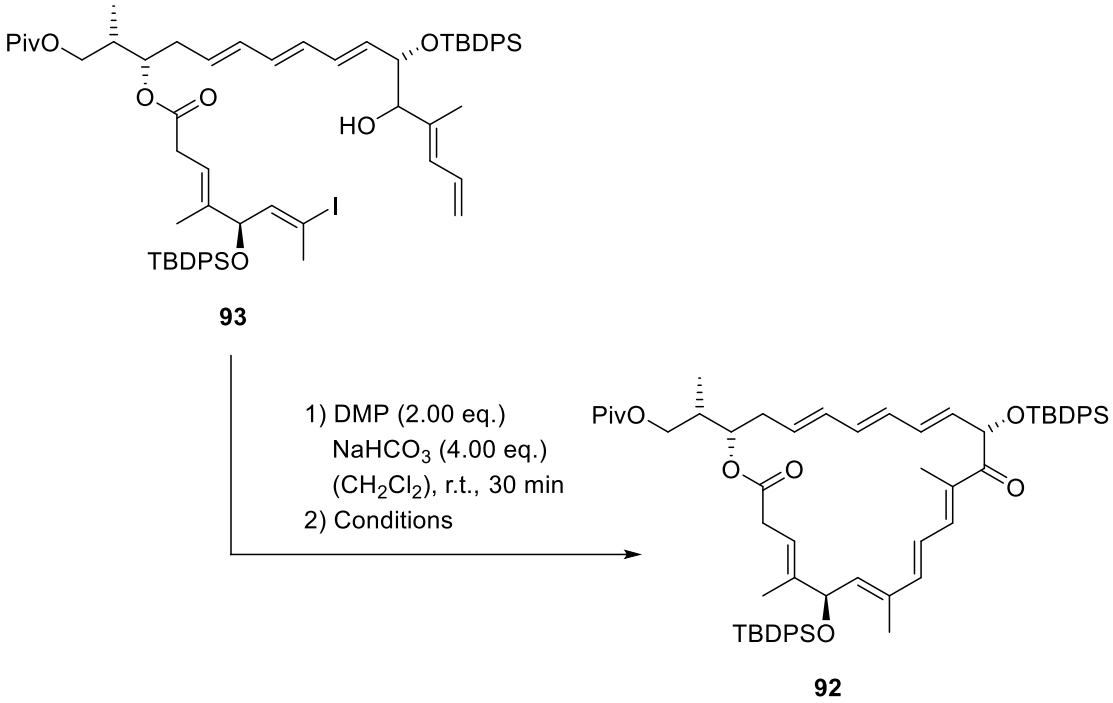
2	$Pd(OAc)_2$ (0.10 eq.) AgOAc (1.50 eq.) TBACl (1.00 eq.)	40 °C	DMF	24 h	traces
3	$Pd(OAc)_2$ (1.00 eq.) Ag_2CO_3 (2.00 eq.) TBACl (1.00 eq.)	40 °C	DMF	1 h	decomp.

Using 50 mol% palladium-(II)-acetate, two equivalents of potassium carbonate, and one equivalent of tetrabutylammonium chloride (TBACl), a product with correct mass (ESI) could be isolated (Table 14, entry 1). However, the NMR still showed the presence of the terminal alkene protons, which suggests a cyclization at the C10 position. Due to the very unclean NMR spectrum, the exact identity of the product could not be resolved. Switching to other bases like silver carbonate and silver acetate only led to decomposition.[93] Therefore, we decided to oxidize alcohol **93** to the ketone before applying the conditions for the *Heck* reaction.

Oxidation of the alcohol **93** using *Dess-Martin* conditions cleanly led to the formation of the desired ketone. Unfortunately, the compound turned out to be very labile and could not be purified by column chromatography. Still, the formation of the ketone could be unambiguously determined by NMR analysis. Due to its lability, the dienone was used without further purification for the subsequent *Heck* cyclization (Table 15). At first, the same conditions as for the free alcohol **93** were applied (entry 1). While there was no conversion at room temperature, the desired cyclized product could be isolated with an 18% yield when the reaction was heated to 40°C. Unfortunately, the reproducibility of the reaction turned out to be difficult, even when the palladium was used stoichiometrically (entry 2). Changing the solvent from DMF to THF led to no conversion (entry 3). Finally, the reaction could be performed reproducibly by omitting the ammonium salt and using potassium phosphate instead of potassium carbonate (entry 4). However, the yield still did not exceed 18%. Changing the solvent from DMF to DMA even further decreased the yield to 10% (entry 5). Reducing the amount of potassium phosphate to one equivalent led to sluggish and incomplete conversion (entry 6), while a larger excess of base increased the yield only marginally (entry 7). When catalytic amounts of palladium were employed, the reaction time drastically increased to 22 hours while further decreasing the yield to 5% (entry 8).[94] By using PPh_3 as the base, the de-iodinated product was observed in the mass, but no material could be isolated (entry 9). The addition of a phosphane ligand to the reaction only led to decomposition (entry 10).[95] Utilizing $Pd(PPh_3)_4$ in DMF also decomposed the starting material (entry 11). A yield of 18% could be achieved using catalytic

amounts of Pd_2dba_3 in DMF (entry 12). However, this single result could not be reproduced. Silver carbonate as base led to no conversion (entry 13).

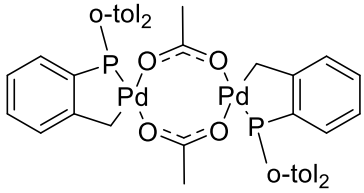
Table 15. *Heck* cyclization with dienone substrate.



	Conditions	T	Solvent	t	Result
1	$Pd(OAc)_2$ (0.50 eq.) K_2CO_3 (2.00 eq.) TBACl (1.00 eq.)	40 °C	DMF	1 h	18% reproducibility
2	$Pd(OAc)_2$ (1.00 eq.) K_2CO_3 (2.00 eq.) TBACl (1.00 eq.)	40 °C	DMF	1 h	18% reproducibility
3	$Pd(OAc)_2$ (1.00 eq.) K_2CO_3 (2.00 eq.) TBACl (1.00 eq.)	40 °C	THF	2 h	n.c.
4	$Pd(OAc)_2$ (1.00 eq.) K_3PO_4 (2.00 eq.)	r.t.	DMF	1.5 h	18%
5	$Pd(OAc)_2$ (1.00 eq.) K_3PO_4 (2.00 eq.)	r.t.	DMA	1.5 h	10%
6	$Pd(OAc)_2$ (1.00 eq.) K_3PO_4 (1.00 eq.)	r.t.	DMF	1.5 h	8%

7	$Pd(OAc)_2$ (1.00 eq.) K_3PO_4 (10.0 eq.)	r.t.	DMF	2 h	19%
8	$Pd(OAc)_2$ (1.00 eq.) K_3PO_4 (2.00 eq.)	r.t.	DMF	22 h	5%
9	$Pd(OAc)_2$ (1.00 eq.) PPh_3 (2.00 eq.)	r.t.	DMF	2 h	-
10	$Pd(OAc)_2$ (0.25 eq.) dppp (0.50 eq.) K_3PO_4 (2.00 eq.)	r.t.	DMF	5 h	decomp.
11	$Pd(PPh_3)_4$ (1.00 eq.), K_3PO_4 (2.00 eq.)	r.t.	DMF	10 min	decomp.
12	$Pd_2(dba)_3$ (0.10 eq.), K_3PO_4 (2.00 eq.)	r.t.	DMF	22 h	"18%"
13	$Pd(OAc)_2$ (1.00 eq.), Ag_2CO_3 (2.00 eq.)	r.t.	DMF	4 h	n.c.
14	$Pd(OAc)_2$ (1.00 eq.), Cy_2NMe (5.00 eq.), $P(oTol)_3$ (2.00 eq.)	r.t.	DMF	4 h	n.c.
15	Pd/C (5 wt%) (0.10 eq.), K_3PO_4 (2.00 eq.)	r.t. ⟶ 50 °C	DMF		decomp.
16	Pd/C (5 wt%) (1.00 eq.), K_3PO_4 (2.00 eq.)	r.t. ⟶ 50 °C	DMF		decomp.
17	$Pd(P^tBu_3)_2$ (0.25 eq.), K_3PO_4 (2.00 eq.)	r.t.	DMF		n.c.
18	*Herrmann*'s catalyst (0.25 eq.) $Na(OAc)_2$ (2.00)	r.t.	DMF		decomp.

Also, literature known conditions employing Cy_2NMe and P(*o*-tol)3 did not show any conversion (entry 14).[96] Experiments with palladium on charcoal only decomposed the material both when used catalytically (entry 15) and stoichiometrically (entry 16).[97] Employing literature known conditions using a $Pd(P^tBu_3)_2$ catalyst did not lead to conversion (entry 17),[89c] while *Herrmann*'s Catalyst (**98**, figure 7) decomposed the starting material (entry 18).[98]

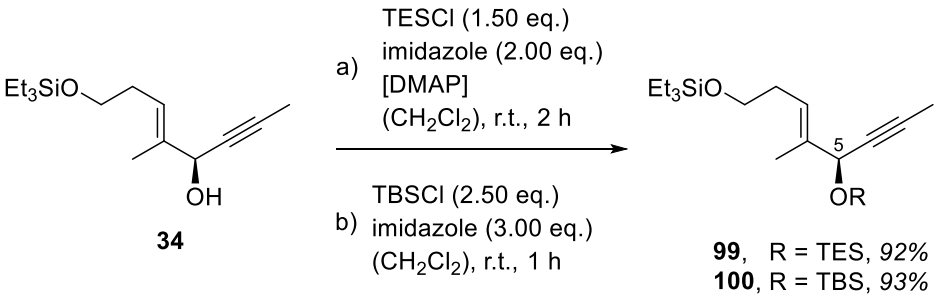


98

Figure 7. Structure of *Herrmann*'s catalyst **98**.

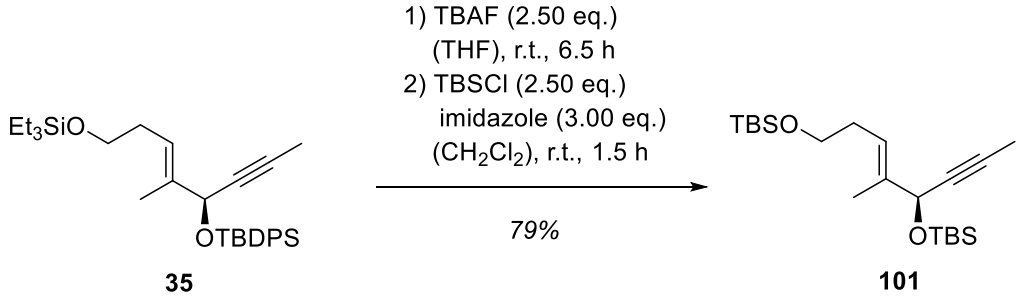
With none of the reaction conditions improving the yield, we turned our attention towards the cyclization precursor itself. We argued that the sterically demanding TBDPS protecting group at C5 might have an influence on the cyclization. Indeed, there is little to no literature precedence for a TBDPS protected allyl alcohol fragment used in a *Heck* reaction. Usually, only TBS or TES groups are employed. Therefore, we decided to synthesize both the TBS- and TES-protected *Heck* precursor to improve the yield of the cyclization.

The double TES-protected compound **99** was synthesized from alcohol **34** with 92% yield. The introduction of the TBS group was accomplished with 93% yield (Scheme 53).



Scheme 53. Preparation of the C5 TES- and TBS-protected compounds.

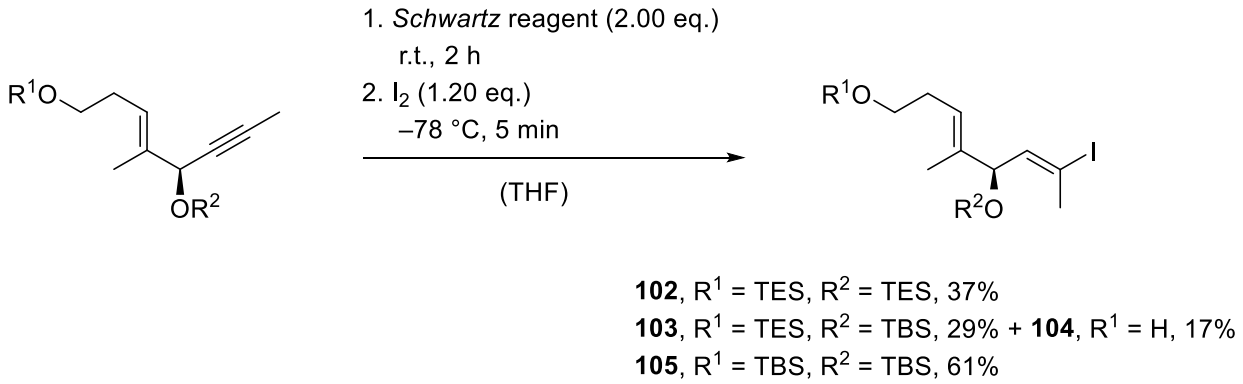
Furthermore, the doubly TBS-protected compound **101** was prepared in a two-step procedure starting from TBDPS protected alkyne **35** (Scheme 54). First, alkyne **35** was converted into diol **39** using TBAF. The crude diol was then protected using TBS chloride and imidazole, delivering the TBS-protected compound **101** in 79% yield.



35 **101**

Scheme 54. Preparation of the double TBS-protected compound **101**.

The fragments were converted into the vinyl iodides by treatment with the *Schwartz* reagent (Scheme 55). In the case of the double TES protected fragment **99**, the desired product **102** could only be isolated in 37% yield. The TES/TBS-protected vinyl iodide **103** was isolated in 29% yield. As a side product, removal of the TES group was observed, leading to alcohol **104** with 17% yield. In the case of the double TBS-protected alkyne **101**, the sequence towards iodide **105** worked smoothly with 61% yield.

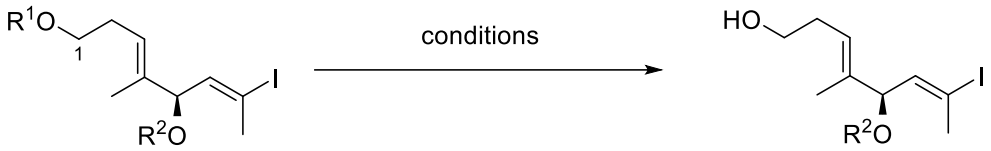


102, R^1 = TES, R^2 = TES, 37%
103, R^1 = TES, R^2 = TBS, 29% + **104**, R^1 = H, 17%
105, R^1 = TBS, R^2 = TBS, 61%

Scheme 55. Conversion of alkynes **99**-**101** into the corresponding vinyl iodides.

The primary alcohol was selectively deprotected using HF · pyridine. Different conditions were needed for the individual substrates (Table 16).

Table 16. Deprotection of the C1 alcohol.

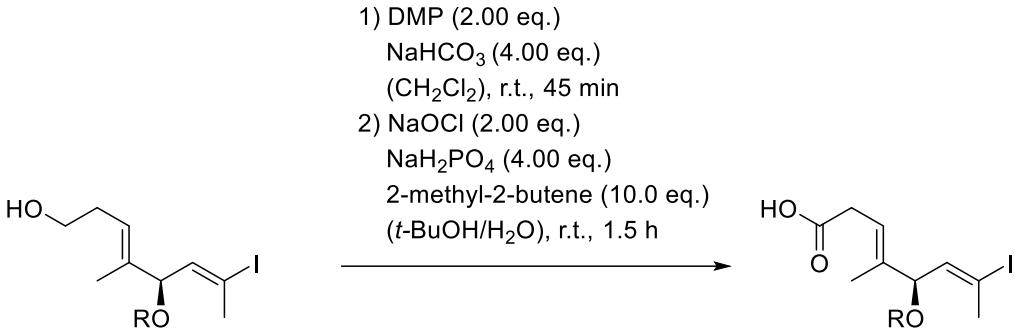


102, R^1 = TES, R^2 = TES
103, R^1 = TES, R^2 = TBS
105, R^1 = TBS, R^2 = TBS

104, R^2 = TBS
107, R^2 = TES
106, R^2 = H

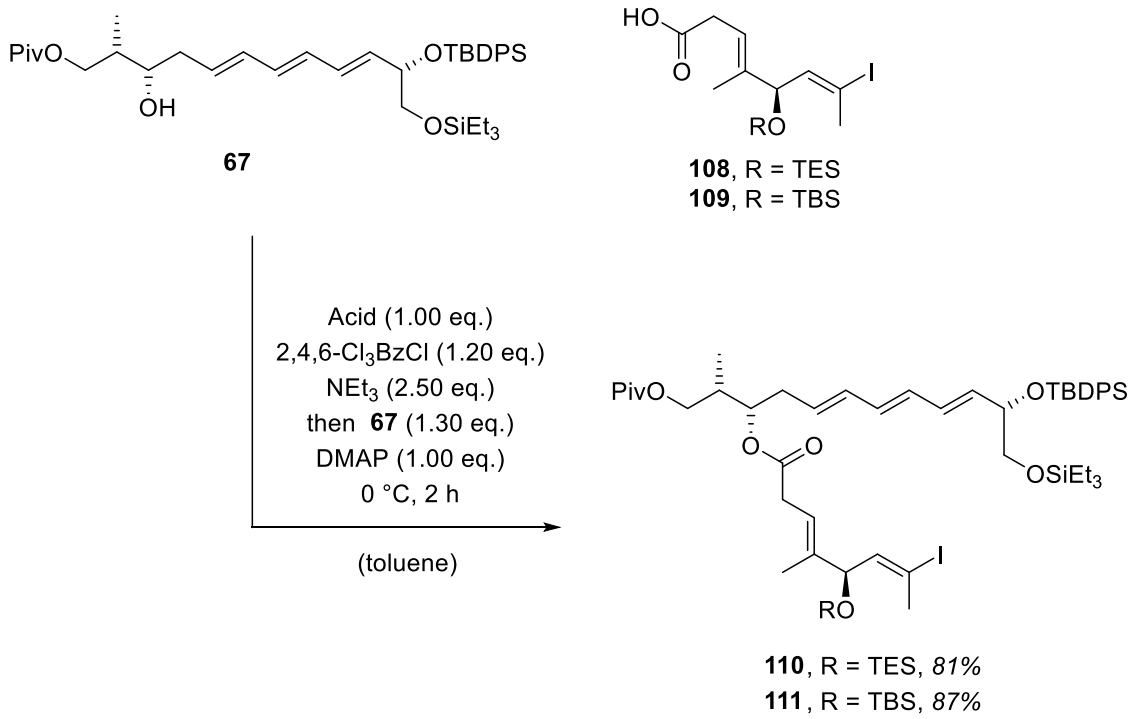
	Starting material	HF · pyridine	Solvent	T	t	Result
1	**103**	10 eq.	THF	0 °C	2 h	76% **104**
2	**102**	17.5 eq.	THF / Et_2O	0 °C	3.5 h	68% **107** 27% **106**
3	**105**	20 eq.	THF	r.t.	1.5 h	67% **104**

In the case of the TES/TBS-protected vinyl iodide **103**, the desired product **104** was isolated cleanly in 76% yield (entry 1). With the double TES-protected substrate **102**, considerable over-deprotection was observed, resulting in the formation of diol **106** in 27% yield and the desired product **107** in 68% (entry 2). Removal of the primary TBS group of fragment **105** required a slightly elevated temperature and furnished the desired alcohol **104** in 67% yield (entry 3). Oxidation to the carboxylic acid under *Pinnick* conditions worked with 81% yield for the TES-protected fragment **108** and 79% for the TBS-protected compound **109** (Scheme 56).



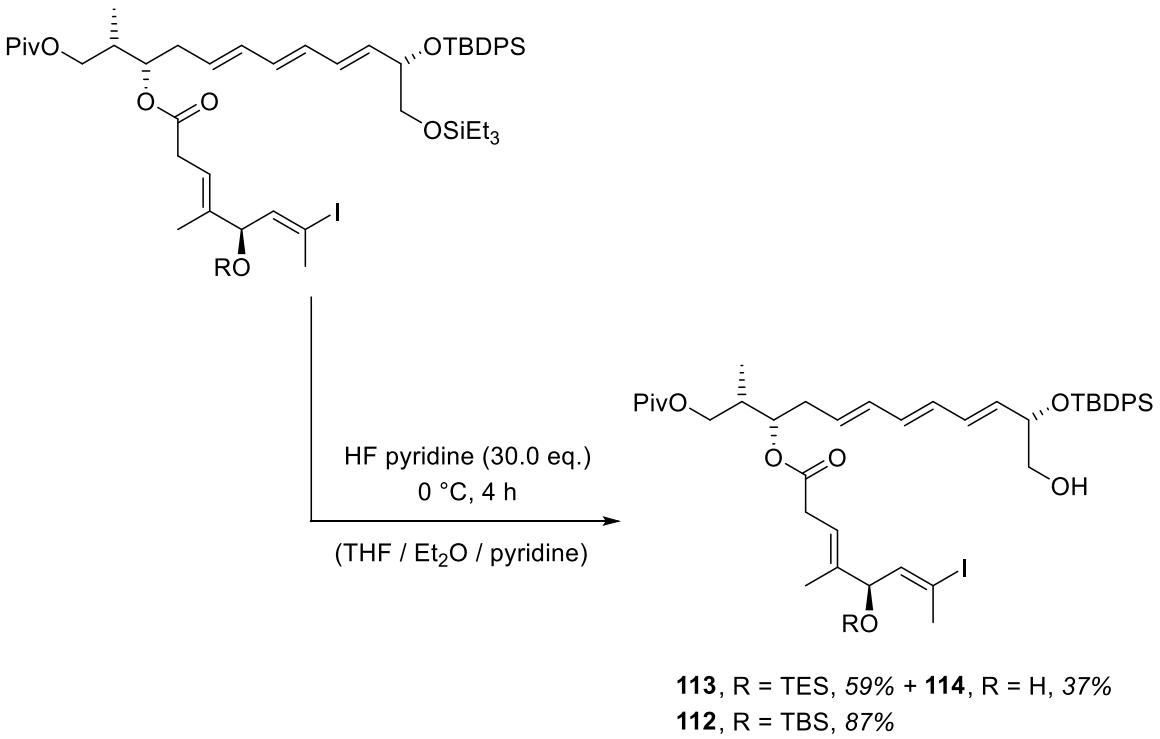
Scheme 56. Oxidation to carboxylic acids **108** and **109**.

Esterification with the northern triene fragment **67** proceeded smoothly to afford TES-protected fragment **110** with 81% and TBS-protected fragment **111** with 87% yield (Scheme 57).



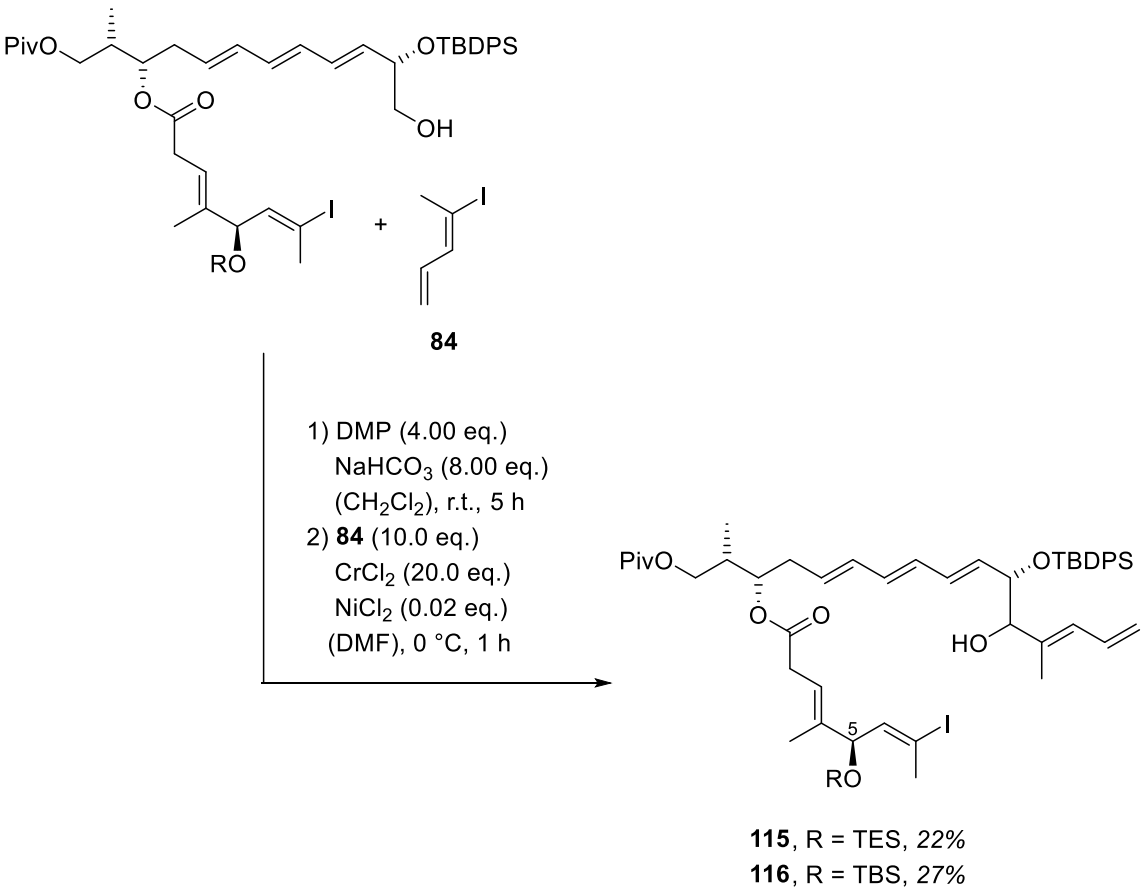
Scheme 57. Esterification of acids **108** and **109** with the northern fragment **67**.

Removal of the primary TES group at C12 worked with a yield of 87% in the case of the TBS-protected fragment **112** (Scheme 58). With the TES-protected compound **110**, only 59% of the desired product **113** were isolated. Again, considerable amounts of double deprotected product **114** (37%) were formed.



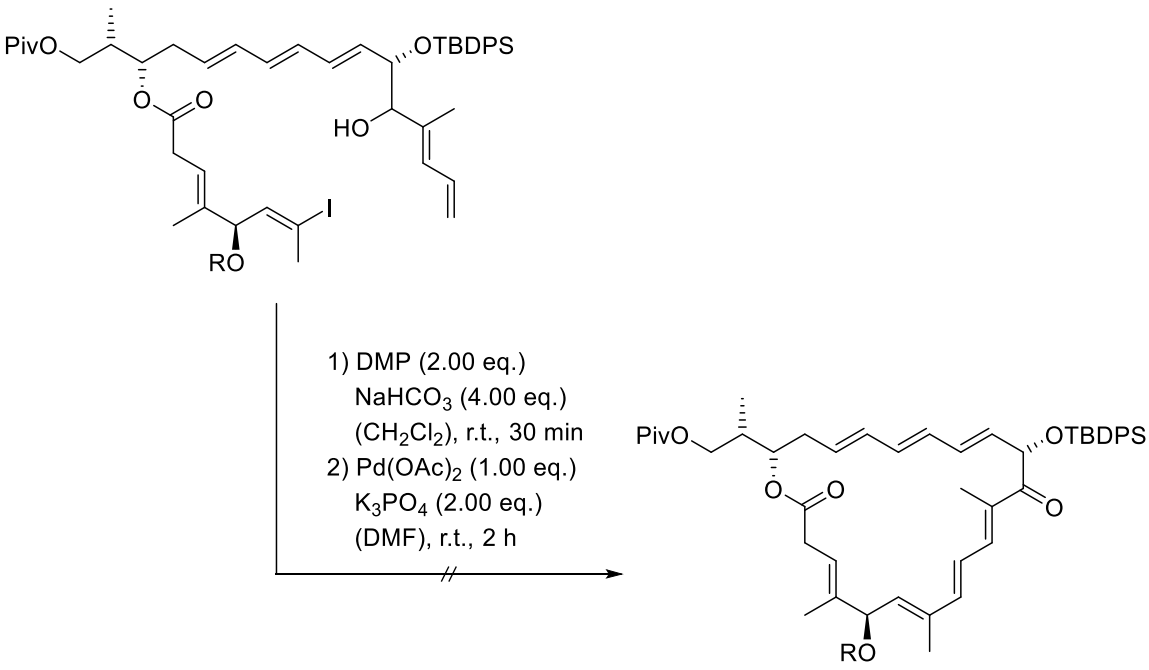
Scheme 58. Removal of the C12 TES group.

In both cases, *Dess-Martin* oxidation and subsequent *Nozaki-Hiyama* reaction with dienyl iodide **84** proceeded with a very low yield of only 22% and 27% (Scheme 59). Furthermore, the oxidations required significantly more oxidant compared to the previously employed TBDPS protected fragment **69**. The reason for this could not be clarified. Cleavage of the silyl ethers at the C5 position seems unlikely because the fragments **108** and **109** could also be prepared using *Dess-Martin* conditions, without noticeable decomposition.



Scheme 59. *Nozaki-Hiyama* coupling with dienyl iodide **84**.

With both cyclization precursors **115** and **116** in hand, we attempted the *Heck* macrocyclization (Scheme 60). Unfortunately, and contrary to our expectations, the *Heck* reaction did not improve in both cases, compared to the C5 TBDPS-protected precursor **93**. In fact, the cyclized products **117** and **118** could only be isolated in traces in both cases.



117, R = TES, *traces*
118, R = TBS, *traces*

Scheme 60. *Heck* cyclization of the TES- and TBS-protected fragments **115** and **116** remained unsuccessful.

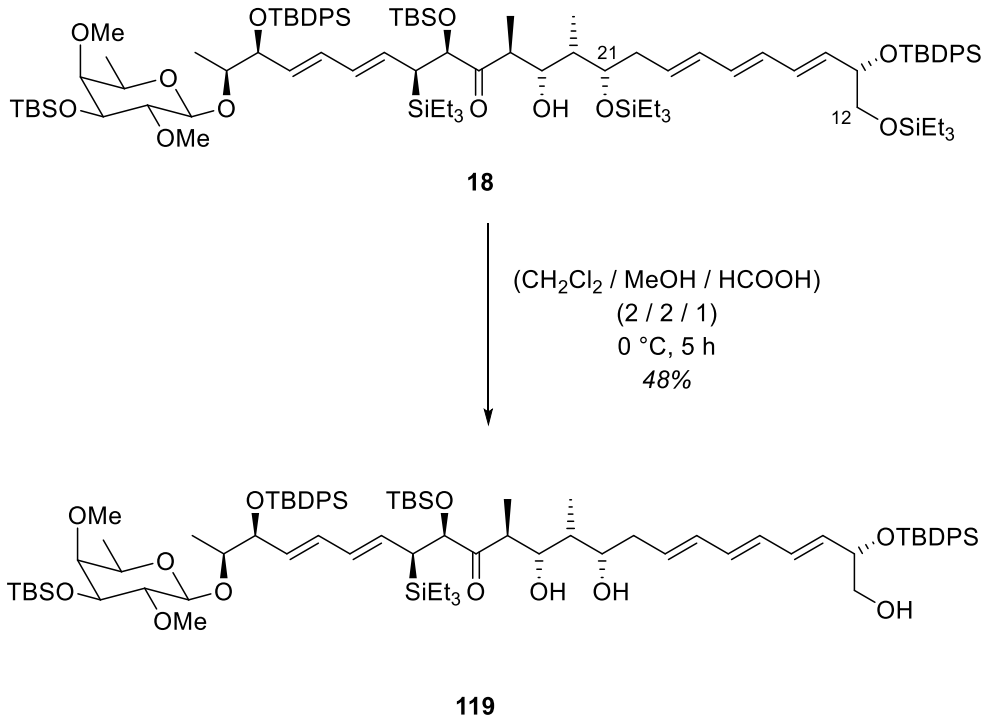
The reason for the low yield could not be finally clarified. It seems as if the protecting groups were not stable under the reaction conditions, which already led to poor yields during the *Nozaki-Hiyama* reaction. It seems like the TBDPS group at the C5 position was mandatory for successful macrocyclization.

7. Synthesis of the C1-C40 fragment

7.1. Linear approach by late-stage *Nozaki-Hiyama* reaction

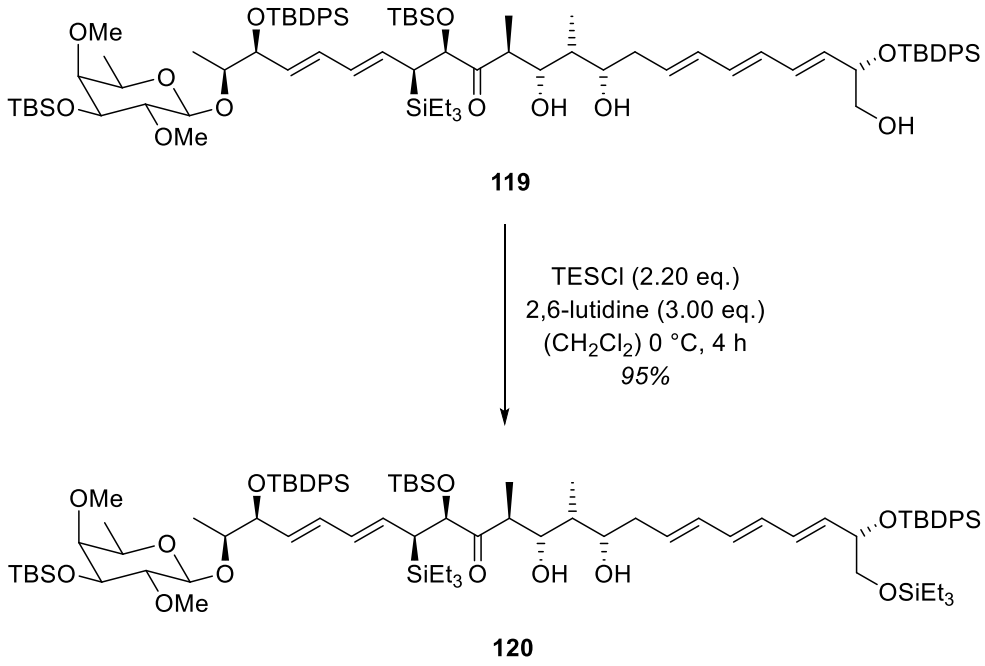
Even though all attempts to optimize the *Heck* cyclization failed, we still envisioned it as the method of choice for the macrocyclization step. Therefore, we focused on the application of the conditions to the complete Pulvomycin scaffold.

The previously (chapter 3) described aldol product **18** was provided by *S. Wienhold* and was converted into the triol **119** by removal of the two TES protecting groups at C12 and C21 (Scheme 61). The deprotection was accomplished by stirring the compound in methanol and dichloromethane with 20% formic acid. The reaction proceeded smoothly, albeit in a moderate yield of only 48%.



Scheme 61. Deprotection of aldol product **18**.

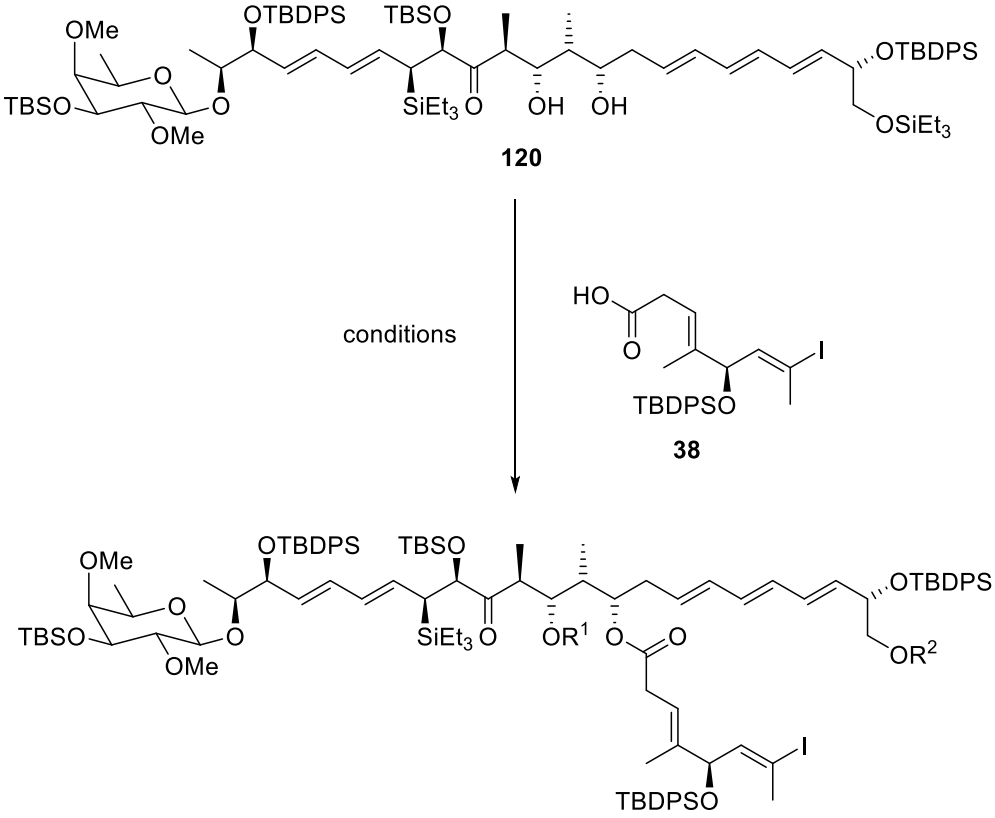
The triol was then selectively TES protected at the C12 position using TESCl and 2,6-lutidine in an excellent yield of 95% (Scheme 62).

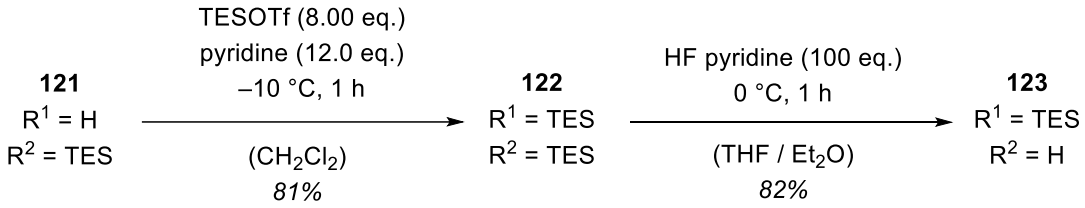


Scheme 62. Selective protection of the primary alcohol **119**.

With the 1,3-diol **120** in hand, we investigated the selective esterification at C21. Employing an excess of the carboxylic acid **38** and the *Yamaguchi* reagent, the desired product was isolated in 42% yield (Table 17, entry 1). However, a significant amount of an unpolar side product was isolated, which probably stems from the elimination of one of the hydroxy groups. Lowering the amount of carboxylic acid and *Yamaguchi* reagent to 1.20 equivalents increased the yield to 64%, although no full conversion was achieved (entry 2). Still, the mass balance of the reaction increased significantly, and 28% of the valuable diol **120** could be recovered. Subsequent TES protection of alcohol **121** using an excess of TESOTf and pyridine, followed by selective deprotection of the primary TES group at C12 using HF · pyridine, led to the desired product **123** in 66% yield over two steps.

Table 17. Optimization of the *Yamaguchi* esterification of unprotected 1,3-diol **120**.

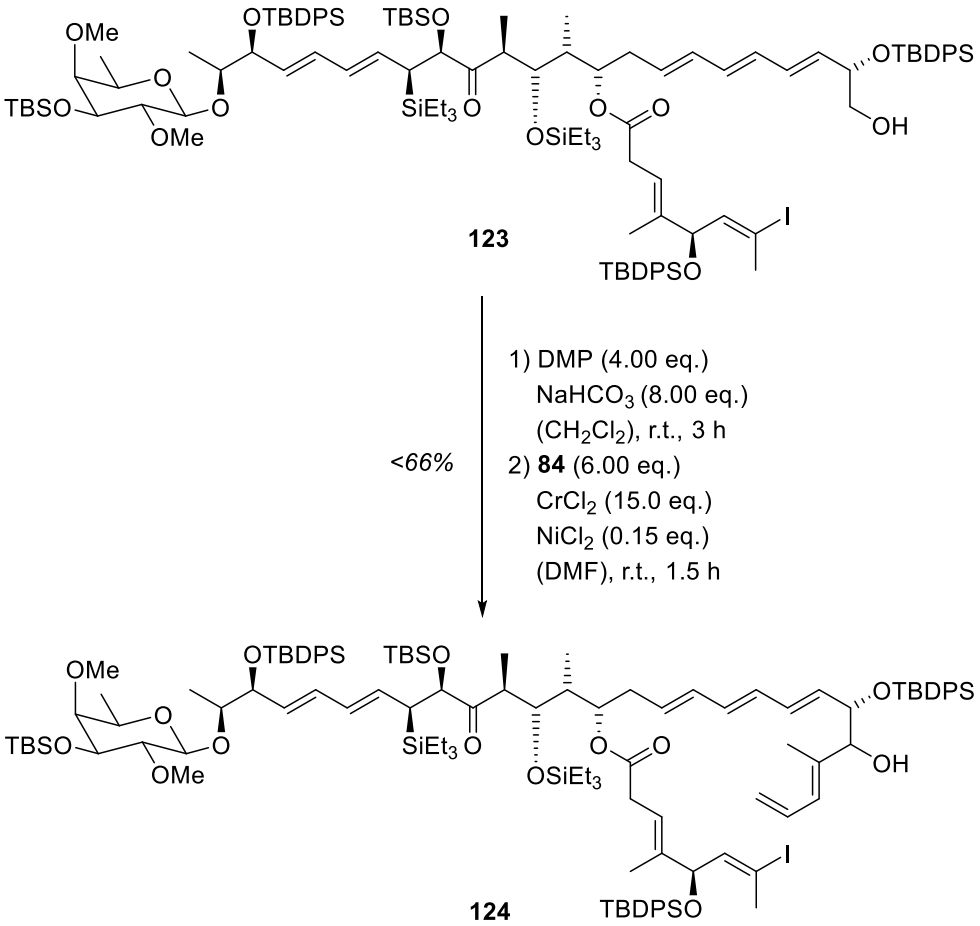




	Conditions	T	t	Result
1	**38** (2.00 eq.) 2,4,6-Cl_3BzCl (2.50 eq.) NEt_3 (4.00 eq.) DMAP (1.00 eq.)	0 °C	3.5 h	42% **121** 17% **120**
2	**38** (1.20 eq.) 2,4,6-Cl_3BzCl (1.20 eq.) NEt_3 (2.40 eq.) DMAP (1.00 eq.)	0 °C	2.5 h	64% **121** 28% **120**

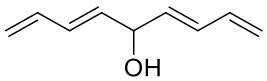
The alcohol was oxidized using *Dess-Martin* conditions, and the aldehyde was used without purification in the subsequent *Nozaki-Hiyama* reaction (Scheme 63). By employing the same

conditions as in the test substrate, the desired product could be isolated in varying yields of 45-66%. Best yields were obtained if the dienyl iodide **84** was freshly prepared.



Scheme 63. Installation of the dienyl linker fragment **84** by a late-stage *Nozaki-Hiyama* reaction.

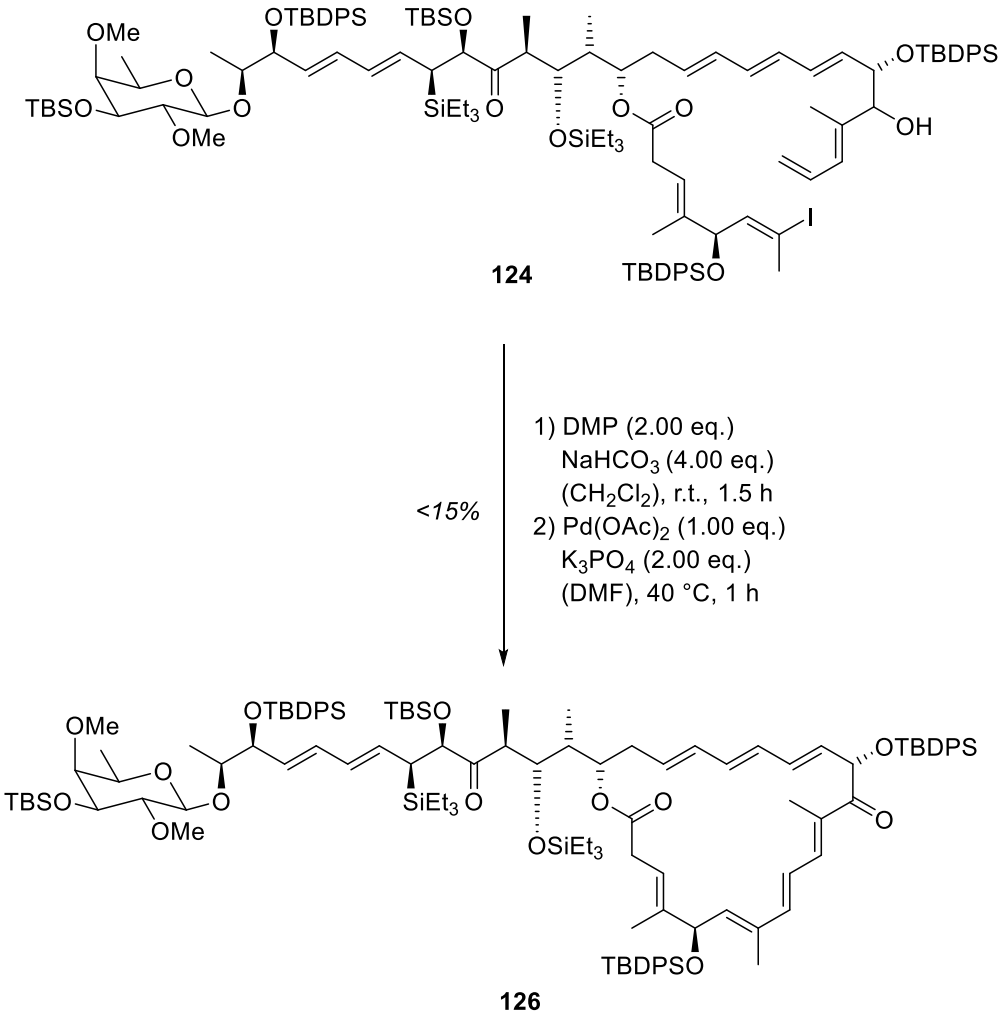
Unfortunately, the product was contaminated with a side product, which could not be finally clarified. According to NMR analysis, the side product correlates to the dimeric structure **125** given in figure 8, although it is not clear how this compound is formed under the reaction conditions.



125

Figure 8. Putative structure of the side product of the *Nozaki-Hiyama* reaction.

Unfortunately, the side product could not be separated by column chromatography because it had the same R_f value as the product. Still, the contaminated product was used in the following *Heck* reaction (Scheme 64).



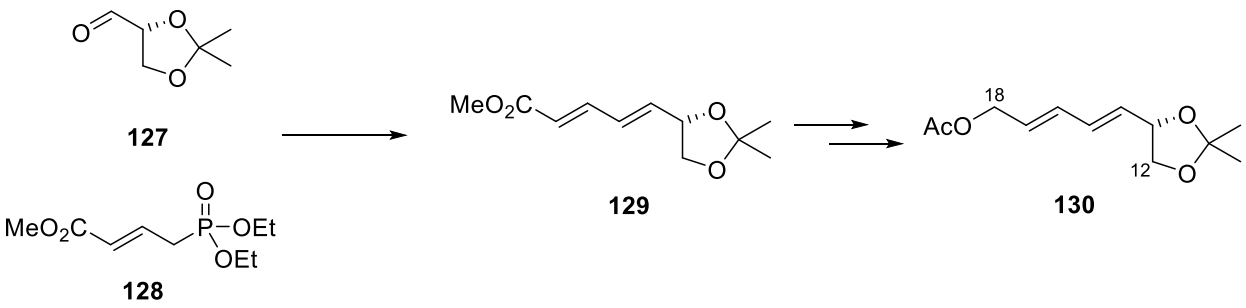
Scheme 64. Macrocyclization of compound **124**.

As with the test substrate, oxidation of the alcohol proceeded smoothly under *Dess-Martin* conditions. To our delight, the formation of the desired macrocycle **126** could be observed when the ketone was subjected to the previously optimized *Heck* conditions. Unfortunately, the yield of the reaction turned out to be even lower than with the test substrate (<15%). Moreover, the compound was still contaminated with impurities from the *Nozaki-Hiyama* reaction, which made detailed characterization of the compound difficult at this point. In the end, we reasoned that the synthetic sequence would not be practical to access larger quantities of the cyclized product **126**. Especially the low and varying yield of the late-stage *Nozaki-Hiyama* reaction, followed by the *Heck* cyclization, limited the synthesis to small milligram amounts of cyclized product. For the subsequent deprotection experiments, larger quantities of the material were required. Thus, we turned our attention towards finding a more sophisticated synthetic route.

7.2. Improved route and late-stage aldol strategy

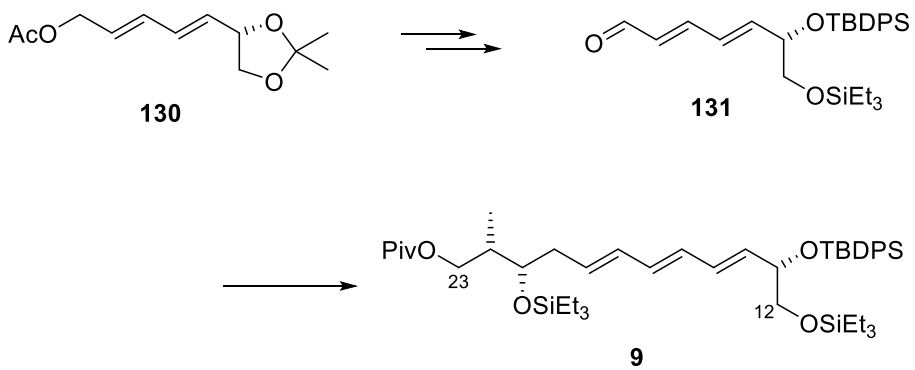
In order to overcome the above-mentioned issues, the C8-C11 dienyl residue was to be incorporated in an earlier step of the synthesis. This should not only lead to a more convergent synthesis and a higher yield but also to a cleaner cyclization precursor **124**. Furthermore, we wanted to explore the possibility of a late-stage aldol reaction between macrocycle **92** and the ketone fragment **11**, which would make the synthetic route even more convergent.

In order to get access to enough material, the synthetic route of the C12-C23 triene fragment needed some general improvements. The original route started from *D*-Mannitol (**15**), which was used as a source for the stereogenic center at C13 (Scheme 65). After acetal protection and glycol cleavage, the aldehyde **127** was coupled with phosphonate **128** in a *Horner-Wadsworth-Emmons* (HWE) reaction.



Scheme 65. Original synthetic route towards the C12-C23 fragment.

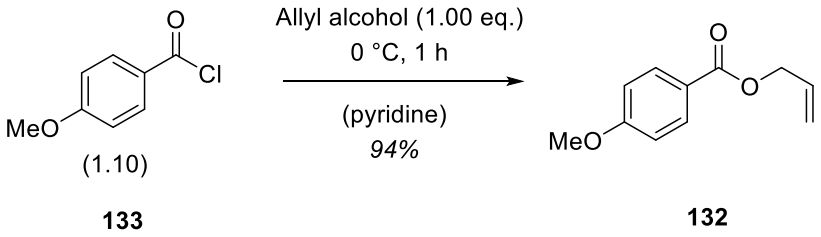
Then, the ester **129** was reduced, and the alcohol was protected as an acetate (Scheme 66). Subsequently, the acetal was removed, and the diol was protected with TES and TBDPS group, followed by removal of the acetate. Allylic oxidation to trienal **131**, followed by *Julia-Kocienksy* olefination, led to the triene fragment **9**.



Scheme 66. Original synthetic route of the C12-C23 fragment **9**.

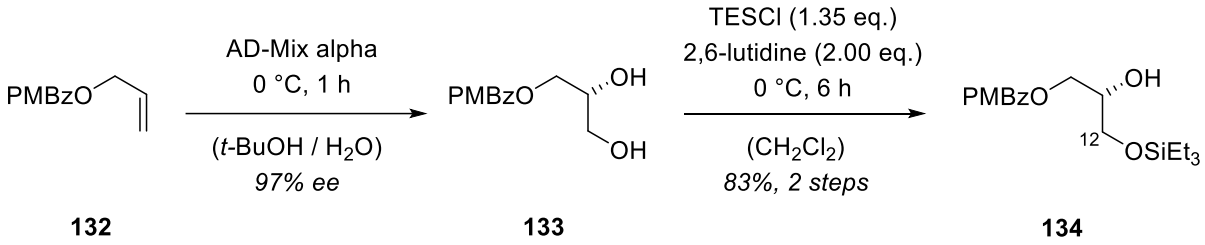
Especially the multiple protecting group operations, involving several Dibal-H reductions, turned out to be problematic in terms of reproducibility and yield. In general, the experimental procedure was very time-consuming and difficult to manage on a larger scale.

For the new strategy, the literature-known asymmetric *Sharpless* dihydroxylation of *para*-methoxybenzoyl protected allyl alcohol **132** was used to introduce the stereogenic center at C13.[99] The protection of allyl alcohol using anisoyl chloride (**133**) worked cleanly with 94% yield (Scheme 67).[100]



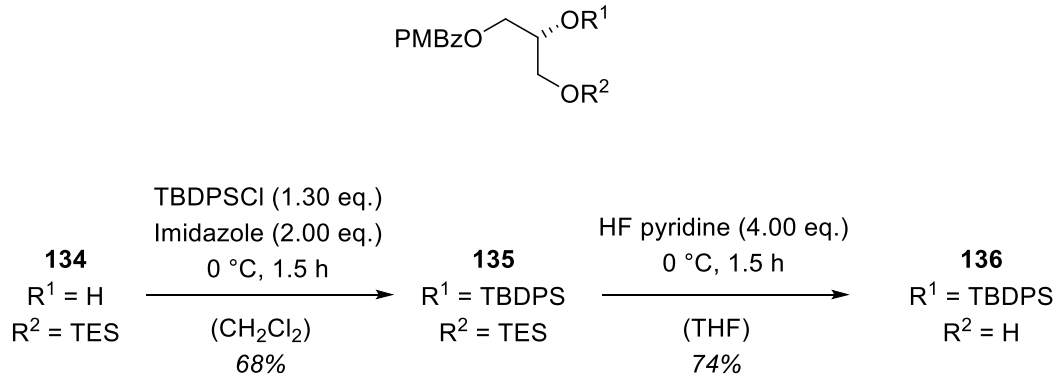
Scheme 67. Protection of allyl alcohol under literature known conditions.

Subsequent *Sharpless* dihydroxylation according to a literature known protocol delivered the desired diol **133** with an excellent enantiomeric excess of 97% (Scheme 68). The crude diol was TES protected using TESCl and 2,6-lutidine with 83% yield over two steps.



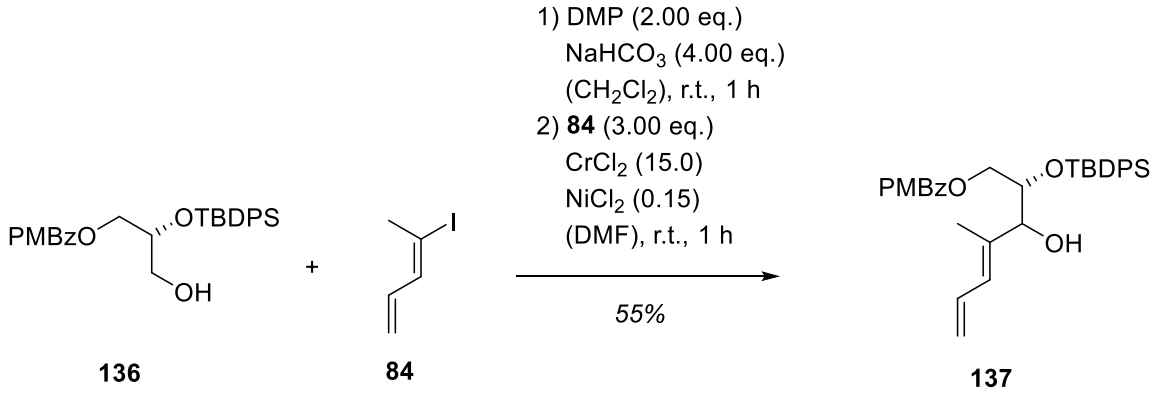
Scheme 68. *Sharpless* dihydroxylation followed by silyl protection. PMBz: *para*-methoxybenzoyl.

TBDPS protection of the secondary alcohol **134**, followed by removal of the primary TES group, proceeded with 68% and 74%, respectively (Scheme 69).



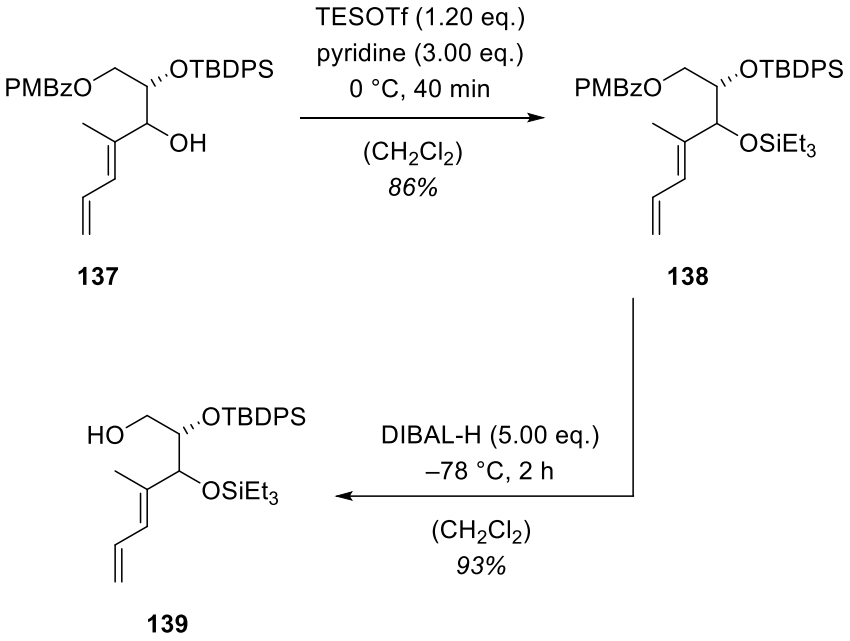
Scheme 69. Preparation of the primary alcohol **136**.

Next, the *Nozaki-Hiyama* coupling with dienyl iodide **84** was attempted (Scheme 70). Alcohol **136** was oxidized to the aldehyde using *Dess-Martin* conditions. Simultaneously, the dienyl iodide **84** was freshly prepared by elimination of the mesylate **89**, as discussed before.[85]



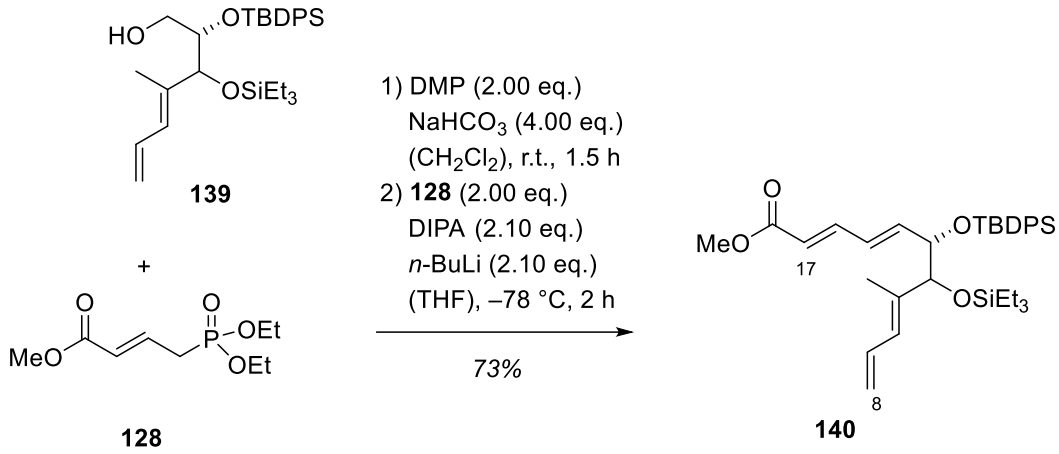
Scheme 70. *Nozaki-Hiyama* reaction starting from alcohol **136** and dienyl iodide **84**.

The aldehyde and a three-fold excess of the dienyl iodide were combined and added to a stirred suspension of chromium-(II)-chloride and nickel-(II)-chloride in DMF. After one hour, full conversion was observed, and the desired product **137** was isolated in 55% yield on a multi-gram scale. TES protection and removal of the ester protecting group using Dibal-H furnished alcohol **138** in 86% and 93% yield, respectively (Scheme 71).



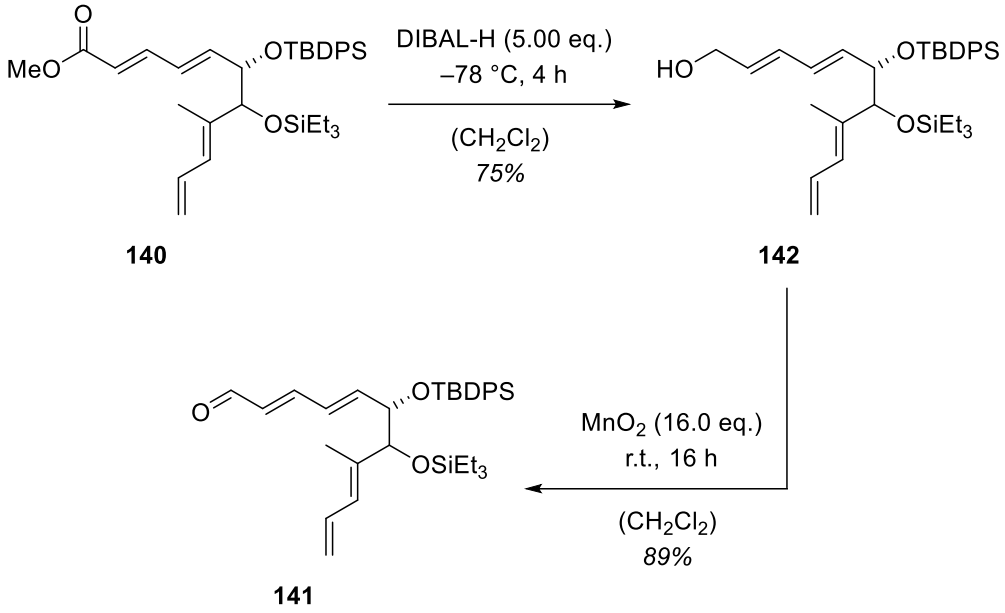
Scheme 71. Preparation of alcohol **139**.

Dess-Martin oxidation, followed by *Horner-Wadsworth-Emmons* reaction with phosphonate **128** under known conditions, led to the desired diene **140** in 73% yield (Scheme 72).[37]



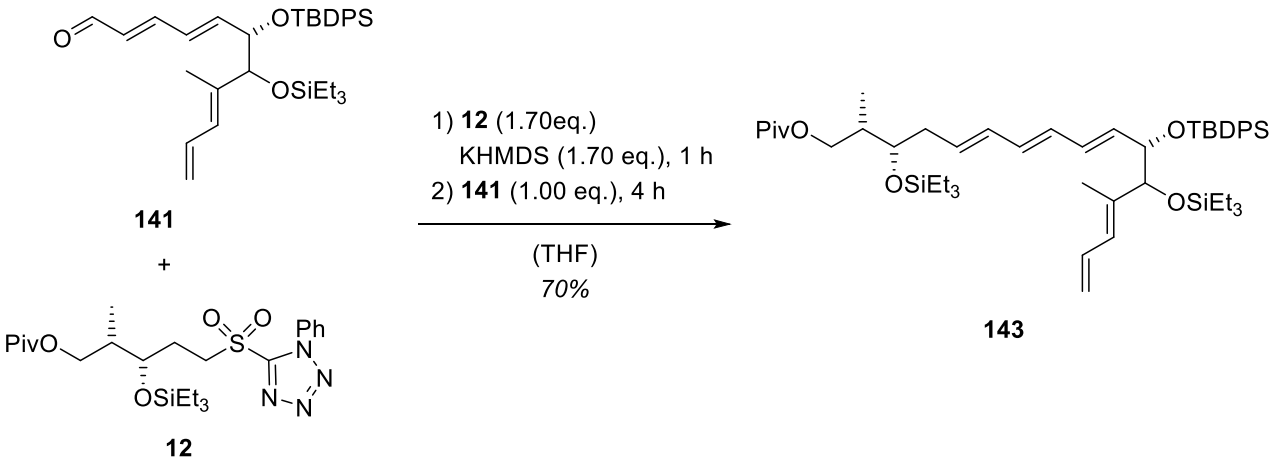
Scheme 72. HWE reaction under known conditions.

The ester was converted into aldehyde **141** by reduction with Dibal-H and allylic oxidation of alcohol **142** with manganese dioxide (Scheme 73).[101]



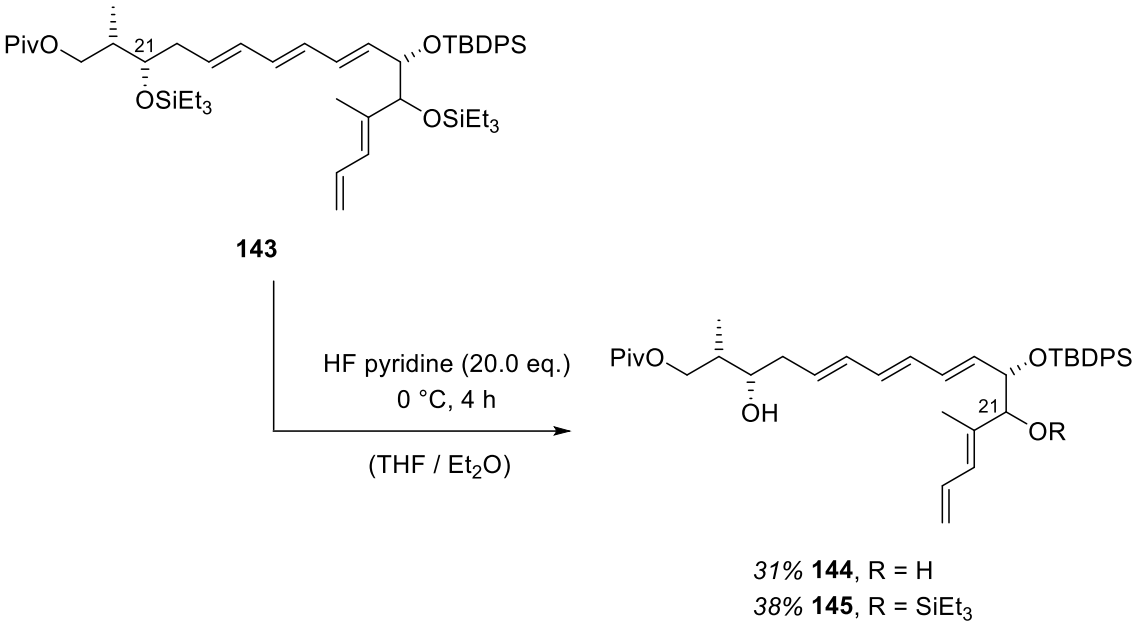
Scheme 73. Reduction/oxidation sequence for the synthesis of trienal **141**.

Julia-Kocienski coupling with literature known sulfone **12** delivered the desired triene **143** with 70% yield (Scheme 74).[37]



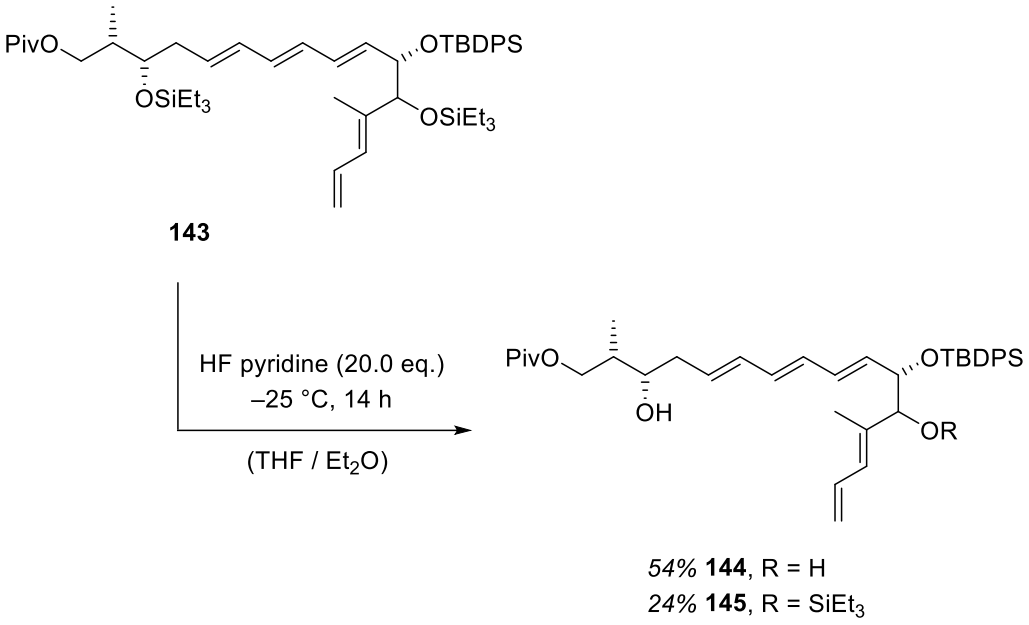
Scheme 74. Julia-Kocienski olefination under known conditions.

In the next step, the TES group at C21 needed to be selectively removed in the presence of the C12 TES group. Unfortunately, treatment of the compound with HF · pyridine only led to a mixture of mono- (**145**) and twofold-deprotected (**144**) compounds (Scheme 75).



Scheme 75. The deprotection of the C21 TES-ether showed little selectivity.

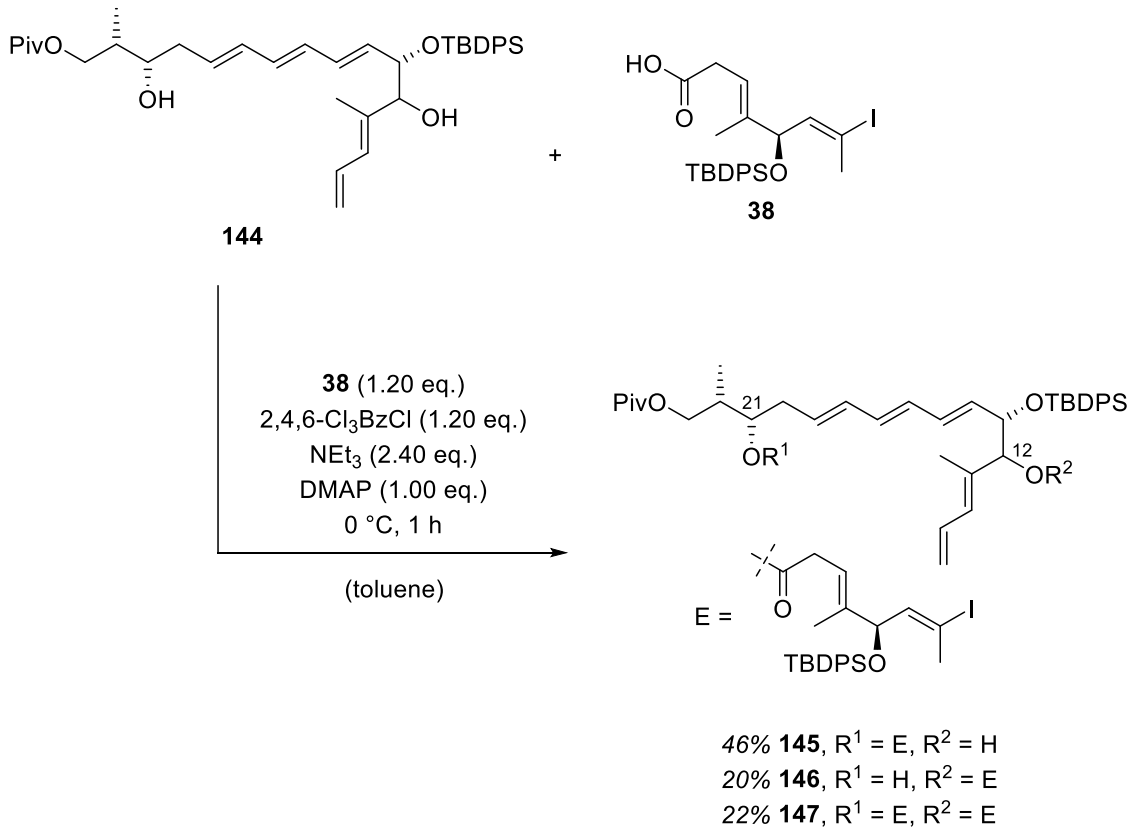
Lowering the temperature did not improve the reaction outcome. In fact, due to the longer reaction time, much more of the double deprotected compound **144** was isolated (Scheme 76).



Scheme 76. Lowering the temperature had no positive effect on selectivity.

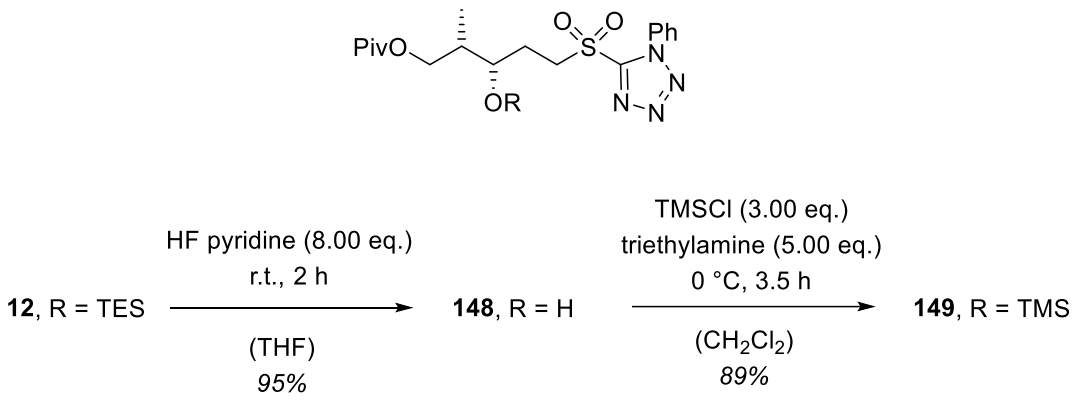
Instead of pursuing a selective deprotection of the C21 TES group, we also wanted to evaluate if selective esterification of the C12-C21 diol would be feasible (Scheme 77). However, conversion of the diol **144** with a slight excess of carboxylic acid **38** under *Yamaguchi*

conditions only led to a complex mixture of products. Besides the desired product **145**, the C12 ester **146** and the double esterified compound **147** were formed as well.



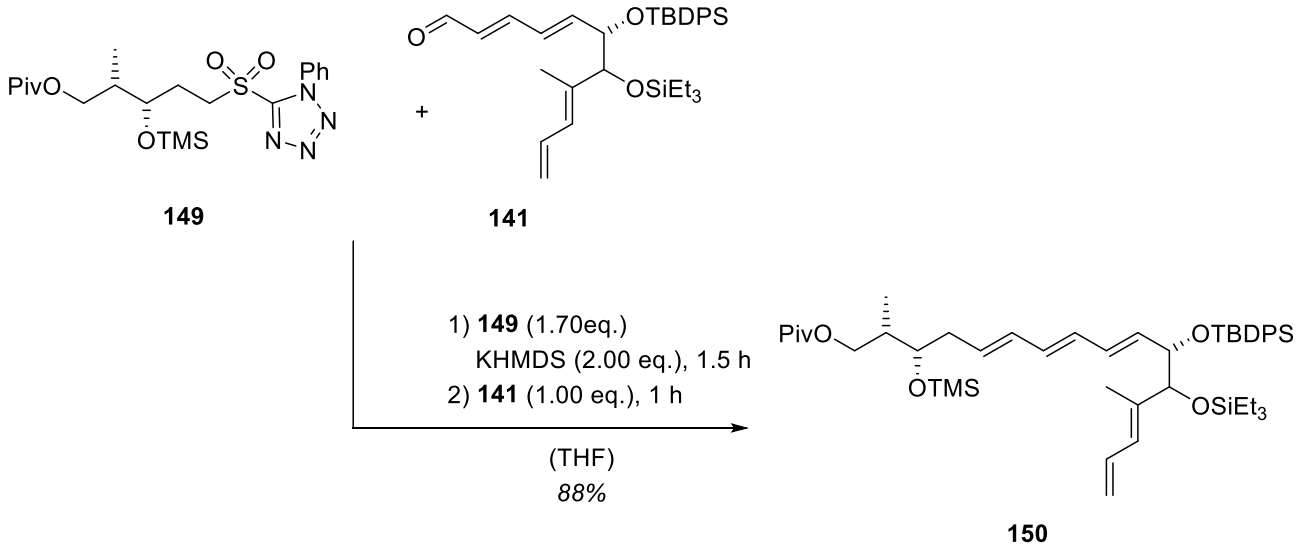
Scheme 77. Selective esterification of diol **144** turned out not to be feasible.

In order to overcome the selectivity problem, the TES group on the sulfone **12** was replaced by the more labile TMS group. Treatment of the sulfone with HF · pyridine cleanly delivered alcohol **148** in an excellent yield of 95% (Scheme 78). TMS protection proceeded with 89% yield using TMS chloride and triethylamine. Compound **149** turned out to be surprisingly stable and endured both aqueous work-up and column chromatography without noticeable silyl ether cleavage.



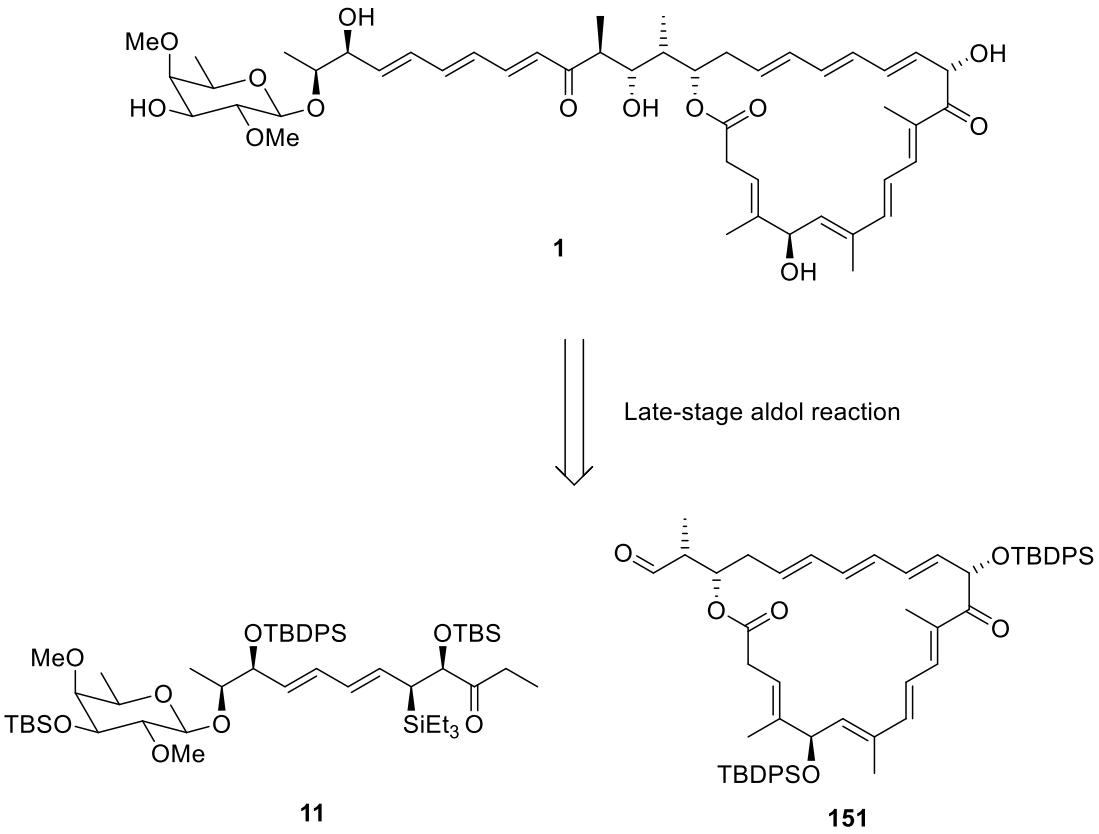
Scheme 78. Synthesis of TMS-protected sulfone **149**.

To our delight, the *Julia-Kocienski* reaction with the TMS-protected sulfone **149** still proceeded smoothly under identical reaction conditions, delivering the desired triene **150** in an excellent yield of 88% (Scheme 79).



Scheme 79. *Julia-Kocienski* reaction with TMS-protected sulfone **149**.

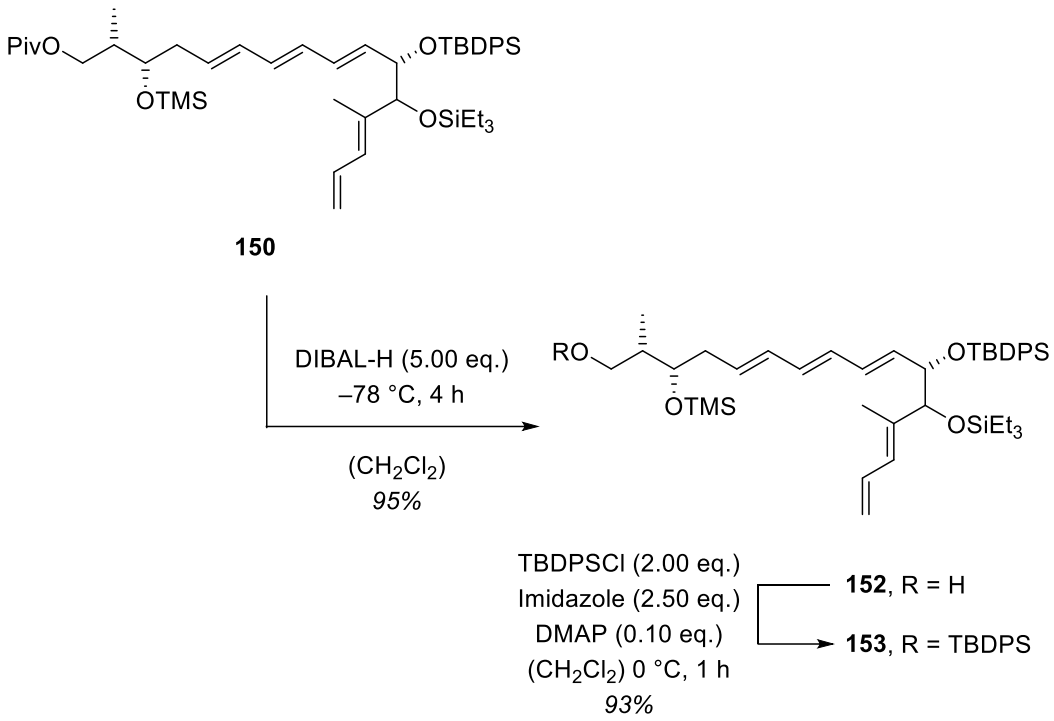
At this point, we wanted to explore the applicability of a late-stage aldol reaction (Scheme 80). Instead of performing the low-yielding *Heck* cyclization in the last synthesis step, we envisioned a more convergent approach using the aldol reaction as the final carbon bond formation step. We reasoned that synthesizing larger amounts of the macrocycle **151** would be easier and more economical than losing most of the material in the last step of the synthesis.



Scheme 80. Construction of the Pulvomycin skeleton by a late-stage aldol reaction between aldehyde **151** and ketone **11**.

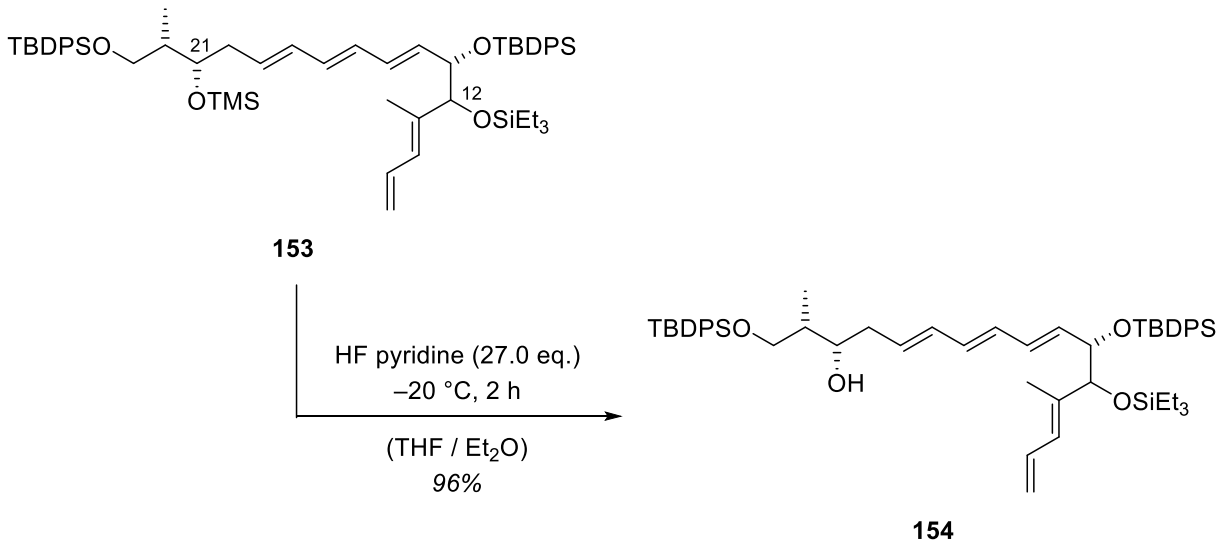
In order to access compound **151**, the protecting group at C23 had to be removed. Removal of the pivaloyl group in the presence of the sensitive lactone moiety and the ketone at C12 seemed not promising. Therefore, the pivaloyl group should be replaced by a TBDPS group, which would enable selective deprotection in the presence of the two secondary TBDPS ethers while providing enough stability to endure the *Heck* conditions.

The pivaloyl group was removed by Dibal-H reduction of compound **150** with an excellent yield of 95%. Then, the TBDPS group was attached using standard conditions (Scheme 81).



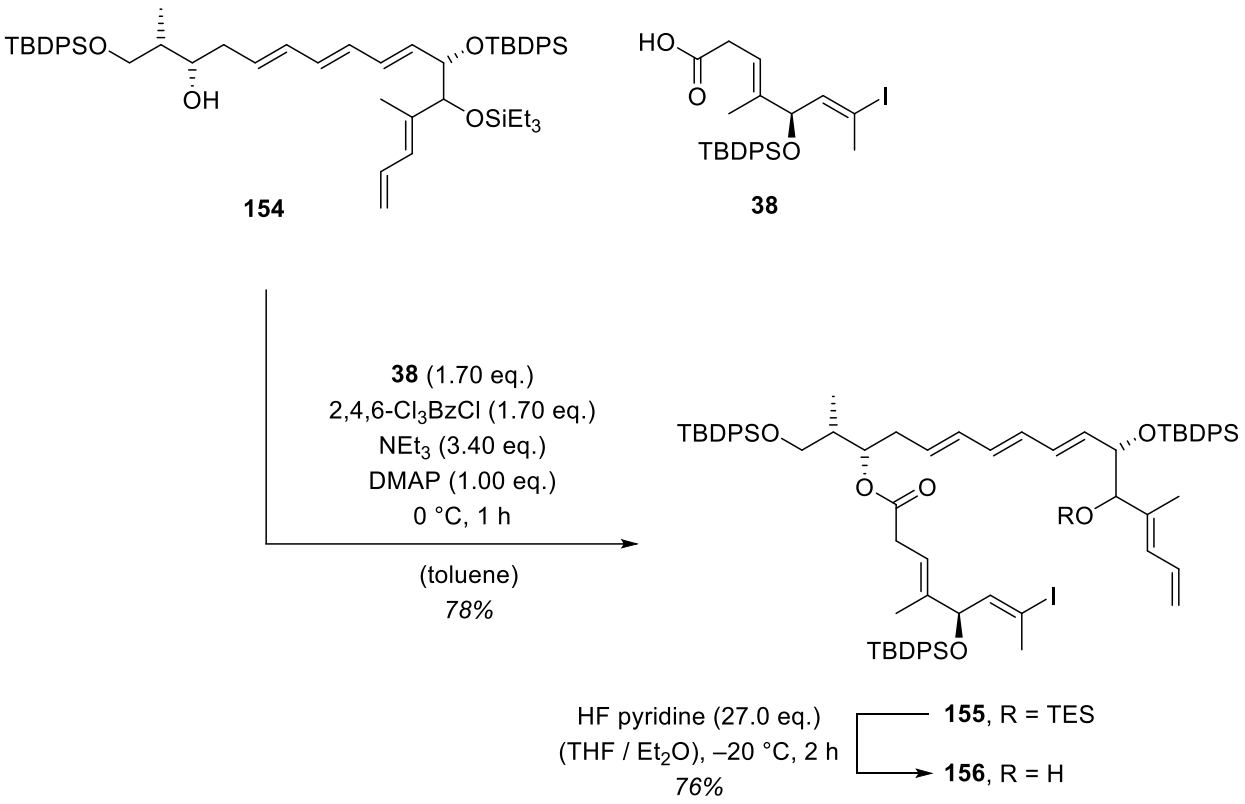
Scheme 81. Replacement of the pivaloyl group with a TBDPS group.

Subsequent removal of the TMS group in the presence of the C12 TES group proceeded with excellent selectivity and a yield of 96% using HF · *pyridine* at low temperatures (Scheme 82).



Scheme 82. Selective deprotection of the C21 TMS ether in the presence of the C12 TES group.

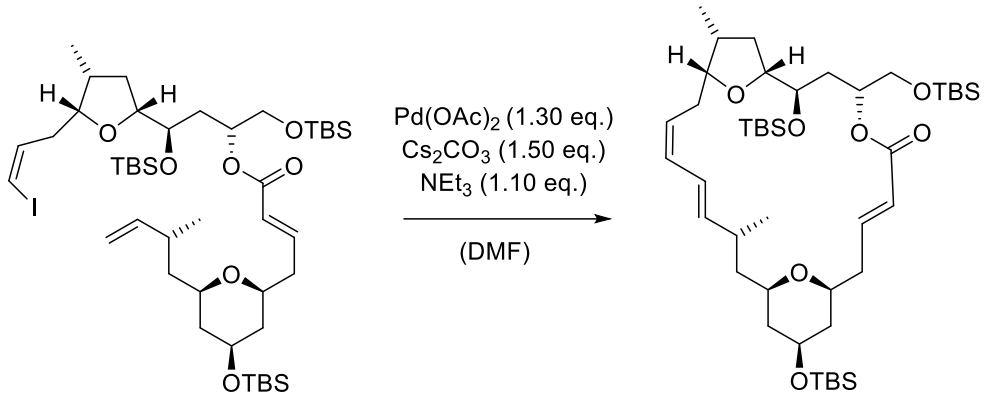
Esterification with the southern fragment, followed by removal of the C12 TES group, proceeded with a yield of 78% and 76%, respectively (Scheme 83).



Scheme 83. The successful synthesis of the cyclization precursor **156**.

Surprisingly, the subsequent *Heck* reaction under previously found *Jeffery* conditions did not work at all. Only decomposition was observed during the reaction. Both on TLC and in the crude NMR, large quantities of residues with a TBDPS group could be observed. No conversion was achieved when the palladium was used catalytically. We concluded that the primary TBDPS group was cleaved under the reaction conditions, and the reactive primary alcohol decomposed thereafter.

A report from *Yamini* et al. from 2018 suggested the use of a combination of cesium carbonate and triethylamine together with palladium-(II)-acetate to facilitate the macrocyclization of compound **157**.[102] Similar to our cyclization precursor, the compound included an ester moiety as well as a primary TBS group (Scheme 84).

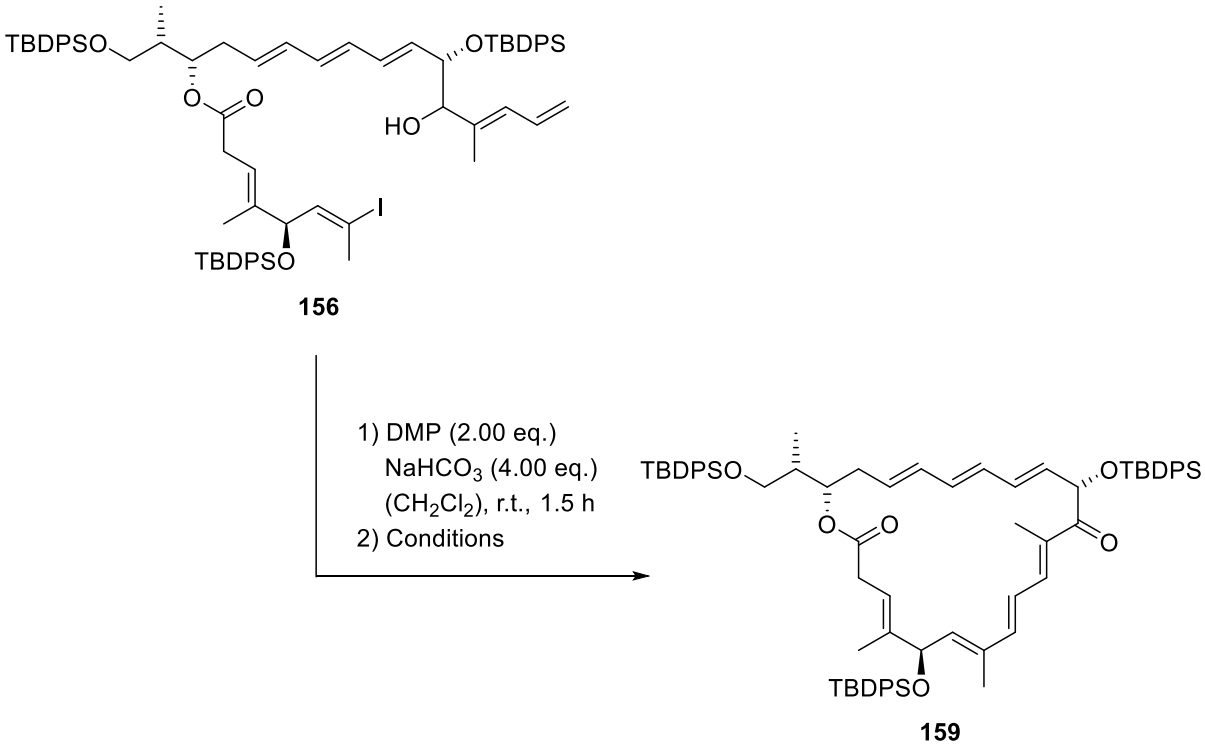


157 **158**

Scheme 84. Successful macrocyclization of compound **157** by *Yamini* and coworkers by employing a combination of an inorganic and organic base.

Indeed, the desired product **159** could be observed by ESI-MS when the literature conditions were applied to our system (Table 18). However, only traces of the product could be isolated (entry 1). By replacing cesium carbonate with potassium phosphate, the product could be isolated in 10%. Unfortunately, the yield dropped drastically when the reaction was performed on a larger (100 mg) scale (entry 2). Performing the reaction without an inorganic base led to no conversion (entry 3).

Table 18. Application of the literature conditions.

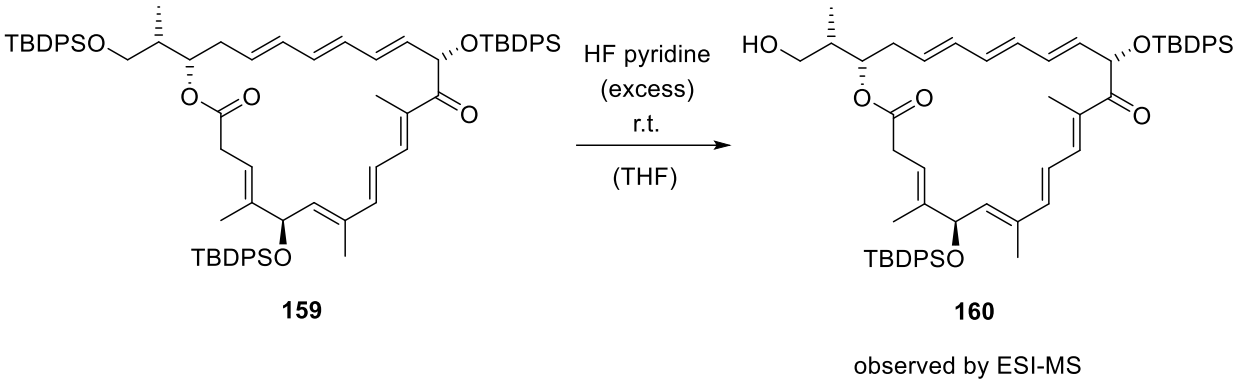


156 **159**

	Conditions	T	t	Result
1	$Pd(OAc)_2$ (1.30 eq.) Cs_2CO_3 (1.50) NEt_3 (1.10)	r.t.	1 h	traces
2	$Pd(OAc)_2$ (1.30 eq.) K_3PO_4 (2.00) NEt_3 (2.00)	r.t.	1.5 h	10 % large scale: 5%
3	$Pd(OAc)_2$ (1.30 eq.) NEt_3 (2.00)	r.t.	6 h	n.c.
4	$Pd(OAc)_2$ (1.30 eq.) $NaHCO_3$ (2.00) NEt_3 (2.00)	40 °C	2.5 h	<12%
5	$Pd(OAc)_2$ (1.30 eq.) $NaHCO_3$ (10.0) NEt_3 (10.0)	r.t.	3 h	15%
6	$Pd(OAc)_2$ (1.30 eq.) $NaHCO_3$ (10.0) TBAI (1.00) NEt_3 (2.00)	r.t.	1.5 h	8%

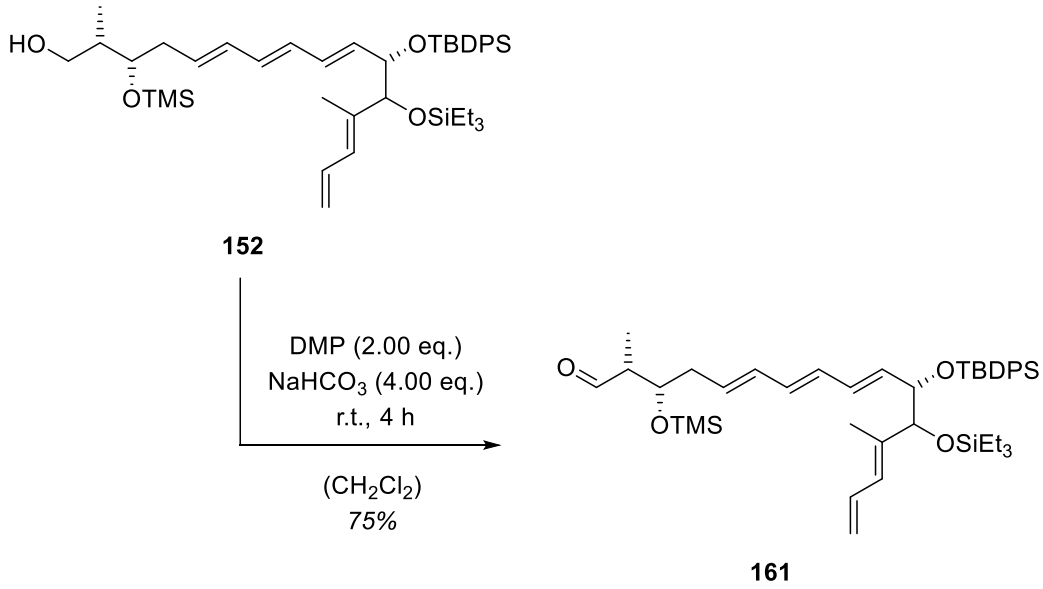
Exchanging potassium phosphate with sodium bicarbonate increased the yield. However, the reaction was very unclean (entry 4). Increasing the amount of base improved the result slightly (entry 5). The addition of tetrabutylammonium iodide (TBAI) did not improve the result (entry 6).

In the end, the results were not convincing, and we decided not to investigate a late-stage aldol approach further. Removal of the primary TBDPS group was attempted in a single experiment using a large excess of HF · *pyridine* at room temperature (Scheme 85). The desired product **160** could be observed by ESI-MS, proving that the concept works in principle. However, due to the low yields of the cyclization, no further attempts were made.



Scheme 85. Removal of the primary TBDPS group in the presence of two secondary TBDPS ethers.

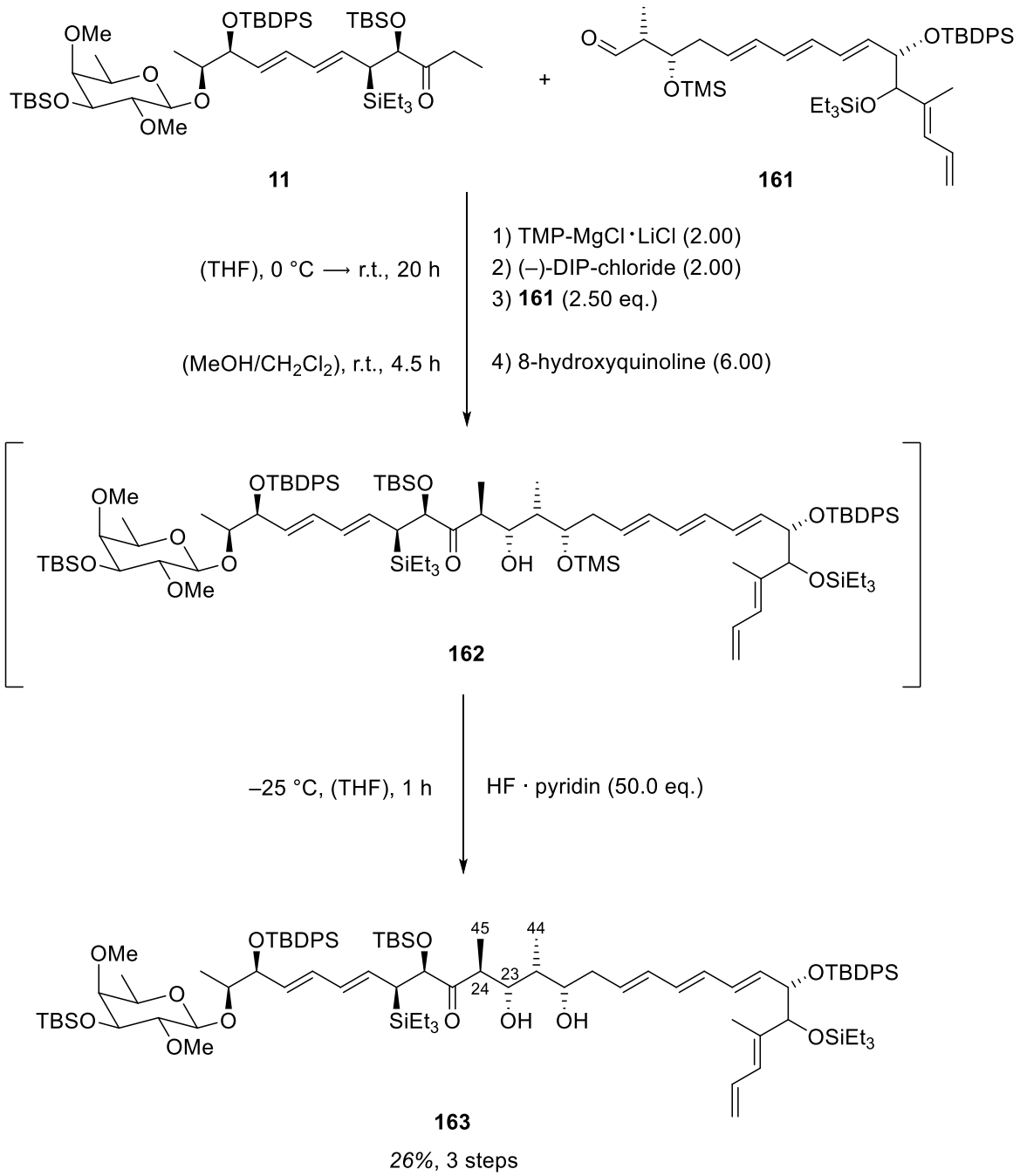
Instead, we pursued the original linear strategy. Oxidation of alcohol **152** under *Dess-Martin* conditions led to the aldehyde **161** in 75% yield (Scheme 86).



Scheme 86. Oxidation of alcohol **152** to aldehyde **161**.

The subsequent aldol reaction with ketone fragment **11**, provided by *S. Hackl*, was carried out under published conditions.[37] First, the ketone was treated with tetramethyl piperidinyl (TMP) magnesium chloride, followed by (–)-*B*-chlorodi-*iso*-pinocinocampheylborane chloride (DIP-Cl) and the addition of aldehyde **161** in 2.5-fold excess (Scheme 87). Unfortunately, the aldol product **162** could not be separated from unreacted ketone **11** due to identical R_f values. Instead, the mixture was treated with HF · *pyridine* to remove the TES group at C21. Now, the resulting 1,3-diol **163** could successfully be separated from the ketone fragment. Starting from ketone

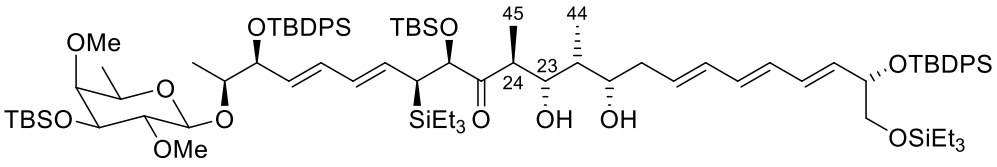
11, the diol **163** was isolated in a 26% yield. 29% of the ketone was reisolated, resulting in a yield for the diol of 36% based on the recovered starting material.



Scheme 87. Aldol reaction and subsequent removal of the C21 TES-group.

In order to verify the correct *anti*-configuration between C23 and C24, the NMR data of compound **163** was compared to the literature known compound **164** (Table 19, synthesized by *S. Wienhold*).[30]

Table 19. Comparison of the chemical shifts of compound **163** with the literature known diol **164**.



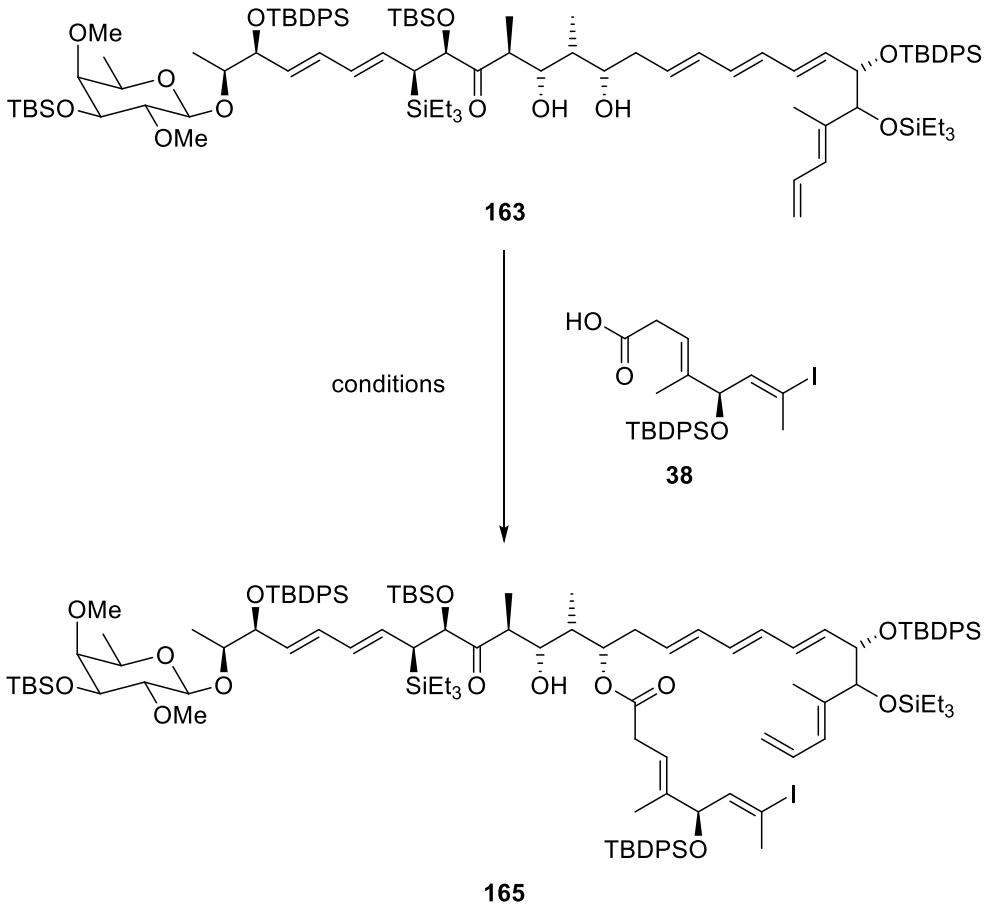
164

Pos	**163**	**164**
23	δ_H = 4.02 ppm δ_C = 78.5 ppm	δ_H = 4.01 ppm δ_C = 78.4 ppm
24	δ_H = 3.17 ppm δ_C = 44.7 ppm	δ_H = 3.17 ppm δ_C = 44.6 ppm
44	δ_H = 0.93-0.89 ppm δ_C = 4.7 ppm	δ_H = 0.90-0.88 ppm δ_C = 4.7 ppm
45	δ_H = 0.93-0.89 ppm δ_C = 13.3 ppm	δ_H = 0.90-0.88 ppm δ_C = 13.2 ppm

Unfortunately, no coupling constants could be extracted from the ^{1}H-NMR spectrum of compound **163** due to overlapping signals. Still, the chemical shifts for both the proton and ^{13}C signals are in perfect agreement with compound **164** synthesized by *S. Wienhold*. This strongly supports that the aldol reaction with aldehyde **161** indeed leads to the desired *anti*-configuration.

Esterification with the C1-C7 carboxylic acid **38** under the previously described *Yamaguchi* conditions only led to a moderate yield of 44% of the desired ester **165** (Table 20, entry 1). Additionally, 46% of the starting material was reisolated.

Table 20. Optimization of the esterification leading to compound **165**.

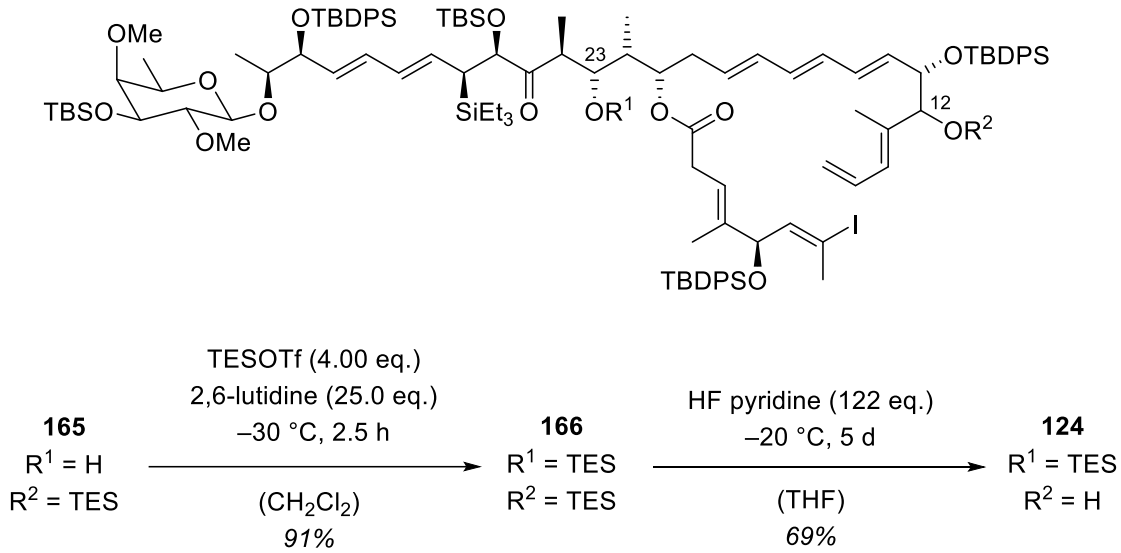


	Conditions	T [°C]	t [h]	Result
1	**38** (1.20 eq.) 2,4,6-Cl_3BzCl (1.20) NEt_3 (2.40) DMAP (1.00)	0	1.5	44% **165** 46% **163**
2	**38** (4.00 eq.) 2,4,6-Cl_3BzCl (3.50) NEt_3 (7.00) DMAP (1.00)	0	3.0	50% **165** 32% **163**

3	**38** (2.50 eq.) 2,4,6-Cl_3BzCl (2.00) NEt_3 (5.00) DMAP (1.00)	–30	2	62% **165** 16% **163**

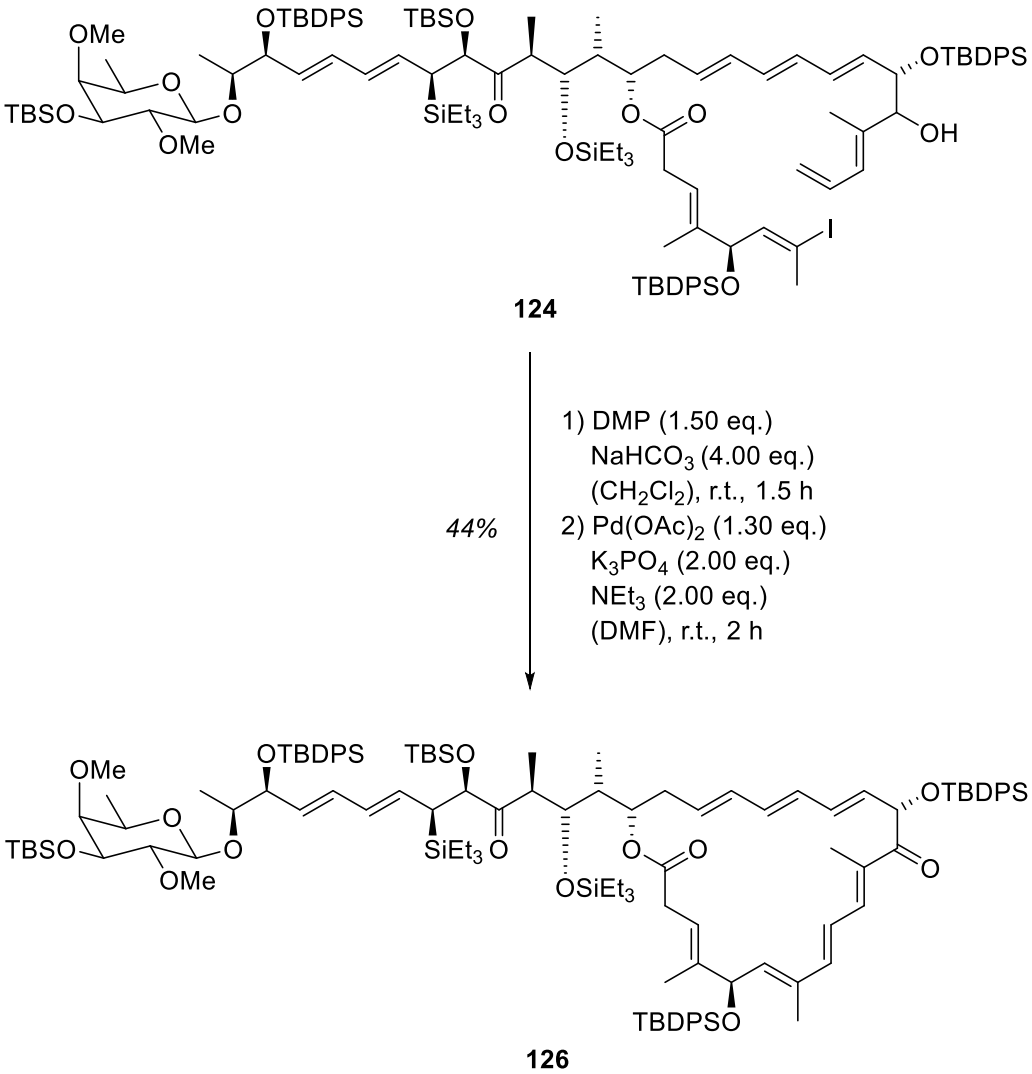
Increasing the amount of carboxylic acid improved the yield slightly but impaired the mass balance (entry 2). Performing the reaction at –30 °C led to an acceptable yield of 62%, while 16% of the valuable starting material could be reisolated (entry 3).

TES protection of the C23 alcohol proceeded smoothly employing TES triflate and 2,6-lutidine at low temperature (Scheme 88). The C12 TES group was removed by treatment with HF · pyridine. To avoid deprotection of the C23 TES group, the reaction was performed at –20 °C. It turned out to be important to add the starting material to the cold HF solution, to avoid overreaction. Despite the very slow reaction progress, the desired alcohol **124** was isolated in 69% yield, together with 18% of the double TES-protected starting material **166**. In contrast to the previous synthetic strategy, the compound was isolated in very pure form as a colorless foam.



Scheme 88. Synthesis of the cyclization precursor **124**.

With the pure alcohol in hand, we proceeded with the *Heck* cyclization. Utilizing the conditions previously found for the TBDPS protected macrocycle **159**, the desired product **126** could be isolated with a yield of 44% (Scheme 89).



Scheme 89. *Heck* cyclization leading to the silyl protected natural product **126**.

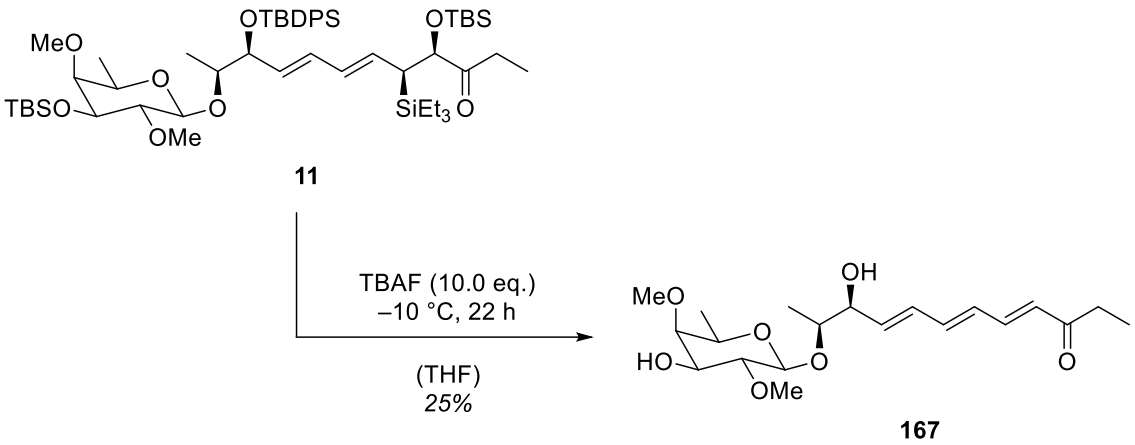
The drastic increase in yield compared to the old synthetic route can be rationalized by the much cleaner starting material and the improved reaction conditions. Apart from the reaction conditions themselves, also the workup was optimized. After adding the metal scavenger resin *QuadrapureTU*, the reaction was filtered over Celite.[103] Then, the solvent was removed at room temperature using an external cooling trap and high vacuum to avoid thermal stress on the sensitive molecule.

8. Deprotection experiments

8.1. Fragment deprotection approaches

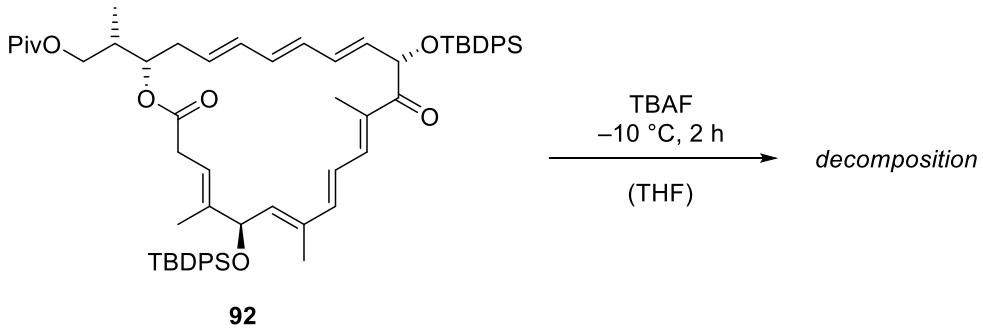
With the macrocycle **126** in hand, the only remaining step was the global deprotection. Thus, we turned our attention towards finding suitable deprotection conditions. We first wanted to explore the deprotection on smaller fragments before trying them on the real Pulvomycin skeleton.

Our experiments commenced with the ketone fragment **11**. The use of ten equivalents of TBAF in THF at –10 °C led to a very slow conversion of the starting material (Scheme 90).



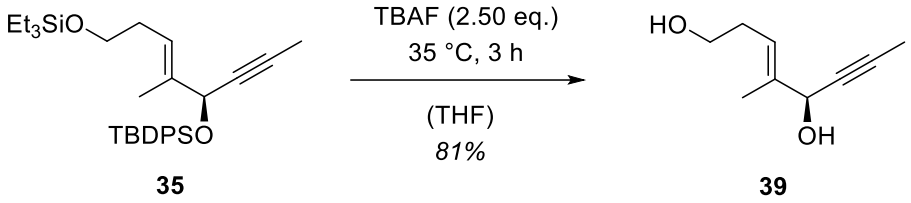
Scheme 90. Global deprotection of ketone fragment **11** at low temperature.

After 22 hours, there still was no full conversion, and only 25% of the fully deprotected product **167** could be isolated. Unfortunately, applying the same conditions to the macrocycle **92** led to rapid decomposition (Scheme 91). The reaction turned red directly after the TBAF addition, and no material could be isolated after workup.



Scheme 91. Treatment of macrocycle **92** with TBAF leads to decomposition, even at low temperature.

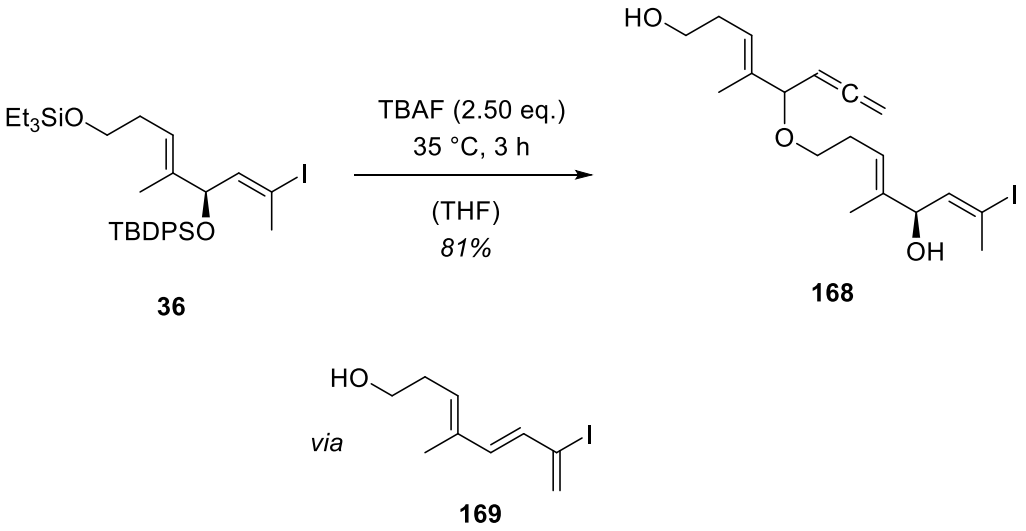
We reasoned that the basicity of the TBAF reagent is the main problem. If alkyne **35** was subjected to TBAF, the deprotection to diol **39** proceeded smoothly even at elevated temperatures (Scheme 92).



35 **39**

Scheme 92. Deprotection of alkyne **35**.

If vinyl iodide **36** was used under identical conditions, the desired product could not be isolated. Instead, NMR analysis suggested the formation of the allene compound **168** (Scheme 93). The double allylic position of the C5 alcohol probably makes it very prone to elimination under basic conditions. The eliminated product **169** can then be attacked by the primary alcohol to form the allene by the elimination of hydrogen iodide.

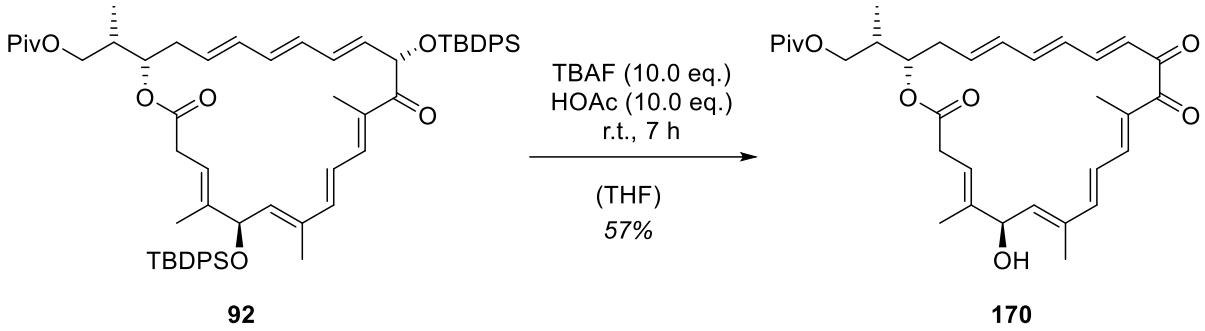


36 **168** **169**

Scheme 93. Formation of the unusual allene **168**.

Therefore, we decided to buffer the TBAF using acetic acid. Using five equivalents of TBAF in a 10:1 mixture of THF and acetic acid completely stopped the reaction, while a 12:1 mixture of TBAF and acetic acid led to complete decomposition. Finally, a one-to-one mixture of TBAF and acetic acid successfully removed both TBDPS groups from the macrocycle **92** (Scheme 94).[104] Although the reaction was carried out at ambient temperature, the deprotection took seven hours. To our surprise, the ^{1}H-NMR spectrum of the isolated product was missing the C13 CH signal. Instead, the ^{13}C spectrum showed an additional signal next to the C12 ketone

signal. After careful analysis of the analytical data, the NMR spectra unambiguously proved the formation of the 1,2-diketone **170**.



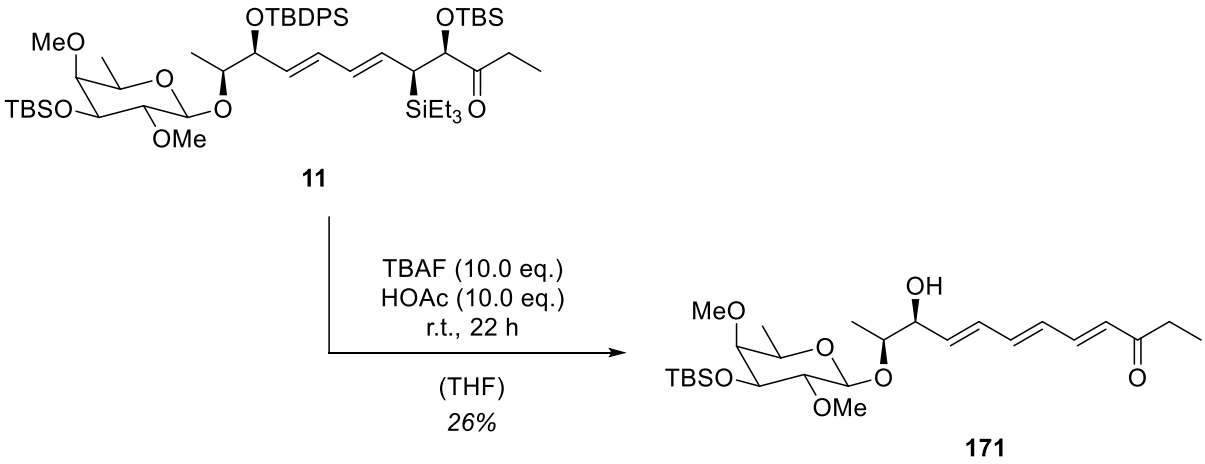
92 **170**

Scheme 94. Formation of 1,2-diketone **170** under TBAF deprotection conditions.

We first suspected aerial oxidation of the C13 alcohol to the ketone. However, the ketone formation was also observed when both the reaction and the workup were conducted under a protective atmosphere. It seems that the TBAF reagent itself acts as the oxidant, as pointed out in the literature.[105]

Around the same time of these findings, the group of *Moon* and coworkers reported the isolation of three new compounds of the Pulvomycin family, as pointed out in chapter 2.[21] These compounds include Pulvomycin D (**4**), which exhibits the same 1,2-diketone structure between C12 and C13. We reasoned that Pulvomycin D (**4**) would be an interesting target for our total synthesis and did not focus on strategies to avoid the oxidation at C13 further.

Applying the above-mentioned buffered TBAF conditions to ketone **11** successfully triggered the *Peterson* olefination and removed the TBDPS group (Scheme 95). However, the TBS group at C37 remained untouched under these conditions. No full conversion was achieved after 22 hours, resulting in a low yield of only 26% for the TBS-protected fragment **171**.



Scheme 95. Application of the buffered TBAF conditions to ketone fragment **11**.

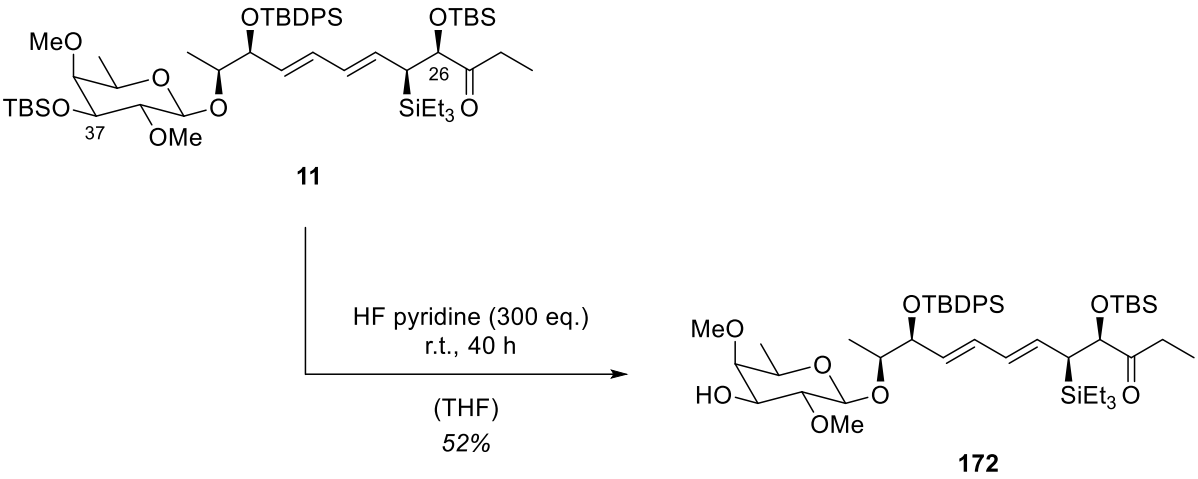
A variety of other known deprotection conditions were applied to the ketone fragment to facilitate the removal of the C37 TBS group (Table 21). However, most conditions only triggered the *Peterson* elimination while leaving the TBDPS and TBS group untouched.
The combination of potassium fluoride and TBACl is known for the *in-situ* formation of TBAF. However, only 51% of the eliminated product could be isolated. Combinations of potassium fluoride and crown ether are known to generate highly reactive fluoride species.[106] In our case, only eliminated product was isolated as well under these conditions. The use of ammonium fluoride in combination with HF led to no conversion.[107] The TASF-reagent was not able to remove neither the TBDPS nor the TBS group.[108]

Table 21. Application of other known silyl deprotection conditions to ketone **11**.

	Conditions	solvent	t	T	Result
1	KF · 2 H_2O (18.0 eq.) NBu_4Cl (19.0 eq.)	MeCN	22 h	r.t.	51% Peterson elimination product
2	KF (10.0 eq.) 18-crown-6 (5.00 eq.)	DMF	3 d	–20°C	53% Peterson elimination product
3	NH_4F · HF (20.0 eq.)	DMF:NMP 1:1	3 d	0°C ⟶ r.t.	n.c.
4	TASF (3.00 eq.)	pyridine	3 d	0°C ⟶ r.t.	Traces of Peterson elimination product

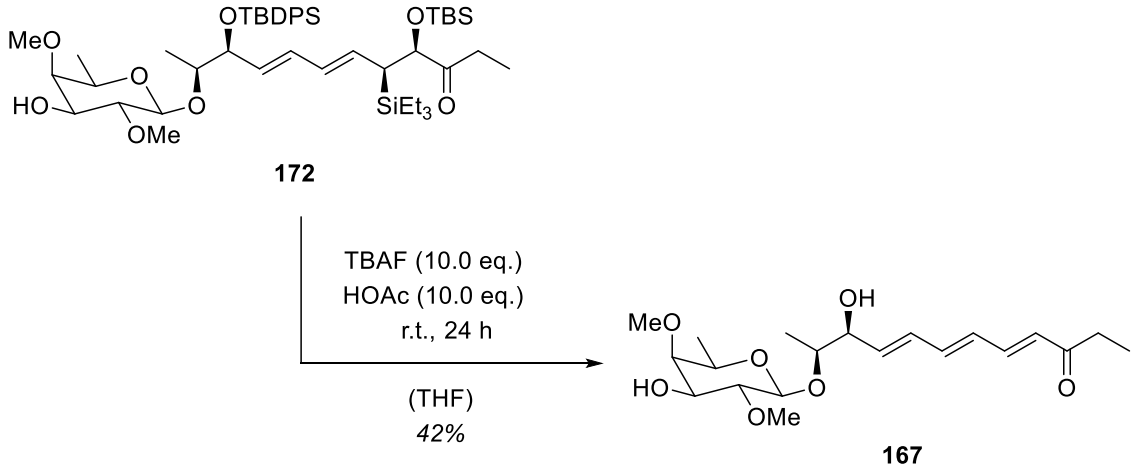
Finally, we came across a literature report of *Paterson* and coworkers from 2006, where they successfully removed a TBS group from a similar sugar unit.[109] Employing a large excess of HF · pyridine, they were able to remove the TBS group in 79% yield. Applying these conditions

to the ketone fragment indeed led to the deprotection of the desired TBS group, although only in a moderate yield of 52% for alcohol **172** (Scheme 96). Interestingly, the TBS group on the sugar was cleaved selectively in the presence of the C26 TBS group, as proven by exclusive NOE contacts between the methyl protons of the remaining TBS group and the ethyl group of the ketone.



Scheme 96. Successful removal of the C37 TBS group by using an excess of HF · pyridine.

Due to the orthogonality of the TBS group at C37 we reasoned, that a two-step deprotection sequence would be the best choice for the global deprotection. Indeed, treatment of the partially deprotected fragment **172** with buffered TBAF for 24 hours finally furnished the fully deprotected triene fragment **167** in 42% yield (Scheme 97).

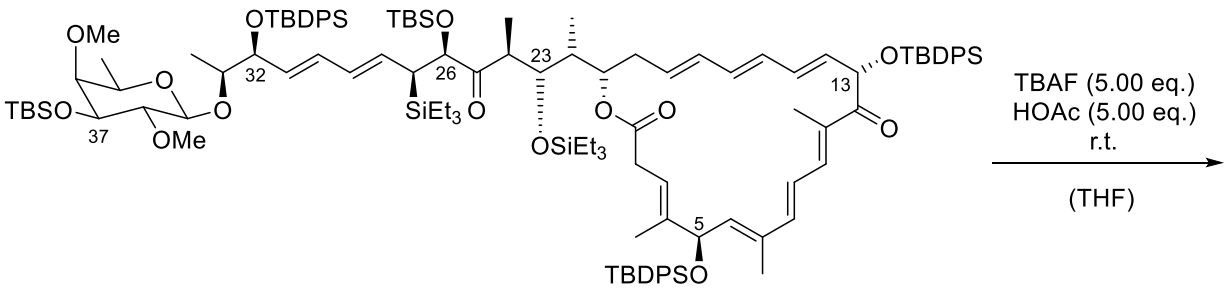


Scheme 97. Complete deprotection of ketone **172** *via* two-step deprotection sequence.

8.2. Global deprotection of the C1-C40 fragment

With the macrocycle **126** in hand, we could proceed towards the global deprotection. The majority of the silyl groups should be cleavable using buffered TBAF conditions, while the TBS group at the C37 position should be removed using HF · pyridine. Furthermore, we already suspected the oxidation of the alcohol at C13 during the deprotection sequence, as observed in the fragment deprotection.

At first, the order of the two reactions was established. In an initial experiment, macrocycle **126** was treated with five equivalents of TBAF, buffered with five equivalents of acetic acid in THF (Scheme 98). The reaction progress was followed by ESI-MS.



126

$M + Na^+ = 2050.15$

Scheme 98. Treatment of macrocycle **126** with a slight excess of TBAF and acetic acid.

After 13 hours at ambient temperature, ESI-MS indicated the successive loss of two TBDPS groups (M_{TBDPS} = 239, Figure 9, $M+Na^+$ = 1812, 1573).

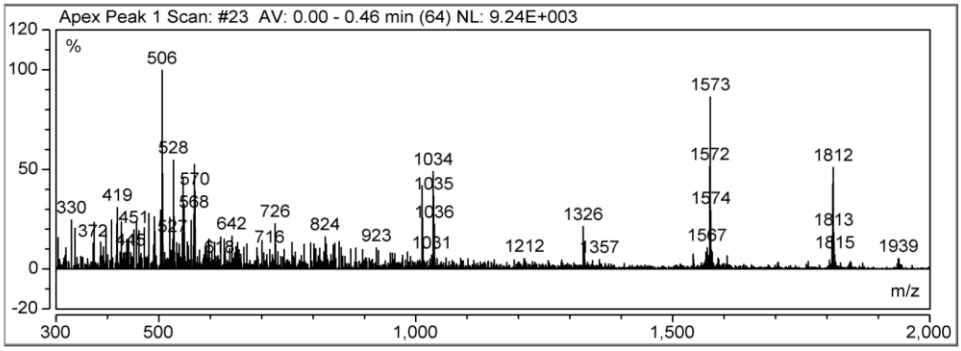


Figure 9. ESI-MS spectrum after 13 hours.

In order to increase the reaction rate, further 50 equivalents of acetic acid and TBAF were added at this point. Three hours later, ESI-MS showed complete removal of the two TBDPS groups (Figure 10).

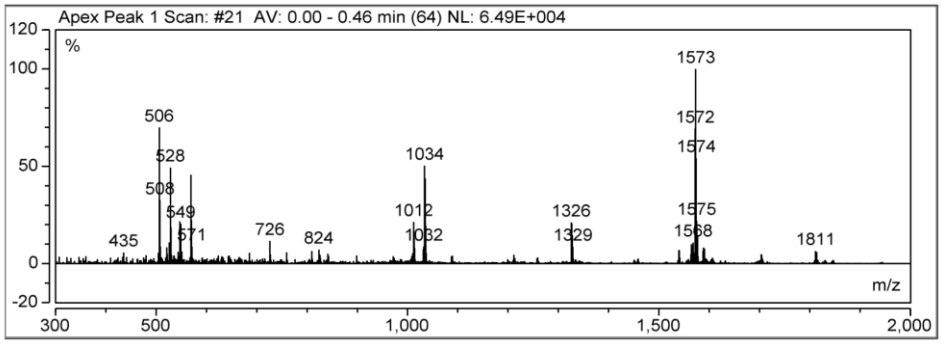


Figure 10. ESI-MS spectrum after 16 hours.

After another 18 hours, the subsequent loss of a TBS group ($M+Na^+ = 1459$), followed by the *Peterson* elimination ($M+Na^+ = 1327$) and the cleavage of the C23 TES group ($M+Na^+ = 1212$), was observed (Figure 11).

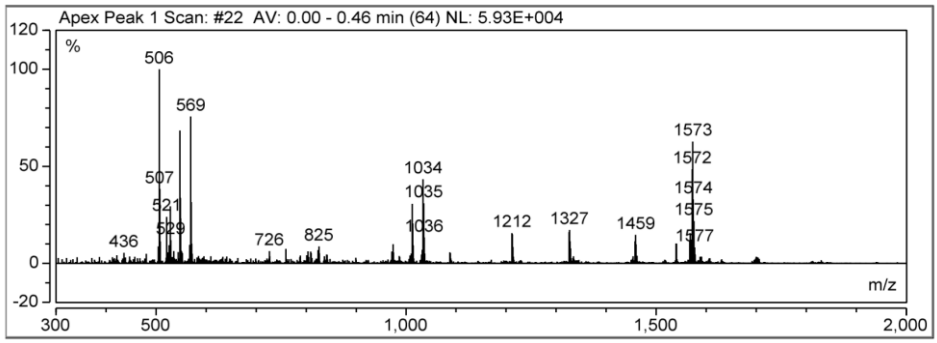


Figure 11. ESI-MS spectrum after 34 hours.

After a total reaction time of 38 hours, the beginning cleavage of the last remaining TBDPS group was observed (Figure 12, $M+Na^+ = 974$). However, the signal-to-noise ratio of the measurements became worse, and after 58 hours, no material could be detected anymore.

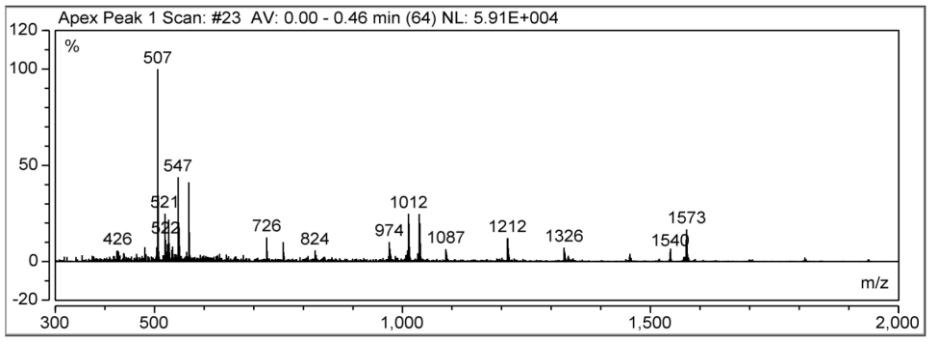
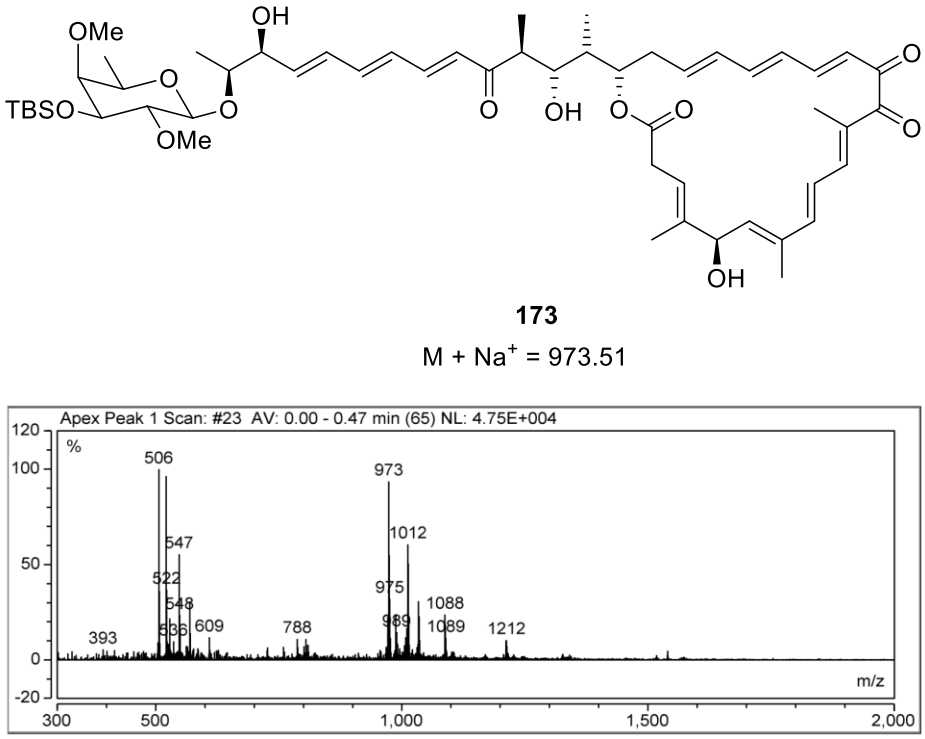


Figure 12. ESI-MS spectrum after 38 hours.

In order to increase the reaction rate, the experiment was repeated using 210 equivalents of TBAF and 200 equivalents of acetic acid. We hoped that shortening the reaction time would decrease the amount of decomposition. Indeed, the formation of the solely TBS-protected compound **173** was observed by ESI-MS after 29 hours, substantially faster than before (Figure 13). However, the reaction was still accompanied by a considerable amount of decomposition.



173

$M + Na^+ = 973.51$

Figure 13. Supposed formation of the TBS-protected natural product **173** ($M+Na^+ = 973$) after 29 hours.

At this point, the observed mass of 973 in the ESI-MS spectrum already suggested that compound **173** exhibited the 1,2-diketone ($M+Na^+ = 973$) rather than the free hydroxy group ($M+Na^+ = 975$).

The reaction proceeded much cleaner when THF was substituted for acetonitrile. Even after a long reaction time of three days, ESI-MS showed the clean formation of the TBS-protected natural product (Figure 14).

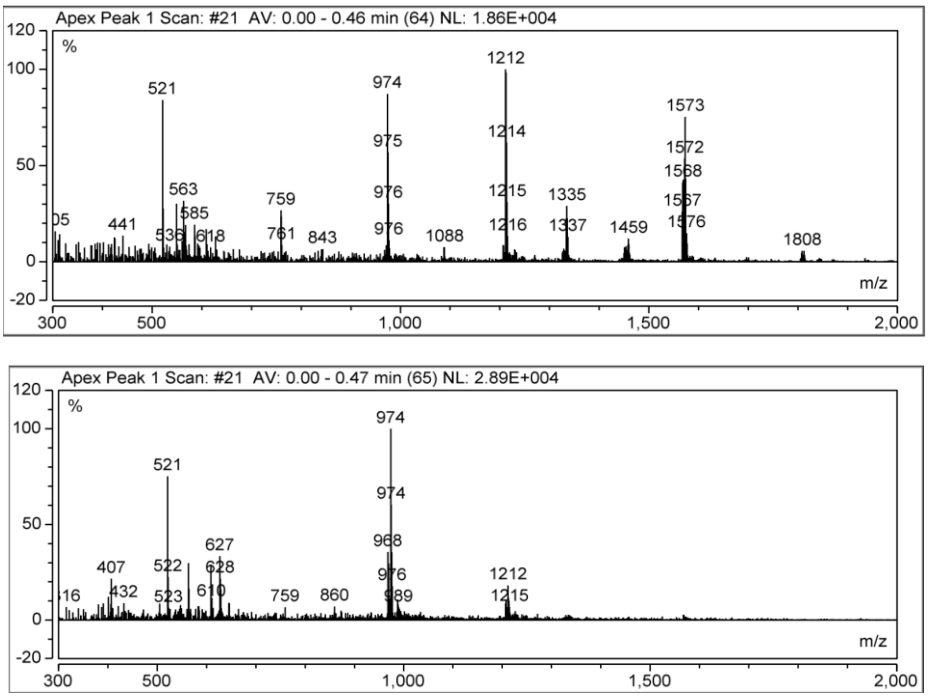


Figure 14. Deprotection using buffered TBAF in acetonitrile after 27h (top) and 72h (bottom).

Due to the small amounts of material, isolation of the compound was attempted by preparative TLC. A bright yellow fraction could be isolated, which mainly contained the TBS-protected natural product according to ESI-MS. However, no characterization by NMR was possible due to the small quantities. We decided to subject the material to HF · pyridine conditions to facilitate the removal of the last remaining TBS group at C37. Unfortunately, though, only decomposition could be observed.

In hindsight, preparative TLC probably was not the method of choice for isolating the very sensitive compound. It seems possible that some of the decomposition already happened during the isolation step and that only traces of material were actually used in the following HF deprotection. Unfortunately, no attempts to isolate the compound using preparative HPLC were made at the time. Treatment of the crude product of the TBAF reaction with HF only led to decomposition, too. The reason might be residues of the TBAF reagent, which cannot be removed by a simple aqueous workup. Therefore, a chromatographic purification step seems to be unavoidable.

Eventually, we decided to reverse the reaction order and perform HF deprotection prior to the treatment with TBAF. In an initial experiment, macrocycle **126** was subjected to a large excess (1000 eq.) of HF · pyridine complex in THF at room temperature. After 1.5 hours, ESI-MS analysis showed the clean formation of a single product that had one TBDPS group removed (Figure 15, $M+Na^+ = 1813$).

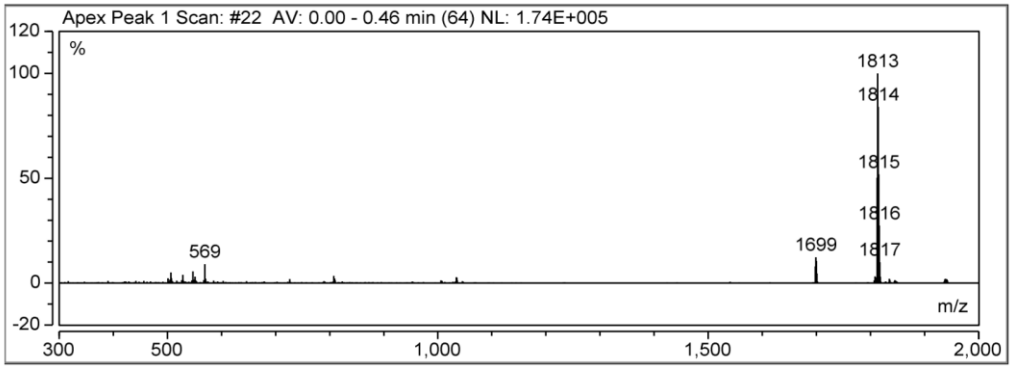


Figure 15. ESI-MS spectrum after 1.5 hours.

Continued stirring for 20 hours led to the cleavage of a TES or TBS group (Figure 16, $M+Na^+ = 1699$). We hoped that the C37 TBS group had been cleaved. However, due to the same molecular weight of TES and TBS (M = 115), no statement could be made from ESI-MS analysis alone.

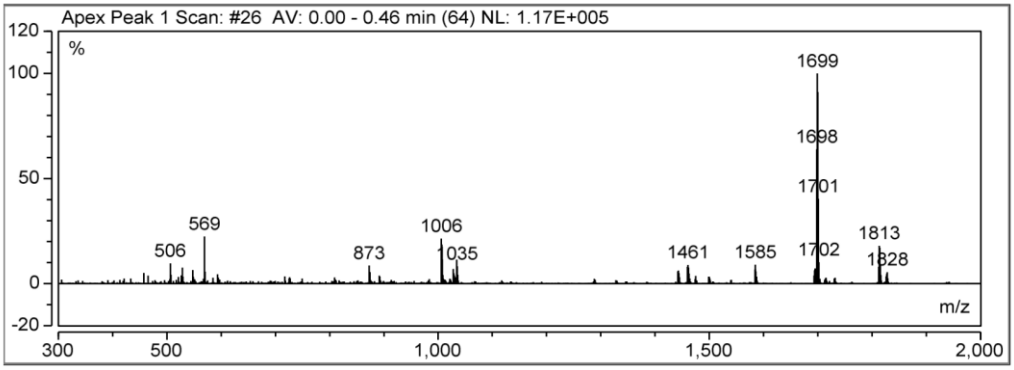
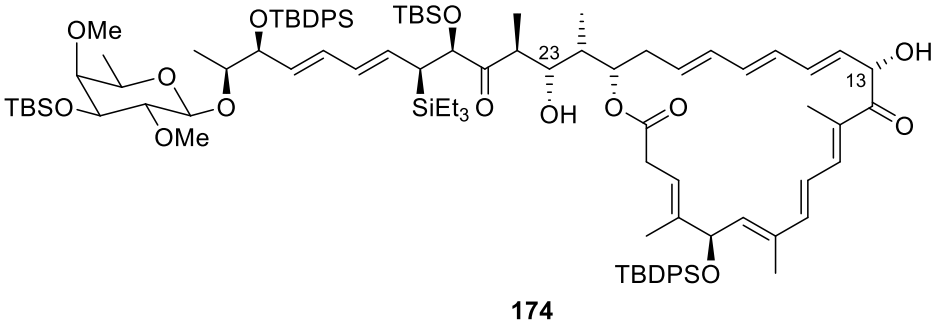


Figure 16. ESI-MS spectrum after 21.5 hours.

Hence, the reaction was stopped at this point, and the material was isolated by column chromatography. NMR analysis unambiguously showed the cleavage of the C23 TES group and the C13 TBDPS group (Compound **174**, Figure 17).



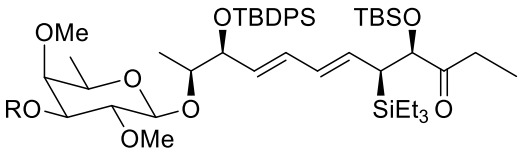
174

M + Na^+ = 1697.95

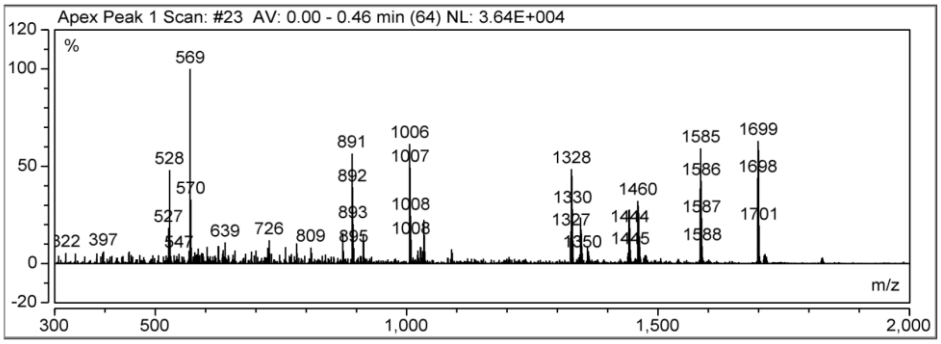
Figure 17. Isolated compound after deprotection with HF · pyridine for 21.5 hours, characterized by NMR.

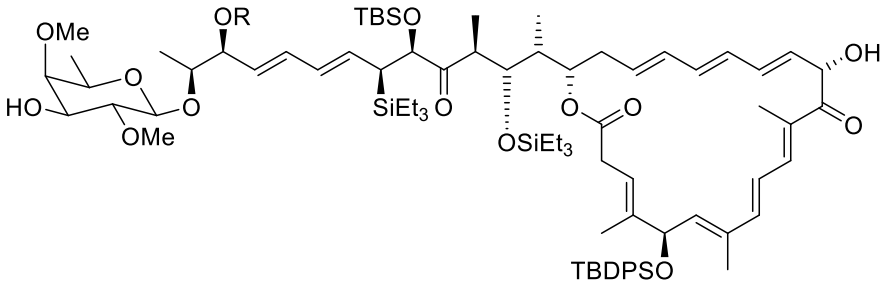
Interestingly, the C13 hydroxy group was still intact at this point. No 1,2-diketone was observed, substantiating that aerial oxidation probably is not the cause for its formation.

The experiment was repeated with a much longer reaction time. After stirring for five days at room temperature, several new intermediates were formed, including the desired C37 deprotected products **175** and **176** (Figure 18, M+Na^+ = 1460, 1585). Unfortunately, the reaction was accompanied by significant decomposition. The fragments with *m/z* = 891 and 1006 can be correlated to the ketone fragments **177** and **178** (M+Na^+), indicating a beginning retro-aldol reaction between C23 and C24. The retro-aldol reaction is probably triggered once the C23 TES group is cleaved.



178, R = TBS, M + Na^+ = 1005.59
177, R = H, M + Na^+ = 891.51

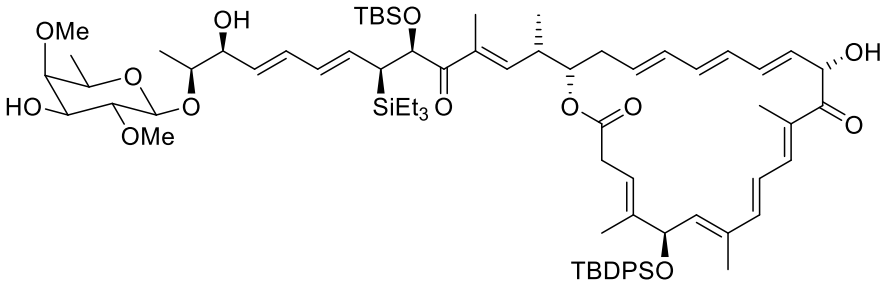




175, R = H M + Na^+ = 1459.83
176, R = TBDPS M + Na^+ = 1583.86

Figure 18. ESI-MS spectrum after five day HF · pyridine reaction and putative structure assignments.

Furthermore, the fragment with *m/z* = 1328 suggests the elimination of the C23 alcohol (Compound **179**, figure 19). At the same time, a significant amount of the diol **174** (M+Na^+ = 1699) was still present, indicating incomplete conversion.

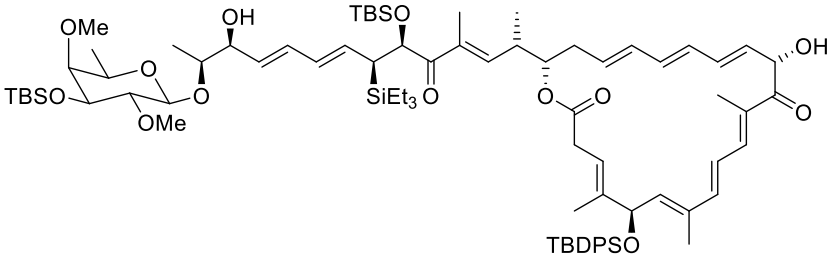


179

M +Na^+ = 1327.73

Figure 19. Putative structure of the elimination product of the C23 alcohol.

Considering the positive effect of acetonitrile on the TBAF reaction, we tried HF · pyridine reaction in acetonitrile as well. However, after 27 hours, mainly elimination product **180** was observed (Figure 20, $M+Na^+ = 1443$).



180

$M + Na^+ = 1441.82$

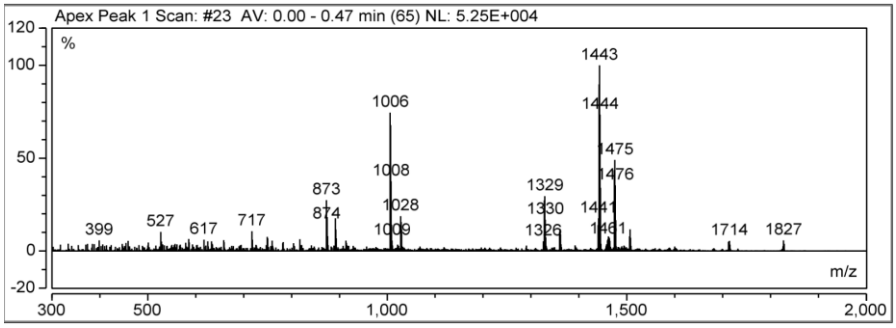


Figure 20. Performing HF deprotection in acetonitrile mainly leads to elimination product **180**.

When HF was added in seven portions of 300 equivalents over the course of three days, mainly eliminated product **179** ($M+Na^+ = 1329$) was formed as well (Figure 21).

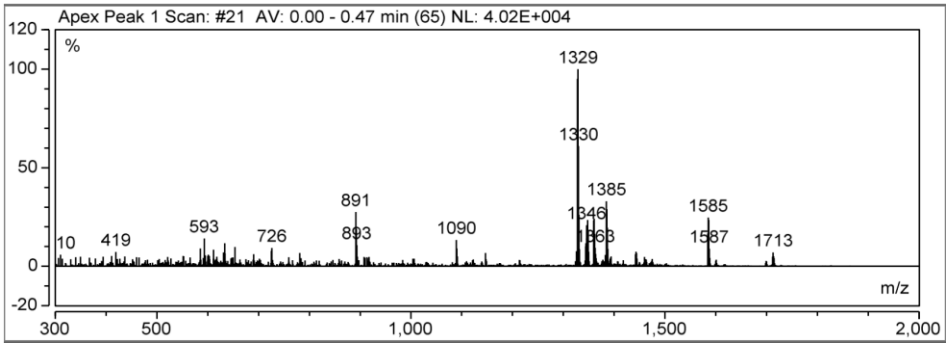
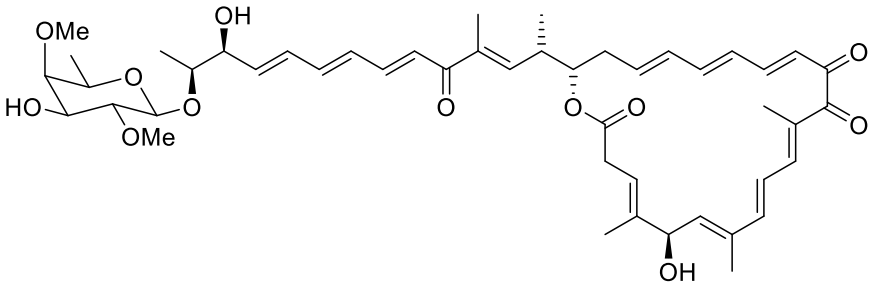


Figure 21. The addition of HF in small portions over a longer time period had no positive effect.

Treatment of compound **179** with the previously found buffered TBAF conditions in acetonitrile for 27 hours led to the clean formation of a product with m/z = 841 (Figure 22). This probably correlates to the C23 eliminated Pulvomycin D (**181**, $M+Na^+ = 841$). No further

attempts to characterize this compound were made. However, the very clean formation of this product, without severe decomposition, suggests that the C23 alcohol is a key factor for the sensitivity of the Pulvomycins.



181

$M + Na^+ = 841.41$

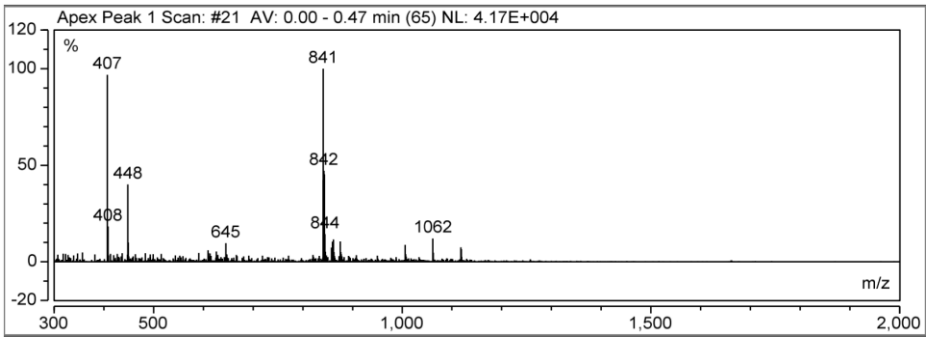
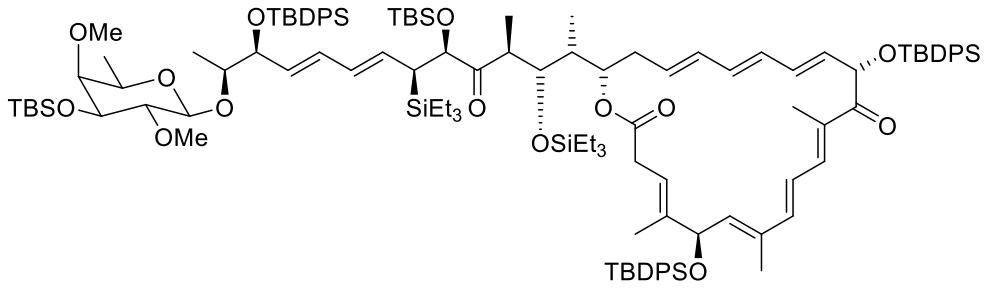
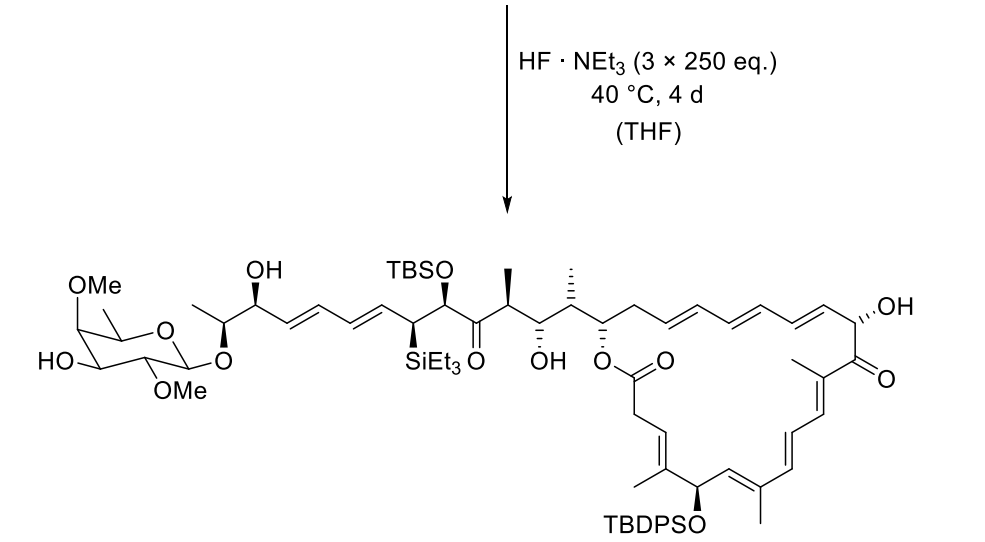


Figure 22. Supposed formation of eliminated Pulvomycin D derivative **181**.

Switching from HF · pyridine to the less common HF · triethylamine derivative had a significant impact on the reaction (Scheme 99).[110] To our delight, neither retro-aldol reaction nor elimination of the C23 alcohol was observed, even after a reaction time of four days and a total of 750 equivalents of the reagent.

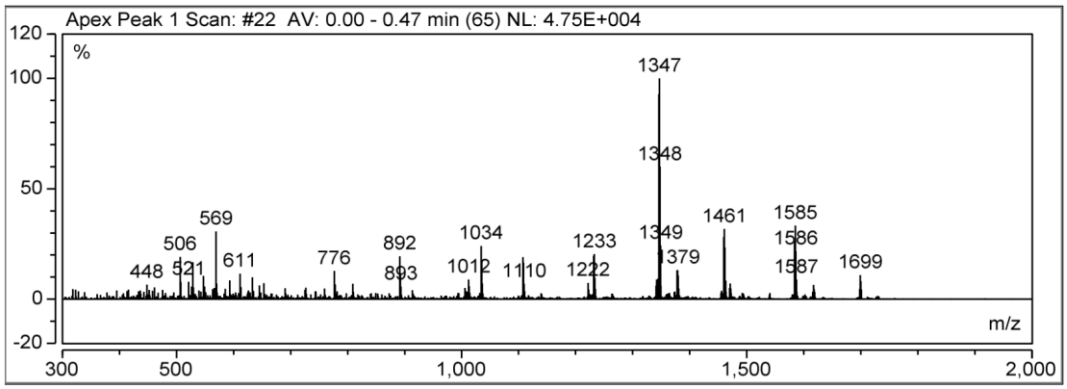


126



182

$M + Na^+ = 1345.74$



Scheme 99. The use of HF triethylamine complex significantly improved the reaction.

Instead, the reaction seemed to converge towards a fragment with *m/z* = 1347, which most likely correlates to compound **182** ($M+Na^+$). We decided not to attempt any purification or isolation of the compound mixture and instead subjected the crude material to the above-mentioned buffered TBAF conditions in acetonitrile (210 eq. TBAF, 200 eq. HOAc). After 20 hours at

room temperature, HPLC-MS analysis revealed the formation of a compound with an *m/z* ratio of 859 (Figure 23).

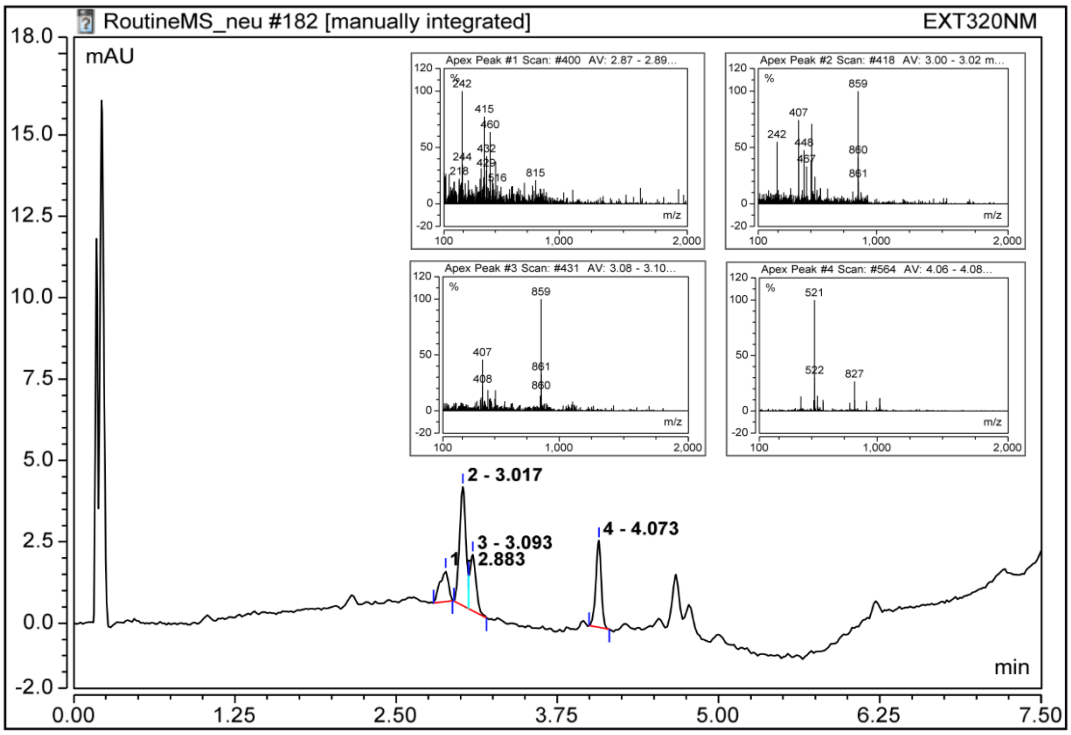


Figure 23. HPLC-MS analysis of the crude reaction mixture after 20 hours (PolarPremium C18 column, 50x2.1mm, H_2O/MeCN = 20-100%).

HRMS analysis proved the formation of a product with *m/z* = 859.4241, which is in perfect agreement with Pulvomycin D (Figure 24, M+Na = 859.4245). Comparison with an authentic sample of Pulvomycin A showed no agreement of the HPLC retention time. Therefore, the oxidation to the 1,2-diketone seems to occur quantitatively during the TBAF deprotection.

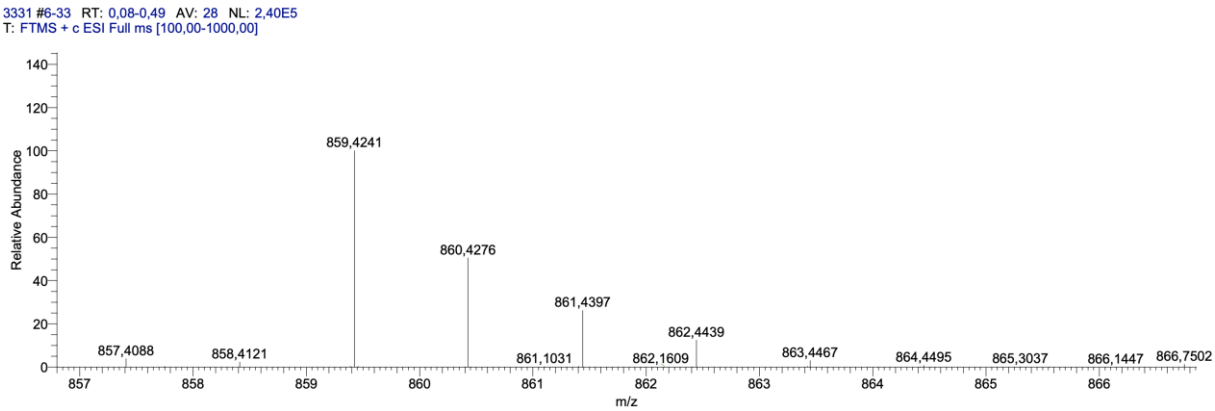


Figure 24. HRMS measurement (ESI) of the isolated compound.

Unfortunately, the isolation of the compound turned out to be complicated. HPLC conditions for Pulvomycin D were published in the literature. However, essential values like the diameter of the used column were missing, and the exact HPLC run could not be reproduced. The isolation was further complicated by a large number of different peaks in the chromatogram, as well as the different HPLC columns used for HPLC-MS and preparative HPLC (Figure 25).

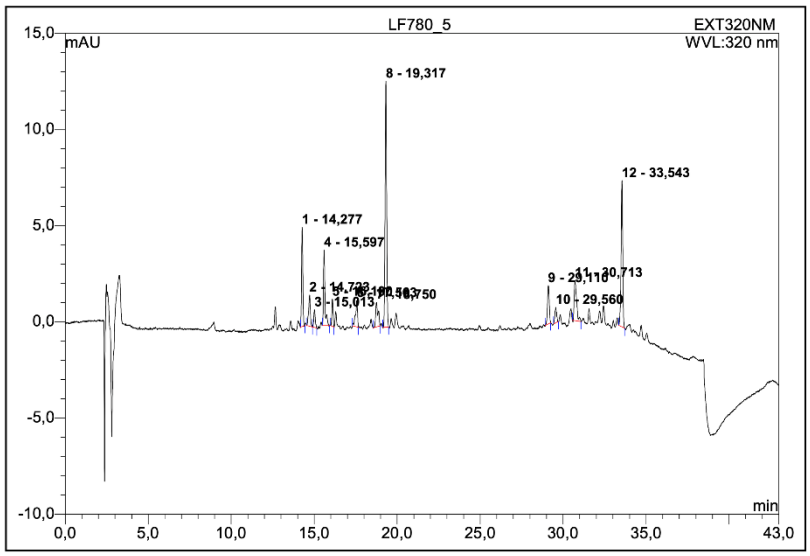


Figure 25. Typical HPLC trace of the crude reaction mixture (Kromasil C18 column, 250x4.6mm, H_2O/MeCN = 20-100%).

Eventually, the peak at 19.3 min could be identified as the natural product containing fraction. The peak at 33.5 min contains TBS protected Pulvomcin D, according to ESI-MS analysis. Although no full conversion was achieved, the reaction was usually stopped at this point in order to avoid decomposition of the sensitive natural product. A prolonged reaction time usually resulted in the complete decomposition of the material.

Using a preparative Kromasil C18 column, the desired peak could be isolated. To our delight, the ^{1}H-NMR shifts of the isolated material perfectly matched those reported for Pulvomycin D (see the experimental section). Unfortunately, though, the spectrum was contaminated with several unidentified impurities. The HPLC trace of the isolated product shows mainly one peak at 19.3 min. However, smaller impurities are still visible in the chromatogram (Figure 26).

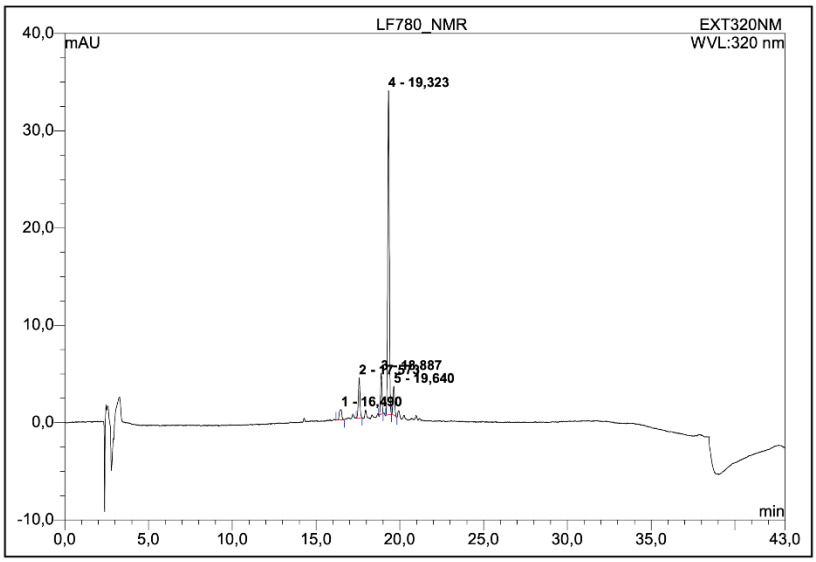
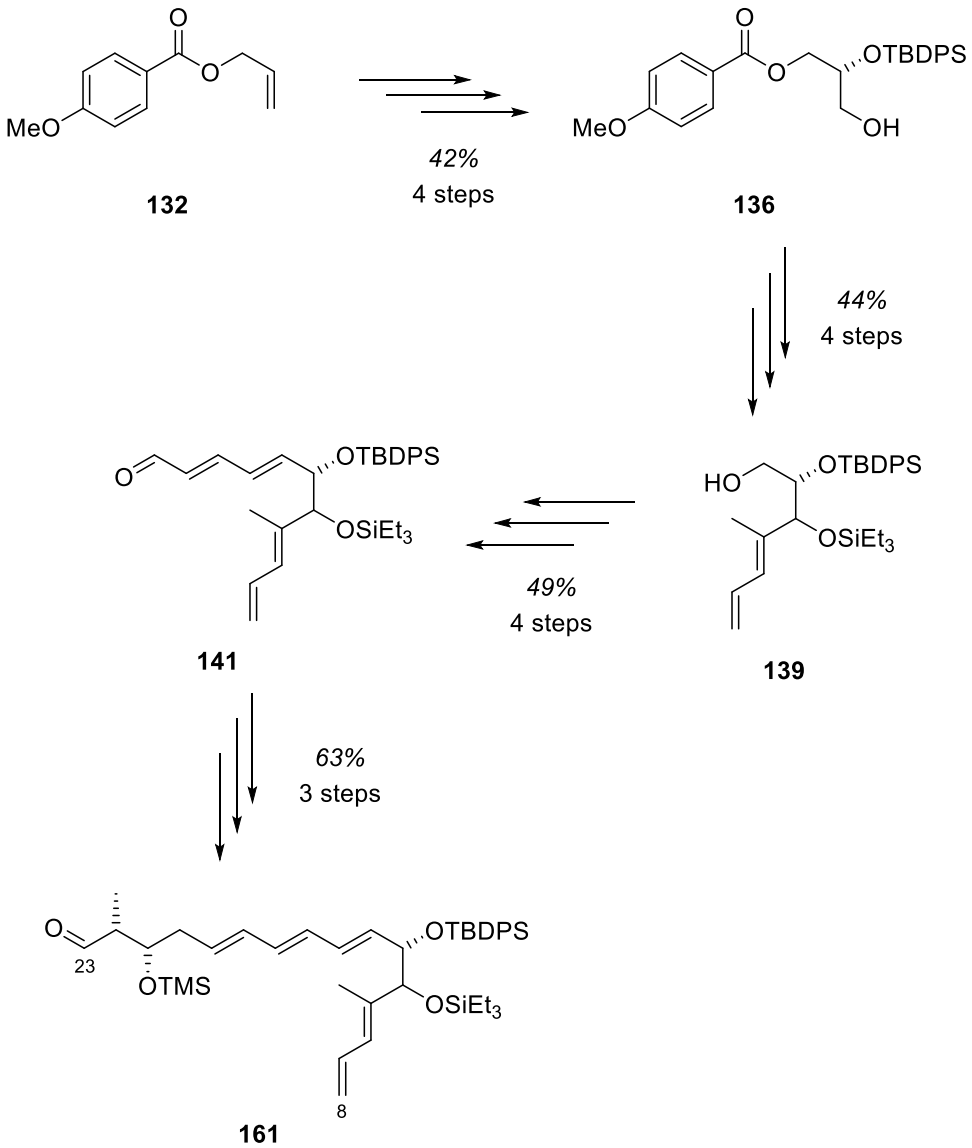


Figure 26. HPLC trace of the purified compound.

Despite numerous attempts to improve the HPLC conditions, the material could never be isolated in pure form. Switching to a bigger HPLC column had no effect on the separation. Changing the gradient to an isocratic method also led to no improvement. Also, due to the very small amounts of material, no ^{13}C spectrum could be recorded, even with very high scan numbers. Typically, around 0.5 mg of the (contaminated) natural product **4** were isolated from the deprotection of 10 mg of macrocycle **126**, resulting in a yield of around 12%.

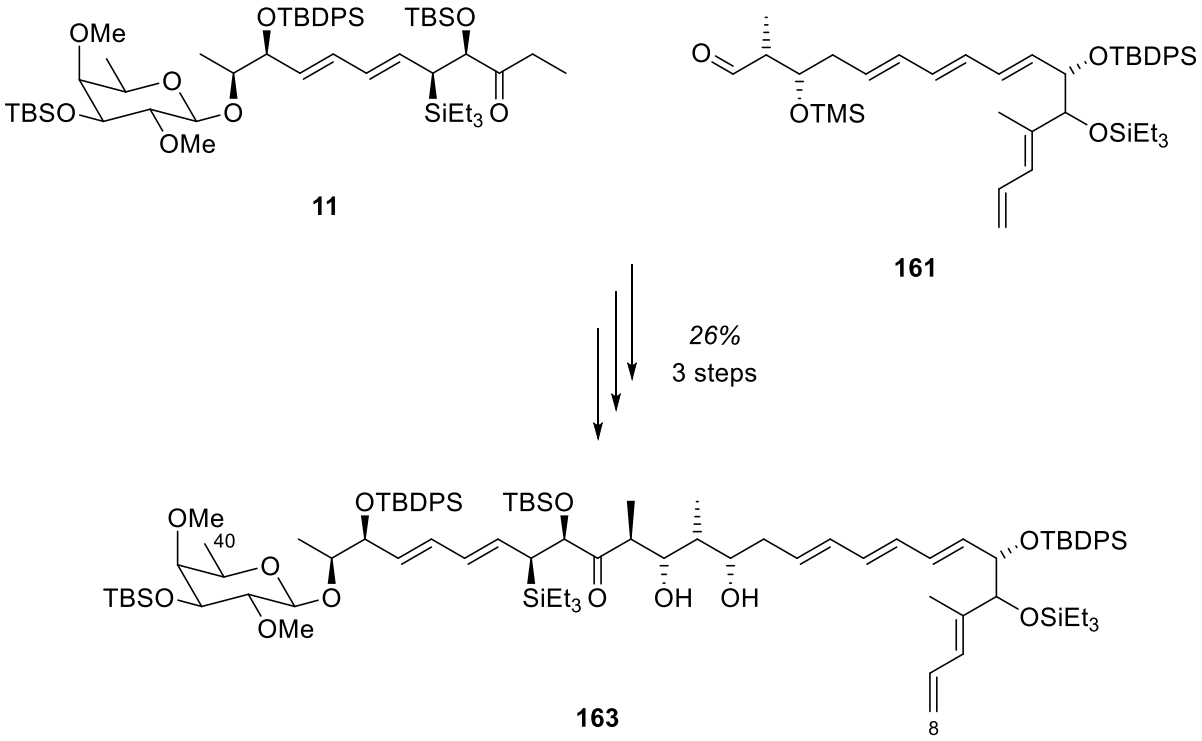
9. Summary

Among various strategies to close the 22 membered macrocycle of the Pulvomycin core, the intramolecular *Heck* reaction turned out to be the only feasible method. Still, the reaction required extensive screening of the reaction conditions. Furthermore, the *Heck* cyclization turned out to be relatively limited in respect to the protecting group strategy, requiring a TBDPS group at the C5 alcohol. Other cyclization strategies *via Nozaki-Hiyama* or *Suzuki* coupling failed due to instable intermediates. Ring closing metathesis only delivered traces of product.
Overall, the natural product Pulvomycin D (**4**) has been synthesized in the longest linear sequence of 24 steps starting from protected allyl alcohol fragment **132**. After dihydroxylation, silyl protection, and reduction, alcohol **139** was isolated in 19% yield over eight steps (Scheme 100).



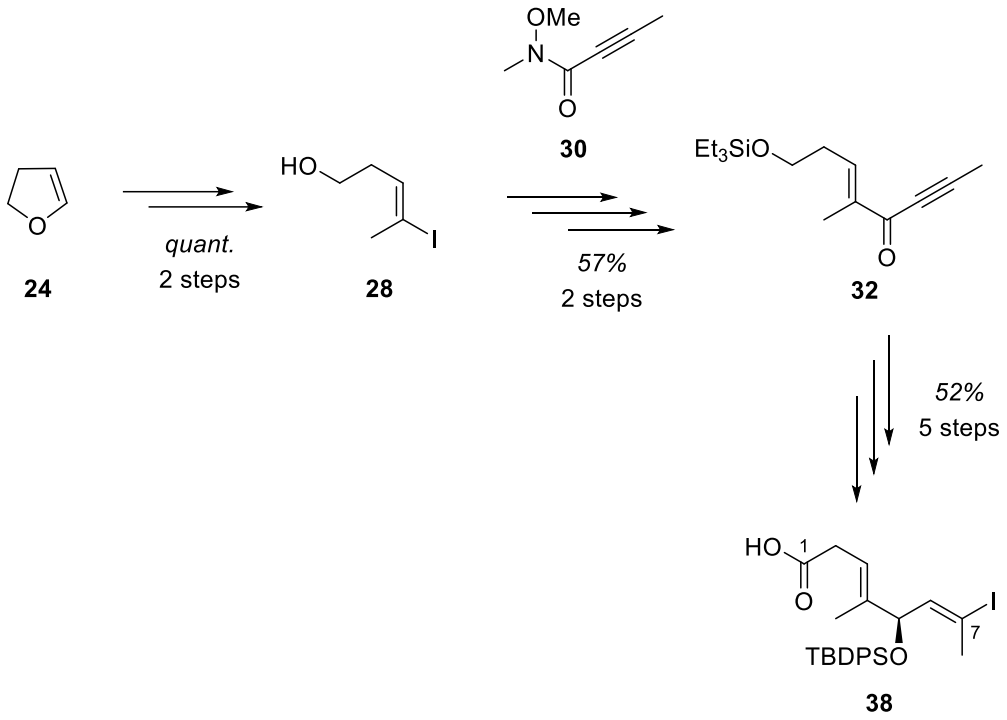
Scheme 100. Synthesis of the C8-C23 fragment **161**.

Horner-Wadsworth-Emmons reaction, followed by *Julia-Kocienski* olefination and oxidation, led to the aldehyde fragment **161** in 31% yield over seven steps. The aldol reaction with ketone **11**, followed by deprotection of the TMS group, proceeded with a yield of 26% over three steps (Scheme 101).



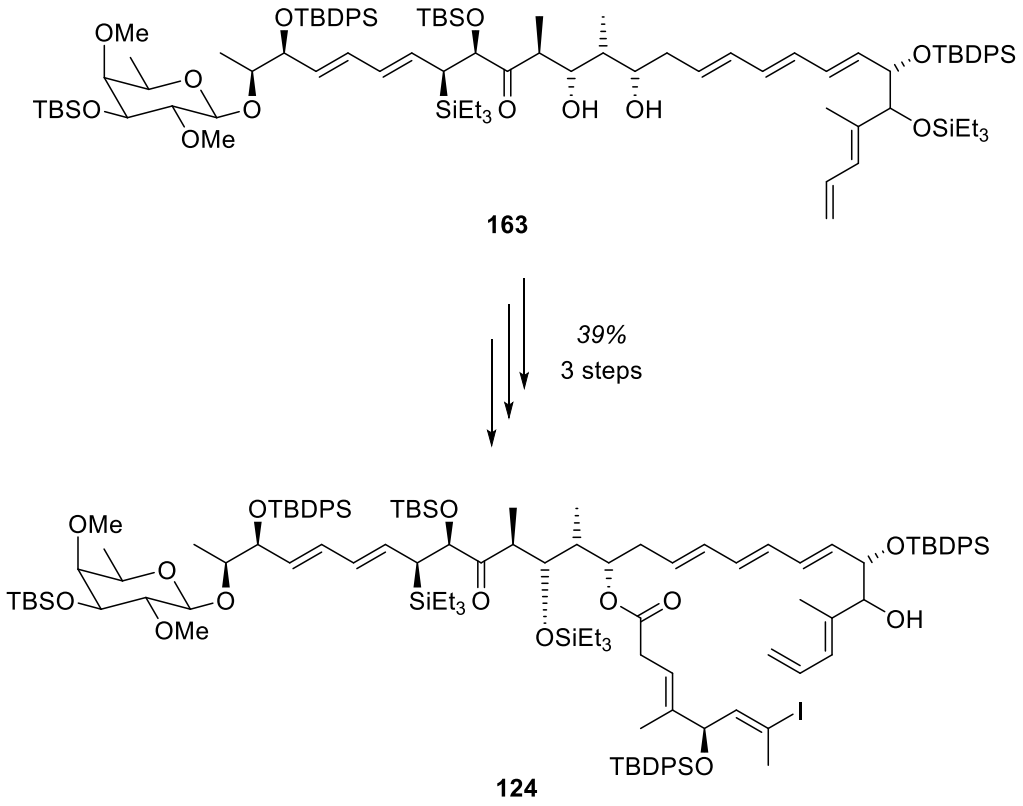
Scheme 101. Aldol reaction and TMS deprotection leading tot he C8-C40 fragment **163**.

The southern C1-C7 fragment was synthesized starting from 2,4-dihydrofuran (**24**) in nine linear steps (Scheme 102). First, the furan was converted into alcohol **28** by a dyotropic rearrangement. Addition to Weinreb amide **30** delivered ketone **32** in 57% over two steps. Stereoselective reduction with the (*S*)-CBS catalyst, installation of the vinyl iodide with the *Schwartz* reagent and oxidation of the C1 alcohol led to carboxylic acid **38** in 52% over five steps.



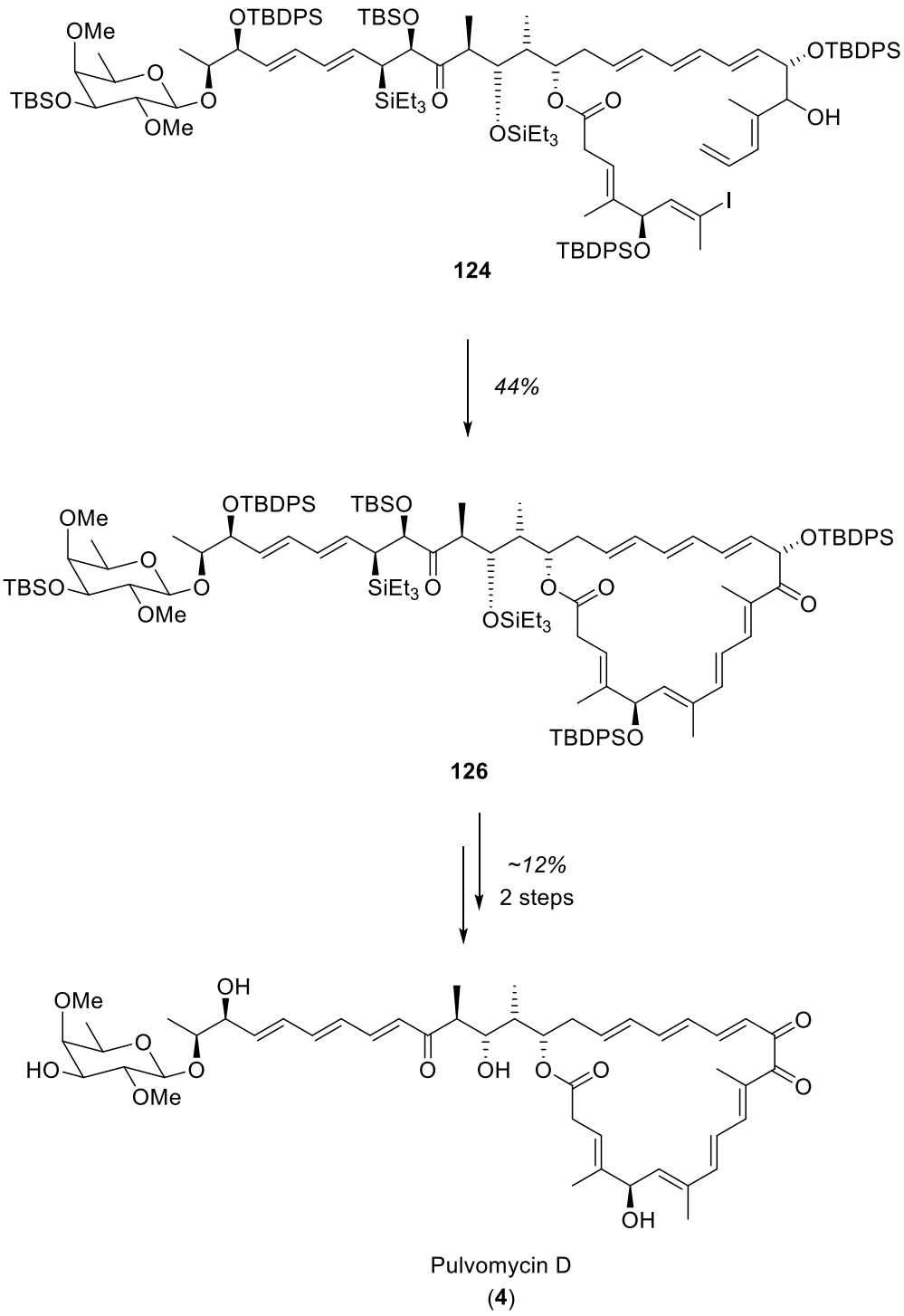
Scheme 102. Synthesis of the C1-C7 fragment **38**.

Esterification of acid **38** with diol **163**, followed by silyl protection and deprotection sequence delivered cyclization precursor **124** in 39% over three steps (Scheme 103).



Scheme 103. Synthesis of the cyclization precursor **124**.

The *Heck* cyclization delivered the macrocycle **126** with a yield of 44%. The following global deprotection led to the natural product **4** in 12% over two steps.



Scheme 104. Cyclization and global deprotection leading to Pulvomycin D (**4**).

In summary, the macrocycle **126** was reached with a yield of 0.23% after 22 steps (average of 76% per step) starting from protected allyl alcohol fragment **132**. The subsequent two-step

deprotection sequence delivered the natural product in approximately 12% yield. The total yield over 24 steps is 0.028% (average of 71% per step). However, due to the unknown contamination of the final product, no exact statement about the deprotection yield can be made.

10. General methods

The numbering in the carbon chain is based on the final position of the carbon atom in the natural product. Inseparable diastereomeric mixtures are marked with „A“ (major diastereoisomer) and „B“ (minor diastereoisomer).

10.1. Experimental techniques

All reactions involving air-sensitive or moisture-sensitive reagents were performed under an argon atmosphere. The used glass devices were heated under vacuum with a heat gun (650 °C). Solid reagents were added under argon counter flow and liquid reagents *via* disposable syringes and needles.

The ratios of solvent mixtures are given in volume units.

The calculated yields refer to the limiting reagent component.

Paraffin oil baths were used as heat baths. The temperature was set and controlled *via* an adjustable contact thermometer. Depending on the temperature, mixtures of ice/water (0 °C), acetone/dry ice (−78 °C) were used for ice baths. If applicable, the aimed temperature was set *via* a HAAKE EK90 cooling device (−78 °C - 0 °C) in Dewar flasks.

Reagents

All commercially available reagents were used without purification.

Solvents

Dried solvents for moisture-sensitive reactions were taken from a MB-SPS-800 device by M. Braun GmbH. The solvents ran through the following columns:

Dichloromethane:	*Merck Emsure*®, p.a., 99.8%, <0.03% H_2O, Column: 2×MB-KOL-A.
Diethyl ether:	*Merck Emsure*®, p.a., 99.7%, <0.03% H_2O, Column: 1×MB-KOL-A, 1×MB-KOL-M Typ 2.
Tetrahydrofuran (THF):	*Merck Emsure*®, p.a., 99.8%, <0.03% H_2O, Column: 2×MB-KOL-M Typ 2.

Dried solvents from the given companies were used with the corresponding quality grades. The solvents were stored above molecular sieve and used without further purification:

Dioxane	*Acros Organics*, Extra Dry, 99.8%, <0.005% H_2O
N,*N*-Dimethylformamide (DMF):	*Acros Organics*, Extra Dry, 99.8%, <0.005% H_2O

Ethanol:	*Acros Organics*, Extra Dry, 99.8%, <0.005% H_2O
Methanol:	*Acros Organics*, Extra Dry, 99.8%, <0.005% H_2O.
Toluene:	*Acros Organics*, Extra Dry, 99.8%, <0.005% H_2O

For thin-layer chromatography (TLC) and column chromatography, the following solvents were distilled before use: dichloromethane, diethyl ether, ethyl acetate, methanol, pentane, hexane.

The used sodium chloride, ammonium chloride, sodium hydrogen carbonate and sodium thiosulfate solutions were saturated aqueous solutions.

10.2 Analytics

Column Chromatography and Thin Layer Chromatography

For the column chromatography, silica gel Si 60 (230-400 mesh, ASTM) with a particle size of 40-63 µm by the company *Merck* was used. The corresponding eluent ratios are given in the individual experimental procedures.

Thin-layer chromatography silica gel 600G F254 glass plates by *Merck* were used as the stationary phase. The substances were verified *via* fluorescence detection. Therefore, the TLC-plates were analyzed under UV-light (λ = 254 nm) and, if necessary, evaluated by the following solution heat treatment included (250 °C):

Potassium permanganate-solution [$KMnO_4$]:	$KMnO_4$ (2.25 g), K_2CO_3 (15.0 g) and NaOH (250 mg) in water (250 mL).
Cerium ammonium molybdate [CAM]:	$CeSO_4$ 4 H_2O (1.00 g), $(NH_4)_2MoO_4$ (25.0 g) and H_2SO_4 (25 mL) in water (250 mL)

NMR Spectroscopy

Nuclear magnetic resonance spectra were recorded on the instruments AVHD300, AVHD400, and AVHD500 by the company *Bruker* at 300 K or on a *Bruker* AV-II-500 equipped with a cryoprobe head.

The chemical shifts are given in δ-values (ppm). Deuterated chloroform $CDCl_3$ (*Deutero GmbH*, 99.8%), benzene-d_6 (*Deutero GmbH*, 99.8%) or methanol-d_4 (*Deutero GmbH*, 99.8%) were used as the solvent. When chloroform was used, the signals of the solvent were used in the ^{1}H-NMR-spectra (δ = 7.26 ppm) and ^{13}C-NMR-spectra (δ = 77.16 ppm) as an internal standard for calibration. When methanol was used, the signals of the solvent were used in the

^{1}H-NMR-spectra (δ = 4.87 ppm) and ^{13}C-NMR-spectra (δ = 49.00 ppm) as an internal standard for calibration. When benzene was used, the signals of the solvent were used in the ^{1}H-NMR-spectra (δ = 7.16 ppm) and ^{13}C-NMR-spectra (δ = 128.06 ppm) as an internal standard for calibration.

The spectra were viewed *via* MestReNova 14.2 of the company *Mestrelab Research*. The chemical shifts δ are given in [ppm] (parts per million). For a clear assignment of the signals, the following abbreviations were used for the spin multiplicities: s – singlet, d – doublet, t – triplet, q – quartet, p – quintet, h – sextet, hept – septet, m – multiplet, *br.* – broad. Apparent multiplets which occur as a result of accidental equality of coupling constants to those of magnetically non-equivalent protons are marked as *virt.* – virtual. To fully characterize compounds, standard NMR measurements like DEPT-, HSQC-, HMBC-, and ^{1}H-^{1}H- COSY-experiments were carried out.

Infrared Spectroscopy

IR spectra were recorded using a *Perkin-Elmer* 1600 FT-IR (film). The intensities were designated with the following abbreviations: w (weak), m (medium), s (strong), vs (very strong), br (broad).

Mass Spectrometry

ESI-MS: Mass spectrometry (MS) and high-resolution mass spectrometry (HRMS) were performed on an LTQ FT Ultra (*Thermo*), a linear ion trap with a Fourier Transform Ion Cyclotron Resonance (FT-ICR) MS detector. The instrument is coupled online to an analytical HPLC (UltiMate 3000 HPLC system Dionex). Mass spectra were measured with electrospray ionization (ESI).

Melting Points

Melting points of solids were measured using a *Kofler* apparatus (“Thermopan”, *Reichert*, Vienna) or an IA9100 melting point measuring device from *Electrothermal* and are not corrected.

High performance liquid chromatography (HPLC)

HPLC was performed (Dionex Ultimate 3000 pump, Dionex Ultimate 3000 Autosampler, Dionex Ultimate 3000 photodiode array detector) using different stationary phases (Daicel

ChiralCel, *Chemical Industries*) and UV detection (λ = 215, 254 and 320 nm) at 20 °C or 25 °C.

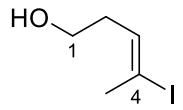
Specific Rotation

The specific rotation was determined using an ADP440+ polarimeter (Fa *Bellingham+Stanley*) and is reported as follows: $[\alpha]_D^T$ (c in g per 100 mL solvent).

11. Synthetic procedures

11.1. C1-C7 fragment

(*E*)-4-iodopent-3-enol (28)



28

C_5H_9IO
212.03 g/mol

To a cold (–78 °C) solution of 2,3-dihydrofuran (10.8 mL, 10.0 g, 143 mmol, 1.00 eq.) in THF (120 mL) was added *tert*-butyllithium (98.0 mL, 1.9M in pentane, 157 mmol, 1.10 eq.) and the yellow solution was stirred for 45 minutes. In a separate flask, copper-(I)-cyanide (12.7 g, 142 mmol, 1.00 eq.) was suspended in diethyl ether (150 mL) and THF (240 mL), and *n*-butyllithium (114 mL, 2.5M in hexane, 285 mmol, 2.00 eq.) was added at –78 °C. The reaction was warmed to 0 °C and stirred for 20 minutes. Subsequently, the reaction was cooled to –40 °C, and tributyltin hydride (76.8 mL, 83.0 g, 285 mmol, 2.00 eq.) was added. The yellow solution turned into a dark golden color. After ten minutes, the lithiated dihydrofuran was carefully cannulated into the cuprate solution. The reaction was warmed to 0 °C and stirred for two hours. Afterward, the solution was cooled to –30 °C, and methyl iodide (43.0 mL, 99.2 g, 699 mmol, 5.00 eq.) was added (violent gas evolution). The dark red suspension was warmed to room temperature and stirred for 1.5 hours. Saturated aqueous ammonium chloride solution (400 mL) and ammonia solution (100 mL) were added, and stirring was continued for 30 minutes. The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 400 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to give a colorless oil.

The oil was dissolved in diethyl ether (300 mL) and cooled to 0 °C. Iodine (43.0 g, 171 mmol, 1.20 eq.) was added, and stirring was continued until the iodine was dissolved. Subsequently, saturated aqueous sodium thiosulphate solution (50 mL) was added, and stirring was continued until the dark brown solution became colorless. A solution of potassium fluoride (17.0 g, 293 mmol, 2.05 eq.) in water (100 mL) and acetone (100 mL) was added. After stirring for three hours at room temperature, the suspension was filtered over Celite, and the layers were separated. The aqueous layer was extracted with diethyl ether (2 × 100 mL). The combined

organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 10:1 ⟶ 1:1), vinyl iodide **28** was obtained as a yellowish oil (29.8 g, 99%).

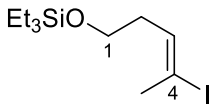
TLC: R_f = 0.25 (pentane:diethyl ether = 1:1) [$KMnO_4$].

^{1}H-NMR: (400 MHz, $CDCl_3$, 300K) δ 6.20 (tq, ^3J = 7.6, ^4J = 1.6 Hz, 1 H, H-3), 3.73 (t, ^3J = 6.4 Hz, 2 H, H-1), 2.42 (d, ^4J = 1.6 Hz, 3 H, H-41), 2.3-2.3 (m, 2 H, H-2).

^{13}C-NMR: (101 MHz, $CDCl_3$, 300K) δ 137.2 (d, C-3), 96.3 (s, C-4), 61.6 (t, C-1), 34.1 (t, C-2), 27.9 (q, C-41).

The analytical data obtained matched those reported in the literature.[43]

TES-protected vinyl iodide 29



29

$C_{11}H_{23}IOSi$
326.29 g/mol

To a cold (0 °C) solution of alcohol (*E*)-4-iodopent-3-enol (**28**, 15.0 g, 70.7 mmol, 1.00 eq.) in dichloromethane (250 mL) was added triethylamine (19.7 mL,14.3 g, 142 mmol, 2.00 eq.) and triethylsilyl chloride (14.2 mL, 12.8 g, 84.9 mmol, 1.20 eq.). The colorless suspension was stirred for one hour and then quenched by the addition of a saturated aqueous ammonium chloride solution (100 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 100 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 80:1), silyl ether **29** was obtained as a colorless oil (21.3 g, 64.3 mmol, 75%).

TLC: R_f = 0.2 (pentane) [$KMnO_4$].

^{1}H-NMR: (300 MHz, $CDCl_3$, 300K) δ 6.18 (tq, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1 H, H-3), 3.61 (t, ^3J = 6.7 Hz, 2 H, H-1), 2.38 (dt, ^4J = 1.6 Hz, ^5J = 0.9 Hz, 3 H, H-5), 2.26 (dtq, ^3J = 7.6 Hz,

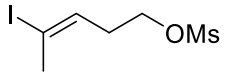
^{3}J = 6.7 Hz, ^{5}J = 0.9 Hz, 2 H, H-2), 0.96 [t, ^{3}J = 7.9 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.60 [q, ^{3}J = 7.9 Hz, 6 H, $Si(CH_2CH_3)_3$].

^{13}C-NMR: (75 MHz, $CDCl_3$, 300K) δ 137.8 (d, C-3), 95.5 (s, C-4), 61.6 (t, C-1), 34.4 (t, C-2), 27.8 (q, C-5), 6.9 [q, $Si(CH_2CH_3)_3$], 4.6 [t, $Si(CH_2CH_3)_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2954 (vs, sp^3-C–H), 2919 (s, sp^3-C–H), 2876 (vs, sp^3-C–H), 1638 (w, C=C), 1458 (m), 1414 (m, sp^3-C–H), 1380 (m), 1239 (m, C–O), 1098 (vs, C–O), 1016 (s, C–O), 745 (vs).

HRMS (ESI): no ionisation possible.

Mesylate 89



89
$C_6H_{11}IO_3S$
290.12 g/mol

To a cold (0 °C) solution of alcohol **28** (5.00 g, 23.6 mmol, 1.00 eq.) in dichloromethane (210 mL) and triethylamine (21 mL) was added mesyl chloride (3.65 mL, 5.40 g, 47.2 mmol, 2.00 eq.). After stirring for three hours, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (100 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 100 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 4:1 ⟶ 1:1), mesylate **89** was obtained as a colorless oil (5.84 g, 20.1 mmol, 85%).

TLC: R_f = 0.46 (pentane:diethyl ether = 1:1) [$KMnO_4$].

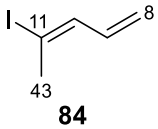
^{1}H-NMR: (400 MHz, $CDCl_3$) δ 6.15 (tq, ^{3}J = 7.5 Hz, ^{4}J = 1.6 Hz, 1 H, =CH), 4.20 (t, ^{3}J = 6.6 Hz, 2 H, CH_2O), 3.01 (s, 3 H, SO_2CH_3), 2.48 (*virt.* q, $^{3}J \approx {}^{3}J$ = 6.6 Hz, 2 H, CH_2), 2.41-2.40 (m, 3 H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$) δ 134.5 (d, =CH), 97.7 (s, =C–I), 67.8 (t, CH_2O), 37.7 (q, SO_2CH_3), 30.5 (t, CH_2), 27.9 (q, CH_3).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3027 (vw) 2960 (vw, C_{sp3}-H), 1332 (vs, S=O), 1168 (vs), 954 (vs), 910 (vs).

HRMS (ESI): no ionization possible.

Dienyl iodide 84



84

C_5H_7I

194.02 g/mol

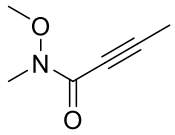
To a cold (0 °C) solution of mesylate **89** (1.00 g, 3.45 mmol, 1.00 eq.) in diethyl ether (50 mL) was added potassium *tert*-butanolate (387 mg, 3.45 mmol, 1.00 eq.). After 15 minutes, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (50 mL). The layers were separated, and the aqueous layer was extracted with pentane (2 x 50 mL). The organic layers were combined, dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure (>300 mbar). Dienyl iodide **84** was isolated as a 40% solution in diethyl ether (69%, 2.38 mmol).

TLC: R_f = 1.0 (pentane:diethyl ether = 1:0).

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 6.78 (d, ^3J = 11.4 Hz, 1 H, H-10), 6.44 (*virt.* dt, ^3J =16.8 Hz, $^3J \approx {}^3J$ = 10.5 Hz, 1 H, H-9), 5.18 (d, ^3J = 16.8 Hz, 1 H, H-8a), 5.07 (d, ^3J = 10.2 Hz, 1 H, H-8b), 2.52 (d, ^4J = 1.5 Hz, 3 H, CH_3).

^{13}**C-NMR**: (126 MHz, $CDCl_3$) δ 141.1 (d, C-10), 131.8 (d, C-9), 117.8 (t, C-8), 98.4 (s, C-11), 31.2 (q, CH_3).

Weinreb amide 30



30

$C_6H_9NO_2$

127.14 g/mol

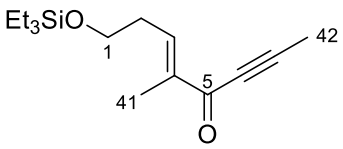
To a cold (0 °C) suspension of tetrolic acid (**31**, 6.00 g, 71.4 mmol, 1.00 eq.) and *N*,*O*-dimethylhydroxylamine hydrochloride (8.35 g, 85.6 mmol, 1.20 eq.) in dichloromethane (80 mL) was added triethylamine (24.7 mL, 18.1 g, 178 mmol, 2.50 eq.) and tetrabromomethane (23.7 g, 71.4 mmol, 1.00 eq.). A solution of triphenylphosphane (18.7 g, 71.4 mmol, 1.00 eq.) in dichloromethane (150 mL) was added dropwise over the course of one hour. After stirring for two hours at ambient temperature, the solvent was removed under reduced pressure. The residue was suspended in ethyl acetate (30 mL) and pentane (60 mL) and filtered over Celite. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:ethyl acetate = 4:1), Weinreb amide **30** was obtained as an orange oil (6.90 g, 54.2 mmol, 76%).

TLC: Rf = 0.50 (pentane:diethyl ether = 1:1) [$KMnO_4$].

^{1}H-NMR: (500 MHz, $CDCl_3$) δ 3.76 (s, 3 H, OMe), 3.21 (s, 3 H, NHC*H*$_3$), 2.02 (s, 3 H, CCH_3).

The analytical data obtained matched those reported in the literature.[47]

Ketone 32



32

$C_{15}H_{26}O_2Si$

266.46 g/mol

To a cold (–78 °C) solution of vinyl iodide **29** (15.0 g, 46.0 mmol, 1.00 eq.) in diethyl ether (150 mL) was added *tert*-butyllithium (1.9M in pentane, 48.4 mL, 91.9 mmol, 2.00 eq.). After five minutes, a solution of Weinreb amide **30** (8.77 g, 69.9 mmol, 1.50 eq.) in diethyl ether

(150 mL) was added slowly over the course of 20 minutes. The yellow suspension was stirred for two hours at –78 °C before saturated aqueous ammonium chloride solution (150 mL) and water (50 mL) were added. The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 150 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 10:1 ⟶ 4:1), ketone **32** was obtained as a colorless oil (9.23 g, 76%).

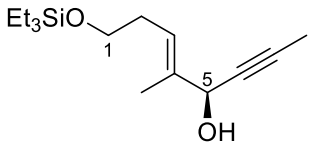
TLC: R_f = 0.70 (pentane:diethyl ether = 4:1) [$KMnO_4$].

^{1}H-NMR: (500 MHz, $CDCl_3$) δ 7.18 [tq, ^3J = 7.4 Hz, ^4J = 1.4 Hz, 1 H, H-3], 3.77 [t, ^3J = 6.1 Hz, 2 H, H-1], 2.53 [td, ^3J = 7.4 Hz, 6.1 Hz, 2 H, H-2], 2.03 [s, 3 H, C-42], 1.80 [d, ^4J = 1.4 Hz, 3 H, H-41], 0.97 [t, ^3J = 8.0 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.62 [q, ^3J = 8.0 Hz, 6 H, $Si(CH_2CH_3)_3$].

^{13}C-NMR: (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 4.3 (q, C-42), 4.5 [t, $Si(CH_2CH_3)_3$], 6.9 [q, $OSi(CH_2CH_3)_3$], 10.8 (q, C-41), 33.1 (t, C-2), 61.3 (t, C-1), 78.2 (s, C-6), 90.3 (s, C-7), 139.5 (s, C-4), 146.8 (d, C-3), 180.7 (s, C-5).

The analytical data obtained matched those reported in the literature.[30]

Alcohol 34



34
$C_{15}H_{28}O_2Si$
268.47 g/mol

To a cold (0 °C) solution of ketone **32** (9.29 g, 34.9 mmol, 1.00eq.) in THF (100 mL) was added (*S*)-2-methyl-CBS catalyst (**33**, 4.84 g, 17.4 mmol, 50 mol%). Borane dimethylsulfide complex (1 M in THF, 20.9 mL, 20.9 mmol, 0.60 eq.) was added slowly over the course of two hours. The reaction was quenched by the careful addition of a saturated aqueous sodium bicarbonate solution (200 mL). The layers were separated, and the aqueous layer was extracted with

dichloromethane (3 × 150 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 6:1 ⟶ 3:1), alcohol **34** was obtained as a colorless oil (7.95 g, 29.6 mmol, 86%).

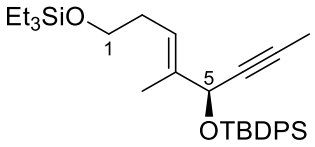
TLC: R_f = 0.30 (pentane:diethyl ether = 4:1) [$KMnO_4$].

Enantiomeric excess: *ee* = 96%.

^{1}H-NMR: (300 MHz, $CDCl_3$) δ 5.68-5.55 (m, 1 H, H-3), 4.79-4.66 (m, 1 H, H-5), 3.63 (t, ^3J = 7.1 Hz, 2 H, H-1), 2.30 (*virt*. q, $^3J \approx {}^3J$ = 7.1 Hz, 2 H, H-2), 1.87 (d, ^3J = 2.1 Hz, 3 H, H-42), 1.79-1.73 (m, 3 H, H-41), 1.70 (d, ^3J = 5.4 Hz, 1 H, OH), 0.96 [t, ^3J = 7.9 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.60 [q, ^3J = 7.9 Hz, 6 H, $Si(CH_2CH_3)_3$].

The analytical data obtained matched those reported in the literature.[30]

TBDPS-protected alkyne 35



35

$C_{31}H_{46}O_2Si_2$
506.88 g/mol

To a cold (0 °C) solution of ketone **32** (12.5 g, 46.7 mmol, 1.00eq.) in THF (200 mL) was added (*S*)-2-methyl-CBS catalyst (**33**, 6.49 g, 23.4 mmol, 50 mol%). Borane dimethylsulfide complex (2M in THF, 16.5 mL, 33 mmol, 0.70 eq.) was added slowly over the course of two hours. The reaction was quenched by the careful addition of a saturated aqueous sodium bicarbonate solution (200 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 150 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. The crude alcohol **34** was dissolved in dichloromethane (300 mL) and cooled to 0 °C. Imidazole (6.37 g, 93.6 mmol, 2.00 eq.), DMAP (567 mg, 4.71 mmol, 0.10 eq.), and *tert*-butyldiphenylsilyl chloride (20 mL, 77.9 mmol, 1.70 eq.) was added to the solution. After four hours, the reaction was quenched by the careful addition of saturated aqueous ammonium chloride solution (150 mL). The layers

were separated, and the aqueous layer was extracted with dichloromethane (3 × 200 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 30:1), silyl ether **35** was obtained as a colorless oil (20.3 g, 40.1 mmol, 86%).

TLC: R_f = 0.88 (pentane:diethyl ether = 4:1) [UV, $KMnO_4$].

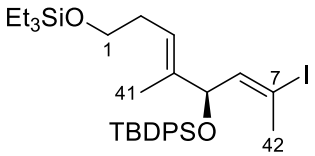
^{1}H-NMR: (400 MHz, $CDCl_3$) δ 7.79-7.63 (m, 4 H, C_{Ar}-H), 7.42-7.33 (m, 6 H, C_{Ar}-H), 5.22 (*virt*. tquint., ^3J = 7.3 Hz, $^4J \approx {}^4J \approx$ 1.2 Hz, 1 H, H-3), 4.66 (q, ^4J = 2.2 Hz, 1 H, H-5), 3.51 (t, ^3J = 7.4 Hz, 2 H, H-1), 2.22 (*virt.* q, $^3J \approx {}^3J \approx$ 7.3 Hz, 2 H, H-2), 1.75 (d, ^4J = 1.2 Hz, 3 H, H-41), 1.72 (d, ^4J = 2.2 Hz, 3 H, H-42), 1.07 (s, 9 H, $SiC(CH_3)_3$), 0.95 [t, ^3J = 7.9 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.59 [q, ^3J = 7.9 Hz, 6 H, $Si(CH_2CH_3)_3$].

^{13}C-NMR: (101 MHz, $CDCl_3$) δ 137.1 (s, C-4), 136.2 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 134.1 (s, C_{Ar}), 133.9 (s, C_{Ar}), 129.7 (d, C_{Ar}-H), 129.6 (d, C_{Ar}-H), 127.5 (d, C_{Ar}-H), 127.4 (d, C_{Ar}-H), 122.3 (d, C-3), 81.4 (s, C-7)*, 79.7 (s, C-6)*, 69.7 (d, C-5), 62.4 (t, C-1), 31.7 (t, C-2), 27.0 [q, $SiC(CH_3)_3$], 19.5 [s, $SiC(CH_3)_3$], 12.3 (q, C-41), 6.93 [q, $Si(CH_2CH_3)_3$], 4.60 [t, $Si(CH_2CH_3)_3$], 3.73 (q, C-42).

*interchangeable signals.

The analytical data obtained matched those reported in the literature.[30]

TBDPS-protected vinyl iodide 36



36

$C_{31}H_{47}IO_2Si_2$
634.79 g/mol

To a solution of alkyne **35** (5.00 g, 9.86 mmol, 1.00 eq.) in THF (50 mL) was added *Schwartz* reagent (5.00 g, 19.7 mmol, 2.00 eq.) at room temperature. The orange suspension was stirred for two hours and then cooled to –78 °C. A solution of iodine (3.00 g, 11.8 mmol, 1.20 eq.) in THF (10 mL) was added and stirred for five minutes. The brown solution was poured into a vigorously stirred mixture of saturated aqueous sodium thiosulphate solution (150 mL) and

diethyl ether (150 mL). A colorless precipitate was separated by filtration over Celite, and the layers were separated. The aqueous phase was extracted with diethyl ether (2 x 50 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 300:1), vinyl iodide **36** was obtained as a colorless oil (3.25 g, 52%).

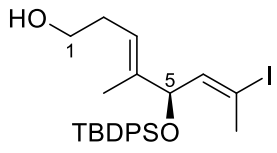
TLC: R_f = 0.53 (pentane:diethyl ether = 30:1) [UV, $KMnO_4$].

^{1}H-NMR: (400 MHz, $CDCl_3$, 300K) δ 7.69-7.61 (m, 4 H, C_{Ar}-H), 7.44-7.33 (m, 6 H, C_{Ar}-H), 6.19 (dq, ^3J = 8.9, 1.6 Hz, 1 H, H-6), 5.39-5.30 (m, 1 H, H-3), 4.53 (d, ^3J = 8.8 Hz, 1 H, H-5), 3.60-3.49 (m, 2 H, H-1), 2.23 (*virt*. q, $^3J \approx {}^3J \approx$ 7.2 Hz, 2 H, H-2), 1.84 (d, ^4J = 1.6 Hz, 3 H, H-42), 1.59 (d, ^4J = 1.4 Hz, 3 H, H-41), 1.05 [s, 9 H, $SiC(CH_3)_3$], 0.96 [t, ^3J = 7.9 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.60 [q, ^3J = 7.9 Hz, 6 H, $Si(CH_2CH_3)_3$].

^{13}C-NMR: (101 MHz, $CDCl_3$, 300K) δ 142.7 (d, C-6), 137.2 (s, C-4), 136.1 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 133.8 (s, C_{Ar}), 129.8 (d, C_{Ar}-H), 127.6 (d, C_{Ar}-H), 127.6 (d, C_{Ar}-H), 121.9 (d, C-3), 96.0 (s, C-7), 75.8 (d, C-5), 62.4 (t, C-1), 31.6 (t, C-2), 27.9 (q, C-42), 27.0 [q, $SiC(CH_3)_3$], 19.5 [s, $SiC(CH_3)_3$], 12.4 (q, C-41), 6.95 [q, $Si(CH_2CH_3)_3$], 4.61 [t, $Si(CH_2CH_3)_3$].

The analytical data obtained matched those reported in the literature.[30]

Alcohol 37



37

$C_{25}H_{33}IO_2Si$
520.53 g/mol

To a cold (0 °C) solution of silyl ether **36** (3.25 g, 5.13 mmol, 1.00 eq.) in THF (55 mL) was added HF · pyridine complex (2.70 mL, 30 wt.%, 20.3 eq.). After two hours, another 0.50 mL HF · pyridine complex (3.74 eq.) was added. After stirring for one hour, the solution was poured into 100 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 100 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column

chromatography (silica, pentane/diethyl ether = 4:1 ⟶ 3:1), alcohol **37** was obtained as a yellowish oil (2.37 g, 4.55 mmol, 89%).

TLC: R_f = 0.49 (pentane:diethyl ether = 1:1) [UV, $KMnO_4$].

^{1}H-NMR: (500 MHz, $CDCl_3$, 300K) δ 7.69 - 7.60 (m, 4 H, C_{Ar}-H), 7.46-7.32 (m, 6 H, C_{Ar}-H), 6.20 (dq, ^3J = 8.6 Hz, ^4J = 1.7 Hz, 1 H, H-6), 5.33 (*virt*. tquint, ^3J = 7.4 Hz, $^4J \approx {}^4J \approx$ 1.3 Hz, 1 H, H-3), 4.55 (d, ^3J = 8.8 Hz, 1 H, H-5), 3.57 (*virt*. q, $^3J \approx {}^3J \approx$ 6.2 Hz, 2 H, H-1), 2.31-2-18 (m, 2 H, H-2), 1.89 (s, 3 H, H-41), 1.60 (s, 3 H, H-42), 1.05 [s, 9 H, $SiC(CH_3)_3$].

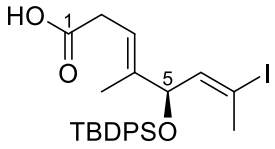
^{13}C-NMR: (126 MHz, $CDCl_3$, 300K) δ 142.5 (d, C-6), 138.8 (s, C-4), 136.1 (d, C_{Ar}-H), 135.9 (d, C_{Ar}-H), 133.8 (s, C_{Ar}), 133.6 (s, C_{Ar}), 129.9 (d, C_{Ar}-H), 127.7 (d, C_{Ar}-H), 121.3 (d, C-3), 96.1 (s, C-7), 75.7 (d, C-5), 62.4 (t, C-1), 31.3 (t, C-2), 28.0 (q, C-42), 27.0 [q, $SiC(\mathit{C}H_3)_3$], 19.5 [q, $Si\mathit{C}(CH_3)_3$], 12.5 (q, C-41).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3337 (*br* m, OH), 3071 (w, C_{sp2}-H), 3049 (w, C_{sp2}-H), 2957 (m, C_{sp3}-H), 2931 (m, C_{sp3}-H), 2890 (m, C_{sp2}-H), 2857 (m, C_{sp2}-H), 1635 (w), 1427 (s), 1111 (vs, C–O).

Specific rotation: $[\alpha]_D^{20} = -50.0$ (*c* = 2.06, $CHCl_3$).

HRMS (ESI): *m/z* $[C_{25}H_{33}IO_2Si + NH_4]^+$ calcd.: 538.1632; found: 538.1626.

Carboxylic acid 38



38

$C_{25}H_{31}IO_3Si$
534.51 g/mol

To a solution of primary alcohol **37** (1.17 g, 2.25 mmol, 1.00 eq.) in dichloromethane (20 mL) was added sodium bicarbonate (756 mg, 9.00 mmol, 4.00 eq.) and *Dess-Martin* periodinane (1.91 g, 4.50 mmol, 2.00 eq.). After 45 minutes, the yellow suspension was poured into a mixture of 30 mL saturated aqueous sodium bicarbonate solution and 30 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 40 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced

pressure to yield the corresponding aldehyde as a yellow oil. The aldehyde was dissolved in 11 mL *tert*-butanol, and 2-methyl-2-buten was added (1.58 g, 22.5 mmol, 10.0 eq.). Subsequently, a solution of sodium dihydrogen phosphate (1.41 g, 9.01 mmol, 4.00 eq.) and sodium chlorite (408 mg, 4.51 mmol, 2.00 eq.) in water (11 mL) was added. The yellow solution was stirred for 1.5 hours and then quenched by the addition of saturated aqueous ammonium chloride solution (100 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 100 mL). The organic layers were combined, dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/diethyl ether = 2:1 ⟶ 1/2), carboxylic acid **38** was obtained as a yellowish oil (1.07 g, 89%).

TLC: R_f = 0.55 (pentane:diethyl ether = 3:1) [UV, $KMnO_4$].

^{1}H-NMR: (300 MHz, $CDCl_3$, 300K) δ 7.69-7.61 (m, 4 H, C_{Ar}-H), 7.44-7.30 (m, 6 H, C_{Ar}-H), 6.16 (dd, ^3J = 8.8 Hz, ^4J = 1.6 Hz, 1 H, H-6), 5.61 (*virt.* tquint., ^3J = 7.3 Hz, $^4J \approx {}^4J$ = 1.3 Hz, 1 H, H-3), 4.56 (d, ^3J = 8.8 Hz, 1 H, H-5), 3.09 (d, ^3J = 7.3 Hz, 2 H, H-2), 1.84 (s, 3 H, H-41), 1.60 (s, 3 H, H-42), 1.05 [s, 9 H, SiC(CH_3)$_3$].

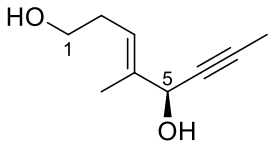
^{13}C-NMR: (100 MHz, $CDCl_3$, 300K) δ 176.2 (s, C-1), 142.0 (d, C-6), 139.4 (s, C-4), 136.0 (d, C_{Ar}-H), 135.9 (d, C_{Ar}-H), 133.4 (s, C_{Ar}), 133.3 (s, C_{Ar}), 129.7 (d, C_{Ar}-H), 127.6 (d, C_{Ar}-H), 116.4 (d, C-3), 96.6 (s, C-7), 75.1 (d, C-5), 32.8 (t, C-2), 27.9 [q, C-42], 26.8 [q, SiC(*C*H_3)$_3$], 19.4 [s, Si*C*(CH$_3$)$_3$], 12.6 (q, C-41).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3071.76 (*br* m, OH), 2930.83 (w, C_{sp3}-H), 2857.87 (w, C_{sp3}-H), 1710.29 (s, C=O), 1636.42 (m, C=C), 1472.36 (s, C–H), 1074.54 (m), 1041.93 (m), 740 (vs).

Specific rotation: $[\alpha]_D^{20} = -16.0$ (*c* = 1.00, $CHCl_3$).

HRMS (ESI): *m/z* $[C_{25}H_{31}IO_3Si + NH_4]^+$ calcd.: 552.1425; found: 552.1422.

Diol 39



39

$C_9H_{14}O_2$
154.21 g/mol

a) Conditions using TBAF

To a solution of alkyne **35** (2.00 g, 3.95 mmol, 1.00 eq.) in THF (30 mL) was added TBAF (1M in THF, 9.86 mL, 9.86 mmol, 2.50 eq.). The yellow solution was heated to 35 °C and stirred for three hours. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (30 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 1:1), diol **39** was obtained as a colorless oil (493 mg, 81%).

b) Conditions using TBAF buffered with acetic acid

To a solution of alkyne **35** (17.5 mg, 34.6 µmol, 1.00 eq.) in THF (1 mL) was added acetic acid (10.0 µL, 173 µmol, 5.00 eq.) and TBAF (1M in THF, 173 µL, 1.73 µmol, 5.00 eq.). The colorless solution was stirred for 18 hours at room temperature and then quenched by the addition of saturated aqueous ammonium chloride solution (5 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 1:1), diol **39** was obtained as a colorless oil (5.30 mg, 34.6 µmol, *quant.*).

TLC: R_f = 0.16 (pentane:diethyl ether = 1:4) [CAM].

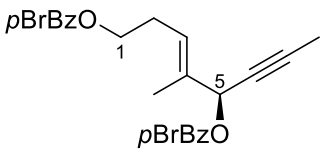
^{1}H-NMR: (300 MHz, $CDCl_3$) δ 5.61 (*virt.* tquint, ^3J = 7.3 Hz, $^4J \approx {}^4J$ = 1.2 Hz, 1 H, H-3), 4.74 (m, 1 H, H-5), 3.68 (t, ^3J = 6.6 Hz, 2 H, H-1), 2.34 (*virt.* q, $^3J \approx {}^3J$ = 6.8 Hz, 2 H, H-2), 2.04 (d, ^3J = 5.1 Hz, 1 H, 5-OH), 1.87 (d, ^5J = 2.2 Hz, 3 H, H-42), 1.78 (dt, ^4J = 1.6 Hz, ^5J = 0.8 Hz, 3 H, H-41), 1.63 (s, 1 H, 1-OH).

^{13}C-NMR: (101 MHz, $CDCl_3$) δ 138.1 (s, C-4), 123.4 (d, C-3), 82.5 (s, C-6), 78.7 (s, C-7), 68.2 (d, C-5), 62.2 (t, C-1), 31.4 (t, C-2), 12.6 (q, C-41), 3.81 (q, C-42).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3322 (br vs, OH), 2920 (s, sp^3-C–H), 2880 (s, sp^3-C–H), 2226 (w, CC), 1438 (s, sp^3-C–H), 1263 (m), 1137 (m), 1048 (vs, C–O), 999 (vs), 884 (m).

Specific rotation: $[\alpha]_D^{20} = +38.8$ (*c* = 1.80, $CHCl_3$).

***para*-Bromobenzoate 42**



42

$C_{23}H_{20}Br_2O_4$
520.22 g/mol

To a cold (0 °C) solution of diol **39** (10.0 mg, 65.0 µmol, 1.00 eq.) in dichloromethane (1 mL) was added triethyl amine (27.0 µL, 19.7 mg, 195 µmol, 3.00 eq.), *p*-bromobenzoyl chloride (42.7 mg, 195 µmol, 3.00 eq.) and a crystal of DMAP. After 1.5 hours, the reaction was quenched by the addition of saturated aqueous sodium bicarbonate solution. The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 4:1), benzoyl ester **42** was obtained as a colorless oil (28.5 mg, 54.8 µmol, 85%).

TLC: R_f = 0.60 (pentane:diethyl ether = 4:1).

^{1}H-NMR: (500 MHz, $CDCl_3$) δ 7.90-7.84 (m, 4 H, C_{ar}-H), 7.59-7.50 (m, 4 H, C_{ar}-H), 5.99 (q, ^5J = 2.3 Hz, 1 H, H-5), 5.81 (*virt.* tquint, ^3J = 7.3 Hz, $^4J \approx {}^4J$ = 1.2 Hz, 1 H, H-3), 4.36 (td, ^3J = 6.7 Hz, ^4J = 1.4 Hz, 2 H, H-1), 2.56 (q, $^3J \approx {}^3J$ = 7.0 Hz, 2 H, H-2), 1.87 (d, ^5J = 2.3 Hz, 3 H, H-42), 1.84 (d, ^4J = 1.3 Hz, 3 H, H-41).

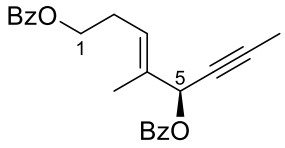
^{13}C-NMR: (101 MHz, $CDCl_3$) δ 165.9 (s, 1 C=O), 164.8 (s, 5 C=O), 134.4 (s, C-4), 131.9 (d, C_{ar}-H), 131.8 (d, C_{ar}-H), 131.4 (d, C_{ar}-H), 131.2 (d, C_{ar}-H), 125.4 (d, C-3), 83.7 (s, C-6), 75.2 (s, C-7), 70.2 (d, C-5), 64.1 (t, C-1), 27.6 (t, C-2), 13.0 (q, C-41), 3.9 (q, C-42).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2921 (w, sp^3-C–H), 2852 (w, sp^3-C–H), 1722 (vs, C=O), 1591 (s, C_{ar}=C_{ar}), 1484 (w, C_{ar}=C_{ar}), 1398 (m), 1264 (vs), 1098 (vs, C–O), 1012 (s, C–O), 754 (s).

Specific rotation: $[\alpha]_D^{20} = +12.0$ (*c* = 1.33, $CHCl_3$).

HRMS (ESI): *m/z* $[C_{23}H_{20}Br_2O_4 + Na]^+$ calcd.: 540.9620; found: 540.9617.

Benzoate 41



41

$C_{23}H_{22}O_4$

362.43 g/mol

To a cold (0 °C) solution of diol **39** (10.0 mg, 65.0 µmol, 1.00 eq.) in dichloromethane (1 mL) was added triethyl amine (27.0 µL, 19.7 mg, 195 µmol, 3.00 eq.), benzoyl chloride (23.0 µL, 27.3 mg, 195 µmol, 3.00 eq.) and a crystal of DMAP. After 1.5 hours, the reaction was quenched by the addition of saturated aqueous sodium bicarbonate solution. The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 4:1), benzoyl ester **41** was obtained as a colorless oil (8.9 mg, 24.6 µmol, 38%).

TLC: R_f = 0.40 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}H-NMR: (500 MHz, $CDCl_3$) δ 8.10-7.96 (m, 4 H, C_{ar}-H), 7.61-7.33 (m, 6 H, C_{ar}-H), 6.02 (q, ^5J = 2.3 Hz, 1 H, H-5), 5.86 (*virt.* tquint, ^3J = 7.3 Hz, $^4J \approx {}^4J$ = 1.3 Hz, 1 H, H-3), 4.37 (td, ^3J = 6.8 Hz, ^2J = 2.9 Hz, 2 H, H-1), 2.57 (*virt.* q, $^3J \approx {}^3J$ = 7.0 Hz, 2 H, H-2), 1.88-1.85 (m, 6 H, H-41, H-42).

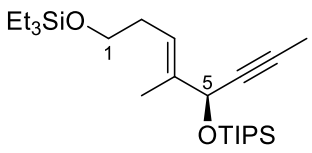
^{13}C-NMR: (101 MHz, $CDCl_3$) δ 166.7 (s, OCOPh), 165.5 (s, OCOPh), 134.4 (s, C-41), 133.2 (C_{ar}-H), 133.0 (C_{ar}-H), 130.5 (s, C_{ar}), 130.3 (s, C_{ar}), 129.9 (d, C_{ar}-H), 129.7 (d, C_{ar}-H), 128.5 (d, C_{ar}-H), 128.5 (d, C_{ar}-H), 125.2 (d, C-3), 83.4 (s, C-6), 75.4 (s, C-7), 69.9 (d, C-5), 63.9 (t, C-1), 27.7 (t, C-2), 13.1 (q, C-41), 3.89 (q, C-42).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2921 (w, sp^3-C–H), 2243 (w), 1789 (s, C=O), 1720 (vs, C=O), 1601 (w), 1452 (m), 1264 (s), 1106 (s, C–O), 709 (vs).

Specific rotation: $[\alpha]_D^{20} = +19.6$ (*c* = 0.714, $CHCl_3$).

HRMS (ESI): *m/z* $[C_{23}H_{22}O_4+Na]^+$ calcd.: 385.1410; found: 385.1411.

TIPS-protected alkyne 46



46

$C_{24}H_{48}O_2Si_2$

424.82 g/mol

To a cold (0 °C) solution of alcohol **34** (190 mg, 708 µmol, 1.00 eq.) in dichloromethane (3 mL) was added 2,6-lutidine (163 µL, 150 mg, 1.42 mmol, 2.00 eq.) and tri-*iso*-propylsilyl triflate (286 µL, 325 mg, 1.06 mmol, 1.50 eq). After stirring for 45 minute, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (5 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 100:1), silyl ether **46** was obtained as a colorless oil (179 mg, 421 µmol, 60%).

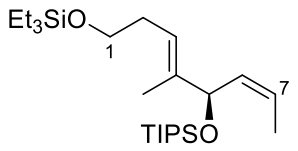
TLC: R_f = 0.95 (pentane:diethyl ether = 4:1).

^{1}H-NMR: (500 MHz, $CDCl_3$, 300K) δ 5.47 (t, ^3J=7.3 Hz, 1 H, H-3), 4.81-4.73 (m, 1 H, H-5), 3.60 (t, ^3J = 7.2 Hz, 2 H, H-1), 2.29 (*virt.* q, $^3J \approx {}^3J$ =7.4 Hz, 2 H, H-2), 1.82 (d, ^5J = 2.1 Hz, 3 H, H-42), 1.73 (d, ^4J = 1.3 Hz, 3 H, H-41), 1.11-1.04 (m, 21 H, TIPS), 0.96 [t, ^3J = 7.9 Hz, 9 H, $Si(CH_2C\mathit{H}_3)_3$], 0.60 [q, ^3J = 7.9 Hz, 6 H, $Si(C\mathit{H}_2CH_3)_3$].

^{13}C-NMR: (75 MHz, $CDCl_3$, 300K) δ 137.8 (s, C-4), 121.6 (d, C-3), 80.2 (s, C-6), 77.4 (s, C-7), 68.7 (d, C-5), 62.5 (t, C-1), 31.7 (t, C-2), 18.1 {q, $Si[CH(\mathit{C}H_3)_2]_3$}, 12.4 {d, $Si[\mathit{C}H(CH_3)_2]_3$, q, C-41}, 6.9 [q, $(Si(CH_2\mathit{C}H_3)_3$], 4.6 [t, $(Si(\mathit{C}H_2CH_3)_3$], 3.8 (q, C-42).

HRMS (ESI): no ionization possible.

Diene 45



45

$C_{24}H_{50}O_2Si_2$
426.83 g/mol

To a solution of alkyne **46** (178 mg, 0.420 mmol, 1.00 eq.) in THF (2.5 mL) was added *Schwartz* reagent (271 mg, 1.05 mmol, 2.50 eq.). The yellow suspension was stirred for two hours at room temperature and then quenched by the addition of saturated aqueous ammonium chloride solution (10 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The organic layers were combined, filtered over a silica plug, dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 200:1), diene **45** was obtained as a colorless oil (120 mg, 67%).

TLC: R_f = 0.38 (pentane:diethyl ether = 100:1).

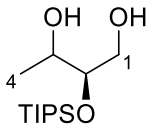
^{1}H-NMR: (500 MHz, $CDCl_3$, 300K) δ 5.46-5.41 (m, 3 H, H-3, H-6, H-7), 4.84 (d, ^3J = 6.8 Hz, 1 H, H-5), 3.58 (t, ^3J = 7.3 Hz, 2 H, H-1), 2.31-2.24 (m, 2 H, H-2), 1.66-1.63 (m, 3 H, H-42), 1.60 (s, 3 H, H-41), 1.05-1.02 (m, 21 H, TIPS), 0.96 [t, ^3J = 8.0 Hz, 9 H, $Si(CH_2C\mathit{H}_3)_3$], 0.60 [q, ^3J = 8.0 Hz, 6 H, $Si(C\mathit{H}_2CH_3)_3$].

^{13}C-NMR: (126 MHz, $CDCl_3$, 300K) δ 139.5 (s, C-4), 134.16 (), 122.98 (), 120.02 (), 73.6 (d, C-5), 62.6 (t, C-1), 31.6 (t, C-2), 18.2 {q, $Si[CH(\mathit{C}H_3)_2]_3$}, 13.6 (q, C-42), 12.4 {d, $Si[\mathit{C}H(CH_3)_2]_3$, 12.2 (q, C-41), 6.9 [q, $(Si(CH_2\mathit{C}H_3)_3$], 4.6 [t, $(Si(\mathit{C}H_2CH_3)_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2945 (vs, C_{sp3}-H), 2868 (vs, C_{sp2}-H), 1463 (m), 1097 (vs), 744 (s).

HRMS (ESI): no ionization possible.

Diol 44



44

$C_{13}H_{30}O_3Si$
262.47 g/mol

Diene **45** (20.0 mg, 46.9 µmol, 1.00 eq.) was dissolved in dry methanol (1 mL) and cooled to –78 °C. Ozone was bubbled through the solution for one minute, followed by three minutes argon. Sodium hydride (11.3 mg, 469 µmol, 10.0 eq.) was added to the blue solution, and stirring was continued for two hours while warming to room temperature. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (10 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 10 mL). The organic layers were combined, dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 2:1 ⟶ 1:2), diol **44** was obtained as a colorless oil (3.4 mg, 28%).

Diastereomeric ratio: d.r. ≈ 1:1.

TLC: R_f = 0.39 (pentane:diethyl ether = 1:1).

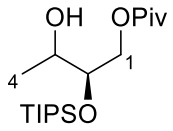
^{1}H-NMR: (400 MHz, $CDCl_3$, 300K) δ 4.01-3.89 (m, 1 H, H-$3_{A/B}$), 3.89-3.64 (m, 3 H, H-$2_{A/B}$, H-$1_{A/B}$), 2.44 (br s, 0.5 H, OH), 2.30 (br s, 0.5 H, OH), 2.18 (br s, 0.5 H, OH), 2.07 (br s, 0.5 H, OH), 1.24 (d, ^3J = 6.4 Hz, 1.5 H, H-4_A), 1.24 (d, ^3J = 6.6 Hz, 1.5 H, H-4_B), 1.11-1.08 {m, 21 H, Si[*CH*(CH_3)$_2$]$_3$}.

^{13}C-NMR: (101 MHz, $CDCl_3$, 300K) δ 76.1 (d, C-2_A), 75.8 (d, C-2_B), 70.8 (d, C-3_A), 68.9 (d, C-3_B), 64.3 (t, C-1_A), 63.7 (t, C-1_B), 19.2 (q, C-4_A), 18.7 (q, C-4_B), 18.2 {q, Si[CH(*C*H_3)$_2$]$_3$}, 12.8 {d, Si[*C*H(CH_3)$_2$]$_{3A}$}, 12.7 {d, Si[*C*H(CH_3)$_2$]$_{3B}$}.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3383 (*br* m, OH), 2944 (vs, C_{sp3}-H), 2868 (vs, C_{sp3}-H), 1464 (m, C–H), 1384 (m, C–H), 1248 (w), 1101 (s, C–O), 882 (s, C–H), 836 (w) 749 (w, C–H), 679 (s).

HRMS (ESI): *m/z* $[C_{13}H_{30}O_3Si+H]^+$ calcd.: 263.2036; found: 263.2036.

Pivalate 47



47

$C_{18}H_{38}O_4Si$
346.58 g/mol

To a solution of diol **44** (4.5 mg, 17.0 µmol, 1.00 eq.) in dichloromethane (500 µL) was added pyridine (3.7 µL, 2.7 mg, 34.0 µmol, 2.00 eq.), pivaloyl chloride (2.1 µL, 17.0 µmol, 1.00 eq.) and a small crystal of DMAP. The solution was stirred for 20 hours at room temperature. The reaction was quenched by the addition of saturated aqueous sodium bicarbonate solution (10 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 10 mL). The organic layers were combined, dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/diethyl ether = 20:1 ⟶ 10:1), pivalate **47** was obtained as a colorless oil (3.1 mg, 52%).

Diastereomeric ratio: d.r. ≈ 1:1.

TLC: R_f = 0.58 (hexane:ethyl acetate = 4:1).

^{1}H-NMR: (500 MHz, $CDCl_3$, 300K) δ 4.24 (dd, ^2J = 11.6 Hz, ^3J = 4.2 Hz, 1 H, H-1a$_A$), 4.17 (dd, ^2J = 11.4 Hz, ^3J = 3.6 Hz, 1 H, H-1a$_B$), 4.09 (dd, ^2J = 11.6 Hz, ^3J = 5.9 Hz, 1 H, H-1b$_A$), 4.09 (dd, ^2J = 11.4 Hz, ^3J = 5.9 Hz, 1 H, H-1b$_B$), 3.95-3.90 (m, 1 H, H-2$_A$), 3.86-3.78 (m, 3 H, H-2$_B$, H-3$_{A/B}$), 2.39 (d, ^3J = 4.6 Hz, 1 H, OH$_A$)*, 2.26 (d, ^3J = 5.9 Hz, 1 H, OH$_B$)*, 1.25-1.17 (m, 6 H, H-4$_{A/B}$), 1.20 [s, 9 H, OCOC(CH$_3$)$_3$], 1.10-1.07 {m, 21 H, Si[CH(CH$_3$)$_2$]$_3$}.

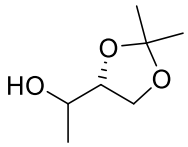
^{13}C-NMR: (101 MHz, $CDCl_3$, 300K) δ 74.6 (d, C-2$_B$), 74.3 (d, C-2$_A$), 69.3 (d, C-3$_B$), 68.2 (d, C-3$_B$), 65.1 (t, C-1$_B$), 64.8 (t, C-1$_B$), 38.9 [s, OCO*C*(CH$_3$)], 27.3 [q, OCOC(*C*H$_3$)], 19.5 (q, C-4$_A$)*, 18.2 {q, Si[CH(*C*H$_3$)$_3$]$_{3A/B}$}, 17.7 (q, C-4$_B$)*, 12.8 {d, Si[*C*H(CH$_3$)$_3$]$_{3A}$}*, 12.7 {d, Si[*C*H(CH$_3$)$_3$]$_{3B}$}*.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3488 (w, b, OH), 2961 (vs, C_{sp3}-H), 2868 (vs, C_{sp3}-H), 1731 (vs, C=O), 1463 (s, C–H), 1397 (m), 1284 (s), 1157 (vs, C–O), 1068 (s), 1028 (m), 800 (w), 679 (s).

HRMS (ESI): $[C_{18}H_{38}O_4Si + H]^+$ calcd.: 347.2611; found: 347.2611.

*interchangeable signals.

Alcohol 49



49
$C_7H_{14}O_3$
146.19 g/mol

Diol **48** (1.00 g, 3.81 mmol, 1.00 eq.) was dissolved in dichloromethane (10 mL) and cooled to 0 °C. Saturated aqueous sodium bicarbonate solution (407 µL) and sodium periodate (1.63 g, 7.63 mmol, 2.00 eq.) was added and the yellow suspension was stirred at room temperature for three hours. The organic layer was separated and the solvent was removed under reduced pressure, to give crude aldehyde **127** as a yellow oil. The aldehyde was dissolved in diethyl ether (15 mL), cooled to 0°C, and methylmagnesium bromide solution (3M in diethyl ether, 11.4 mmol, 1.50 eq.) was added. After stirring for one hour, the reaction was stopped by the addition of saturated aqueous ammonium chloride solution (10 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 5 mL). Following flash column chromatography (silica, pentane:diethyl ether = 1:1), alcohol **49** was obtained as a colorless oil (666 mg, 60%).

Diastereomeric ratio: d.r. ≈ 1:3.

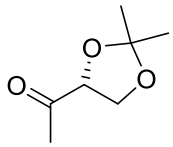
TLC: R_f = 0.21 (pentane:diethyl ether = 1:1) [$KMnO_4$].

^{1}**H-NMR**: (400 MHz, $CDCl_3$) δ 4.05-3.88 (m, 3.5 H, $CHO_{A/B}$, C*H*HO_A, C*HH*O_B, CH_3C*H*O_B), 3.71-3.66 (m, 0.5 H, CH_3C*H*O_A, CH*H*O_A), 2.29 (d, ^3J = 4.0 Hz, 0.25 H, OH_A), 1.99 (d, ^3J = 2.7 Hz, 0.75 H, OH_B), 1.43 [s, 3 H, $C(CH_3)_2]_{A/B}$, 1.36 [s, 3 H, $C(CH_3)_2]_{A/B}$, 1.15 (d, ^3J = 6.4 Hz, 2.25 H, C*H*$_3$CHO_B), 1.15 (d, ^3J = 6.3 Hz, 0.75 H, C*H*$_3$CHO_A).

^{13}**C-NMR**: (101 MHz, $CDCl_3$) δ 109.7 [s, *C*$(CH_3)_2]_A$, 109.2 [s, *C*$(CH_3)_2]_B$, 80.6 (d, $CHO)_A$, 79.6 (d, $CHO)_B$, 69.0 (d, CH_3*C*$HO)_A$, 66.9 (d, CH_3*C*$HO)_B$, 66.3 (t, $CH_2)_A$, 64.7 (t, $CH_2)_B$, 26.9 [q, C(*C*$H_3)_2]_A$, 26.6 [q, C(*C*$H_3)_2]_B$, 25.5 [q, C(*C*$H_3)_2]_A$, 25.3 [q, C(*C*$H_3)_2]_B$, 19.1 [q, $CH_3]_A$, 18.4 [q, $CH_3]_B$.

The analytical data obtained matched those reported in the literature.[58]

Ketone 50



50
$C_7H_{12}O_3$
144,17 g/mol

To a solution of alcohol **49** (666 mg, 4.55 mmol, 1.00 eq.) in dichloromethane (15 mL) was added pyridinium chlorochromate (1.47 g, 6.83 mmol, 1.50 eq.). After 20 hours, the brown suspension was diluted with 20 mL diethyl ether and filtered over Celite. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 2:1), ketone **50** was obtained as a colorless oil (350 mg, 53%).

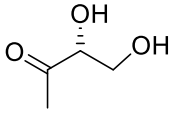
TLC: R_f = 0.78 (pentane:diethyl ether = 1:1) [UV, $KMnO_4$].

^{1}**H-NMR**: (400 MHz, $CDCl_3$) δ 4.40 (dd, ^3J = 7.7 Hz, ^3J = 5.5 Hz, 1 H, CHO), 4.19 (dd, ^2J = 8.7 Hz, ^3J = 7.7 Hz, 1 H, C*H*HO), 3.99 (dd, ^3J = 8.7 Hz, ^3J = 5.5 Hz, 1 H, CH*H*O), 2.25 (s, 3 H, CH_3), 1.49 [s, 3 H, $C(CH_3)_2$], 1.39 [s, 3 H, $C(CH_3)_2$].

^{13}**C-NMR**: (101 MHz, $CDCl_3$) δ 209.3 (s, CO), 111.2 [s, *C*$(CH_3)_2$], 80.6 (d, CHO), 66.6 (t, CH_2O), 26.4 [q, CH_3], 26.2 [q, $C(CH_3)_2$], 25.2 [q, $C(CH_3)_2$].

The analytical data obtained matched those reported in the literature.[58]

Diol 51



51
$C_4H_8O_3$
104.11 g/mol

A solution of acetal **50** (212 mg, 1.47 mmol, 1.00 eq.) in water (1 mL) and acetic acid (4 mL) was heated to 50 °C on the rotary evaporator at a pressure of 400 mbar. After 30 min, the solvent was removed under reduced pressure. The residue was dissolved in toluene (10 mL) and the solvent was again removed under reduced pressure. This procedure was repeated two times.

Following flash column chromatography (silica, 100% ethyl acetate), diol **51** was obtained as a colorless oil (80.0 mg, 53%).

TLC: R_f = 0.25 (ethyl acetate) [UV, $KMnO_4$].

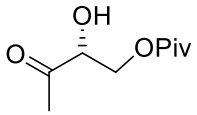
^{1}**H-NMR**: (400 MHz, $CDCl_3$) δ 4.22 (t, ^3J = 3.4 Hz, 1 H, C*H*OH), 4.01-3.85 (m, 3 H, C*H*$_2$OH, CHO*H*), 2.74 (s, 1 H, CH_2O*H*), 2.26 (s, 3 H, CH_3).

^{13}**C-NMR**: (101 MHz, $CDCl_3$) δ 208.0 (s, CO), 78.2 (d, CHO), 63.6 (t, CH_2O), 25.6 (q, CH_3).

Specific rotation: $[\alpha]_D^{20} = -82.0$ (c = 1.00, $CHCl_3$).

The scalar analytical data obtained matched those reported in the literature.[58]

Pivalate 184



184
$C_9H_{16}O_4$
188.22 g/mol

To a solution of diol **51** (83.3 mg, 798 µmol, 1.00 eq.) in dichloromethane (5 mL) was added pyridine (350 µL, 255 mg, 3.23 mmol, 4.00 eq.) and pivaloyl chloride (200 µL, 196 mg, 1.63 mmol, 2.00 eq.). After one hour, saturated aqueous sodium bicarbonate solution (5 mL) was added, and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 10 mL). The organic layers were combined, dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/diethyl ether = 1:1), pivalate **184** was obtained as a yellowish oil (81.2 mg, 54%).

TLC: R_f = 0.77 (ethyl acetate) [UV, $KMnO_4$].

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 4.41 (*virt.* t, $^3J \approx {}^2J$ = 3.4 Hz, 2 H, CH_2O), 4.36 (*virt.* q, $^3J \approx {}^3J$ = 4.2 Hz, 1 H, CHO), 3.68 (d, ^3J = 5.0 Hz, 1 H, OH), 2.27 (s, 3 H, CH_3), 1.17 [s, 9 H, $OCOC(CH_3)_3$].

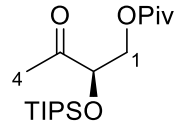
^{13}C-NMR: (126 MHz, $CDCl_3$) δ 206.5 (s, CO), 178.4 [s, O*C*OC(CH_3)], 75.8 (d, CHO), 64.8 (t, CH_2O), 39.0 [s, OCO*C*(CH_3)], 27.2 [q, OCOC(*C*H_3)], 25.7 (q, CH_3).

Specific rotation: $[\alpha]_D^{20} = -74.0$ (*c* = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3476 (w, b, O–H), 2974 (m, sp^3-C–H), 1722 (vs, C=O), 1481 (m, C=C), 1283 (s), 1151 (vs, C–O), 1119 (s, C–O), 1040 (m), 779 (w), 678 (w).

HRMS (ESI): $[C_9H_{16}O_4 + Na]^+$ calcd.: 211.0941; found: 211.0941.

Ketone 43



43

$C_{18}H_{36}O_4Si$

344.57 g/mol

a) *Via* oxidation of alcohol **47**

To a cold (0 °C) solution of alcohol **47** (3.2 mg, 9.00 µmol, 1.00 eq.) in dichloromethane (200 µL) and DMSO (100 µL) was added DIPEA (10 µL, 7.2 mg, 55.0 µmol, 6.00 eq.) and sulfur trioxide pyridine complex (5.9 mg, 37.0 µmol, 4.00 eq.). The solution was stirred for 1.5 hours and then quenched by the addition of saturated aqueous ammonium chloride solution (10 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The organic layers were combined and washed with water (2 × 5 mL). The organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/diethyl ether 40:1), pivalate **43** was obtained as a colorless oil (1.6 mg, 50%).

b) *Via* TIPS protection of alcohol **184**

To a cold (0 °C) solution of alcohol **184** (10.0 mg, 53.0 µmol, 1.00 eq.) in dichloromethane (2 mL) was added pyridine (29 µL, 21.0 mg, 266 µmol, 5.00 eq.) and TIPSOTf (29 µL, 32.6 mg, 106 µmol, 2.00 eq.). The solution was stirred for 2.5 hours and then quenched by the addition of saturated aqueous sodium bicarbonate solution (5 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The organic layers were combined, dried over sodium sulfate and filtered. The solvent was removed under reduced

pressure. Following flash column chromatography (silica, pentane/diethyl ether 50:1), silyl ether **43** was obtained as a colorless oil (13.0 mg, 71%).

TLC: R_f = 0.76 (hexane:ethyl acetate = 4:1); 0.69 (pentane:diethyl ether = 1:1).

^{1}H-NMR: (500 MHz, $CDCl_3$) δ 4.32-4.27 (m, 2 H, H-1a, H-2), 4.22-4.17 (m, 1 H, H-1b), 2.29 (s, 3 H, H-4), 1.18 [s, 9 H, OCOC(CH_3)$_3$], 1.15-1.09 {m, 3 H, Si[C*H*(CH_3)$_2$]$_3$}, 1.08 - 1.04 {m, 18 H, Si[CH(C*H*$_3$)$_2$]$_3$}.

^{13}C-NMR: (101 MHz, $CDCl_3$) δ 210.6 (s, CO), 178.2 [s, O*C*OC(CH_3)], 77.1 (d, C-2), 66.4 (t, C-1), 38.9 [s, OCO*C*(CH_3)], 27.3 [q, OCOC(*C*H$_3$)], 26.3 (q, C-4), 18.0 {q, Si[CH(*C*H$_3$)$_3$]$_3$}, 12.3 {d, Si[*C*H(CH_3)$_3$]$_3$}.

Specific rotation: $[\alpha]_D^{20} = +18.0$ (*c* = 1.01, $CHCl_3$) (*via* Route A).

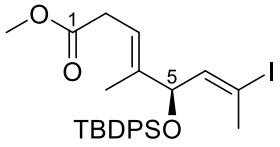
$[\alpha]_D^{20} = +11.0$ (*c* = 1.00, $CHCl_3$) (*via* Route B).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2945 (s, C_{sp3}-H), 2868 (s, C_{sp3}-H), 1786 (vs, C=O), 1463 (m), 1142 (vs, C-O).

HRMS (ESI): $[C_{18}H_{36}O_4Si + H]^+$ calcd.: 345.2454; found: 345.2455.

The scalar analytical data match those reported in the literature.[56]

Methyl ester 64



64

$C_{26}H_{33}IO_3Si$
548.54 g/mol

To a cold (0 °C) solution of carboxylic acid **38** (44.1 mg, 80.0 µmol, 1.00 eq.) in toluene (2 ml) and methanol (2 mL) was added trimethylsilyl diazomethane (63.0 µL, 120 µmol, 1.50 eq.). After stirring for two hours, the reaction was quenched by the addition of saturated aqueous sodium thiosulphate solution (5 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column

chromatography (silica, pentane:diethyl ether = 10:1), methyl ester **64** was obtained as a colorless oil (34.9 mg, 60.0 µmol, 77%).

TLC: R_f = 0.84 (pentane:diethyl ether = 3:1).

^{1}H-NMR: (300 MHz, $CDCl_3$) δ 7.65-7.60 (m, 4 H, C_{Ar}-H), 7.45-7.31 (m, 6 H, C_{Ar}-H), 6.16 (dq, ^3J = 8.8 Hz, ^4J = 1.6 Hz, 1 H, H-6), 5.61 (*virt.* tquint., ^3J = 7.3 Hz, $^4J \approx {}^4J$ = 1.3 Hz, 1 H, H-3), 4.55 (d, ^3J = 8.8 Hz, 1 H, H-5), 3.69 (s, 3 H, $COOCH_3$), 3.04 (d, ^3J = 7.3 Hz, 2 H, H-2), 1.84 (s, 3 H, H-42), 1.58 (s, 3 H, H-41), 1.05 [s, 9 H, $SiC(CH_3)_3$].

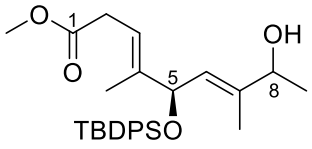
^{13}C-NMR: **(**100 MHz, $CDCl_3$) δ 172.2 (s, C-1), 142.1 (d, C-6), 138.7 (s, C-4), 135.9 (d, C_{Ar}-H), 135.8 (d, C_{Ar}-H), 129.7 (d, C_{Ar}-H), 127.6 (d, C_{Ar}-H), 117.2 (d, C-3), 96.4 (s, C-7), 75.2 (d, C-5), 55.8 (q, $COOCH_3$) 33.2 (t, C-2), 27.9 (q, C-42), 26.8 [q, $SiC(CH_3)_3$], 19.4 [q, $SiC(CH_3)_3$], 12.5 (q, C-41).

Specific rotation: $[\alpha]_D^{20} = -20.0$ (c = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3071 (w, sp^2-C–H), 2953 (w, sp^3-C–H), 2931 (w, sp^3-C–H), 2857 (w, sp^3-C–H), 1742 (s, C=O), 1428 (m), 1111 (s, C–O), 702 (s).

HRMS (ESI): *m/z* $[C_{26}H_{33}IO_3Si + NH_4]^+$ calcd.: 566.1582; found: 566.1577.

Alcohol 65



65

$C_{28}H_{38}O_4Si$

466.69 g/mol

Vinyl iodide **64** (10.0 mg, 20.0 µmol, 1.00 eq.) and acetaldehyde (5 µL, 90 µmol, 5.00 eq.) were dissolved in DMSO (500 µL) and added to a stirred suspension of chromium-(II)-chloride (8.70 mg, 60.0 µmol, 3.00 eq.) and nickel-(II)-chloride (87.0 µg, 3 mol%) in DMSO (300 µL). After 1.5 hours, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (5 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 100 mL). The combined organic layers were dried over sodium sulfate and

filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 1:1), alcohol **65** was obtained as a colorless oil (6.66 mg, 64.0 µmol, 80%).

TLC: R_f = 0.50 & 0.56 (pentane:diethyl ether = 1:1).

Diastereomeric ratio: d.r ≈ 1:1.

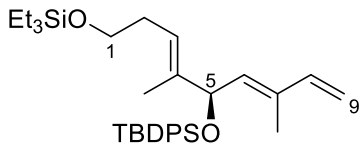
^{1}H-NMR: (400 MHz, $CDCl_3$) δ 7.72-7.60 (m, 4 H, C_{Ar}-H), 7.45-7.29 (m, 6 H, C_{Ar}-H), 5.67-5.57 (m, 1 H, H-3), 5.47-5.32 (m, 1 H, H-6), 4.73 (t, ^3J = 8.7 Hz, 1 H, H-5), 4.04-3.91 (m, 1 H, H-8), 3.69 (s, 3 H, COOMe), 3.06 (d, ^3J = 7.3 Hz, 1 H, H-2_A), 3.05 (d, ^3J = 7.2 Hz, 1 H, H-2_B), 1.60 (d, ^4J = 1.8 Hz, 3 H, H-41), 1.17 (d, ^4J = 1.2 Hz, 3 H, H-42), 1.09 (d, ^3J = 6.4 Hz, 3 H, H-9), 1.08 (d, ^3J = 6.4 Hz, 3 H, H-9), 1.04 [s, 9 H, SiC(CH_3)$_3$].

^{13}C-NMR: (101 MHz, $CDCl_3$) δ 172.6 (s, C=O), 140.2 (d, C-4_A), 140.1 (d, C-4_B), 139.5 (d, C-7_A), 139.3 (d, C-7_B), 136.1 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 134.8 (s, C_{Ar}), 134.7 (s, C_{Ar}), 129.7 (d, C_{Ar}-H), 129.6 (d, C_{Ar}-H), 127.6 (d, C_{Ar}-H), 127.5 (d, C_{Ar}-H), 127.0 (d, C-6_A), 126.4 (d, C-6_B), 116.3 (d, C-3_A), 116.2 (d, C-3_B), 74.7 (d, C-5_A), 74.5 (d, C-5_B), 73.0 (d, C-8_A), 73.0 (d, C-8_B), 51.9 (q, COOMe), 33.4 (t, C-2), 27.1 [q, SiC(*C*H_3)$_3$], 21.4 (q, C-9_A), 21.1 (q, C-9_B), 19.5 [s, Si*C*(CH_3)$_3$], 12.6 (q, C-41), 12.1 (q, C-42_A), 11.7 (q, C-42_B).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3436 (br, OH), 3071 (w, sp^2-C–H), 3049 (w, sp^2-C–H), 2960 (m, sp^3-C–H), 2930 (m, sp^3-C–H), 2892 (m, sp^3-C–H), 2857 (m, sp^3-C–H), 1739 (vs, C=O), 1428 (m), 701 (vs).

HRMS (ESI): *m/z* $[C_{28}H_{38}O_4Si + NH_4]^+$ calcd.: 484.2877; found: 484.2876.

Diene 85



85

$C_{33}H_{50}O_2Si_2$

534.93 g/mol

a) *Via* Stille coupling

To a solution of vinyl iodide **36** (208 mg, 328 µmol, 1.00 eq.) in DMF (10 mL) was added tributylvinyl tin (312 mg, 988 µmol, 3.00 eq.), triphenylphosphine (34.3 mg, 135 µmol, 0.40 eq.) and $Pd_2(dba)_3$ (60.3 mg, 65.9 µmol, 0.20 eq.). After stirring for 30 minutes at 50 °C, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution. The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with water (2 × 10 mL), dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 1:0), diene **85** was obtained as a colorless oil (20.8 mg, 12%).

b) *Via* Suzuki coupling with vinylboronic acid pinacol ester

To a solution of vinyl iodide **36** (200 mg, 315 µmol, 1.00 eq.) in THF (4 mL) and water (0.4 mL) was added vinylboronic acid pinacol ester (146 mg, 945 µmol, 3.00 eq.), triphenylarsane (116 mg, 378 µmol, 1.20 eq.), $Pd_2(dba)_3$ (43.3 mg, 47.0 µmol, 30 mol%) and silver oxide (365 mg, 1.57 mmol, 5.00 eq.). After stirring for 30 minutes at room temperature, pentane (10 mL) and diethyl ether (1 mL) were added, and the suspension was filtered over a silica plug. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 100:1), diene **85** was obtained as a colorless oil (142 mg, 265 µmol, 85%).

c) *Via* Suzuki Coupling with potassium vinyltrifluoroborate

To a solution of vinyl iodide **36** (1.89 g, 2.98 mmol, 1.00 eq.) in THF (28 mL) and water (2.8 mL) was added potassium vinyltrifluoroborate (1.20 g, 8.93 mmol, 3.00 eq.), triphenylarsane (1.09 g, 3.57 mmol, 1.20 eq.), Pd2(dba)3 (141 mg, 446 µmol, 30 mol%) and

silver oxide (3.45 g, 14.9 mmol, 5.00 eq.). After stirring for two hours at room temperature, pentane (100 mL) and diethyl ether (10 mL) were added, and the suspension was filtered over a silica plug. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 300:1 ⟶ 100:1), diene **85** was obtained as a colorless oil (1.22 g, 2.28 mmol, 77%).

TLC: R_f = 0.51 (pentane:diethyl ether = 30:1).

^{1}**H-NMR**: (400 MHz, $CDCl_3$) δ 7.67-7.59 (m, 4 H, C_{Ar}-H), 7.43-7.30 (m, 6 H, C_{Ar}-H), 6.29 (dd, ^3J = 17.4 Hz, ^3J = 10.7 Hz, 1 H, H-8), 5.54 (d, ^3J = 8.7 Hz, 1 H, H-6), 5.28 (*virt*. tquint, ^3J = 7.1 Hz, $^4J \approx {}^4J$ = 1.2 Hz 1 H, H-3), 5.04 (d, ^3J = 17.4 Hz, 1 H, H-9a), 4.96 (d, ^3J = 10.7 Hz, 1 H, H-9b), 4.75 (d, ^3J = 8.7 Hz, 1 H, H-5), 3.52-3.46 (m, 2 H, H-1), 2.21 (*virt.* q, $^3J \approx {}^3J$ = 7.4 Hz, 2 H, H-2), 1.59 (d, ^4J = 1.4 Hz, 3 H, H-41), 1.30 (d, ^4J = 1.3 Hz, 3 H, H-42), 1.04 [s, 9 H, $Si(CH_3)_3$], 0.95 [t, ^3J = 8.0 Hz, 9 H, $Si(CH_2C\mathit{H}_3)_3$], 0.59 [q, ^3J = 7.9 Hz, 6 H, $Si(C\mathit{H}_2CH_3)_3$].

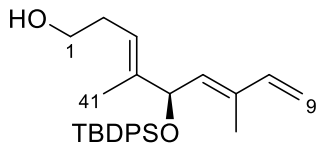
^{13}C-NMR: (101 MHz, $CDCl_3$) δ 141.5 (d, C-8), 138.4 (s, C-4), 136.0 (d, C_{Ar}-H), 134.4 (d, C-6), 133.4 (s, C-7), 129.5 (d, C_{Ar}-H), 127.5 (d, C_{Ar}-H), 121.1 (d, C-3), 112.2 (t, C-9), 75.5 (d, C-5), 62.5 (t, C-1), 31.6 (t, C-2), 27.1 [q, $SiC(\mathit{C}H_3)_3$], 19.5 [s, $Si\mathit{C}(CH_3)_3$], 12.4 (q, C-41), 11.9 (q, C-42), 6.9 [q, $Si(CH_2\mathit{C}H_3)_3$], 4.6 [t, $Si(\mathit{C}H_2\mathit{C}H_3)_3$].

Specific rotation: $[\alpha]_D^{20} = -20.0$ (c = 2.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3071 (w, sp^2-C–H), 2955 (s, sp^3-C–H), 1472 (m), 1428 (m, C=C), 1106 (vs, C–O), 1017 (s, C–O), 939 (w), 822 (m, C–H), 739 (s), 701 (vs).

HRMS (ESI): *m/z* $[C_{33}H_{50}O_2Si_2 + Na]^+$ calcd.: 557.3241; found: 557.3233.

Alcohol 185



185
$C_{27}H_{36}O_2Si$
420.67 g/mol

To a cold (0 °C) solution of silyl ether **85** (590 mg, 1.10 mmol, 1.00 eq.) in THF (13 mL) was added HF · pyridine complex (30 wt.% HF, 573 µL, 22.0 mmol, 20.0 eq.) and 1 mL pyridine. After 30 minutes, the solution was poured into 100 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 4:1), alcohol **185** was obtained as a colorless oil (346 mg, 75%).

TLC: R_f = 0.50 (pentane:diethyl ether = 1:1).

^{1}**H-NMR**: (300 MHz, $CDCl_3$) δ 7.68-7.60 (m, 4 H, C_{Ar}-H), 7.42-7.30 (m, 6 H, C_{Ar}-H), 6.31 (dd, ^3J = 17.4 Hz, ^3J = 10.6 Hz, 1 H, H-8), 5.55 (d, ^3J = 8.7 Hz, 1 H, H-6), 5.27 (*virt.* tquint, ^3J = 7.4 Hz, $^4J \approx {}^4J$ = 1.3 Hz, 1 H, H-3), 5.06 (d, ^3J = 17.4 Hz, 1 H, H-9a), 4.98 (d, ^3J = 10.6 Hz, 1 H, H-9b), 4.79 (d, ^3J = 8.7 Hz, H-5), 3.54 (q, ^3J = 6.4 Hz, 2 H, H-1), 2.22 (*virt.* q, $^3J \approx {}^3J$ = 6.8 Hz, 2 H, H-2), 1.61 (d, ^4J = 1.4, 0.8 Hz, 3 H, H-41), 1.35 (d, ^4J = 1.2 Hz, 3 H, H-42), 1.05 [s, 9 H, $SiC(CH_3)_3$].

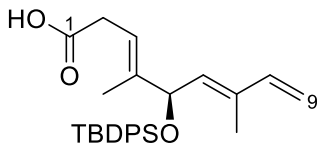
^{13}**C-NMR**: (75 MHz, $CDCl_3$) δ 141.4 (d, C-8), 140.1 (s, C-4), 136.0 (d, C_{Ar}-H), 134.4 (s, C_{Ar}), 134.2 (d, C-6), 134.0 (s, C_{Ar}), 133.6 (s, C-7), 129.7 (d, C_{Ar}-H), 127.6 (d, C_{Ar}-H), 120.7 (d, C-3), 112.4 (t, C-9), 75.4 (d, C-5), 62.4 (t, C-1), 31.3 (t, C-2), 27.1 [q, $SiC(CH_3)_3$], 19.5 [s, $SiC(CH_3)_3$], 12.5 (q, C-41), 12.0 (q, C-42).

Specific rotation: $[\alpha]_D^{20} = -43.0$ (c = 2.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3356 (w, b, O–H), 3071 (w, sp^2-C–H), 2931 (m, sp^3-C–H), 2857 (m), 1607 (w, C=C), 1427 (m, C–H), 1111 (s, C–O), 1044 (s, C–O), 822 (w, C–H), 701 (vs).

HRMS (ESI): no ionisation possible.

Carboxylic acid 86



86
$C_{27}H_{34}O_3Si$
434.65 g/mol

To a solution of primary alcohol **185** (336 mg, 798 µmol, 1.00 eq.) in dichloromethane (20 mL) was added sodium bicarbonate (268 mg, 3.19 mmol, 4.00 eq.) and *Dess-Martin* periodinane (677 mg, 1.59 mmol, 2.00 eq.). After 45 minutes, the yellow suspension was poured into a mixture of 20 mL saturated aqueous sodium bicarbonate solution and 20 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the corresponding aldehyde as a yellow oil. The aldehyde was dissolved in 4 mL *tert*-butanol, and 2-methyl-2-butene was added (0.93 mL, 615 mg, 8.77 mmol, 11.0 eq.). Subsequently, a solution of sodium dihydrogen phosphate (624 mg, 3.99 mmol, 5.00 eq.) and sodium chlorite (217 mg, 2.39 mmol, 3.00 eq.) in water (4 mL) was added. The yellow solution was cooled to 0 °C and stirred for two hours before saturated aqueous ammonium chloride solution was added (100 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 50 mL). The organic layers were combined, dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether 2:1 ⟶ 1:2), carboxylic acid **86** was obtained as a yellowish oil (152 mg, 350 µmol, 44%).

TLC: R_f = 0.51 (pentane:diethyl ether = 1:1).

^{1}**H-NMR**: (400 MHz, $CDCl_3$) δ 7.72-7.62 (m, 4 H, C_{Ar}-H), 7.46-7.30 (m, 6 H, C_{Ar}-H), 6.31 (dd, ^3J = 17.4 Hz, ^3J = 10.7 Hz, 1 H, H-8), 5.58 (*virt.* tquint., ^3J = 7.1 Hz, $^4J \approx {}^4J$ = 1.3 Hz, 1 H, H-3), 5.53 (d, ^3J = 8.7 Hz, 1 H, H-6), 5.07 (d, ^3J = 17.4 Hz, 1 H, H-9a), 4.99 (d, ^3J = 10.7 Hz, 1 H, H-9b), 4.82 (d, ^3J = 8.7 Hz, 1 H, H-5), 3.07 (d, ^3J = 7.1 Hz, 2 H, H-2), 1.61 (d, ^4J = 1.4 Hz, 3 H, H-41), 1.32 (d, ^4J = 1.2 Hz, 3 H, H-42), 1.07 [s, 9 H, $SiC(CH_3)_3$].

^{13}**C-NMR**: (101 MHz, $CDCl_3$) δ 177.1 (s, C-1), 141.1 (d, C-8), 140.6 (s, C-4), 135.9 (d, C_{Ar}-H), 133.9 (s, C-7), 133.6 (d, C-6), 129.5 (d, C_{Ar}-H), 127.4 (d, C_{Ar}-H), 115.8 (d, C-3), 112.4 (t,

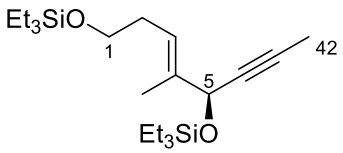
C-9), 74.8 (d, C-5), 32.9 (t, C-2), 26.9 [q, SiC(*C*H$_3$)$_3$], [s, Si*C*(CH$_3$)$_3$], 12.5 (q, C-41), 11.8 (q, C-42).

Specific rotation: $[\alpha]_D^{20} = -34.0$ (c = 2.00, CHCl$_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3071 (w, sp^2-C–H), 2957 (m, sp^3-C–H), 2857 (m), 1709 (vs, C=O), 1607 (w, C=C), 1427 (m, C–H), 1298 (w), 1110 (s, C–O), 1059 (m, C–O), 822 (w, C–H), 701 (vs).

HRMS (ESI): [C$_{27}$H$_{34}$O$_3$Si + Na]$^+$ calcd.: 457.2169; found: 457.2168.

TES protected alkyne 99



99
$C_{21}H_{42}O_2Si_2$
382.74 g/mol

To a solution of alcohol **34** (124 mg, 462 µmol, 1.00 eq.) in dichloromethane (5 mL) was added imidazole (62.9 mg, 924 µmol, 2.00 eq.), 4-(dimethylamino)-pyridine (5.64 mg, 46.2 µmol, 0.100 eq.) and triethylsilyl chloride (116 µL, 105 mg, 693 µmol, 1.50 eq). After stirring for two hours at room temperature, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (5 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 100:1), alkyne **99** was obtained as a colorless oil (164 mg, 428 µmol, 92%).

TLC: R_f = 0.50 (pentane:diethyl ether = 30:1).

^{1}**H-NMR**: (400 MHz, CDCl$_3$) δ 5.51 (*virt.* tquint, ^3J = 7.2 Hz, $^4J \approx {}^3J \approx$ 1.3 Hz, 1 H, H-3), 4.70 (q, ^4J = 2.2 Hz, 1 H, H-5), 3.61 (t, ^3J = 7.2 Hz, 2 H, H-1), 2.28 (*virt.* q, $^3J \approx {}^3J \approx$ 7.2 Hz, 2 H, H-2), 1.83 (d, ^4J = 2.2 Hz, 3 H, H-42), 1.72 (d, ^4J = 1.3 Hz, 3 H, H-41), 1.00-0.92 [m, 18 H, Si(CH$_2$C*H*$_3$)$_3$], 0.71-0.54 [m, 12 H, Si(C*H*$_2$CH$_3$)$_3$].

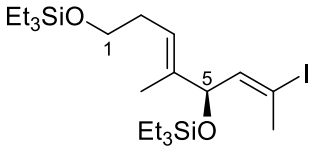
^{13}C-NMR: (101 MHz, $CDCl_3$) δ 137.5 (s, C-4), 122.1 (d, C-3), 80.9 (s, C-6), 79.7 (s, C-7), 68.5 (d, C-5), 62.4 (t, C-1), 31.7 (t, C-2), 12.4 (q, C-41), 6.9 [q, $Si(CH_2\mathit{C}H_3)_3$], 5.0 [t, C_5-$OSi(\mathit{C}H_2CH_3)_3$], 4.6 [t, C_1-$OSi(\mathit{C}H_2CH_3)_3$], 3.8 (q, C-42).

Specific rotation: $[\alpha]_D^{20} = +10.0$ (c = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2954 (vs) 2912 (s) 2877 (vs) (C_{sp3}-H), 1102 (vs), 1047 (vs), 742 (vs).

HRMS (ESI): *m/z* $[C_{21}H_{42}O_2Si_2 + NH_4]^+$ calcd.: 400.3067; found: 400.3061.

TES-protected vinyl iodide 102



102
$C_{21}H_{43}IO_2Si_2$
510.65 g/mol

To a solution of alkyne **99** (728 mg, 1.91 mmol, 1.00 eq.) in THF (12 mL) was added *Schwartz* reagent (985 mg, 3.82 mmol, 2.00 eq.) at room temperature. The orange suspension was stirred for 2.5 hours and then cooled to –78 °C. A solution of iodine (581 mg, 2.29 mmol, 1.20 eq.) in THF (5 mL) was added and stirred for five minutes. The brown solution was poured into a vigorously stirred mixture of saturated aqueous sodium thiosulphate solution (20 mL) and diethyl ether (20 mL). A colorless precipitate was separated by filtration over Celite and the layers were separated. The aqueous phase was extracted with diethyl ether (2 x 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether 400:1 ⟶ 300:1), vinyl iodide **102** was obtained as a colorless oil (359 mg, 704 µmol, 37%).

TLC: R_f = 0.63 (pentane:diethyl ether = 30:1).

^{1}H-NMR: (500 MHz, $CDCl_3$) δ 6.16 (dq, ^3J = 8.5 Hz, ^4J = 1.5 Hz, 1 H, H-6), 5.45 (*virt.* tquint, ^3J = 7.1 Hz, $^4J \approx {}^3J \approx$ 1.3 Hz, 1 H, H-3), 4.62 (d, ^3J = 8.4 Hz, 1 H, H-5), 3.59 (t, ^3J = 7.1 Hz, 2 H, H-1), 2.44 (d, ^4J = 1.5 Hz, 3 H, H-42), 2.31-2.20 (m, 2 H, H-2), 0.96 [t, ^3J = 8.0 Hz, 9 H,

$Si(CH_2CH_3)_3$], 0.94 [t, ^3J = 7.9 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.62 [q, ^3J = 7.9 Hz, 6 H, C_1-$OSi(CH_2CH_3)_3$], 0.60 [d, ^3J = 7.9 Hz, 6 H, C_5-$OSi(CH_2CH_3)_3$].

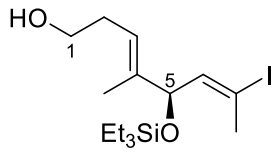
^{13}C-NMR: (75 MHz, $CDCl_3$) δ 143.6 (d, C-6), 137.6 (s, C-4), 121.7 (d, C-3), 95.0 (s, C-7), 75.1 (d, C-5), 62.4 (t, C-1), 31.6 (t, C-2), 28.4 (q, C-42), 12.4 (q, C-41), 6.9 [q, $Si(CH_2CH_3)_3$], 5.0 [t, $C_5OSi(CH_2CH_3)_3$], 4.6 [t, $C_1OSi(CH_2CH_3)_3$].

Specific rotation: $[\alpha]_D^{20} = -12.0$ (c = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2955 (s, C-H), 2923 (s, C-H), 2876 (m, C-H) 2856 (m, C-H), 1634 (w, C=C), 1459 (m, C-H), 1097 (m, C-O), 745 (m, C-I).

HRMS (ESI): no ionization possible.

Alcohol 107



107
$C_{15}H_{29}IO_2Si$
396.38 g/mol

To a cold (0 °C) solution of silyl ether **102** (359 mg, 0.703 mmol, 1.00 eq.) in THF (15 mL) and diethyl ether (15 mL) was added pyridine (3 mL) and HF · pyridine complex (30 w% HF, 350 µL, 0.523 mmol, 17.5 eq.). After 3.5 hours, the solution was poured into 30 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 30 mL). The combined organic layers were washed with 10% copper sulfate solution (2 × 15 mL), water (1 × 15 mL), brine (1 × 15 mL), dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 2:1), alcohol **107** was obtained as a colorless oil (189 mg, 68%). Additionally, 16.0 mg of diol **106** were isolated (56.7 µmol, 27%).

TLC: R_f = 0.50 (pentane:diethyl ether = 1:1).

^{1}**H-NMR**: (300 MHz, $CDCl_3$) δ 6.15 (dq, ^3J = 8.5 Hz, ^4J = 1.5 Hz, 1 H, H-6), 5.47 (*virt.* tquint, ^3J = 7.3 Hz, $^4J \approx {}^4J \approx$ 1.4 Hz, 1 H, H-3), 4.63 (d, ^3J = 8.5 Hz, 1 H, H-5), 3.65 (t,

^{3}J = 6.6 Hz, 2 H, H-1), 2.45 (d, ^{4}J = 1.5 Hz, 3 H, H-42), 2.35 - 2.26 (m, 2 H, H-2), 1.61 (d, ^{4}J = 1.3 Hz, 3 H, H-41), 0.95 [t, ^{3}J = 7.9 Hz, 9 H, $Si(CH_2C\mathit{H}_3)_3$], 0.57 [q, ^{3}J = 7.9 Hz, 6 H, $Si(C\mathit{H}_2CH_3)_3$].

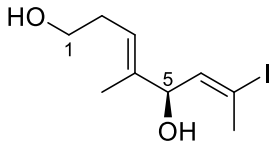
^{13}C-NMR: (75 MHz, $CDCl_3$) δ 143.4 (d, C-6), 139.1 (s, C-4), 120.8 (d, C-3), 95.1 (s, C-7), 74.8 (d, C-5), 62.4 (t, C-1), 31.3 (t, C-2), 28.5 (q, C-42), 12.6 (q, C-41), 6.9 [q, $Si(CH_2\mathit{C}H_3)_3$], 5.0 [t, $Si(\mathit{C}H_2CH_3)_3$].

Specific rotation: $[\alpha]_D^{20} = -20.0$ (c = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3335 (b, OH), 2922 (s, C-H), 2856 (s, C-H), 1635 (w, C=C), 1429 (m, C-H), 1048 (m, C-O), 880 (m, C-I).

HRMS (ESI): no ionization possible.

Diol 106



106
$C_9H_{15}IO_2$
282.12 g/mol

TLC: R_f = 0.24 (pentane:diethyl ether = 1:4) [$KMnO_4$].

^{1}H-NMR: (300 MHz, $CDCl_3$) δ 6.22 (dq, ^{3}J = 8.5 Hz, ^{4}J = 1.5 Hz, 1 H, H-6), 5.52 (*virt.* tquint, ^{3}J = 7.3 Hz, $^{4}J \approx {}^{4}J \approx$ 1.4 Hz, 1 H, H-3), 4.70 (d, ^{3}J = 6.9 Hz, 1 H, H-5), 3.67 (t, ^{3}J = 8.5 Hz, 2 H, H-1), 2.48 (d, ^{4}J = 1.5 Hz, 3 H, H-42), 2.36 - 2.27 (m, 2 H, H-2), 1.67 (d, ^{4}J = 1.6 Hz, 3 H, H-41).

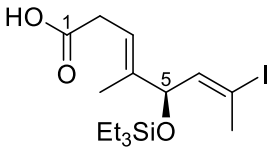
^{13}C-NMR: (75 MHz, $CDCl_3$) δ 141.8 (d, C-6), 138.4 (s, C-4), 122.4 (d, C-3), 98.0 (s, C-7), 74.5 (d, C-5), 62.3 (t, C-1), 31.2 (t, C-2), 28.5 (q, C-42), 12.7 (q, C-41).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3350 (b, OH), 2954 (s, C-H), 2923 (s, C-H), 2876 (m, C-H), 1636 (w, C=C), 1459 (m, C-H), 1044 (m, C-O), 745 (m, C-I).

Specific rotation: $[\alpha]_D^{20} = +6.00$ (c = 1.00, $CHCl_3$).

HRMS (ESI): no ionization possible.

Carboxylic acid 108



108
$C_{15}H_{27}IO_3Si$
410.37 g/mol

To a solution of primary alcohol **107** (189 mg, 478 µmol, 1.00 eq.) in dichloromethane (10 mL) was added sodium bicarbonate (161 mg, 1.91 mmol, 4.00 eq.) and *Dess-Martin* periodinane (405 mg, 0.956 mmol, 2.00 eq.). After 45 minutes, the yellow suspension was poured into a mixture of 10 mL saturated aqueous sodium bicarbonate solution and 10 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the corresponding aldehyde as a yellow oil. The aldehyde was dissolved in 5 mL *tert*-butanol, and 2-methyl-2-buten was added (0.5 mL, 335 mg, 4.78 mmol, 10.0 eq.). Subsequently, a solution of sodium dihydrogen phosphate (299 mg, 1.91 mmol, 4.00 eq.) and sodium chlorite (86.5 mg, 956 µmol, 2.00eq.) in water (5 mL) was added. The yellow solution was stirred for two hours at room temperature before saturated aqueous ammonium chloride solution was added (10 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (5 × 10 mL). The organic layers were combined, dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether 2:1 ⟶ 1:2), carboxylic acid **108** was obtained as a yellowish oil (158 mg, 385 µmol, 81%).

TLC: R_f = 0.23 (pentane:diethyl ether = 1:1) [UV, $KMnO_4$].

^{1}**H-NMR**: (300 MHz, $CDCl_3$) δ 6.15 (dq, ^3J = 8.4 Hz, ^4J = 1.5 Hz, H-6), 5.66 (tp, ^3J = 7.1, $^4J \approx {}^4J \approx$ 1.4 Hz, 1 H, H-3), 4.66 (d, ^3J = 8.4 Hz, 1 H, H-5), 3.11 (d, ^3J = 7.1 Hz, 2 H, H-2), 2.46 (d, ^4J = 1.5 Hz, 3 H, H-42), 1.61 (d, ^4J = 1.2 Hz, 3 H, H-41), 0.94 [t, ^3J = 8.1 Hz, 9 H, $Si(CH_2C\mathit{H}_3)_3$], 0.58 [q, ^3J = 8.1 Hz, 6 H, $Si(C\mathit{H}_2CH_3)_3$].

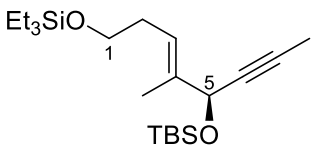
^{13}**C-NMR**: (75 MHz, $CDCl_3$) δ 176.9 (s, C-1), 143.0 (d, C-6), 140.0 (s, C-4), 116.2 (d, C-3), 95.5 (s, C-7), 74.6 (d, C-5), 33.0 (t, C-2), 28.5 (q, C-42), 12.7 (q, C-41), 6.9 [q, $Si(CH_2\mathit{C}H_3)_3$], 5.0 [t, $Si(\mathit{C}H_2CH_3)_3$].

Specific rotation: $[\alpha]_D^{20} = -20.0$ (c = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2956 (s, OH), 2915 (s, C-H), 2877 (m, C-H), 1712 (s, C=O), 1414 (m, C-H), 1077 (m, C-O), 745 (m, C-I).

HRMS (ESI): *m/z* $[C_{15}H_{27}IO_3Si + NH_4]^+$ calcd.: 428.1118; found: 428.1113.

TES-TBS protected alkyne 100



100
$C_{21}H_{42}O_2Si_2$
382.74 g/mol

To a cold (0 °C) solution of ketone **32** (7.06 g, 26.5 mmol, 1.00 eq.) in THF (250 mL) was added (S)-2-methyl-CBS-catalyst (**33**, 3.70 g, 13.3 mmol, 0.50 eq.). Borane dimethylsulfide complex (2M in THF, 9.30 mL, 18.6 mmol, 0.70 eq.) was added *via* a syringe pump over the course of 2.5 hours. The reaction was quenched by the addition of a saturated aqueous sodium bicarbonate solution (150 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 50 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. The crude alcohol was dissolved in dichloromethane (265 mL), and imidazole (3.61 g, 53.0 mmol, 2.00 eq.), 4-(dimethylamino)-pyridine (323 mg, 2.65 µmol, 0.10 eq.) and *tert*-butyldimethylsilyl chloride (6.39 g, 42.4 mmol, 1.60 eq) were added. After stirring for two hours, additional imidazole (2.00 g, 29.4 mmol, 1.12 eq.) and *tert*-butyldimethylsilyl chloride (3.00 g, 23.1 mmol, 0.87 eq) were added. After 20 minutes, the reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (100 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 80 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 100:1 ⟶ 70:1), silyl ether **100** was obtained as a colorless oil (7.80 g, 20.4 mmol, 77%).

TLC: R_f = 0.89 (pentane:diethyl ether = 4:1) [UV, $KMnO_4$].

^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 5.52 (*virt.* tquint, ^3J = 7.1 Hz, $^4J \approx {}^4J$ = 1.4 Hz, 1 H, H-3), 4.73-4.67 (m, 1 H, H-5), 3.61 (t, ^3J = 7.1 Hz, 2 H, H-1), 2.28 (*virt.* q, $^3J \approx {}^3J$ = 7.2 Hz, 2 H, H-2), 1.83 (d, ^3J = 2.2 Hz, 3 H, H-42), 1.71 (s, 3 H, H-41), 0.99-0.85 [m, 18 H, $OSiC(CH_3)_3$, $OSi(CH_2CH_3)_3$], 0.66-0.55 [m, 6 H, $OSi(CH_2CH_3)_3$], 0.13-0.04 [m, 6 H, $OSi(CH_3)_2$].

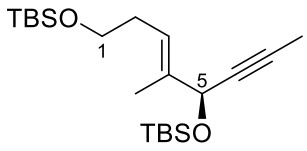
^{3}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 137.5 (s, C-4), 122.1 (d, C-3), 81.0 (s, C-6), 79.7 (s, C-7), 68.5 (d, C-5), 62.4 (t, C-1), 31.7 (t, C-2), 26.0 [q, $OSiC(CH_3)_3$], 19.5 [q, $OSiC(CH_3)_3$], 12.4 (q, C-41), 6.9 [q, $Si(CH_2CH_3)_3$], 5.0 [q, $OSi(CH_3)_2$], 4.6 [t, $Si(CH_2CH_3)_3$], 3.8 (q, C-42).

Specific rotation: $[\alpha]_D^{20} = +8.00$ (c = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2955 (s, C-H), 2936 (s, C-H), 2878 (s, C-H), 1462 (m, C-H), 1252 (s, C-O), 1102 (s, C-O), 837 (s, C-H).

HRMS (ESI): *m/z* $[C_{21}H_{42}O_2Si_2 + Na]^+$ calcd.:405.2621; found: 405.2617.

TBS protected alkyne 101



101
$C_{21}H_{42}O_2Si_2$
382.74 g/mol

TBAF (2.39 mL, 1M in THF, 2.39 mmol, 2.50 eq.) was added to a solution of alkyne **35** (485 mg, 0.956 mmol, 1.00 eq.) in THF. After 6.5 hours, the reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (20 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. The crude diol was dissolved in dichloromethane (10 mL), and imidazole (199 mg, 2.92 mmol, 3.00 eq.), and *tert*-butyldimethylsilyl chloride (367 mg, 2.43 mmol, 2.50 eq.) were added. The colorless suspension was stirred for 1.5 hours before saturated aqueous ammonium chloride solution (40 mL) was added. The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure.

Following flash column chromatography (silica, pentane:diethyl ether = 50:1), silyl ether **101** was obtained as a colorless oil (288 mg, 753 µmol, 79%).

TLC: R_f = 0.95 (pentane:diethyl ether = 4:1) [UV, $KMnO_4$].

^{1}**H-NMR**: (400 MHz, $CDCl_3$) δ 5.53 (*virt.* tquint, ^3J = 7.2, $^4J \approx {}^4J \approx$ 1.3 Hz, 1 H, H-3), 4.70 (s, 1 H, H-5), 3.62 (t, ^3J = 7.0 Hz, 2 H, H-1), 2.26 (*virt*. q, $^3J \approx {}^3J \approx$ 7.1 Hz, 2 H, H-2), 1.83 (d, ^5J = 2.2 Hz, 3 H, H-42), 1.70 (d, ^4J = 1.3 Hz, 3 H, H-41), 0.90 [s, 9 H, $SiC(CH_3)_3$], 0.89 [s, 9 H, $SiC(CH_3)_3$], 0.11 [s, 3 H, $C_5OSi(CH_3)_2$], 0.09 [s, 3 H, $C_5OSi(CH_3)_2$], 0.05 [s, 6 H, $C_1OSi(CH_3)_2$].

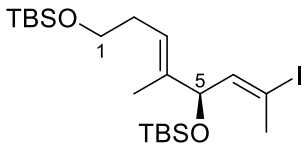
^{13}C-NMR: (101 MHz, $CDCl_3$) δ 137.3 (s, C-4), 122.1 (d, C-3), 80.9 (s, C-6), 79.8 (s, C-8), 68.7 (d, C-5), 62.8 (t, C-1), 31.7 (t, C-2), 26.1 [q, $SiC(CH_3)_3$], 26.0 [q, $SiC(CH_3)_3$], 18.5 [s, $SiC(CH_3)_3$], 12.6 (q, C-41), 3.8 (q, C-42), –4.4 [q, $C_5OSi(CH_3)_2$], –4.8 [q, $C_5OSi(CH_3)_2$], –5.1 [q, $C_1OSi(CH_3)_2$].

Specific rotation: $[\alpha]_D^{20} = +8.00$ (c = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2955 (s) 2929 (s) 2858 (s) (C_{sp3}-H), 1472 (m), 1254 (s), 1103 (s), 836 (vs).

HRMS (ESI): no ionization possible.

TBS protected vinyl iodide 105



105

$C_{21}H_{43}IO_2Si_2$

510.65 g/mol

To a solution of alkyne **101** (281 mg, 0.734 mmol, 1.00 eq.) in THF (5 mL) was added *Schwartz* reagent (379 mg, 1.47 mmol, 2.00 eq.) at room temperature. The orange suspension was stirred for two hours and then cooled to –78 °C. A solution of iodine (223 mg, 0.881 mmol, 1.20 eq.) in THF (2 mL) was added and stirred for five minutes. The brown solution was poured into a vigorously stirred mixture of saturated aqueous sodium thiosulphate solution (40 mL) and

diethyl ether (40 mL). A colorless precipitate was separated by filtration over Celite, and the layers were separated. The aqueous phase was extracted with diethyl ether (2 × 30 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 200:1), vinyl iodide **105** was obtained as a colorless oil (226 mg, 443 µmol, 61%).

TLC: R_f = 0.50 (pentane:diethyl ether = 30:1) [UV, $KMnO_4$].

Specific rotation: $[\alpha]_D^{20} = -14.0$ (c = 1.00, $CHCl_3$).

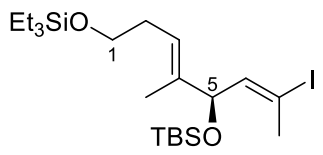
^{1}**H-NMR**: (400 MHz, $CDCl_3$) δ 6.13 (dq, ^3J = 8.4 Hz, ^4J = 1.5 Hz, 1 H, H-6), 5.44 (*virt*. tquint, ^3J = 7.1 Hz, $^4J \approx {}^4J \approx$ 1.3 Hz, 1 H, H-3), 4.61 (d, ^3J = 8.4 Hz, 1 H, H-5), 3.60 (t, ^3J = 6.8 Hz, 2 H, H-1), 2.44 (d, ^4J = 1.5 Hz, 3 H, H-42), 2.24 (*virt*. q, $^3J \approx {}^3J \approx$ 7.0 Hz, 2 H, H-2), 1.58 (d, ^4J = 1.3 Hz, 3 H, H-41), 0.89 [s, 9 H, $SiC(CH_3)_3$], 0.88 [s, 9 H, $SiC(CH_3)_3$], 0.05 [s, 6 H, $C_1OSi(CH_3)_2$], 0.04 [s, 3 H, $C_5OSi(CH_3)_2$], 0.02 [s, 3 H, $C_5OSi(CH_3)_2$].

^{13}**C-NMR**: (101 MHz, $CDCl_3$) δ 143.7 (d, C-6), 137.5 (s, C-4), 121.8 (d, C-3), 94.8 (s, C-7), 75.4 (d, C-5), 62.8 (t, C-1), 31.5 (t, C-2), 28.5 (q, C-42), 26.1 [q, $SiC(CH_3)_3$], 25.9 [q, $SiC(CH_3)_3$], 18.5 [s, $SiC(CH_3)_3$], 18.4 [s, $SiC(CH_3)_3$], 12.5 (q, C-41), –4.6 [q, $C_5OSi(CH_3)_2$], –4.7 [q, $C_5OSi(CH_3)_2$], –5.1 [q, $C_1OSi(CH_3)_2$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2954 (s) 2929 (s) 2857 (s) (C_{sp3}-H), 1463 (m), 1254 (s), 1099 (vs), 835 (vs).

HRMS (ESI): no ionization possible.

TES-TBS-protected vinyl iodide 103



103

$C_{21}H_{43}IO_2Si_2$

510.65 g/mol

To a solution of alkyne **100** (1.36 g, 3.54 mmol, 1.00 eq.) in THF (15 mL) was added *Schwartz* reagent (1.83 g, 7.09 mmol, 2.00 eq.) at room temperature. The orange suspension was stirred

for three hours and then cooled to –78 °C. A solution of iodine (1.08 g, 4.25 mmol, 1.20 eq.) in THF (5 mL) was added and stirred for five minutes. The brown solution was poured into a vigorously stirred mixture of saturated aqueous sodium thiosulphate solution (70 mL) and diethyl ether (70 mL). A colorless precipitate was separated by filtration over Celite, and the layers were separated. The aqueous phase was extracted with diethyl ether (2 x 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether 100:1 ⟶ 4:1), vinyl iodide **103** was obtained as a yellowish oil (516 mg, 29%). Furthermore, 234 mg of alcohol **104** were isolated (0.590 mmol, 17%).

TLC: R_f = 0.60 (pentane:diethyl ether = 30:1) [UV, $KMnO_4$].

^{1}**H-NMR**: (400 MHz, $CDCl_3$) δ 6.13 (dq, ^3J = 8.5 Hz, ^4J = 1.5 Hz, 1 H, H-6), 5.44 (*virt*. tquint., ^3J = 7.1 Hz, ^4J = 1.4 Hz, 1 H, H-3), 4.61 (d, ^3J = 8.4 Hz, 1 H, H-5), 3.59 (t, ^3J = 6.9 Hz, 2 H, H-1), 2.44 (d, ^4J = 1.5 Hz, 3 H, H-42), 2.25 (q, ^3J = 7.1 Hz, 2 H, H-2), 1.58 (d, ^3J = 1.3 Hz, 3 H, H-41), 0.96 [t, ^3J = 8.0 Hz, 9 H, $OSi(CH_2C\mathit{H}_3)_3$], 0.88 [s, 9 H, $SiC(CH_3)_3$], 0.60 [q, ^3J = 8.0 Hz, 6 H, $OSi(C\mathit{H}_2CH_3)_3$], 0.04 [s, $Si(CH_3)_2$], 0.02 [s, $Si(CH_3)_2$].

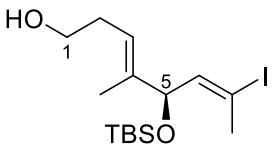
^{13}**C-NMR**: (101 MHz, $CDCl_3$) δ 143.7 (d, C-6), 137.6 (s, C-4), 121.7 (d, C-3), 94.8 (s, C-7), 75.4 (d, C-5), 62.7 (t, C-1), 31.6 (t, C-2), 28.5 (q, C-42), 25.9 [q, $SiC(\mathit{C}H_3)_3$], 18.4 [s, $Si\mathit{C}(CH_3)_3$], 12.5 (q, C-41), 6.9 [q, $Si(CH_2\mathit{C}H_3)_3$], 4.6 [t, $Si(\mathit{C}H_2CH_3)_3$], –4.6 [q, $Si(CH_3)_2$], –4.7 [q, $Si(CH_3)_2$].

Specific rotation: $[\alpha]_D^{20} = -4.00$ (c = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2955 (vs) 2877 (s) 2858 (s) (C_{sp3}-H), 1462 (m), 1253 (s), 1098 (vs).

HRMS (ESI): *m/z* $[C_{21}H_{43}IO_2Si_2 + Na]^+$ found: 533.1737; calcd.: 533.1744.

TBS protected fragment 104



104
$C_{15}H_{29}IO_2Si$
396.38 g/mol

To a cold (0 °C) solution of silyl ether **103** (1.32 g, 2.58 mmol, 1.00 eq.) in THF (30 mL) was added HF · pyridine complex (30 wt.% HF, 671 µL, 25.8 mmol, 10.0 eq.). After two hours, the solution was poured into 30 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 60 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 100:1 ⟶ 4:1), alcohol **104** was obtained as a yellowish oil (775 mg, 1.96 mmol, 76%).

TLC: R_f = 0.50 (pentane:diethyl ether = 1:1) [UV, $KMnO_4$].

^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 6.13 (dq, ^3J = 8.4 Hz, ^4J = 1.5 Hz, 1 H, H-6), 5.45 (*virt.* tquint, ^3J = 7.2, Hz, $^4J \approx {}^4J$ = 1.4 Hz, 1 H, H-3), 4.63 (d, ^3J = 8.4 Hz, 1 H, H-5), 3.64 (t, ^3J = 7.0 Hz, 2 H, H-1), 2.45 (d, ^4J = 1.5 Hz, 3 H, H-42), 2.35 (*virt.* q, $^3J \approx {}^3J$ = 7.1 Hz, 2 H, H-2), 1.61 (s, 3 H, H-41), 0.88 [s, 9 H, $OSiC(CH_3)_3$], 0.06-0.03 [m, 6 H, $OSi(CH_3)_2$].

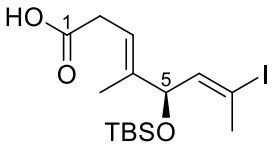
^{3}C-NMR (75 MHz, $CDCl_3$): δ [ppm] = 143.5 (d, C-6), 139.1 (s, C-4), 120.8 (d, C-3), 95.0 (s, C-7), 75.2 (d, C-5), 62.5 (t, C-1), 31.3 (t, C-2), 28.5 (q, C-42), 25.8 [q, $OSiC(\mathit{C}H_3)_3$], 18.4 [s, $OSi\mathit{C}(CH_3)_3$], 12.6 (q, C-41).

Specific rotation: $[\alpha]_D^{20} = -14.0$ (c = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3342 (*br.* s, OH), 2955 (s) 2929 (s) 2857 (s) (C_{sp3}-H), 1252 (m), 1043 (vs), 836 (vs).

HRMS (ESI): no ionization possible.

TBS-protected carboxylic acid fragment 109



109
$C_{15}H_{27}IO_3Si$
410.37 g/mol

To a solution of primary alcohol **104** (973 mg, 2.46 mmol, 1.00 eq.) in dichloromethane (25 mL) was added sodium bicarbonate (827 mg, 9.84 mmol, 4.00 eq.) and *Dess-Martin* periodinane (2.09 g, 4.92 mmol, 2.00 eq.). After one hour, the yellow suspension was poured into a mixture of 50 mL saturated aqueous sodium bicarbonate solution and 50 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 50 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the corresponding aldehyde as a yellow oil. The aldehyde was dissolved in 20 mL *tert*-butanol, and 2-methyl-2-buten was added (2.61 mL, 1.72 g, 24.6 mmol, 10.0 eq.). Subsequently, a solution of sodium dihydrogen phosphate (1.54 g, 9.84 mmol, 4.00 eq.) and sodium chlorite (445 mg, 4.92 mmol, 2.00 eq.) in water (20 mL) was added. The yellow solution was stirred for 30 minutes at room temperature before saturated aqueous ammonium chloride solution was added (50 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (5 × 40 mL). The organic layers were combined, dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether 2:1 ⟶ 1:2), carboxylic acid **109** was obtained as a yellowish oil (792 mg, 1.93 mmol, 79%).

TLC: R_f = 0.18 (pentane:diethyl ether = 1:1) [UV, $KMnO_4$].

Specific rotation: $[\alpha]_D^{20} = -20.0$ (c = 1.00, $CHCl_3$).

^{1}**H-NMR**: (300 MHz, $CDCl_3$) δ 6.13 (dq, ^3J = 8.4, ^4J = 1.5 Hz, 1 H, H-6), 5.64 (tt, ^3J = 7.1 Hz, ^4J = 1.3 Hz, 1 H, H-3), 4.66 (d, ^3J = 8.7 Hz, 1 H, H-5), 3.11 (d, ^3J = 7.1 Hz, 2 H, H-2), 2.46 (d, ^4J = 1.5 Hz, 3 H, H-), 1.60 (d, ^4J = 1.2 Hz, 3 H, H-), 0.88 [s, 9 H, $SiC(CH_3)_3$], 0.05 [s, 3 H, $Si(CH_3)_2$], 0.03 [s, 3 H, $Si(CH_3)_2$].

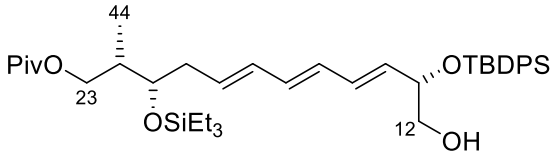
^{13}C-NMR: (75 MHz, $CDCl_3$) δ 177.3 (s, C-1), 143.1 (d, C-6), 140.0 (s, C-4), 116.1 (d, C-3), 95.4 (s, C-7), 74.9 (d, C-5), 33.1 (t, C-2), 28.5 (q, C-42), 25.9 [q, SiC(CH$_3$)$_3$], 18.4 [s, SiC(CH$_3$)$_3$], 12.7 (q, C-41), –4.6 [q, Si(CH$_3$)$_2$], –4.8 [q, Si(CH$_3$)$_2$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2955 (s, OH), 2929 (s, C-H), 2888 (m, C-H), 1712 (s, C=O), 1472 (m, C-H), 1077 (m, C-O), 777 (m, C-I).

HRMS (ESI): *m/z* [$C_{15}H_{27}IO_3Si$ + Na]$^+$ found: 433.0668; calcd.: 433.0672.

11.2. C8-C23 fragment

Alcohol 55



55
$C_{40}H_{62}O_5Si_2$
679.10 g/mol

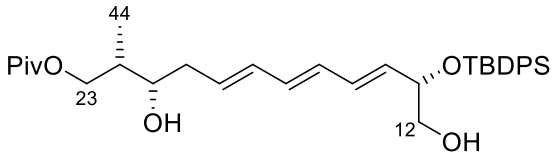
To a cold (–20 °C) solution of silyl ether **9** (502 mg, 633 µmol, 1.00 eq.) in dichloromethane (6 mL) and methanol (600 µL) was added pyridinium *para*-toluenesulfonate (477 mg, 1.90 mmol, 3.00 eq.). After four hours, the reaction was quenched by the addition of saturated aqueous sodium bicarbonate solution. The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 15 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 4:1), alcohol **55** was obtained as a colorless oil (307 mg, 452 µmol, 72%).

TLC: R_f = 0.40 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}H-NMR: (400 MHz, $CDCl_3$): δ 7.64-7.70 (m, 4 H, C_{Ar}-H), 7.33-7.42 (m, 6 H, C_{Ar}-H), 5.88-6.11 (m, 4 H, H-15-18), 5.55-5.62 (m, 2 H, H-14, H-19), 4.28 (td, ^3J = 6.3, 3.0 Hz, 1 H, H-13), 3.92-4.01 (m, 2 H, H-23), 3.79 (td, ^3J = 6.6, 3.1 Hz, 1 H, H-21), 3.47-3.50 (m, 2 H, H-12), 2.23-2.32 (m, 2 H, H-20), 1.87 (*virt*. qd, $^3J \approx {}^3J$ = 6.8, 3.1 Hz, 1 H, H-22), 1.20 [s, 9 H, $COC(CH_3)_3$], 1.08 [s, 9 H, $SiC(CH_3)_3$], 0.95 [t, ^3J = 7.8 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.89 (d, ^3J = 6.9 Hz, 3 H, H-44), 0.59 [q, ^3J = 7.8 Hz, 6 H, $Si(CH_2CH_3)_3$]

The analytical data obtained matched those reported in the literature.[30]

Diol 66



66

$C_{34}H_{48}O_5Si$

564.84 g/mol

To a cold (0 °C) solution of silyl ether **9** (2.85 g, 3.60 mmol, 1.00 eq.) in dichloromethane (21 mL) and methanol (21 mL) was added formic acid (2.1 mL). After 2.5 hours, the solution was poured into 50 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane/ethyl acetate 1:0 ⟶ 4:1), diol **66** was obtained as a colorless oil (1.74 g, 86%).

TLC: R_f = 0.20 (pentane:diethyl ether = 1:1) [UV, CAM].

^{1}H-NMR: (400 MHz, $CDCl_3$) δ 7.7-7.6 (m, 4 H, C_{Ar}-H), 7.5-7.3 (m, 6 H, C_{Ar}-H) 6.17-5.92 (m, 4 H, H-15-18), 5.7 (dt, ^3J = 14.7 Hz, ^3J = 7.4 Hz, 1 H, H-19), 5.6 (dd, ^3J = 14.5 Hz, ^3J = 7.0 Hz, 1 H, H-14), 4.28 (*virt.* q, $^3J \approx {}^3J$ = 5.2 Hz, 1 H, H-13), 4.18 (dd, ^2J = 11.0 Hz, ^3J = 7.3 Hz, 1 H, H-23a), 3.95 (dd, ^2J = 11.0 Hz, ^3J = 5.8 Hz, 1 H, H-23b), 3.7-3.6 (m, 1 H, H-21), 2.28 (*virt.* t, $^3J \approx {}^3J$ = 7.0 Hz, 2 H, H-20), 1.89 (m, 1 H, H-22), 1.87 (d, ^3J = 4.3 Hz, C_{21}-OH), 1.81 (t, ^3J = 6.6 Hz, 1 H, C_{12}-OH), 1.21 [s, 9 H, OCOC(CH_3)$_3$], 1.08 [s, 9 H, SiC(CH_3)$_3$], 0.95 (d, ^3J = 6.9 Hz, 3 H, H-44).

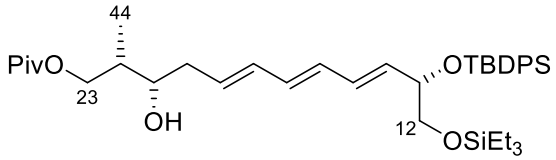
^{13}C-NMR: **(**101 MHz, $CDCl_3$) δ 179.0 [s, O*C*OC(CH_3)], 136.1 (d, C_{Ar}-H), 135.9 (d, C_{Ar}-H), 134.0 (s, C_{Ar}), 133.6 (s, C_{Ar}), 133.4 (d, C=C), 133.1 (d, C=C), 132.4 (d, C=C), 132.2 (d, C-14), 131.0 (d, C-19), 130.9 (d, C=C), 130.0 (d, C_{Ar}-H), 129.9 (d, C_{Ar}-H), 127.9 (d, C_{Ar}-H), 127.7 (d, C_{Ar}-H), 75.0 (d, C-13), 71.3 (d, C-21), 67.0 (t, C-12), 66.8 (t, C-23), 39.0 [s, OCO*C*(CH_3)], 38.2 (t, C-20), 37.6 (d, C-22), 27.4 [q, OCOC(*C*H_3)], 27.2 [q, SiC(*C*H_3)], 19.5 [s, Si*C*(CH_3)], 10.6 (q, C-44).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3441 (br, OH), 3071 (w, sp^2-C–H), 2962 (s, sp^3-C–H), 2933 (s, sp^3-C–H), 2859 (s, sp^3-C–H), 1727 (vs, C=O), 1590 (w), 702 (vs).

Specific rotation: $[\alpha]_D^{20} = +22.0$ (*c* = 1.00, $CHCl_3$).

HRMS (ESI): *m/z* $[C_{34}H_{48}O_5Si + NH_4]^+$ calcd.: 582.3609; found: 582.3605.

Silyl ether 67



67
$C_{40}H_{62}O_5Si_2$
679.10 g/mol

To a cold (0 °C) solution of diol **66** (1.74 g, 3.09 mmol, 1.00 eq.) in dichloromethane (35 mL) was added 2,6-lutidine (538 µL, 497 mg, 4.64 mmol, 1.50 eq.) and triethylsilyl chloride (621 µL, 559 mg, 3.71 mmol, 1.20 eq). After stirring for three hours, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (50 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 1:0 ⟶ 10:1), silyl ether **67** was obtained as a colorless oil (1.80 g, 2.65 mmol, 86%).

TLC: R_f = 0.70 (pentane:diethyl ether = 1:1) [UV, CAM].

^{1}H-NMR: (400 MHz, $CDCl_3$) δ 7.72-7.62 (m, 4 H, C_{Ar}-H), 7.45-7.30 (m, 6 H, C_{Ar}-H), 6.23-5.93 (m, 4 H, H-15-H-18), 5.78-5.57 (m, 2 H, H-14, H-19), 4.25-4.15 (m, 2 H, H-13, H-23a), 3.96 (dd, 1 H, ^2J = 11.0 Hz, ^3J = 5.8 Hz, H-23b), 3.66 (m, 1 H, H-21), 3.54 (dd, ^2J = 9.8 Hz, ^3J = 5.8 Hz, 1 H, H-12a), 3.40 (dd, ^2J = 9.8 Hz, ^3J = 6.9 Hz, 1 H, H-12b), 2.28 (*virt.* t, $^3J \approx {}^3J \approx$ 7.0 Hz, 2 H, H-20), 1.94-1.88 (m, 1 H, H-22), 1.87 (d, ^3J = 4.2 Hz, 1 H, C_{21}-OH)., 1.21 [s, 9 H, $OCOC(CH_3)_3$], 1.07 [s, 9 H, $SiC(CH_3)_3$], 0.96 (d, ^3J = 6.9 Hz, 3 H, H-44), 0.85 [t, ^3J = 8.0 Hz, 9 H, $Si(CH_2C\mathit{H}_3)_3$], 0.45 [q, ^3J = 8.0 Hz, 6 H, $Si(C\mathit{H}_2CH_3)_3$].

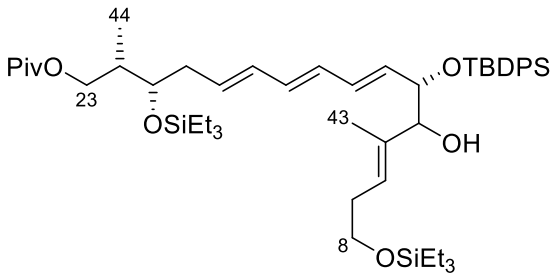
^{13}C-NMR: (100 MHz, $CDCl_3$) δ 178.9 [s, $OCOC(CH_3)_3$], 136.1 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 134.4 (s, C_{Ar}), 134.2 (d, C-14), 134.1 (s, C_{Ar}), 133.7 (d, C=C), 132.1 (d, C=C), 131.6 (d, C=C), 131.0 (d, C=C), 130.2 (d, C-19), 129.7 (C_{Ar}-H), 127.6 (d, C_{Ar}-H), 74.6 (d, C-13), 71.3 (d, C-21), 67.3 (t, C-12), 66.8 (t, C-23), 39.0 [s, $OCOC(CH_3)_3$], 38.2 (t, C-20), 37.5 (d, C-22), 27.4 [q, $OCOC(CH_3)_3$], 27.2 [q, $SiC(CH_3)_3$], 19.5 [s, $SiC(CH_3)_3$], 10.6 (q, C-44), 6.83 [q, $Si(CH_2CH_3)_3$], 4.40 [t, $Si(CH_2CH_3)_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3476 (*br* m, OH), 2957 (s, sp^3-CH), 2932 (s, sp^3-CH), 2876 (s, sp^3-CH), 2858 (s, sp^3-CH), 1729 (s, CO), 1112 (vs, C–O).

Specific rotation: $[\alpha]_D^{20} = +28.0$ (*c* = 1.00, $CHCl_3$).

HRMS (ESI): *m/z* $[C_{40}H_{62}O_5Si_2 + NH_4]^+$ calcd.: 696.4474; found: 696.4470.

C8-C23 fragment 56



56

$C_{51}H_{84}O_6Si_3$
877.48 g/mol

To a solution of alcohol **55** (307 mg, 453 µmol, 1.00 eq.) in dichloromethane (2 mL) was added sodium bicarbonate (152 mg, 1.81 mmol, 4.00 eq.) followed by *Dess-Martin* periodinane (384 mg, 905 µmol, 2.00 eq.). The colorless suspension was stirred for 25 minutes and then poured into a mixture of saturated aqueous sodium thiosulphate solution (5 mL) and saturated aqueous sodium bicarbonate solution (5 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to give the aldehyde as a yellow oil.

In a separate flask, vinyl iodide **29** (591 mg, 1.81 mmol, 4.00 eq.) was dissolved in diethyl ether (1 mL) and cooled to –78 °C. *Tert*-butyllithium (1.9M in pentane, 1.91 mL, 3.62 mmol, 8.00 eq.) was added, and the colorless suspension was stirred for five minutes. Then, dimethyl zinc (1M in heptane, 1.81 mL, 1.81 mmol, 4.00 eq.) was added, and stirring was continued for 30 minutes. The previously prepared aldehyde was added as a solution in diethyl ether (2 mL), and the orange suspension was stirred for two hours at –78 °C. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (10 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under

reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 10:1 ⟶ 1:1), alcohol **56** was obtained as a colorless oil (187 mg, 47%).

TLC: R_f = 0.67 (pentane:diethyl ether = 4:1) [UV, CAM].

Diastereomeric ratio: d.r. ≈ 8:1.

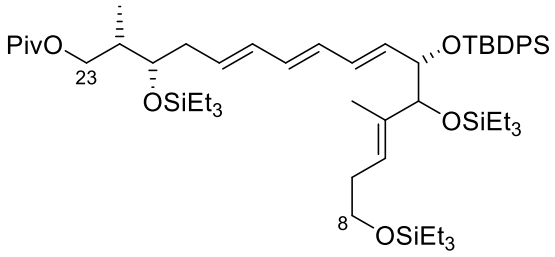
^{1}H-NMR: (300 MHz, $CDCl_3$) δ 7.69-7.59 (m, 4 H, C_{ar}-H), 7.46-7.32 (m, 6 H, C_{ar}-H), 6.13-5.80 (m, 4 H, H-15-18), 5.56 (m, 2 H, H-14, H-19), 5.41-5.31 (m, 1 H, H-10), 4.18 (dd, ^3J = 7.3 Hz, ^3J = 4.6 Hz, 1 H, H-13), 3.97 (dd, ^3J = 6.6 Hz, ^2J = 2.0 Hz, 2 H, H-23a/b), 3.92 (s, 1 H, H-12), 3.80 (td, ^3J = 6.7 Hz, ^3J = 3.2 Hz, 1 H, H-21), 3.54-3.48 (m, 2 H, H-8), 2.32-2.18 (m, 4 H, H-9, H-20), 1.88 (qtd, ^3J = 10.2 Hz, ^3J = 6.6 Hz, ^3J = 3.2 Hz, 1 H, H-22), 1.36-1.34 (m, 3 H, H-43), 1.21-1.18 [m, 9 H, $OCOC(CH_3)_3$], 1.08-1.05 [m, 9 H, $SiC(CH_3)_3$], 1.00-0.90 [m, 18 H, $Si(CH_2C\mathit{H}_3)_3$], 0.89-0.88 (m, 3 H, H-44), 0.64-0.55 [m, 12 H, $Si(C\mathit{H}_2CH_3)_3$].

^{13}C-NMR: (126 MHz, $CDCl_3$) δ 178.6 [s, $OCOC(CH_3)$], 136.1 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 134.7 (s, C-11), 133.8 (s, C_{Ar}), 133.6 (s, C_{Ar}), 133.3 (d, C=C), 133.2 (d, C=C), 132.7 (d, C=C), 131.2 (d, C-14)*, 130.5 (d, C-19)*, 130.0 (d, C_{Ar}-H), 129.8 (d, C_{Ar}-H), 127.8 (d, C_{Ar}-H), 127.6 (d, C_{Ar}-H), 123.1 (d, C-10), 79.2 (d, C-12), 76.1 (d, C-13), 72.2 (d, C-21), 66.7 (t, C-23), 62.4 (t, C-8), 38.9 [s, $OCOC(CH_3)$], 38.6 (t, C-20), 37.2 (d, C-22), 31.6 (t, C-9), 27.4 [q, $OCOC(CH_3)$], 27.2 [q, $SiC(CH_3)_3$], 19.5 [s, $SiC(CH_3)_3$], 13.0 (q, C-43), 10.6 (q, C-44), 7.1 [q, $C_{21}OSi(CH_2CH_3)_3$], 6.9 [q, $C_8OSi(CH_2CH_3)_3$], 5.2 [t, $C_{21}OSi(CH_2CH_3)_3$], 4.5 [t, $C_8OSi(CH_2CH_3)_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3478 (br w, OH), 2956 (s, sp^3-C–H), 2934 (s, sp^2-C–H), 2911 (s, sp^3-C–H), 2876 (s, sp^3-C–H), 1730 (s, C=O), 1460 (m), 1428 (m), 1383 (m), 1363 (m), 1154 (s), 1111 (vs), 998 (vs), 823 (m), 740 (vs), 702 (vs).

HRMS (ESI): *m/z* $[C_{51}H_{84}O_6Si_3 + NH_4]^+$ calcd.: 894.5914; found: 894.5915.

Silyl protected C8-C23 fragment 57



57

$C_{57}H_{98}O_6Si_4$
991.75 g/mol

To a solution of alcohol **56** (187 mg, 213 µmol, 1.00 eq.) in dichloromethane (5 mL) was added imidazole (36.2 mg, 531 µmol, 2.50 eq.), 4-(dimethylamino)-pyridine (2.60 mg, 21.0 µmol, 0.100 eq.) and triethylsilyl chloride (71.0 µL, 64.1 mg, 425 µmol, 2.00 eq). After stirring for three hours at room temperature, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (5 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 20:1), silyl ether **57** was obtained as a colorless oil (141 mg, 142 µmol, 67%).

TLC: R_f = 0.95 (pentane:diethyl ether = 4:1) [UV, CAM].

Diastereomeric ratio: d.r. ≈ 8:1.

^{1}H-NMR: (500 MHz, $CDCl_3$) δ 7.72-7.57 (m, 4 H, C_{Ar}-H), 7.43-7.28 (m, 6 H, C_{Ar}-H), 6.05-5.96 (m, 1 H, C=C), 5.94-5.85 (m, 2 H, C=C), 5.62-5.44 (m, 3 H, H-14, H-19, C=C), 5.32 (t, ^3J = 7.2 Hz, 1 H, H-10), 4.01-3.93 (m, 3 H, H-23, H-13), 3.86 (d, ^3J = 6.5 Hz, 1 H, H-12), 3.78 (td, ^3J = 6.6 Hz, 3.0 Hz, 1 H, H-21), 3.55 (t, ^3J = 6.9 Hz, 2 H, H-8), 2.31-2.17 (m, 3 H, H-20, H-9), 1.87 (dt, ^3J = 13.6 Hz, ^3J = 6.9 Hz, ^3J = 3.0 Hz, 1 H), 1.40 (s, 3 H, H-43), 1.21 [s, 9 H, $OCOC(CH_3)_3$], 1.00 [m, 9 H, $SiC(CH_3)_3$], 0.98-0.92 [m, 18 H, C_8/C_{21}-$OSi(CH_2CH_3)_3$], 0.89 (d, ^3J = 6.9 Hz, 3 H, H-44), 0.85 (t, ^3J = 8.0 Hz, 9 H, C_{12}-$OSi(CH_2CH_3)_3$), 0.62-0.56 [m, 12 H, C_8/C_{21}-$OSi(CH_2CH_3)_3$], 0.53-0.45 [m, 6 H, C_{12}-$OSi(CH_2CH_3)_3$].

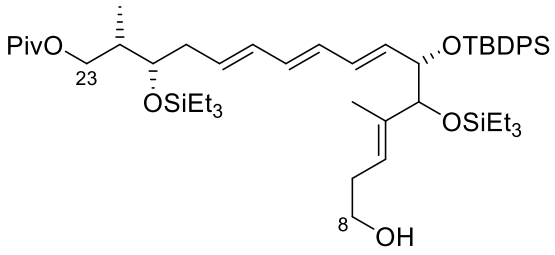
^{13}C-NMR: (126 MHz, $CDCl_3$) δ 178.6 [s, $OCOC(CH_3)$], 137.5 (s, C-11), 136.3 (d, C_{Ar}-H), 136.3 (d, C_{Ar}-H), 134.5 (d, C_{Ar}-H), 134.2 (d, C_{Ar}-H), 134.1 (d, C-14), 133.0 (d, C=C), 132.7 (d, C=C), 132.2 (d, C=C), 131.0 (d, C=C), 130.4 (d, C-19), 129.5 (d, C_{Ar}-H), 129.4 (d, C_{Ar}-H), 127.4 (d, C_{Ar}-H), 127.3 (d, C_{Ar}-H), 124.3 (d, C-10), 82.2 (d, C-12), 76.6 (d, C-13), 72.3 (d, C-

21), 66.7 (t, C-23), 62.4 (t, C-8), 38.9 [s, OCO*C*(CH_3)], 38.6 (t, C-20), 37.3 (d, C-22), 31.9 (t, C-9), 27.4 [q, OCOC(*C*H_3)], 27.2 [q, SiC(*C*H_3)$_3$], 19.5 [s, Si*C*(CH_3)$_3$], 12.0 (q, C-43), 10.6 (q, C-44), 7.1 [C_{21}OSi(CH_2*C*H_3)$_3$], 7.0 [q, C_8/C_{12}OSi(CH_2*C*H_3)$_3$], 5.2 [t, C_{21}OSi(*C*$H_2$$CH_3$)$_3$], 4.9 [t, C_{12}OSi(*C*$H_2$$CH_3$)$_3$], 4.6 [t, C_8OSi(*C*$H_2$$CH_3$)$_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2956 (s, sp^3-C–H), 2877(s, sp^3-C–H), 1731 (s, C=O), 1460 (m, C–H), 1414 (m), 1154 (s, C–O), 1105 (vs, C–O), 1005 (s, C–O), 822 (m, C=C), 739 (vs, C–H), 702 (s)

HRMS (ESI): *m/z* $[C_{57}H_{98}O_6Si_4 + NH_4]^+$ calcd.: 1008.6778; found: 1008.6762.

Primary alcohol 58



58

$C_{51}H_{84}O_6Si_3$
877.48 g/mol

To a cold (–20 °C) solution of silyl ether **57** (133 mg, 134 µmol, 1.00 eq.) in dichloromethane (9 mL) and methanol (900 µL) was added pyridinium *para*-toluenesulfonate (106 mg, 421 µmol, 3.00 eq.). After three hours, the reaction was quenched by the addition of saturated aqueous sodium bicarbonate solution. The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 4:1), alcohol **58** was obtained as a colorless oil (88.4 mg, 101 µmol, 75%).

TLC: R_f = 0.23 (pentane:diethyl ether = 4:1) [UV, CAM].

Diastereomeric ratio: d.r. ≈ 8:1

^{1}H-NMR: (500 MHz, $CDCl_3$) δ 7.74-7.55 (m, 4 H, C_{Ar}-H), 7.45-7.28 (m, 6 H, C_{Ar}-H), 6.06-5.97 (m, 1 H, C=C), 5.97-5.86 (m, 2 H, C=C), 5.63-5.46 (m, 3 H, H-14, H-19, C=C), 5.33 (t, ^{3}J = 7.5 Hz, 1 H, H-10), 4.04-3.94 (m, 3 H, H-23, H-13), 3.91 (d, ^{3}J = 6.1 Hz, 1 H, H-12), 3.79 (td, ^{3}J = 6.6 Hz, ^{3}J = 3.0 Hz, 1 H, H-21), 3.64-3.54 (m, ^{3}J = 6.2 Hz, 2 H, H-8), 2.35-2.16 (m, 4 H, H-9, H-20), 1.87 (ddq, ^{3}J = 13.5 Hz, ^{3}J = 7.1 Hz, ^{3}J = 3.0 Hz, 1 H, H-22), 1.42 (s, 3 H, H-43), 1.20 [s, 9 H, $OCOC(CH_3)_3$], 1.01 [s, 9 H, $SiC(CH_3)_3$], 0.95 [t, ^{3}J = 7.9 Hz, 9 H, C_{21}-$OSi(CH_2CH_3)_3$], 0.89 (d, ^{3}J = 7.1 Hz, 3 H, H-44), 0.86 (t, ^{3}J = 7.9 Hz, 9 H, C_{12}-$OSi(CH_2CH_3)_3$], 0.58 (q, ^{3}J = 7.9 Hz, 6 H, C_{21}-$OSi(CH_2CH_3)_3$], 0.50 (q, ^{3}J = 7.9 Hz, 6 H, C_{12}-$OSi(CH_2CH_3)_3$].

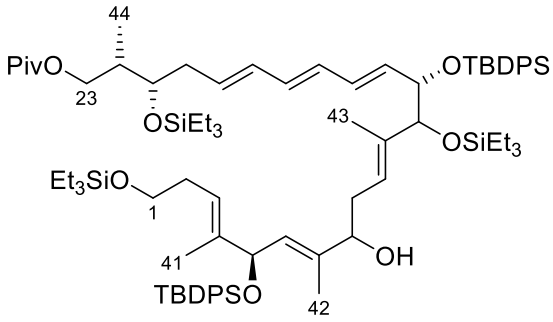
^{13}C-NMR: (126 MHz, $CDCl_3$) δ 178.6 [s, $OCOC(CH_3)$], 138.9 (d, C-11), 136.3 (d, C_{Ar}-H), 136.2 (d, C_{Ar}-H), 134.3 (s, C_{Ar}), 134.3 (s, C_{Ar}), 133.7 (d, C-14), 132.9 (d, C=C), 132.7 (d, C=C), 132.4 (d, C=C), 130.9 (d, C=C), 130.6 (d, C-19), 129.6 (d, C_{Ar}-H), 129.5 (d, C_{Ar}-H), 127.4 (d, C_{Ar}-H), 127.4 (d, C_{Ar}-H), 123.7 (d, C-10), 82.0 (d, C-12), 76.7 (d, C-13), 72.2 (d, C-21), 66.7 (t, C-23), 62.4 (t, C-8), 38.9 [s, $OCOC(CH_3)$], 38.5 (t, C-20), 37.3 (d, C-22), 31.5 (t, C-9), 27.4 [q, $OCOC(CH_3)$], 27.2 [q, $SiC(CH_3)_3$], 19.5 [s, $SiC(CH_3)_3$], 12.3 (q, C-43), 10.7 (q, C-44), 7.1 [q, C_{21}-$OSi(CH_2CH_3)_3$], 7.0 [q, C_{12}-$OSi(CH_2CH_3)_3$], 5.2 [t, C_{21}-$OSi(CH_2CH_3)_3$], 5.0 [t, C_{12}-$OSi(CH_2CH_3)_3$].

IR (ATR):): $\tilde{\nu}$ (cm^{-1}) = 3447 (w, b, O–H), 3072 (w, sp^2-C–H), 2956 (s, sp^3-C–H), 2876 (s, sp^3-C–H), 1731 (s, C=O), 1590 (w, C=C), 1460 (m, C–H), 1427 (m, C–H), 1238 (m), 1154 (s, C–O), 1111 (vs, C–O), 1050 (s, C–O), 997 (vs, C=C), 822 (m, C=C), 738 (vs, C–H), 701 (vs).

HRMS (ESI): *m/z* $[C_{51}H_{84}O_6Si_3 + NH_4]^+$ calcd.: 894.5914; found: 894.5915.

11.3. C1-C23 fragment

C1-C23 fragment 53



53

$C_{82}H_{130}O_8Si_5$

1384.36 g/mol

To a solution of alcohol **58** (178 mg, 203 µmol, 1.00 eq.) in dichloromethane (5 mL) was added sodium bicarbonate (68.1 mg, 810 µmol, 4.00 eq.) followed by *Dess-Martin* periodinane (172 mg, 405 µmol, 2.00 eq.). The colorless suspension was stirred for 40 minutes and then poured into a mixture of saturated aqueous sodium thiosulphate solution (5 mL) and saturated aqueous sodium bicarbonate solution (5 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to give the aldehyde as a yellow oil.

In a separate flask, vinyl iodide **36** (257 mg, 405 µmol, 2.00 eq.) was dissolved in diethyl ether (1 mL) and cooled to –78 °C. *Tert*-butyllithium (1.9M in pentane, 426 µL, 810 µmol, 4.00 eq.) was added, and the colorless suspension was stirred for ten minutes. Then, dimethyl zinc (1M in heptane, 425 µL, 425 µmol, 2.10 eq.) was added, and stirring was continued for 30 minutes. The previously prepared aldehyde was added as a solution in diethyl ether (2 mL), and the orange suspension was stirred for 3.5 hours at –78 °C. The reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (10 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 20:1 ⟶ 4:1), alcohol **53** was obtained as a colorless oil (194 mg, 69%).

TLC: R_f = 0.76 (pentane:diethyl ether = 4:1) [UV, CAM].

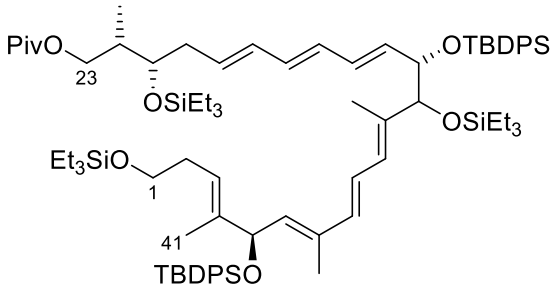
^{1}H-NMR: (500 MHz, C_6D_6) δ 7.88-7.71 (m, 8 H, C_{Ar}-H), 7.31-7.19 (m, 12 H, C_{Ar}-H), 6.07-5.98 (m, 3 H, alkene), 5.77 (d, ^{3}J = 7.8 Hz, 0.5 H, H-6$_A$), 5.70 (d, ^{3}J = 7.8 Hz, 0.5 H, H-6$_B$), 5.66 (t, ^{3}J = 4.3 Hz, 1 H, H-3), 5.48 (dd, ^{3}J = 14.3, 7.1 Hz, 1 H, H-19), 5.01-4.91 (m, 1 H, H-5), 4.37-4.30 (m, 1 H, H-13), 4.15 (dd, ^{3}J = 13.3, 6.1 Hz, 1 H, H-12), 4.11 (d, ^{3}J = 6.7 Hz, 2 H, H-23), 3.88 (d, ^{3}J = 6.7 Hz, 1 H, H-8), 3.83-3.78 (m, 1 H, H-21), 3.69-3.56 (m, 2 H, H-1), 2.43-2.32 (m, 2 H, H-2), 2.27-2.20 (m, 4 H, H-9, H-20), 1.91-1.87 (m, 1 H, H-22), 1.77 (s, 3 H, H-41), 1.30 (s, 3 H, H-42), 1.25-1.19 [m, 27 H, $SiC(CH_3)_3$, $OCOC(CH_3)_3$], 1.06-0.98 [m, 27 H, $Si(CH_2CH_3)_3$], 0.90 (d, ^{3}J = 6.9 Hz, 3 H, H-44), 0.70-0.55 [m, 18 H, $Si(CH_2CH_3)_3$].

^{13}C-NMR: (126 MHz, C_6D_6) δ 177.6 [s, $OCOC(CH_3)_3$], 128.5 (d, C-6$_A$), 127.5 (d, C-6$_B$), 121.6 (d, C-3$_A$), 121.5 (d, C-3$_B$), 82.7 (C-12$_A$), 82.61 (C-12$_B$), 77.5 (C-13$_A$), 77.2 (C-13$_B$), 76.9 (C-8$_A$), 76.6 (C-8$_B$), 75.7 (C-5$_A$), 75.5 (C-5$_B$), 72.5 (d, C-21), 66.7 (t, C-23), 62.7 (t, C-1), 38.9 (Piv, C-9), 37.5 (d, C-22), 34.4 (t, C-20), 32.0 (t, C-2), 27.4 (Piv, TBDPS), 10.5 (q, C-44), 7.26 (q, TES-CH_3), 5.54 (t, TES-CH_2).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3499 (w, OH), 2955 (m) 2934 (m) 2910 (m) (C_{sp3}-H), 1731 (m, CO), 1110 (vs).

HRMS (ESI): *m/z* $[C_{82}H_{130}O_8Si_5+NH_4]^+$ calcd.: 1400.8950; found: 1400.8952.

Triene 52



52

$C_{82}H_{128}O_7Si_5$
1366.34 g/mol

To a solution of alcohol **53** (11.3 mg, 8.16 µmol, 1.00 eq.) in toluene (1 mL) was added *Burgess* reagent (17 mg, 71.4 µmol, 8.75 eq.). The solution was warmed to 50 °C and stirred for two hours. The reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (5 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 100:1 ⟶ 50:1), triene **52** was obtained as a colorless oil (5.0 mg, 3.66 µmol, 55%).

TLC: R_f = 0.82 (pentane:diethyl ether = 10:1) [UV, CAM].

Diastereomeric ratio: d.r. ≈ 3.6:1.

^{1}H-NMR: (500 MHz, C_6D_6) δ 7.87 - 7.78 (m, 8 H, C_{Ar}–H), 7.28-7.20 (m, 12 H, C_{Ar}–H), 6.50 - 6.41 (m, 1 H, H-9), 6.31 - 6.24 (m, 2 H, H-8, H-10), 6.08 – 5.96 (m, 3 H, H-18, H-17, H-16), 5.92 (dd, ^3J = 15.0 Hz, ^3J = 9.0 Hz, 1 H, H-15), 5.85 (d, ^3J = 7.7 Hz, 1 H, H-14), 5.81 (d, ^3J = 8.0 Hz, 1 H, H-6), 5.59 (t, ^3J = 7.1 Hz, 1 H, H-3), 5.53 - 5.47 (m, 1 H, H-19), 5.04 (d, ^3J = 8.9 Hz, 1 H, H-5), 4.38 - 4.33 (m, 1 H, H-13), 4.20 (d, ^3J = 6.0 Hz, 1 H, H-12), 4.15-4.10 (m, 2 H, H-23), 3.85 - 3.78 (m, 1 H, H-21), 3.61 - 3.55 (m, 2 H, H-1), 2.31 (q, ^3J = 7.0 Hz, 2 H, H-2), 2.27 - 2.22 (m, 2 H, H-20), 1.94 - 1.89 (m, 1 H, H-22), 1.73 (s, 3 H, H-43), 1.72 (s, 3 H, H-41), 1.47 (d, ^3J = 2.2 Hz, 3 H, H-42), 1.23 [s, 9 H, OCOC$(CH_3)_3$], 1.21 [s, 18 H, SiC$(CH_3)_3$], 1.05 – 0.98 [m, 27 H, Si$(CH_2CH_3)_3$], 0.90 (d, ^3J = 6.9 Hz, 3 H, H-44), 0.67 - 0.59 [m, 18 H, Si$(CH_2CH_3)_3$].

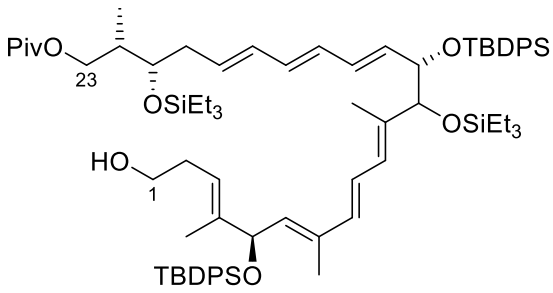
^{13}C-NMR: (126 MHz, C_6D_6) δ 177.6 [s, O*C*OC(CH_3)], 138.6 (d, C-4*), 138.4 (d, C-11*), 137.5 (d, C-8), 136.8 (d, C_{Ar}-H), 136.7 (d, C_{Ar}-H), 136.4 (d, C_{Ar}-H), 134.5 (d, C-6), 134.0 (s, C-7),

133.3 (d, C-17*), 133.3 (d, C-16*), 133.1 (d, C-15*), 131.2 (d, C-18), 130.7 (d, C-19), 130.0 - 129.8 (m, C_{Ar}-H), 128.9 (d, C-10), 124.2 (d, C-9), 122.0 (d, C-3), 82.6 (d, C-12), 77.8 (d, C-13), 76.1 (d, C-5), 72.5 (d, C-21), 66.8 (t, C-23), 62.7 (t, C-1), 38.9 [s, OCO*C*(CH_3), C-20], 37.6 (d, C-22), 32.0 (t, C-2), 27.4 [q, SiC(*C*H_3)$_3$], 27.3 [q, OCOC(*C*H_3)], 19.7 [s, Si*C*(CH_3)$_3$], 13.1 (q, C-41*), 12.9 (q, C-42), 12.6 (C-43*), 10.6 (d, C-22), 7.3 - 7.1 [q, Si(CH_2*C*H_3)$_3$], 5.5 [t, C_{12}-OSi(*C*$H_2$$CH_3$)$_3$], 5.4 [t, C_{21}-OSi(*C*$H_2$$CH_3$)$_3$], 5.0 [t, C_1-OSi(*C*$H_2$$CH_3$)$_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2956 (vs, sp^3-C–H), 2876 (s, sp^3-C–H), 1731 (m, C=O), 1460 (m, C–H), 1428 (m, C–H), 1389 (m), 1362 (w), 1282 (w), 1151 (m, C–O), 1111 (vs, C–O), 1004 (s, C–O), 962 (m), 822 (m, C=C), 739 (s, C–H), 701 (vs).

HRMS (ESI): *m/z* [$C_{82}H_{128}O_7Si_5 + NH_4$]$^+$ calcd.: 1382.8844; found: 1382.8843.

Alcohol 54



54

$C_{76}H_{114}O_7Si_4$

1252.08 g/mol

In a polyethylene flask, silyl ether **52** (5.80 mg, 4.24 µmol, 1.00 eq.) was dissolved in diethyl ether (800 µL) and THF (800 µL) and cooled to 0 °C. Pyridine (10 µL) and HF · pyridine complex (10 µL, 357 µmol, 84.0 eq.) were added, and the colorless solution was stirred for four hours. The reaction was quenched by the addition of saturated aqueous sodium bicarbonate solution (5 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 2:1), alcohol **54** was obtained as a colorless oil (3.30 mg, 2.64 µmol, 62%).

TLC: R_f = 0.40 (pentane:diethyl ether = 2:1) [UV, CAM].

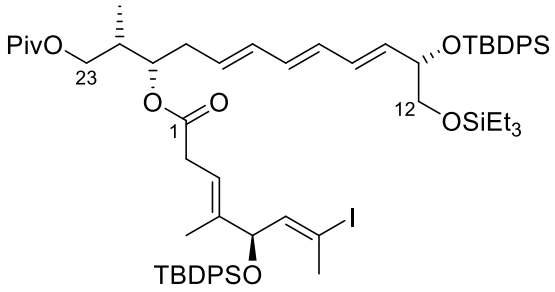
^{1}H-NMR: (500 MHz, C_6D_6) δ 7.86 - 7.78 (m, 8 H, C_{Ar}-H), 7.29 - 7.19 (m, 12 H, C_{Ar}-H), 6.48 (dd, ^{3}J = 15.1 Hz, ^{3}J = 11.0 Hz, 1 H, H-9), 6.34 - 6.23 (m, 2 H, H-8, H-10), 6.07 – 5.98 (m, 3 H, H-16-18), 5.93 (dd, ^{3}J = 15.5 Hz, ^{3}J = 9.1 Hz, 1 H, H-15), 5.87 - 5.76 (m, 2 H, H-6, H-14), 5.54 - 5.45 (m, 1 H, H-19), 5.42 (t, ^{3}J = 7.6 Hz, 1 H, H-3), 5.01 (d, ^{3}J = 8.8 Hz, 1 H, H-5), 4.39 - 4.34 (m, H-13), 4.24 - 4.18 (m, 1 H, H-12), 4.17 - 4.09 (m, 1 H, H-23), 3.86 - 3.77 (m, 1 H, H-21), 3.38 - 3.31 (m, 2 H, H-1), 2.29 - 2.21 (m, 2 H, H-20), 2.13 - 2.00 (m, 2 H, H-2), 1.96 - 1.87 (m, 1 H, H-22), 1.73 (s, 3 H, H-43), 1.65 (s, 3 H, H-41), 1.48 (s, 3 H, H-42), 1.23-1.18 [m, 27 H, $SiC(CH_3)_3$, $OCOC(CH_3)_3$], 1.03-0.99 [m, 18 H, $Si(CH_2C\mathit{H}_3)_3$], 0.90 (d, ^{3}J = 7.0 Hz, 3 H, H-44), 0.68 - 0.57 [m, 12 H, $Si(C\mathit{H}_2CH_3)_3$].

^{13}C-NMR: (126 MHz, C_6D_6) δ 177.6 [s, $OCOC(CH_3)$], 139.4 (s, C-4), 138.5 (s, C-11), 137.4 (d, C-8), 136.8 (d, C_{Ar}-H), 136.7 (d, C_{Ar}-H), 136.4 (d, C_{Ar}-H), 136.3 (d, C_{Ar}-H), 134.5 (d, C-6), 134.4 (d, C-14), 133.3 (d, C-15*), 133.3 (d, C-16*), 133.1 (d, C-17*), 131.2 (d, C-18), 130.8 (d, C-19), 130.0 (d, C_{Ar}-H), 129.9 (d, C_{Ar}-H), 128.8 (d, C-10), 124.3 (d, C-9), 121.8 (d, C-3), 82.6 (d, C-12), 77.9 (d, C-13), 76.1 (d, C-5), 72.5 (d, C-21), 66.8 (t, C-23), 62.2 (t, C-1), 38.9 [m, $OCO\mathit{C}(CH_3)$, C-20], 37.5 (d, C-22), 31.6 (t, C-2), 27.4 [q, $SiC(\mathit{C}H_3)_3$], 27.2 [q, $OCOC(\mathit{C}H_3)$], 19.7 [s, $Si\mathit{C}(CH_3)_3$], 13.1 (q, C-43), 12.9 (q, C-42), 12.5 (q, C-41), 10.6 (q, C-44), 7.3 [q, $Si(CH_2\mathit{C}H_3)_3$], 5.5 [t, C_{12}-$OSi(\mathit{C}H_2CH_3)_3$], 5.3 [t, C_{21}-$OSi(\mathit{C}H_2CH_3)_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3404 (w, b, O–H), 3071 (w, sp^2-C–H), 2956 (s, sp^3-C–H), 2877 (s, sp^3-C–H), 1731 (m, C=O), 1590 (w, C=C), 1461 (w, C–H), 1427 (m, C–H), 1390 (w), 1283 (w), 1111 (vs, C–O), 1050 (s, C–O), 998 (s, C–O), 822 (m, C=C), 739 (s, C–H), 702 (vs).

HRMS (ESI): *m/z* $[C_{76}H_{114}O_7Si_4+NH_4]^+$ calcd.: 1268.7979; found: 1268.7991.

Ester 68



68
$C_{65}H_{91}IO_7Si_3$
1195.60 g/mol

To a cold (0 °C) solution of carboxylic acid **38** (1.02 g, 1.91 mmol, 1.30 eq.) in toluene (20 mL) was added triethylamine (572 µL, 417 mg, 4.12 mmol, 2.80 eq.), followed by 2,4,6-trichlorobenzoyl chloride (311 µL, 485 mg, 1.99 mmol, 1.35 eq.). After stirring for 20 minutes, a solution of alcohol **67** (1.00 g, 1.47 mmol, 1.00 eq.) in toluene (20 mL) and 4-(dimethylamino)-pyridine (180 mg, 1.47 mmol, 1.00 eq.) was added. While stirring for 45 minutes at 0 °C, the solution turned into an orange suspension. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (50 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 1:0 ⟶ 15:1), ester **68** was obtained as a colorless oil (1.51 g, 1.26 mmol, 86%).

TLC: R_f = 0.71 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}H-NMR: (500 MHz, $CDCl_3$) δ 7.71-7.61 (m, 8 H, C_{Ar}-H), 7.45-7.28 (m, 12 H, C_{Ar}-H), 6.16-6.12 (m, 1 H, H-6), 6.11-6.00 (m, 4 H, H-15-18), 5.72-5.66 (m, 1 H, H-14), 5.64-5.57 (m, 1 H, H-3), 5.57-5.49 (m, 1 H, H-19), 5.00 (td, ^3J = 6.7, 4.1 Hz, 1 H, H-21), 4.57 (d, ^3J = 8.8 Hz, 1 H, H-5), 4.22 (*virt.* q, $^3J \approx {}^3J \approx$ 6.3 Hz, 1 H, H-13), 3.92 (d, ^3J = 6.4 Hz, 2 H, H-23), 3.52 (dd, ^2J = 9.9 Hz, ^3J = 5.7 Hz, 1 H, H-12a), 3.39 (dd, ^2J = 9.9 Hz, ^3J = 6.7 Hz, 1 H, H-12b), 3.09-2.94 (m, 2 H, H-2), 2.46-2.29 (m, 2 H, H-20), 2.06 (qd, ^3J = 6.8 Hz, ^3J = 4.4 Hz, 1 H, H-22), 1.82 (d, ^4J = 1.6 Hz, 3 H, H-41), 1.59 (s, 3 H, H-42), 1.20 [s, 9 H, $OCOC(CH_3)_3$], 1.07 [s, 9 H, $SiC(CH_3)_3$], 1.05 [s, 9 H, $SiC(CH_3)_3$], 0.95 (d, ^3J = 6.9 Hz, 3 H, H-43), 0.85 [t, ^3J = 8.0 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.45 [q, ^3J = 8.0 Hz, 6 H, $Si(CH_2CH_3)_3$].

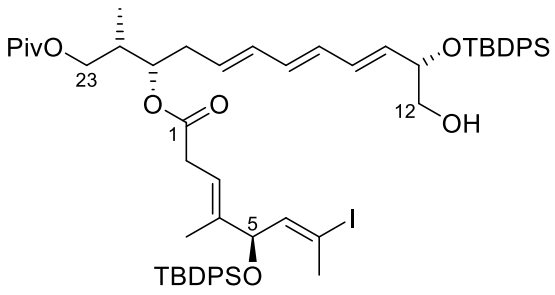
^{13}C-NMR: (101 MHz, $CDCl_3$) δ 178.5 [s, O*C*OC(CH_3)], 171.1 (s, C-1), 142.2 (d, C-6), 139.1 (s, C-4), 136.1 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 134.4 (d, C-14), 134.2 (s, C_{Ar}), 134.1 (s, C_{Ar}), 133.6 (s, C_{Ar}), 133.5 (d, C-18*), 132.1 (d, C-17*), 131.7 (d, C-16*), 131.0 (d, C-15*), 129.8 (d, C_{Ar}-H), 129.7 (d, C_{Ar}-H), 128.6 (d, C-19), 127.7 (d, C_{Ar}-H), 127.7 (d, C_{Ar}-H), 127.6 (d, C_{Ar}-H), 117.1 (d, C-3), 96.6 (s, C-7), 75.3 (d, C-5), 74.6 (d, C-13), 73.4 (d, C-21), 67.3 (t, C-12), 65.8 (t, C-23), 39.0 [s, OCO*C*(CH_3)], 35.5 (d, C-22), 35.3 (t, C-20), 33.7 (t, C-2), 28.0 (q, C-41), 27.4 [q, OCOC(*C*H_3)], 27.2 [q, SiC(*C*H_3)$_3$], 27.0 [q, SiC(*C*H_3)$_3$], 19.5 [s, Si*C*(CH_3)$_3$], 12.7 (q, C-42), 11.4 (q, C-44), 6.8 [q, Si(CH_2*C*H_3)$_3$], 4.4 [t, Si(*C*H_2CH$_3$)$_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3072 (w, sp^2-C–H), 3048 (w, sp^2-CH), 2957 (m, sp^3-CH), 2932 (m, sp^3-CH), 1732 (s, C=O), 1637 (m, *ν*(-C=C)), 1589 (m, C=C), 1472 (m, C–H), 1112 (s, C–O), 1042 (s, C–O), 998 (m), 940 (m), 702 (vs).

Specific rotation: $[\alpha]_D^{20} = -6.00$ (*c* = 1.00, $CHCl_3$).

HRMS (ESI): no ionization possible.

Alcohol 69



69
$C_{59}H_{77}IO_7Si_2$
1081.33 g/mol

To a cold (0 °C) solution of silyl ether **68** (1.58 g, 1.32 mmol, 1.00 eq.) in THF (15 mL) was added HF · pyridine complex (30 wt.% HF, 700 µL). After three hours, the solution was poured into 50 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 1:0 ⟶ 4:1), alcohol **69** was obtained as a yellowish oil (1.00 g, 70%).

TLC: R_f = 0.19 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}H-NMR: (500 MHz, $CDCl_3$) δ 7.69-7.59 (m, 4 H, C_{Ar}-H), 7.43-7.31 (m, 6 H, C_{Ar}-H), 6.13 (dq, ^3J = 8.8 Hz, ^4J = 1.5 Hz, 1 H, H-6), 6.07-5.91 (m, 4 H, H-15-18), 5.65-5.53 (m, 3 H, H-3, H-14, H-19), 5.00 (td, ^3J = 6.6 Hz, ^3J = 4.1 Hz, 1 H, H-21), 4.56 (d, ^3J = 8.8 Hz, 1 H, H-5), 4.28 (*virt.* q, $^3J \approx {}^3J \approx$ 5.6 Hz, 1 H, H-13), 3.92 (d, ^3J = 6.4 Hz, 2 H, H-23), 3.51-3.44 (m, 2 H, H-12), 3.09-2.95 (m, 2 H, H-2), 2.45-2.32 (m, 2 H, H-20), 2.06 (q, ^3J = 3.8 Hz, 1 H, H-22), 1.81 (d, ^4J = 1.5 Hz, 3 H, H-42), 1.57 (s, 3 H, H-41), 1.19 [s, 9 H, $OCOC(CH_3)_3$], 1.07 [s, 9 H, $SiC(CH_3)_3$], 1.04 [s, 9 H, $SiC(CH_3)_3$], 0.95 (d, ^3J = 6.9 Hz, 3 H, H-44).

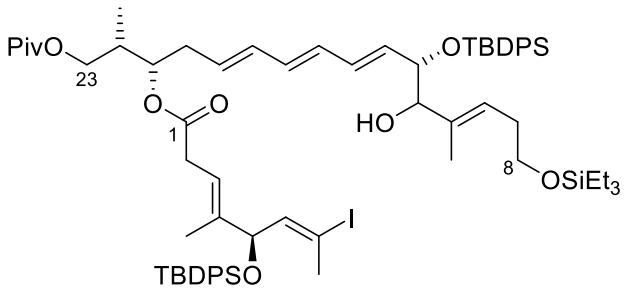
^{13}C-NMR: (126 MHz, $CDCl_3$) δ 178.5 [s, O*C*OC(CH_3)], 171.1 (s, C-1), 142.1 (d, C-6), 139.1 (s, C-4), 136.1 (d, C_{Ar}-H), 135.9 (d, C_{Ar}-H), 135.9 (d, C_{Ar}-H), 133.9 (s, C_{Ar}), 133.6 (s, C_{Ar}), 133.5 (s, C_{Ar}), 133.5 (s, C_{Ar}), 133.3 (d, C-18), 133.0 (d, C-16*), 132.3 (d, C-15), 132.2 (d, C-14), 130.9 (d, C-17*), 130.0 (d, C_{Ar}-H), 129.9 (d, C_{Ar}-H), 129.8 (d, C_{Ar}-H), 129.4 (d, C-19), 127.9 (d, C_{Ar}-H), 127.7 (d, C_{Ar}-H), 127.7 (d, C_{Ar}-H), 117.0 (d, C-3), 96.7 (s, C-7), 75.2 (d, C-5), 75.0 (d, C-13), 73.2 (d, C-21), 67.0 (t, C-12), 65.8 (t, C-23), 39.0 [s, OCO*C*(CH_3)], 35.5 (d, C-22), 33.7 (t, C-2), 27.9 (q, C-41), 27.3 [q, OCOC(*C*H_3)], 27.2 [q, SiC(*C*H_3)$_3$], 27.0 [q, SiC(*C*H_3)$_3$], 19.5 [s, Si*C*(CH_3)$_3$], 12.7 (q, C-42), 11.4 (q, C-44).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3454 (*br* s, OH), 3072 (w, sp^2-CH), 2959 (m, sp^3-CH), 2931 (m, sp^3-CH), 2858 (m, sp^3-CH), 1728 (vs, CO), 1428 (m), 1158 (s), 1112 (vs, C-O), 703 (vs).

Specific rotation: $[\alpha]_D^{20} = +6.00$ (*c* = 1.00, $CHCl_3$).

HRMS (ESI): *m/z* $[C_{59}H_{77}IO_7Si_2 + Na]^+$ calcd.: 1103.4144; found: 1103.4143.

Alcohol 70



70

$C_{70}H_{99}IO_8Si_3$

1279.71 g/mol

To a solution of primary alcohol **69** (36.7 mg, 34.0 µmol, 1.00 eq.) in dichloromethane (2 mL) was added sodium bicarbonate (17.1 mg, 204 µmol, 6.00 eq.) and *Dess-Martin* periodinane (43.2 mg, 102 µmol, 3.00 eq.). After 45 minutes, the yellow suspension was poured into a mixture of 5 mL saturated aqueous sodium bicarbonate solution and 5 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the aldehyde as a yellow oil. Chromium-(II)-chloride (26.9 mg, 219 µmol, 6.40 eq.) and nickel-(II)-chloride (0.27 mg, 2.09 µmol, 6.1 mol%) were suspended in DMSO (400 µL). A solution of vinyl iodide **29** (111 mg, 339 µmol, 10.0 eq.) in DMSO (500 µL) was added and sonicated for five minutes. Subsequently, a solution of previously prepared aldehyde in DMSO (500 µL) was added. The dark green solution was stirred for two hours. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (5 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 6:1), alcohol **70** was obtained as a colorless oil (18.4 mg, 14.4 µmol, 42%).

TLC: R_f = 0.29 & 0.18 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}H-NMR: (500 MHz, C_6D_6) δ 7.83-7.68 (m, 8 H, C_{Ar}-H), 7.31-7.20 (m, 12 H, C_{Ar}-H), 6.41-6.35 (m, 1 H, H-6), 6.06-5.95 (m, 3 H, H-16*, H-17*, H-18), 5.90-5.74 (m, 2.5 H, H-3, H-14$_A$, H-15*), 5.72-5.67 (m, 0.5 H, H-10$_A$), 5.67-5.62 (m, 0.5 H, H-14$_B$), 5.62-5.58 (m, 0.5 H, H-10$_B$), 5.53-5.38 (m, 1 H, H-19), 5.19 (*virt.* qd, $^3J \approx {}^3J \approx$ 6.8 Hz, 1 H, H-21), 4.67 (d, ^3J = 8.8 Hz, 1 H, H-5), 4.42-4.37 (m, 1 H, H-13), 4.14 (d, ^3J = 4.3 Hz, 0.5 H, H-12$_A$), 4.10 (d, ^3J = 6.4 Hz, 0.5 H,

H-12$_B$), 4.06-4.00 (m, 1 H, H-23a), 3.93-3.87 (m, 1 H, H-23b), 3.62-3.52 (m, 2 H, H-8), 2.95-2.86 (m, 2 H, H-2), 2.41-2.26 (m, 3 H, H-9, H-20a), 2.24-2.16 (m, 1 H, H-20b), 1.95 (dq, ^3J = 11.2, 7.0 Hz, 1 H, H-22), 1.74-1.72 (m, 3 H, H-42), 1.58-1.54 (m, 1.5 H, H-43$_B$), 1.45 (s, 4.5 H, H-43$_A$, H-41), 1.22 [s, 9 H, OCOC(CH$_3$)$_3$], 1.19-1.15 [s, 18 H, SiC(CH$_3$)$_3$], 1.05-0.99 [m, 9 H, Si(CH$_2$C*H*$_3$)$_3$], 0.84 (d, ^3J = 7.0 Hz, 3 H, H-44), 0.65-0.59 [m, 6 H, Si(C*H*$_2$CH$_3$)$_3$].

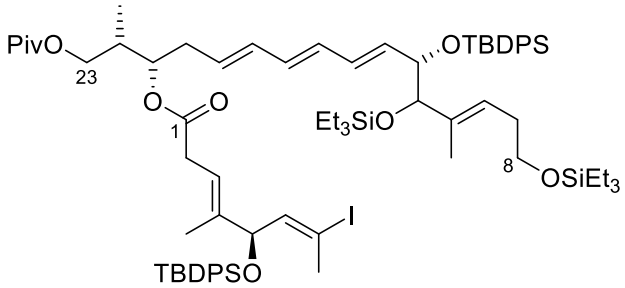
^{13}C-NMR: (**, C$_6$D$_6$) δ 177.0 [s, O*C*OC(CH$_3$)], 170.3 (s, C-1), 142.1 (d, C-6), 138.9 (s, C-4), 136.0 (d, C$_{Ar}$-H), 135.6 (s, C-11$_A$), 134.6 (s, C-11$_B$), 133.0 (d, C-18), 129.8 (d, C$_{Ar}$-H), 129.1 (d, C-19), 127.6 (d, C$_{Ar}$-H), 124.4 (d, C-10$_B$), 123.3 (d, C-10$_A$), 117.0 (d, C-3), 96.5 (s, C-7), 80.9 (d, C-12$_A$), 79.3 (d, C-12$_B$), 76.8 (d, C-13), 75.1 (d, C-5), 72.3 (d, C-21), 65.0 (t, C-23), 62.1 (t, C-8), 35.2 (d, C-22), 35.1 (t, C-20), 33.2 (t, C-2), 31.6 (t, C-9), 27.5 (q, C-42), 26.9 [q, OCOC(*C*H$_3$)], 26.7 [q, SiC(*C*H$_3$)$_3$], 12.4 (q, C-43), 12.2 (q, C-41), 10.7 (q, C-44), 6.62 [q, Si(CH$_2$*C*H$_3$)$_3$], 4.52 [t, Si(*C*H$_2$CH$_3$)$_3$].

HRMS (ESI): *m/z* [C$_{70}$H$_{99}$IO$_8$Si$_3$ + NH$_4$]$^+$ calcd.: 1296.6030; found: 1296.6033.

*exchangeable signals

**^{13}C signals extracted from HSQC and HMBC

Silyl protected fragment 71



71
$C_{76}H_{113}IO_8Si_4$
1393.98 g/mol

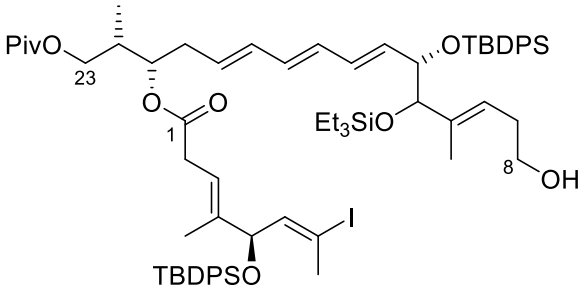
To a cold (0 °C) solution of alcohol **70** (92.3 mg, 72.0 µmol, 1.00 eq.) in dichloromethane (3 mL) was added pyridine (29.0 µL, 28.5 mg, 361 µmol, 5.00 eq.) and triethylsilyl triflate (41.0 µL, 47.7 mg, 180 µmol, 2.50 eq.). After stirring for one hour, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (12 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 8 mL). The combined

organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 10:1), silyl ether **71** was obtained as a colorless oil (46.8 mg, 33.6 µmol, 70%).

TLC: R_f = 0.86 (pentane:diethyl ether = 4:1).

MS (ESI): 1412 (M+Na).

Alcohol 72



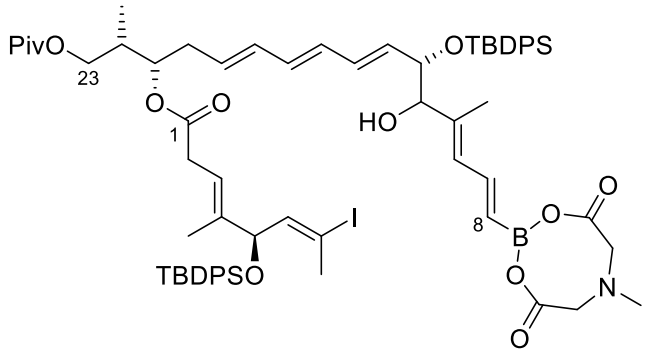
72
$C_{70}H_{99}IO_8Si_3$
1279.71 g/mol

To a cold (0 °C) solution of silyl ether **71** (14.0 mg, 10.0 µmol, 1.00 eq.) in THF (1 mL), diethyl ether (1 mL) and pyridine (300 µL) was added HF · pyridine complex (30 w% HF, 4 µL, 15 eq.). After 20 minutes, an additional 12 µL HF · pyridine complex was added (45 eq.). After 40 minutes, further 40 µL HF · pyridine complex was added (150 eq.). After 20 minutes, the colorless suspension was poured into 10 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 4:1 ⟶ 2:1), alcohol **72** was obtained as a yellowish oil (11.5 mg, 89%).

TLC: R_f = 0.29 (pentane:diethyl ether = 3:1) [UV, CAM].

MS (ESI): 1302 (M+Na).

BMIDA fragment 73



73

$C_{69}H_{89}BINO_{11}Si_2$

1302.35 g/mol

To a solution of primary alcohol **69** (200 mg, 184 µmol, 1.00 eq.) in dichloromethane (8 mL) was added sodium bicarbonate (62.0 mg, 738 µmol, 4.00 eq.) and *Dess-Martin* periodinane (156 mg, 369 µmol, 2.00 eq.). After 20 minutes, the yellow suspension was poured into a mixture of 10 mL saturated aqueous sodium bicarbonate solution and 10 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the aldehyde as a yellow oil. Chromium-(II)-chloride (468 mg, 3.81 mmol, 20.7 eq.) and nickel-(II)-chloride (4.68 mg, 36.1 µmol, 20.0 mol%) were suspended in DMF (6 mL). A solution of vinyl iodide **10** (258 mg, 738 µmol, 4.00 eq.) and previously prepared aldehyde in DMF (5 mL) was added. The dark green solution was stirred for two hours and then poured into cold (0 °C) saturated aqueous ammonium chloride solution (10 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL) and dichloromethane (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, cyclohexane:ethyl acetate = 3:2), alcohol **73** was obtained as a colorless oil (31.5 mg, 24.2 µmol, 13%). NMR analysis showed that the compound was contaminated with 25% of the protodeiodinated product.

TLC: R_f = 0.65 (diethyl ether:acetonitrile = 4:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, C_6D_6) δ 7.90-7.70 (m, 8 H, C_{Ar}-H), 7.33-7.19 (m, 12 H, C_{Ar}-H), 7.14-7.08 (m, 1 H, H-9), 6.52 (d, ^3J = 11.1 Hz, 0.5 H, H-10$_A$), 6.42 (d, ^3J = 11.1 Hz, 0.5 H, H-10$_B$), 6.38 (dq, ^3J = 9.0 Hz, ^4J = 1.9 Hz, 1 H, H-6), 6.01-5.94 (m, 2 H, H-18, H-17*), 5.91-5.76 (m, 3.5 H, H-3, H-14$_A$, H-15*, H-16*), 5.70 (dd, ^3J = 14.2, 7.4 Hz, 0.5 H, H-14$_B$), 5.53-5.46 (m,

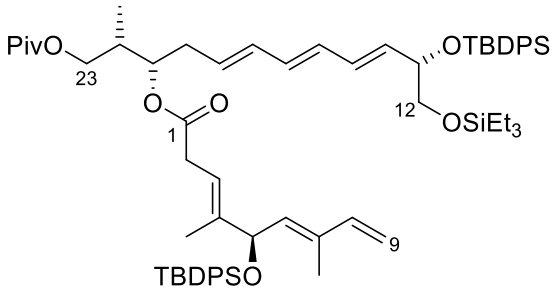
1 H, H-19), 5.42 (d, ^{3}J = 17.3 Hz, 1 H, H-8), 5.23-5.15 (m, 1 H, H-21), 4.68 (d, ^{3}J = 8.8 Hz, 1 H, H-5), 4.47-4.42 (m, 0.5 H, H-13_A), 4.42-4.37 (m, 0.5 H, H-13_B), 4.18-4.14 (m, 0.5 H, H-12_A), 4.13-4.08 (m, 0.5 H, H-12_B), 4.07-4.00 (m, 1 H, H-23a), 3.95-3.90 (m, 1 H, H-23b), 2.97-2.84 (m, 2 H, H-2), 2.57-2.46 (m, 2 H, NCH_2), 2.41-2.28 (m, 3 H, H-20a, NCH_2), 2.25-2.15 (m, 1 H, H-20b), 2.01-1.90 (m, 1 H, H-22), 1.77-1.72 (m, 3 H, H-42), 1.57 (s, 1.5 H, H-43_A), 1.46 (s, 4.5 H, H-41, H-43_B), 1.24-1.21 [m, 9 H, $OCOC(CH_3)_3$], 1.18-1.14 [m, 18 H, $SiC(CH_3)_3$], 0.85 (d, ^{3}J = 7.0 Hz, 3 H, H-44).

^{13}C-NMR: (126 MHz, C_6D_6) δ 177.7 [s, O*C*OC$(CH_3)_3$], 170.7 (s, C-1), 167.0 [s, (*C*O$CH_2)_2$N], 142.5 (d, C-6), 139.38 (s, C-4), 139.1 (d, C-9), 138.9 (s, C-11), 136.4 (d, C_{Ar}-H), 136.4 (d, C_{Ar}-H), 136.3 (d, C_{Ar}-H), 132.8 (d, C-14), 130.3 (d, C-19), 128.6 (d, C-10), 127.5 (d, C-8), 117.7 (d, C-3), 97.1 (s, C-7), 79.4 (d, C-12), 77.2 (d, C-13_A), 76.4 (d, C-13_B), 75.6 (d, C-5), 72.9 (d, C-21), 65.7 (t, C-23), 60.7 [t, (CO*C*$H_2)_2$N], 45.0 (q, NCH_3), 38.9 [s, OCO*C*$(CH_3)_3$], 35.7 (d, C-22), 35.6 (t, C-20), 33.6 (d, C-2), 27.9 (q, C-42), 27.4 (q, tBu), 27.1 (q, tBu), 13.7 (q, C-43_A), 13.2 (q, C-43_B), 12.6 (q, C-41), 11.1 (q, C-44).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3523 (w, b, O–H), 3071 (w, sp2-C–H), 2958 (m, sp2-C–H), 1732 (s, C=O), 1600 (w), 1427 (m, C=C), 1284 (m), 1152 (s), 1110 (vs, C–O), 996 (vs, C–O), 821 (m, C–H), 701 (vs).

HRMS (ESI): *m/z* $[C_{69}H_{89}BINO_{11}Si_2+NH_4]^+$ calcd.: 1319.5450; found: 1319.5453..

Ester 87



87

$C_{67}H_{94}O_7Si_3$

1095.74 g/mol

To a cold (0 °C) solution of carboxylic acid **86** (148 mg, 341 µmol, 1.10 eq.) in toluene (4 mL) was added triethylamine (86.0 µL, 62.7 mg, 620 µmol, 2.00 eq.), followed by 2,4,6-trichlorobenzoyl chloride (73.0 µL, 113 mg, 465 µmol, 1.50 eq.). After stirring for 15 minutes, a solution of alcohol **67** (211 mg, 310 µmol, 1.00 eq.) in toluene (3 mL) and 4-(dimethylamino)-pyridine (37.9 mg, 310 µmol, 1.00 eq.) was added. While stirring for three hours at 0°C, the solution turned into an orange suspension. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (25 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 15 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 10:1), ester **87** was obtained as a colorless oil (260 mg, 237 µmol, 77%).

TLC: R_f = 0.79 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}**H-NMR**: (400 MHz, $CDCl_3$) δ 7.73-7.59 (m, 8 H, C_{Ar}-H), 7.43-7.30 (m, 12 H, C_{Ar}-H), 6.25 (dd, ^3J = 17.4 Hz, ^3J = 10.7 Hz, 1 H, H-8), 6.10-6.00 (m, 4 H, H-15-18), 5.69 (dd, ^3J = 14.1 Hz, ^3J = 6.2 Hz, 1 H, H-14), 5.59-5.48 (m, 2 H, H-3, H-19), 5.48 (d, ^3J = 8.6 Hz, 1 H, H-6), 5.06-4.91 (m, 3 H, H-9, H-21), 4.79 (d, ^3J = 8.6 Hz, 1 H, H-5), 4.22 (*virt.* q, $^3J \approx {}^3J \approx$ 6.3 Hz, 1 H, H-13), 3.94 (d, ^3J = 6.6 Hz 2 H, H-23), 3.53 (dd, ^2J = 9.8, ^3J = 5.8 Hz, 1 H, H-12a), 3.39 (dd, ^2J = 9.8, ^3J = 6.8 Hz, 1 H, H-12b), 3.07-2.89 (m, 2 H, H-2), 2.36-2.30 (m, 2 H, H-20), 2.10-2.00 (m, 1 H, H-22), 1.58 (d, ^4J = 1.3 Hz, 3 H, H-41), 1.27 (d, ^4J = 1.5 Hz, 3 H, H-42), 1.23-1.16 (m, 9 H, Piv), 1.07 [s, 9 H, $SiC(CH_3)_3$], 1.04 [s, 9 H, $SiC(CH_3)_3$], 0.92 (d, ^3J = 6.9 Hz, 3 H, H-43), 0.85 [t, ^3J = 8.0 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.45 [q, ^3J = 8.0 Hz, 6 H, $Si(CH_2CH_3)_3$].

^{13}**C-NMR**: (101 MHz, $CDCl_3$) δ 178.0 (s, $(CH_3)_3CCO$), 170.9 (s, C-1), 141.6 (d, C-8), 140.3 (s, C-4), 136.1 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 134.4 (s, C_{Ar}), 134.1 (d, C-14), 133.9 (s, C-7), 133.8

(d, C-6), 133.6 (d, C-18[a]), 132.1 (d, C-17[a]), 131.6 (d, C-16[a]), 131.0 (d, C-15[a]), 128.6 (d, C-19), 127.6, 127.5, 116.4 (d, C-3), 112.5 (t, C-9), 74.9 (d, C-5), 74.6 (d, C-13), 73.3 (d, C-21), 67.3 (t, C-12), 66.3 (t, C-23), 39.0 [s, $(CH_3)_3CCO$], 35.4 (d, C-22), 35.3 (t, C-20), 33.7 (t, C-2), 27.3 [q, $(CH_3)_3CCO$], 27.2 [q, $SiC(CH_3)_3$], 27.1 [q, $SiC(CH_3)_3$], 18.1 [q, $SiC(CH_3)_3$], 12.7 (q, C-41), 12.0 (q, C-42), 11.4 (q, C-44), 7.83 [q, $Si(CH_2CH_3)_3$], 4.40 [t, $Si(CH_2CH_3)_3$].

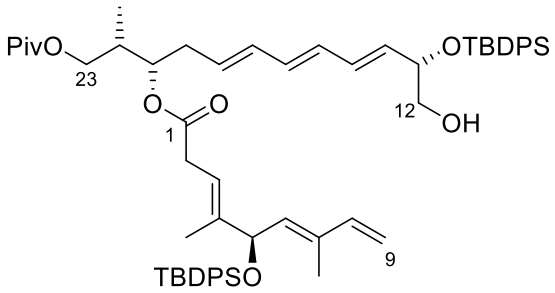
Specific rotation: $[\alpha]_D^{20} = +6.00$ (c = 2.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3071 (w), 2957 (s, sp^3-CH), 2933 (s, sp^3-CH), 2858 (m, sp^3-CH), 1732 (vs, CO), 1427 (m), 1111 (vs, C-O), 701 (vs).

HRMS (ESI): $[C_{67}H_{94}O_7Si_3 + Na]^+$ calcd.: 1117.6199; found: 1117.6202 (2264).

a) interchangeable signals

Alcohol 88



88
$C_{61}H_{80}O_7Si_2$
981.47 g/mol

To a cold (0 °C) solution of silyl ether **87** (244 mg, 223 µmol, 1.00 eq.) in THF (5 mL) was added HF pyridinde complex (30 w% HF, 116 µL, 2.25 mmol, 20.0 eq.). After 30 minutes, the solution was poured into 50 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 4:1), alcohol **88** was obtained as a colorless oil (193 mg, 197 µmol, 88%).

TLC: R_f = 0.11 (pentane:diethyl ether = 4:1).

^{1}**H-NMR**: (400 MHz, $CDCl_3$) δ 7.70-7.61 (m, 8 H, C_{Ar}-H), 7.55-7.33 (m, 12 H, C_{Ar}-H), 6.23 (dd, ^3J = 17.4 Hz, ^3J = 10.7 Hz, 1 H, H-8), 6.12-5.91 (m, 4 H, H-15-18), 5.61-5.53 (m, 3 H, H-

3, H-14, H-19), 5.53 (d, ^{3}J = 8.8 Hz, 1 H, H-6), 5.11-4.93 (m, 3 H, H-9, H-21), 4.82 (d, ^{3}J = 8.8 Hz, 1 H, H-5), 4.31-4.21 (m, 1 H, H-13), 3.90 (d, ^{3}J = 6.6 Hz, 2 H, H-23), 3.51-3.45 (m, 2 H, H-12), 3.11-2.90 (m, 2 H, H-2), 2.41-2.32 (m, 2 H, H-20), 2.18-2.02 (m, 1 H, H-22), 1.81-1.78 (m, 1 H, OH), 1.61 (s, 3 H, H-41), 1.32 (d, ^{4}J = 1.3 Hz, 3 H, H-42), 1.21 (s, 9 H, Piv), 1.07 [s, 9 H, SiC(CH_3)$_3$], 1.04 [s, 9 H, SiC(CH_3)$_3$], 0.91 (d, ^{3}J = 6.9 Hz, 3 H, H-43).

^{13}C-NMR: (101 MHz, $CDCl_3$) δ 178.5 [s, (CH_3)$_3$C*C*O], 171.3 (s, C-1), 141.2 (d, C-8), 140.3 (s, C-4), 136.1 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 135.9 (d, C_{Ar}-H), 134.1 (d, C_{Ar}-H), 134.0 (s, C_{Ar}), 133.9 (s, C_{Ar}), 133.8 (d, C-6), 133.6 (d, C-18[a]), 133.3, 133.1, 132.4, 132.2, 130.9, 130.0, 129.9, 129.7, 129.6, 129.5, 127.9, 127.7, 127.6, 127.5, 116.4 (d, C-3), 112.5 (t, C-8), 75.1 (d, C-13), 74.9 (d, C-5), 73.2 (d, C-21), 67.1 (t, C-12), 66.0 (t, C-23), 39.0 [s, (CH_3)$_3$*C*CO], 35.5 (d, C-22), 35.3 (t, C-20), 33.7 (t, C-2), 27.3 [q, (*C*H_3)$_3$CCO], 27.2 [q, SiC(*C*H_3)$_3$], 27.1 [q, SiC(*C*H_3)$_3$], 19.5 [q, Si*C*(CH_3)$_3$], 12.7 (q, C-41), 12.0 (q, C-42), 11.4 (q, C-43).

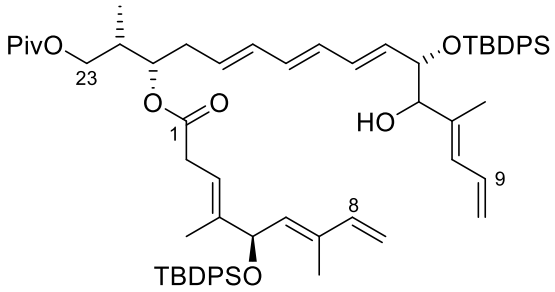
Specific rotation: $[\alpha]_D^{20} = +22.0$ (*c* = 2.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3518 (*br* w, OH), 3071 (w, sp^2-CH), 3015 (w, sp^2-CH), 2959 (m, sp^3-CH), 2931 (m, sp^3-CH), 2858 (m, sp^3-CH), 1731 (vs, CO), 1111 (vs), 701 (vs).

HRMS (ESI): $[C_{61}H_{80}O_7Si_2 + Na]^+$ calcd.: 1003.5334; found: 1003.5336.

$[C_{61}H_{80}O_7Si_2 + NH_4]^+$ calcd.: 998.5780; found: 998.5782.

Alcohol 90



90

$C_{66}H_{86}O_7Si_2$

1047.58 g/mol

To a solution of primary alcohol **88** (307 mg, 313 µmol, 1.00 eq.) in dichloromethane (10 mL) was added sodium bicarbonate (105 mg, 1.25 mmol, 4.00 eq.) and *Dess-Martin* periodinane (265 mg, 626 µmol, 2.00 eq.). After 25 minutes, the yellow suspension was poured into a mixture of 15 mL saturated aqueous sodium bicarbonate solution and 15 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 15 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the aldehyde as a yellow oil. Chromium-(II)-chloride (800 mg, 6.51 mmol, 20.8 eq.) and nickel-(II)-chloride (8.00 mg, 62.0 µmol, 20.0 mol%) were suspended in DMF (10 mL) and cooled to 0 °C. A solution of vinyl iodide **85** (364 mg, 1.87 mmol, 6.00 eq.) and previously prepared aldehyde in DMF (5 mL) was added. The dark green solution was stirred for ten minutes and then poured into cold (0 °C) saturated aqueous ammonium chloride solution (100 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (4 × 30 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 6:1), alcohol **90** was obtained as a colorless oil (111 mg, 106 µmol, 34%).

TLC: R_f = 0.31 & 0.38 (pentane:diethyl ether = 4:1) [UV, CAM].

Diastereomeric ratio: d.r. = 3:2.

^{1}**H-NMR**: (400 MHz, $CDCl_3$) δ 7.72-7.54 (m, 8 H, C_{Ar}-H), 7.46-7.30 (m, 12 H, C_{Ar}-H), 6.57-6.42 (m, 1 H, H-9), 6.25 (dd, ^3J = 17.1, 10.7 Hz, 1 H, H-8), 6.09-5.84 (m, 4 H, H-10, H-15, H-16, H-17), 5.64-5.51 (m, 3 H, H-3, H-14, H-19), 5.47 (d, ^3J = 8.5 Hz, 1 H, H-6), 5.17-5.11 (m, 1 H, C^9=C*H*H), 5.09-4.91 (m, 3 H, H-21, C^9=CH*H*, C^8=CH_2), 4.79 (d, ^3J = 8.5 Hz, 1 H, H-5),

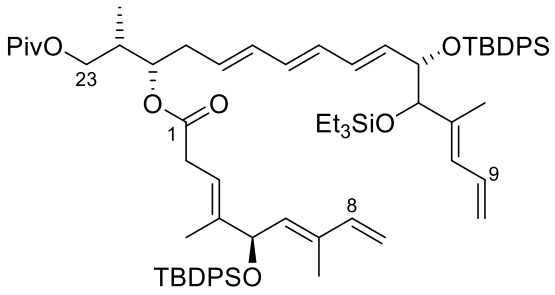
4.23 (dd, ^3J = 7.1, 4.3 Hz, 0.6 H, H-13$_A$), 4.14 (dd, ^3J = 7.7, 5.9 Hz, 0.4 H, H-13$_B$), 3.95 (s, 0.6 H, H-12$_A$), 3.93-3.87 (m, 2.4 H, H-12$_B$, H-23), 3.09-2.87 (m, 2 H, H-2), 2.77 (d, ^3J = 4.5 Hz, 0.6 H, OH$_B$), 2.48-2.26 (m, 2.4 H, H-20, OH$_A$), 2.10-1.96 (m, 1 H, H-22), 1.59-1.56 (m, 3 H, H-41), 1.52 (d, ^4J = 1.3 Hz, 1.2 H, H-43$_B$), 1.44 (s, 1.8 H, H-43$_A$), 1.27 (d, ^4J = 1.4 Hz, 3 H, H-42), 1.21-1.16 [m, 9 H, OCOC(CH$_3$)$_3$], 1.08 [s, 5 H, C$_{12}$OSiC(CH$_3$)$_3$]$_A$, 1.06 [s, 4 H, C$_{12}$OSiC(CH$_3$)$_3$]$_B$, 1.05-1.03 [s, 5 H, C$_5$OSiC(CH$_3$)$_3$], 0.96-0.88 (m, 3 H, H-44).

^{13}C-NMR: (101 MHz, CDCl$_3$) δ 178.5 [s, O*C*OC(CH$_3$)$_3$], 171.3 (s, C-1), 141.2 (d, C-8), 140.3 (s, C-4), 136.3 (s, C-11), 136.2 (d, C$_{Ar}$-H), 136.0 (d, C$_{Ar}$-H), 133.8 (d, C-6), 132.6 (d, C-9), 128.1 (d, C-10$_A$), 127.7 (d, C$_{Ar}$-H), 127.6 (d, C$_{Ar}$-H), 127.5 (d, C$_{Ar}$-H), 127.1 (d, C-10$_B$), 117.1 (t, C^9=*C*H$_2$), 116.4 (d, C-3), 112.5 (t, C^8=*C*H$_2$), 80.4 (d, C-12$_B$), 79.0 (d, C-12$_A$), 76.7 (d, C-13$_A$), 76.1 (d, C-13$_B$), 74.9 (d, C-5), 73.2 (d, C-21), 65.8 (t, C-23), 38.9 [s, OCO*C*(CH$_3$)$_3$], 35.5 (d, C-22), 35.3 (t, C-20), 33.7 (t, C-2), 27.3 [q, OCOC(*C*H$_3$)$_3$], 27.2 [q, C$_{13}$OSiC(*C*H$_3$)$_3$]$_B$, 27.2 [q, C$_{13}$OSiC(*C*H$_3$)$_3$]$_A$, 27.1 [q, C$_5$OSiC(*C*H$_3$)$_3$], 19.5 [s, Si*C*(CH$_3$)$_3$], 13.4 (q, C-43), 12.7 (q, C-41), 11.9 (q, C-42), 11.4 (q, C-44).

HRMS (ESI): *m/z* [C$_{66}$H$_{86}$O$_7$Si$_2$ + Na]$^+$ calcd.: 1069.5804; found: 1069.5803.

[C$_{66}$H$_{86}$O$_7$Si$_2$ + NH$_4$]$^+$ calcd.: 1064.6250; found: 1064.6249.

Silyl protected fragment 91



91

$C_{72}H_{100}O_7Si_3$

1161.84 g/mol

To a cold (0 °C) solution of alcohol **90** (105 mg, 100 µmol, 1.00 eq.) in dichloromethane (5 mL) was added pyridine (65.0 µL, 63.4 mg, 801 µmol, 8.00 eq.) and triethylsilyl triflate (90.5 µL, 106 mg, 401 µmol, 4.00 eq.). After stirring for five minutes, the reaction was quenched by the addition of saturated aqueous sodium bicarbonate solution (5 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers

were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 20:1), silyl ether **91** was isolated as a colorless oil (102 mg, 87.8 µmol, 88 %).

TLC: R_f = 0.78 (pentane:diethyl ether = 4:1) [UV, CAM].

Diastereomeric ratio: d.r. = 3:2.

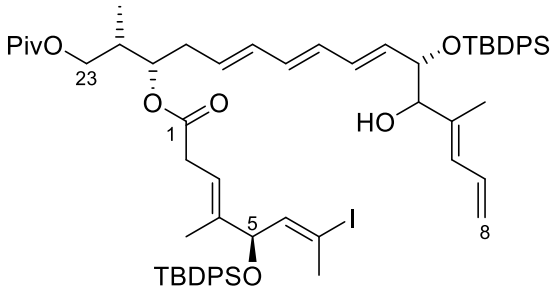
^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.75-7.55 (m, 8 H, C_{Ar}-H), 7.44-7.30 (m, 12 H, C_{Ar}-H), 6.58-6.45 (m, 1 H, H-9), 6.25 (dd, ^3J = 17.4, 10.7 Hz, 1 H, H-8), 6.08-5.83 (m, 4 H, H-10, H-15, H-16, H-17), 5.65-5.59 (m, 1 H, H-3), 5.58-5.50 (m, 2 H, H-14, H-19), 5.48 (d, ^3J = 8.6 Hz, 1 H, H-6), 5.17-4.91 (m, 5 H, C^8=CH_2, C^9=CH_2, H-21), 4.79 (d, ^3J = 8.6 Hz, 1 H, H-5), 4.25 (virt. t, $^3J \approx {}^3J \approx$ 5.8 Hz, H-13_B), 4.01 (dd, ^3J = 7.7, 6.3 Hz, 0.6 H, H-13_A), 3.95-3.86 (m, 3 H, H-12, H-23), 3.07-2.91 (m, 2 H, H-2), 2.45-2.27 (m, 2 H, H-20), 2.04 (qd, ^3J = 6.8, 4.1 Hz, 1 H, H-22), 1.59-1.56 (m, 3 H, H-41), 1.56 (d, ^4J = 1.2 Hz, 1.2 H, H-43_B), 1.49 (d, ^4J = 1.3 Hz, 1.8 H, H-43_A), 1.27 (d, ^4J = 1.3 Hz, 3 H, H-42), 1.19 [s, 9 H, $OCOC(CH_3)_3$], 1.07-0.99 [m, 18 H, $SiC(CH_3)_3$], 0.92 (dd, ^3J = 6.9, 1.3 Hz, 3 H, H-44), 0.84 [t, ^3J = 8.0 Hz, 9 H, $Si(CH_2C\mathit{H}_3)_3$], 0.50 [q, ^3J = 8.0 Hz, 3.5 H $Si(C\mathit{H}_2CH_3)_3]_A$, 0.40 [q, ^3J = 8.0 Hz, 2.5 H, $Si(C\mathit{H}_2C\mathit{H}_3)_3]_B$.

^{13}C-NMR: (126 MHz, $CDCl_3$) δ 178.5 [s, $OCOC(CH_3)_3$], 171.3 (s, C-1), 141.2 (d, C-8), 140.2 (s, C-4), 136.4 (d, C_{Ar}-H), 136.3 (s, C-11), 136.2 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 135.9 (d, C_{Ar}-H), 133.8 (d, C-6), 132.6 (d, C-9), 132.0 (d, C-15*), 131.5 (d, C-16*), 129.6 (d, C-19^+), 129.5 (d, C-14^+), 128.5 (d, C-17*), 128.4 (d, C-18*), 128.2 (d, C-10_B), 128.0 (d, C-10_A), 127.5 (d, C_{Ar}-H), 127.4 (d, C_{Ar}-H), 127.3 (d, C_{Ar}-H), 116.5 (t, C^9=*C*H2), 116.2 (d, C-3), 112.5 (t, C^8=*C*H2), 81.9 (d, C-12_A), 80.2 (d, C-12_B), 76.9 (d, C-13), 74.8 (d, C-5), 73.2 (d, C-21), 65.8 (d, C-23), 38.9 [s, $OCO\mathit{C}(CH_3)_3$], 35.3 (d, C-22), 35.2 (t, C-20), 33.7 (t, C-2), 27.3 [q, $OCOC(\mathit{C}H_3)_3$], 27.2 [q, $C_{13}OSiC(\mathit{C}H_3)_3]_B$, 27.2 [q, $C_{13}OSiC(\mathit{C}H_3)_3]_A$, 27.0 [q, $C_5OSiC(\mathit{C}H_3)_3$], 19.5 [s, $Si\mathit{C}(CH_3)_3$], 14.3 (q, C-43), 12.7 (q, C-41), 11.9 (q, C-42), 11.4 (q, C-44), 6.95 [q, $Si(CH_2\mathit{C}H_3)_3$], 4.91 [t, $Si(\mathit{C}H_2\mathit{C}H_3)_3]_A$, 4.73 [t, $Si(\mathit{C}H_2\mathit{C}H_3)_3]_B$.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2956 (s) 2931 (s) 2857 (s) (C_{sp3}-H), 1733 (vs, CO), 1110 (vs).

HRMS (ESI): *m/z* $[C_{72}H_{100}O_7Si_3 + NH_4]^+$ calcd.: 1178.7115; found: 1178.7108.

Alcohol 93



93

$C_{64}H_{83}IO_7Si_2$

1147.44 g/mol

To a solution of primary alcohol **69** (509 mg, 471 µmol, 1.00 eq.) in dichloromethane (10 mL) was added sodium bicarbonate (158 mg, 1.88 mmol, 4.00 eq.) and *Dess-Martin* periodinane (399 mg, 941 µmol, 2.00 eq.). After 30 minutes, the yellow suspension was poured into a mixture of 15 mL saturated aqueous sodium bicarbonate solution and 15 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 15 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the aldehyde as a yellow oil. Chromium-(II)-chloride (1.19 g, 9.68 mmol, 20.5 eq.) and nickel-(II)-chloride (11.9 mg, 92.2 µmol, 20.0 mol%) were suspended in DMF (12 mL) and cooled to 0 °C. A solution of vinyl iodide **84** (913 mg, 4.70 mmol, 10.0 eq.) and previously prepared aldehyde in DMF (5 mL) was added. The dark green solution was stirred for two hours and then poured into a mixture of cold (0 °C) saturated aqueous ammonium chloride solution (150 mL) and water (100 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (5 × 50 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 5:1), alcohol **93** was obtained as a colorless oil (309 mg, 269 µmol, 57%).

TLC: R_f = 0.29 & 0.37 (pentane:diethyl ether = 4:1) [UV, CAM].

Diastereomeric ratio: d.r. = 3:2.

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.68-7.59 (m, 8 H, C_{Ar}-H), 7.45-7.32 (m, 12 H, C_{Ar}-H), 6.50 (dt, ^3J = 16.8 Hz, ^3J = 10.5 Hz, 1 H, H-9), 6.13 (dq, ^3J = 8.9 Hz, ^4J = 1.3 Hz, 1 H, H-6), 6.10-5.85 (m, 5 H, H-10, H-15-18), 5.66-5.49 (m, 3 H, H-3, H-14, H-19), 5.14 (dd, ^3J = 16.8, ^2J = 2.1 Hz, 1 H, H-8a), 5.08-5.03 (m, 1 H, H-8b), 5.00 (td, ^3J = 6.4 Hz, ^3J = 4.2 Hz, 1 H, H-

21), 4.59-4.52 (m, 1 H, H-5), 4.23 (dd, ^{3}J = 7.1 Hz, ^{3}J = 4.9 Hz, 0.5 H, H-13$_A$), 4.14 (dd, ^{3}J = 7.9 Hz, ^{3}J = 5.7 Hz, 0.5 H, H-13$_B$), 3.98-3.85 (m, 3 H, H-12, H-23), 3.09-2.96 (m, 2 H, H-2), 2.44-2.30 (m, 2 H, H-20), 2.10-2.00 (m, 1 H, H-22), 1.82-1.79 (m, 3 H, H-42), 1.59-1.56 (m, 3 H, H-41), 1.51 (d, ^{4}J = 1.3 Hz, 1.3 H, H-43$_A$), 1.44 (d, ^{4}J = 1.3 Hz, 1.7 H, H-43$_B$), 1.21-1.18 [m, 9 H, OCOC(CH$_3$)$_3$], 1.06-1.02 [m, 9 H, SiC(CH$_3$)$_3$], 0.96-0.93 (m, 3 H, H-44).

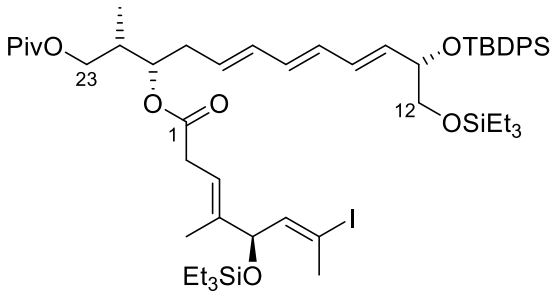
^{13}C-NMR: (126 MHz, CDCl$_3$) δ 178.5 [s, O*C*OC(CH$_3$)], 171.2 (s, C-1), 142.1 (d, C-6), 139.1 (s, C-4), 136.4 (s, C-11$_A$), 136.2-135.9 (m, C$_{Ar}$), 135.8 (s, C-11$_B$), 133.7-132.8 (m, C=C), 132.6 (d, C-9$_A$), 132.6 (d, C-9$_B$), 130.1-129.7 (m, C$_{Ar}$), 128.1 (d, C-10$_A$), 127.0 (d, C-10$_B$), 117.3 (d, C-8$_A$), 117.1 (d, C-8$_B$), 117.0 (t, C-3), 96.7 (s, C-7), 80.3 (d, C-13$_A$), 79.0 (d, C-13$_B$), 76.7 (d, C-12$_A$), 76.0 (d, C-12$_B$), 75.2 (d, C-5), 73.2 (d, C-21), 66.0 (t, C-23), 39.0 [s, OCO*C*(CH$_3$)], 35.4 (t, C-22), 35.3 (t, C-20), 33.7 (t, C-2), 27.9 (q, C-42), 27.3 [q, OCOC(*C*H$_3$)], 27.0 [q, SiC(*C*H$_3$)$_3$], 19.5 [s, Si*C*(CH$_3$)$_3$], 13.6 (q, C-43$_A$), 13.4 (q, C-43$_B$), 12.7 (q, C-41), 11.4 (q, C-44).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3516 (*br* w, OH), 3072 (w, sp^2-CH), 2959 (m, sp^3-CH), 2930 (m, sp^3-CH), 2857 (m, sp^3-CH), 1731 (vs, CO), 1111 (vs), 702 (vs).

HRMS (ESI): *m/z* [C$_{64}$H$_{83}$IO$_7$Si$_2$ + NH$_4$]$^+$ calcd.: 1164.5060; found: 1164.5059.

[C$_{64}$H$_{83}$IO$_7$Si$_2$ + Na]$^+$ calcd.: 1169.4614; found: 1169.4613.

Ester 110



110
C$_{55}$H$_{87}$IO$_7$Si$_3$
1071.45 g/mol

To a cold (0 °C) solution of carboxylic acid **108** (153 mg, 372 µmol, 1.00 eq.) in toluene (10 mL) was added triethylamine (130 µL, 94.1 mg, 930 µmol, 2.50 eq.), followed by 2,4,6-trichlorobenzoyl chloride (70.0 µL, 109 mg, 446 µmol, 1.20 eq.). After stirring for ten minutes,

a solution of alcohol **67** (329 mg, 484 µmol, 1.30 eq.) in toluene (5 mL) and 4-(dimethylamino)-pyridine (45.4 mg, 372 µmol, 1.00 eq.) was added. While stirring for two hours at 0°C, the solution turned into an orange suspension. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (10 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 4:1), ester **110** was obtained as a yellowish oil (325 mg, 303 µmol, 81%).

TLC: R_f = 0.80 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.71-7.62 (m, 4 H, C_{Ar}-H), 7.45-7.28 (m, 6 H, C_{Ar}-H), 6.14 (dq, ^3J = 8.5 Hz, ^4J = 1.6 Hz, 1 H, H-6), 6.12-5.99 (m, 4 H, H-15-18), 5.73-5.67 (m, 1 H, H-14), 5.66-5.61 (m, 1 H, H-3), 5.53 (dt, ^3J = 14.7 Hz, ^3J = 7.3 Hz, 1 H, H-19), 5.00 (td, ^3J = 6.7 Hz, ^3J = 4.0 Hz, 1 H, H-21), 4.65 (d, ^3J = 8.5 Hz, 1 H, H-5), 4.21 (*virt.* q, $^3J \approx {}^3J \approx$ 6.4 Hz, 1 H, H-13), 3.94-3.89 (m, 1 H, H-23), 3.53 (dd, ^2J = 9.8 Hz, ^3J = 5.8 Hz, 1 H, H-12a), 3.40 (dd, ^3J = 9.8 Hz, ^3J = 6.8 Hz, 1 H, H-12b), 3.04 (d, ^3J = 7.2 Hz, 2 H, H-2), 2.45 (d, ^3J = 1.6 Hz, 3 H, H-42), 2.41-2.33 (m, 1 H, H-20), 2.10-2.05 (m, 1 H, H-22), 1.59 (d, ^4J = 1.3 Hz, 3 H, H-41), 1.20 [s, 9 H, $OCOC(CH_3)_3$], 1.07 [s, 9 H, $SiC(CH_3)_3$], 0.96 (d, ^3J = 7.0 Hz, 3 H, H-44), 0.93 [t, ^3J = 8.0 Hz, 9 H, C_5-$OSi(CH_2CH_3)_3$], 0.84 [t, ^3J = 8.0 Hz, 9 H, C_{12}-$OSi(CH_2CH_3)_3$], 0.58 [q, ^3J = 8.0 Hz, 6 H, C_5-$OSi(CH_2CH_3)_3$], 0.45 [q, ^3J = 8.0 Hz, 6 H, C_{12}-$OSi(CH_2CH_3)_3$].

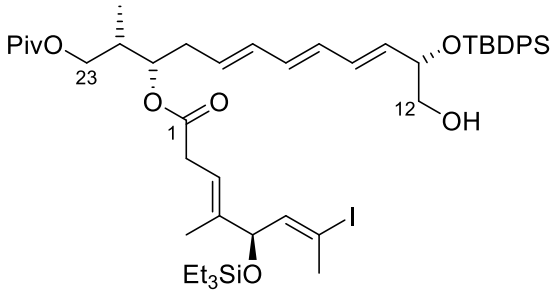
^{13}**C-NMR**: (126 MHz, $CDCl_3$) δ 178.5 [s, $OCOC(CH_3)$], 171.2 (s, C-1), 143.1 (d, C-6), 139.5 (s, C-4), 136.1 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 134.4 (s, C_{Ar}), 134.2 (d, C-14), 134.1 (s, C_{Ar}), 133.6 (d, C-15)*, 132.1 (d, C-16)*, 131.6 (d, C-17)*, 130.9 (d, C-18)*, 129.7 (d, C_{Ar}-H), 128.6 (d, C-19), 127.6 (d, C_{Ar}-H), 116.8 (d, C-3), 95.4 (s, C-7), 74.5 (d, C-5, C-13), 73.3 (d, C-21), 67.3 (t, C-12), 65.8 (t, C-23), 39.0 [s, $OCOC(CH_3)$], 35.4 (d, C-22), 35.3 (t, C-20), 33.7 (t, C-2), 28.5 (q, C-42), 27.3 [q, $OCOC(CH_3)$], 27.2 [q, $SiC(CH_3)_3$], 19.5 [s, $SiC(CH_3)_3$], 12.7 (q, C-41), 11.4 (q, C-44), 6.9 [q, C_5-$OSi(CH_2CH_3)_3$], 6.8 [q, C_{12}-$OSi(CH_2CH_3)_3$], 4.9 [t, C_5-$OSi(CH_2CH_3)_3$], 4.4 [t, C_{12}-$OSi(CH_2CH_3)_3$].

Specific rotation: $[\alpha]_D^{20} = +14.0$ (c = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2956 (s, OH), 2912 (s, C-H), 2877 (m, C-H), 1733 (s, C=O), 1460 (m, C-H), 1112 (m, C-O), 740 (m, C=C).

HRMS (ESI): *m/z* $[C_{55}H_{87}IO_7Si_3 + NH_4]^+$ calcd.: 1088.5148; found: 1088.5143.

Alcohol 113



113
$C_{49}H_{73}IO_7Si_2$
957.19 g/mol

To a cold (0 °C) solution of silyl ether **110** (320 mg, 0.298 mmol, 1.00 eq.) in THF (5 mL) and diethyl ether (5 mL) was added pyridine (1 mL) and HF · pyridine complex (30 wt.% HF, 230 µL, 8.58 mmol, 28.8 eq.). After four hours, the solution was poured into 20 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with 10% copper sulfate solution (3 × 10 mL), water (1 × 10 mL), brine (1 × 10 mL), dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane/ethyl acetate = 4:1), alcohol **113** was obtained as a colorless oil (168 mg, 59%). Additionally, 92.5 mg of diol **114** were isolated as a yellowish oil (113 µmol, 37%).

TLC: R_f = 0.19 (pentane:diethyl ether = 4:1) [UV, $KMnO_4$].

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.71-7.65 (m, 4 H, C_{Ar}-H), 7.48-7.35 (m, 6 H, C_{Ar}-H), 6.16 (dq, ^3J = 8.6 Hz, ^4J = 1.7 Hz, 1 H, H-6), 6.13-5.93 (m, 4 H, H-15-18), 5.71-5.52 (m, 3 H, H-3, H-14, H-19), 5.03 (td, ^3J = 6.5 Hz, ^3J = 4.0 Hz, 1 H, H-21), 4.67 (d, ^3J = 8.7 Hz, 1 H, H-5), 4.34-4.27 (m, 1 H, H-13), 3.98-3.91 (m, 1 H, H-23), 3.51 (t, ^3J = 5.8 Hz, 2 H, H-12), 3.06 (d, ^3J = 7.1 Hz, 2 H, H-2), 2.47 (d, ^4J = 1.5 Hz, 3 H, H-43), 2.43-2.37 (m, 2 H, H-20), 2.13-2.07 (m, 1 H, H-22), 1.80 (d, ^3J = 6.9 Hz, 1 H, OH), 1.62 (d, ^4J = 1.4 Hz, 3 H, H-41), 1.23 [s, 9 H, $OCOC(CH_3)_3$], 1.10 [s, 9 H, $SiC(CH_3)_3$], 0.99 (d, ^3J = 7.0 Hz, 3 H, H-44), 0.96 [t, ^3J = 8.0 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.60 [q, ^3J = 8.0 Hz, 6 H, $Si(CH_2CH_3)_3$] .

^{13}**C-NMR**: (126 MHz, $CDCl_3$) δ 178.5 [s, $OCOC(CH_3)$], 171.3 (s, C-1), 143.1 (d, C-6), 139.6 (s, C-4), 136.1 (d, C_{Ar}-H), 135.9 (d, C_{Ar}-H), 133.9 (s, C_{Ar}), 133.5 (s, C_{Ar})*, 133.3 (d, C-16)*, 133.0 (d, C-18), 132.3 (d, C-15)*, 132.2 (d, C-14)*, 130.9 (d, C-17)*, 130.0 (d, C_{Ar}-H), 129.9 (d, C_{Ar}-H), 129.4 (d, C-19), 127.9 (d, C_{Ar}-H), 127.7 (d, C_{Ar}-H), 116.7 (d, C-3), 95.4 (s, C-7),

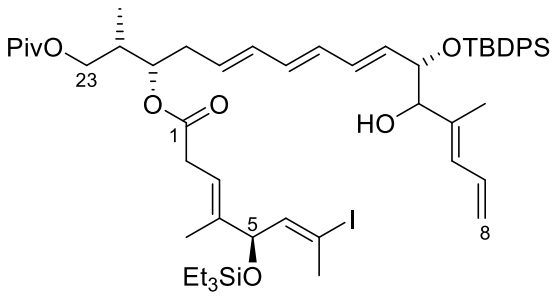
75.0 (d, C-13), 74.5 (d, C-5), 73.3 (d, C-21), 67.0 (t, C-12), 65.8 (t, C-23), 39.0 [s, OCO*C*(CH_3)], 35.5 (d, 22), 35.3 (t, 20), 33.7 (t, C-2), 28.5 (q, C-42), 27.3 [q, OCOC(*C*H_3)], 27.2 [q, SiC(*C*H_3)$_3$], 19.5 [s, Si*C*(CH_3)$_3$], 12.7 (q, C-41), 11.5 (q, C-44), 6.9 [q, Si(CH_2*C*H_3)$_3$], 4.9 [t, Si(*C*$H_2$$CH_3$)$_3$].

Specific rotation: $[\alpha]_D^{20} = +14.0$ (*c* = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3460 (m, OH), 2957 (s, C-H), 2859 (m, C-H), 1731 (s, C=O), 1462 (m, C-H), 1111 (m, C-O), 742 (m, C=C).

HRMS (ESI): *m/z* $[C_{49}H_{73}IO_7Si_2 + NH_4]^+$ calcd.: 974.4283; found: 974.4280.

Alcohol 115



115
$C_{54}H_{79}IO_7Si_2$
1023.29 g/mol

To a solution of primary alcohol **113** (159 mg, 166 µmol, 1.00 eq.) in dichloromethane (5 mL) was added sodium bicarbonate (55.8 mg, 664 µmol, 4.00 eq.) and *Dess-Martin* periodinane (141 mg, 332 µmol, 2.00 eq.). After one hour, additional sodium bicarbonate (27.9 mg, 332 µmol, 2.00 eq.) and *Dess-Martin* periodinane (70.4 mg, 166 µmol, 1.00 eq.) were added. After two hours, the colorless suspension was poured into a mixture of 5 mL saturated aqueous sodium bicarbonate solution and 5 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the aldehyde as a yellow oil. Chromium-(II)-chloride (421 mg, 3.43 mmol, 20.6 eq.) and nickel-(II)-chloride (4.21 mg, 3.02 µmol, 21.0 mol%) were suspended in DMF (5 mL) and cooled to 0 °C. A solution of vinyl iodide **84** (322 mg, 1.66 mmol, 10.0 eq.) and previously prepared aldehyde in DMF (5 mL) was added. The dark green solution was stirred for two hours and then poured

into a mixture of cold (0 °C) saturated aqueous ammonium chloride solution (30 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (6 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 7:1), alcohol **115** was obtained as a yellowish oil (37.5 mg, 36.7 µmol, 22%).

TLC: R_f = 0.40 (pentane:diethyl ether = 4:1) [UV, CAM].

Diastereomeric ratio: d.r. ≈ 3:2

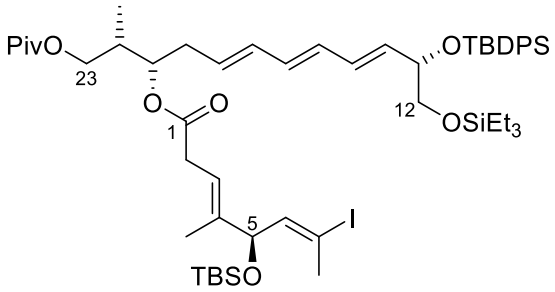
^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.70-7.57 (m, 4 H, C_{Ar}-H), 7.46-7.32 (m, 6 H, C_{Ar}-H), 6.49 (dt, ^3J = 16.8, 10.5 Hz, 1 H, H-9), 6.14 (dq, ^3J = 8.6 Hz, ^4J = 1.9 Hz, 1 H, H-6), 6.08-5.98 (m, 4 H, H-10, H-16-18), 5.96-5.86 (m, 1 H, H-15), 5.65-5.61 (m, 1 H, H-3), 5.61-5.48 (m, 2 H, H-14, H-19), 5.18-5.11 (m, 1 H, H-8a), 5.09-5.03 (m, 1 H, H-8b), 5.03-4.96 (m, 1 H, H-21), 4.69-4.62 (m, 1 H, H-5), 4.23 (dd, ^3J = 7.1, 4.5 Hz, 0.6 H, H-13_A), 4.14 (dd, ^3J = 8.1, 5.8 Hz, 0.4 H, H-13_A), 3.98-3.88 (m, 3 H, H-12, H-23), 3.03 (t, ^3J = 6.7 Hz, 2 H, H-2), 2.78 (d, ^3J = 4.6 Hz, 0.4 H, OH_B), 2.45 (m, 3 H, H-42), 2.41-2.32 (m, 2.6 H, H-20, OH_A), 2.12-2.00 (m, 1 H, H-22), 1.61-1.57 (m, 3 H, H-41), 1.52 (d, ^4J = 1.3 Hz, 1.2 H, H-43_B), 1.47-1.42 (m, 1.8 H, H-43_A), 1.21-1.18 [m, 9 H, OCOC$(CH_3)_3$], 1.08 [s, 5 H, SiC$(CH_3)_3]_A$, 1.05 [s, 4 H, SiC$(CH_3)_3]_B$, 0.98-0.96 (m, 3 H, H-44), 0.95-0.91 [m, 9 H, Si$(CH_2C\mathit{H}_3)_3$], 0.61-0.54 [m, 6 H, Si$(C\mathit{H}_2CH_3)_3$].

^{13}**C-NMR**: (126 MHz, $CDCl_3$) δ 178.5 [s, O*C*OC$(CH_3)_3$], 171.2 (s, C-1), 143.1 (d, C-6), 139.5 (s, C-4), 136.4 (s, C-11_B), 136.3 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 135.8 (s, C-11_A), 132.6 (d, C-9), 130.5 (d, C-14), 129.3 (d, C-19), 128.1 (d, C-10_B), 127.8 (d, C_{Ar}-H), 127.8 (d, C_{Ar}-H), 127.6 (d, C_{Ar}-H), 127.6 (d, C_{Ar}-H), 127.0 (d, C-10_A), 117.3 (d, C-8_B), 117.1 (d, C-8_A), 116.7 (d, C-3), 95.4 (s, C-7), 80.3 (d, C-12_B), 78.9 (d, C-12_A), 76.7 (d, C-13_A), 76.0 (d, C-13_B), 74.5 (d, C-5), 73.3 (d, C-21), 65.7 (t, C-23), 38.9 [s, OCO*C*$(CH_3)_3$], 35.5 (d, C-22), 35.3 (t, C-20), 33.7 (t, C-2), 28.4 (q, C-42), 27.3 [q, OCOC($\mathit{C}H_3)_3$], 27.2 [q, SiC($\mathit{C}H_3)_3$], 27.2 [q, SiC($\mathit{C}H_3)_3$], 19.5 [s, Si*C*$(CH_3)_3$], 19.4 [s, Si*C*$(CH_3)_3$], 13.6 (q, C-43_A), 13.4 (q, C-43_B), 12.7 (q, C-41), 11.4 (q, C-44), 6.91 [q, Si$(CH_2\mathit{C}H_3)_3$], 4.93 [t, Si($\mathit{C}H_2CH_3)_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3405 (m, OH), 2957 (s, C-H), 2931 (s, C-H), 2876 (m, C-H), 1732 (s, C=O), 1461 (m, C-H), 997 (m, C-O), 741 (m, C=C).

HRMS (ESI): *m/z* $[C_{54}H_{79}IO_7Si_2 + NH_4]^+$ calcd.: 1040.4752, found: 1040.4749.

Silyl protected fragment 111



111
$C_{55}H_{87}IO_7Si_3$
1071.45 g/mol

To a cold (0 °C) solution of carboxylic acid **109** (778 mg, 1.90 mmol, 1.00 eq.) in toluene (80 mL) was added triethylamine (659 µL, 481 mg, 4.75 µmol, 2.50 eq.), followed by 2,4,6-trichlorobenzoyl chloride (357 µL, 556 mg, 2.28 mmol, 1.20 eq.). After stirring for ten minutes, a solution of alcohol **67** (1.68 g, 2.47 mmol, 1.30 eq.) in toluene (20 mL) and 4-(dimethylamino)-pyridine (232 mg, 1.90 mmol, 1.00 eq.) was added. While stirring for 2.5 hours at 0 °C, the solution turned into an orange suspension. The reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (100 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 100 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 10:1), ester **111** was obtained as a yellowish oil (1.76 mg, 1.64 mmol, 87%).

TLC: R_f = 0.82 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}**H-NMR**: (400 MHz, $CDCl_3$) δ 7.73-7.60 (m, 4 H, C_{Ar}-H), 7.44-7.31 (m, 6 H, C_{Ar}-H), 6.12 (dq, ^3J = 9.2 Hz, ^4J = 1.9 Hz, 1 H, H-6), 6.09-6.01 (m, 4 H, H-15-18), 5.74-5.67 (m, 1 H, H-14), 5.66-5.60 (m, 1 H, H-3), 5.53 (dt, ^3J = 14.9, 7.4 Hz, 1 H, H-19), 5.01 (td, ^3J = 6.7, 3.9 Hz, 1 H, H-21), 4.65 (d, ^3J = 8.5 Hz, 1 H, H-5), 4.22 (*virt*. q, $^3J \approx {}^3J$ = 6.4 Hz, 1 H, H-13), 3.93 (d, ^3J = 6.4 Hz, 2 H, H-23), 3.52 (dd, ^2J = 9.5 Hz, ^3J = 3.4 Hz, 1 H, H-12a), 3.39 (dd, ^2J = 9.5 Hz, ^3J = 6.8 Hz, 1 H, H-12b), 3.04 (d, ^3J = 7.2 Hz, 2 H, H-2), 2.45 (d, ^4J = 1.5 Hz, 3 H, H-42), 2.41-2.34 (m, 2 H, H-20), 2.12-2.02 (m, 1 H, H-22), 1.59 (d, ^4J = 1.3 Hz, 3 H, H-41), 1.20 [s, 9 H, $OCOC(CH_3)_3$], 1.07 [s, 9 H, $SiC(CH_3)_3$ TBDPS], 0.97 (d, ^3J = 6.9 Hz, 3 H, H-44), 0.88 [s, 9 H, $SiC(CH_3)_3$ TBS], 0.85 [t, ^3J = 8.0 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.45 [q, ^3J = 8.0 Hz, 6 H, $Si(CH_2CH_3)_3$], 0.05 (s, 3 H, $SiCH_3$), 0.03 (s, 3 H, $SiCH_3$).

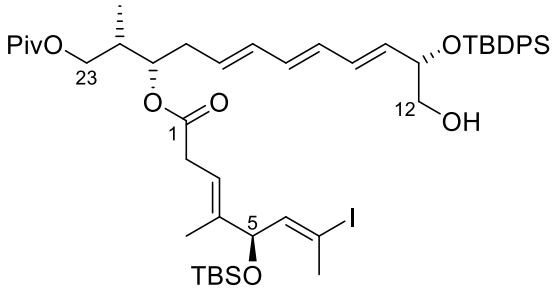
^{13}C-NMR: (101 MHz, $CDCl_3$) δ 178.5 [s, O*C*OC$(CH_3)_3$], 171.2 (s, C-1), 143.2 (d, C-6), 139.5 (s, C-4), 136.1 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 134.4 (d, C-14), 134.2 (d, C_{Ar}), 134.1 (d, C_{Ar}), 133.6 (d, C-18)*, 132.1 (d, C-15)*, 131.6 (d, C-16)*, 130.9 (d, C-17)*, 129.7 (d, C_{Ar}-H), 128.5 (d, C-19), 127.5 (d, C_{Ar}-H), 116.7 (d, C-3), 95.3 (s, C-7), 74.8 (d, C-5), 74.6 (d, C-13), 73.4 (d, C-21), 67.3 (t, C-12), 65.8 (t, C-23), 38.9 [s, OCO*C*$(CH_3)_3$], 35.5 (d, C-22), 35.3 (t, C-20), 33.6 (t, C-2), 28.5 (q, C-42), 27.3 [q, OCOC(*C*$H_3)_3$], 27.2 [q, SiC(*C*$H_3)_3$ TBDPS], 25.9 [q, SiC(*C*$H_3)_3$ TBS], 19.5 [s, Si*C*$(CH_3)_3$ TBDPS], 18.4 [s, Si*C*$(CH_3)_3$ TBS], 12.6 (q, C-41), 11.4 (q, C-44), 6.84 [q, Si(CH_2*C*$H_3)_3$], 4.40 [t, Si(*C*$H_2CH_3)_3$], –4.58 (q, SiCH_3), –4.74 (q, SiCH_3).

Specific rotation: $[\alpha]_D^{20} = +20.0$ (*c* = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2956 (vs) 2857 (s) (C_{sp3}-H), 1733 (vs, CO), 1111 (vs).

HRMS (ESI): *m/z* $[C_{55}H_{87}IO_7Si_3 + NH_4]^+$ found: 1088.5137; calcd.: 1088.5148.

Alcohol 112



112

$C_{49}H_{73}IO_7Si_2$

957.19 g/mol

To a cold (0 °C) solution of silyl ether **111** (1.72 g, 1.60 mmol, 1.00 eq.) in THF (25 mL) and diethyl ether (25 mL) was added pyridine (5 mL) and HF · pyridine complex (30 w% HF, 1.25 mL, 8.58 mmol, 28.8 eq.). After four hours, the solution was poured into 50 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 100 mL). The combined organic layers were washed with 10% copper sulfate solution (3 × 50 mL), brine (2 × 50 mL), dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 4:1), alcohol **112** was obtained as a yellowish oil (1.34 g, 87%).

TLC: R_f = 0.20 (pentane:diethyl ether = 4:1) [UV, CAM].

Specific rotation: $[\alpha]_D^{20} = +48.0$ (c = 1.00, $CHCl_3$).

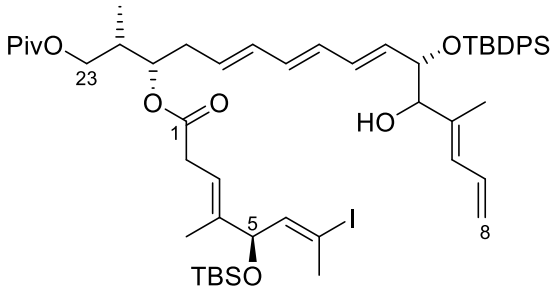
^{1}H-NMR: (400 MHz, $CDCl_3$) δ 7.70-7.60 (m, 2H), 7.45-7.32 (m, 2H), 6.11 (dq, ^3J = 8.5 Hz, ^4J = 1.8 Hz, 1 H, H-6), 6.08-5.91 (m, 4 H, H-15-18), 5.69-5.48 (m, 3 H, H-3, H-14, H-19), 5.04-4.97 (m, 1 H, H-21), 4.64 (d, ^3J = 8.3 Hz, 1 H, H-5), 4.28 (*virt*. q, $^3J \approx {}^3J$ = 5.6 Hz, 1 H, H-13), 3.98-3.87 (m, 2 H, H-23), 3.53-3.43 (m, 2 H, H-12), 3.03 (d, ^3J = 7.2 Hz, 2 H, H-2), 2.46-2.43 (m, 3 H, H-42), 2.42-2.31 (m, 2 H, H-20), 2.06 (dt, ^3J = 11.1, 6.5 Hz, 1 H, H-22), 1.80 (t, ^3J = 6.3 Hz, 1 H, OH), 1.58 (d, ^4J = 1.4 Hz, 1 H, H-41), 1.20 [s, 9 H, $OCOC(CH_3)_3$], 1.08 [s, 9 H, $SiC(CH_3)_3$ TBDPS], 0.96 (d, ^3J = 7.0 Hz, 3 H, H-44), 0.88 [s, 9 H, $SiC(CH_3)_3$ TBS], 0.05 (s, 3 H, $SiCH_3$), 0.03 (s, 3 H, $SiCH_3$).

^{13}C-NMR: (101 MHz, $CDCl_3$) δ 178.5 [s, $OCOC(CH_3)_3$], 171.2 (s, C-1), 143.1 (d, C-6), 139.5 (s, C-4), 136.1 (d, C_{Ar}-H), 135.9 (d, C_{Ar}-H), 134.0 (d, C-15)*, 133.3 (d, C-16)*, 132.3 (d, C-14), 132.2 (d, C-17)*, 130.9 (d, C-18)*, 130.0 (d, C_{Ar}-H), 129.9 (d, C_{Ar}-H), 129.4 (d, C-19), 127.8 (d, C_{Ar}-H), 127.7 (d, C_{Ar}-H), 116.7 (d, C-3), 95.2 (s, C-7), 75.0 (d, C-13), 74.8 (d, C-5), 73.3 (d, C-21), 67.1 (t, C-12), 65.7 (t, C-23), 38.97 [s, $OCOC(CH_3)_3$], 35.5 (d, C-22), 35.3 (t, C-20), 33.7 (t, C-2), 28.5 (q, C-42), 27.4 [q, $OCOC(CH_3)_3$], 27.2 [q, $SiC(CH_3)_3$ TBDPS], 25.9 [q, $SiC(CH_3)_3$ TBS], 19.5 [s, $SiC(CH_3)_3$ TBDPS], 18.4 [s, $SiC(CH_3)_3$ TBS], 12.7 (q, C-41), 11.5 (q, C-44), –4.57 (q, $SiCH_3$), –4.74 (q, $SiCH_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3570 (*br*. w, OH), 2957 (s) 2931 (s) 2858 (s) (C_{sp3}-H), 1732 (vs, CO), 1111 (vs).

HRMS (ESI): *m/z* $[C_{49}H_{73}IO_7Si_2 + NH_4]^+$ found: 974.4277; calcd.: 974.4283.

Alcohol 116



116

$C_{54}H_{79}IO_7Si_2$

1023.29 g/mol

To a solution of primary alcohol **112** (22.9 mg, 24.0 µmol, 1.00 eq.) in dichloromethane (2 mL) was added sodium bicarbonate (16.0 mg, 192 µmol, 8.00 eq.) and *Dess-Martin* periodinane (40.3 mg, 96 µmol, 4.00 eq.). After five hours, the yellow suspension was poured into a mixture of 5 mL saturated aqueous sodium bicarbonate solution and 5 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the aldehyde as a yellow oil. Chromium-(II)-chloride (60.6 mg, 493 µmol, 20.5 eq.) and nickel-(II)-chloride (0.606 mg, 4.70 µmol, 20.0 mol%) were suspended in DMF (1 mL) and cooled to 0 °C. A solution of vinyl iodide **84** (46.4 mg, 239 µmol, 10.0 eq.) and previously prepared aldehyde in DMF (1 mL) was added. The dark green solution was stirred for one hour and then poured into cold (0 °C) saturated aqueous ammonium chloride solution (20 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (5 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 8:1), alcohol **116** was obtained as a colorless oil (6.50 mg, 6.35 µmol, 27%).

TLC: R_f = 0.35 & 0.40 (pentane:diethyl ether = 4:1) [UV, CAM].

Diastereomeric ratio: d.r. ≈ 1:1

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.70-7.59 (m, 4 H, C_{Ar}-H), 7.47-7.31 (m, 6 H, C_{Ar}-H), 6.49 (dt, ^3J = 16.8, 10.6 Hz, 1 H, H-9), 6.17-6.08 (m, 2 H, H-6, H-18), 6.07-5.97 (m, 3 H, H-10, H-16, H-17), 5.96-5.86 (m, 1 H, H-15), 5.69-5.45 (m, 3 H, H-3, H-14, H-19), 5.17-5.12 (m, 1 H, H-8a), 5.08-5.03 (m, 1 H, H-8b), 5.03-4.97 (m, 1 H, H-21), 4.70-4.60 (m, 1 H, H-5), 4.25-4.21 (m, 0.5 H, H-13_A), 4.17-4.13 (m, 0.5 H, H-13_B), 3.99-3.87 (m, 3 H, H-12, H-23), 3.09-2.98 (m,

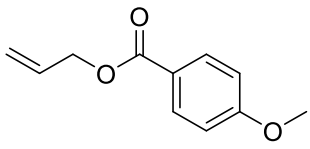
2 H, H-2), 2.45 (d, ^4J = 1.5 Hz, 3 H, H-42), 2.42-2.32 (m, 2 H, H-20), 2.11-2.01 (m, 1 H, H-22), 1.60-1.56 (m, 3 H, H-41), 1.52 (d, ^4J = 1.3 Hz, 1.5 H, H-43$_A$), 1.45 (d, ^4J = 1.3 Hz, 1.5 H, H-43$_B$), 1.21-1.19 [m, 9 H, OCOC(CH$_3$)$_3$], 1.09-1.07 [m, 4.5 H, SiC(CH$_3$)$_3$ TBDPS]$_A$, 1.06 [m, 4.5 H, SiC(CH$_3$)$_3$ TBDPS]$_B$, 0.99-0.95 (m, 3 H, H-44), 0.89-0.87 [m, 9 H, SiC(CH$_3$)$_3$ TBS], 0.05 (s, 3 H, SiCH$_3$), 0.03 (s, 3 H, SiCH$_3$).

^{13}C-NMR: (126 MHz, CDCl$_3$) δ 178.5 [s, O*C*OC(CH$_3$)$_3$], 171.2 (s, C1), 143.1 (d, C-6), 139.5 (s, C-4), 136.2 (s, C-11), 136.1 (s, C$_{Ar}$-H), 136.1 (s, C$_{Ar}$-H), 136.0 (s, C$_{Ar}$-H), 135.8 (s, C$_{Ar}$-H), 135.8 (s, C$_{Ar}$-H), 132.6 (d, C-9), 132.0 (d, C-14), 129.3 (d, C-19), 128.1 (d, C-10$_A$), 127.0 (d, C-10$_B$), 117.3 (t, C-8$_A$), 117.1 (t, C-8$_B$), 116.6 (d, C-3), 95.3 (s, C-7), 80.3 (d, C-12$_A$), 78.9 (d, C-12$_B$), 76.7 (d, C-13$_A$), 76.0 (d, C-13$_B$), 74.8 (d, C-5), 73.3 (d, C-21), 65.8 (t, C-23), 38.9 [s, OCO*C*(CH$_3$)$_3$], 35.4 (d, C-22), 35.3 (t, C-20), 33.7 (t, C-2), 28.5 (q, C-42), 27.3 [q, OCOC(*C*H$_3$)$_3$], 27.2 [q, SiC(*C*H$_3$)$_3$ TBDPS]$_A$, 27.2 [q, SiC(*C*H$_3$)$_3$ TBDPS]$_B$, 25.9 [q, SiC(*C*H$_3$)$_3$ TBS], 19.5 [s, Si*C*(CH$_3$)$_3$ TBDPS]$_A$, 19.49 [s, Si*C*(CH$_3$)$_3$ TBDPS]$_B$, 18.4 [s, Si*C*(CH$_3$)$_3$ TBS], 13.6 (q, C-43$_A$), 13.5 (q, C-43$_B$), 12.7 (q, C-41), 11.4 (q, C-44), –4.57 (q, SiCH$_3$), –4.75 (q, SiCH$_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3567 (*br.* w OH), 2957 (s) 2930 (s) 2857 (s) (C$_{sp3}$-H), 1732 (vs, CO), 1111 (vs), 702 (s).

HRMS (ESI): *m/z* [C$_{54}$H$_{79}$IO$_7$Si$_2$ + NH$_4$]$^+$ found: 1040.4745; calcd.: 1040.4753.

PMBz protected allyl alcohol 132



132
$C_{11}H_{12}O_3$
192.21 g/mol

To a cold (0 °C) solution of allyl alcohol (9.09 mL, 7.73 g, 133 mmol, 1.00 eq.) in pyridine (250 mL) was added anisoyl chloride (19.8 mL, 25.0 g, 146 mmol, 1.10 eq.). The colorless suspension was stirred for 18 hours while warming up to room temperature. Ethyl acetate (500 mL) was added, and the solution was washed with saturated aqueous sodium bicarbonate solution (2 × 500 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (2 × 500 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution, dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 2:1 ⟶ 1:2), ester **132** was obtained as a colorless oil (24.0 mg, 94%)

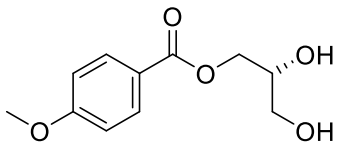
TLC: R_f = 0.80 (pentane:diethyl ether = 2:1) [UV, CAM].

^{1}**H-NMR**: (300 MHz, $CDCl_3$) δ 8.08-7.96 (m, 2 H, C_{Ar}-H), 6.98-6.87 (m, 2 H, C_{Ar}-H), 6.04 (ddt, ^3J = 17.2 Hz, ^3J = 10.4 Hz, ^3J = 5.6 Hz, 1 H, -*H*C=CH_2), 5.40 (*virt*. dq, ^3J = 17.2 Hz, $^2J \approx {}^4J \approx$ 1.6 Hz, 1 H, *H*HC=C), 5.28 (*virt*. dq, ^3J = 10.4 Hz, $^2J \approx {}^4J \approx$ 1.3 Hz, 1 H, H*H*C=C), 4.80 (dt, ^3J = 5.6 Hz, ^4J = 1.4 Hz, 2 H, CH_2O), 3.86 (s, 3 H, OMe).

^{13}**C-NMR**: (75 MHz, $CDCl_3$) δ 166.2 (s, CO), 163.6 (s, C-OMe), 132.6 (d, -H*C*=CH_2), 131.8 (d, C_{Ar}-H), 122.8 (s, C_{Ar}), 118.1 (t, -HC=*C*H_2), 113.8 (d, C_{Ar}-H), 65.4 (t, CH_2O), 55.6 (q, OMe).

The analytical data obtained matched those reported in the literature.[100]

Diol 133



133
$C_{11}H_{14}O_5$
226.23 g/mol

To a cold (0 °C) solution of AD-Mix-alpha (50 g) in water (150 mL) and *tert*-butanol (100 mL) was slowly added allyl ester **132** (6.00 g, 31.2 mmol, 1.00 eq.) over a period of 15 minutes. The orange solution turns into a yellow suspension. After stirring for one hour, sodium thiosulfate (60 g) was added, and stirring was continued for 30 minutes. The yellow suspension turned into a red solution. Ethyl acetate (150 mL) and water (100 mL) were added, and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (50 mL), dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Diol **133** was obtained as a colorless solid (7.00 g, *quant.*) and used without further purification.

TLC: R_f = 0.50 (ethyl acetate) [UV, CAM].

Enantiomeric excess: *ee* = 97%.

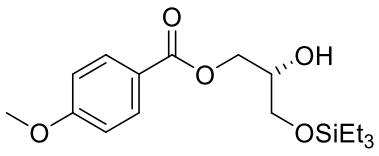
Specific rotation: $[\alpha]_D^{20}$ = –26.0 (*c* = 1.00, $CHCl_3$), –11.3 (*c* = 1.36, pyridine).

^{1}**H-NMR**: (400 MHz, $CDCl_3$, 300K) δ 8.05-7.95 (m, 2 H, C_{Ar}-H), 6.96-6.88 (m, 2 H, C_{Ar}-H), 4.46-4.33 (m, 2 H, CH_2OR), 4.08-4.01 (m, 1 H, C*H*OH), 3.86 (s, 3 H, OMe), 3.76 (dd, ^3J = 11.5 Hz, ^3J = 4.0 Hz, 1 H, C*H*HOH), 3.67 (dd, ^3J = 11.5 Hz, ^3J = 5.7 Hz, 1 H, CH*H*OH).

^{13}**C-NMR**: (101 MHz, $CDCl_3$, 300K) δ 167.0 (s, CO), 163.9 (s, COMe), 132.0 (d, C_{Ar}-H), 122.0 (s, C_{Ar}), 113.9 (d, C_{Ar}-H), 70.6 (d, CHOH), 65.7 (t, CH_2OR), 63.5 (t, CH_2OH), 55.6 (q, OMe).

The analytical data obtained matched those reported in the literature.[99c]

TES protected fragment 134



134
$C_{17}H_{28}O_5Si$
340.49 g/mol

To a cold (0 °C) solution of diol **133** (7.00 g, 31.2 mmol, 1.00 eq.) in dichloromethane (100 mL) was added 2,6-lutidine (7.27 mL, 62.4 mmol, 2.00 eq.) and triethylsilyl chloride (5.49 mL, 4.94 g, 32.7 mmol, 1.05 eq.). After stirring for six hours at 0 °C, further 1.50 mL triethylsilyl chloride (9.36 mmol, 0.3 eq.) was added. After 1.5 hours, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (100 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 100 mL). The combined organic layers were washed with copper sulfate solution (10 wt.%, 3 × 50 mL), dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 4:1 ⟶ 2:1), silyl ether **134** was obtained as a colorless oil (8.86 g, 83%).

TLC: R_f = 0.60 (pentane:diethyl ether = 1:1), [UV, CAM].

Specific rotation: $[\alpha]_D^{20} = -2.0$ (c = 1.00, $CHCl_3$).

^{1}H-NMR: (300 MHz, $CDCl_3$, 300K) δ 8.03-7.97 (m, 2 H, C_{Ar}-H), 6.97-6.86 (m, 2 H, C_{Ar}-H), 4.36 (dd, ^3J = 5.4 Hz, ^2J = 1.0 Hz, 2 H, CH_2OR), 4.01 (*virt.* p, $^3J \approx {}^3J$ = 5.3 Hz, 1 H, C*H*OH), 3.85 (s, 3 H, OMe), 3.76 (dd, ^2J = 10.1 Hz, ^3J = 4.7 Hz, 1 H, C*H*HOSiEt$_3$), 3.69 (dd, ^2J = 10.1 Hz, ^3J = 5.6 Hz, 1 H, CH*H*OSiEt$_3$), 0.97 [t, ^3J = 7.9 Hz, 9 H, Si(CH_2CH_3)$_3$], 0.63 [q, ^3J = 7.9 Hz, 6 H, Si(CH_2CH_3)$_3$].

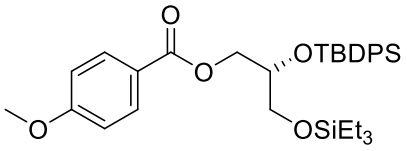
^{13}C-NMR: (75 MHz, $CDCl_3$, 300K) δ 166.6 (s, CO), 163.7 (s, COMe), 131.9 (d, C_{Ar}-H), 122.5 (s, C_{Ar}), 113.8 (d, C_{Ar}-H), 70.4 (d, CHOH), 65.6 (t, CH_2OR), 63.6 (t, CH_2OSiEt_3), 55.6 (q, OMe), 6.8 [q, Si(CH_2CH_3)$_3$], 4.5 [t, Si(CH_2CH_3)$_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3478 (*br* m, OH), 2955 (m, C_{sp3}-H), 2912 (m, C_{sp3}-H), 2877 (m, C_{sp2}-H), 1715 (s, C=O), 1607 (s), 1257 (vs), 1102 (s).

HRMS (ESI): *m/z* $[C_{17}H_{28}O_5Si+H]^+$ calcd.: 341.1784; found: 341.1783.

$[C_{17}H_{28}O_5Si+Na]^+$ calcd.: 363.1604; found: 363.1603.

TES-TBDPS protected fragment 135



135
$C_{33}H_{46}O_5Si_2$
578.90 g/mol

To a cold (0 °C) solution of alcohol **134** (8.86 g, 26.0 mmol, 1.00 eq.) in dichloromethane (60 mL) was added imidazole (3.54 g, 52.0 mmol, 2.00 eq.) and *tert*-butyldiphenylsilyl chloride (8.79 mL, 9.29 g, 33.8 mmol, 1.30 eq.). After stirring for 1.5 hours at 0 °C, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (100 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 100 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 100:1 ⟶ 10:1), silyl ether **135** was obtained as a colorless oil (10.2 g, 68%)

TLC: R_f = 0.60 (pentane:diethyl ether = 10:1), [UV, CAM].

Specific rotation: $[\alpha]_D^{20} = +18.0$ (c = 1.00, $CHCl_3$).

^{1}**H-NMR**: (400 MHz, $CDCl_3$, 300K) δ 7.94-7.86 (m, 2 H, C_{Ar}-H), 7.70-7.62 (m, 4 H, C_{Ar}-H TBDPS), 7.46-7.27 (m, 6 H, C_{Ar}-H TBDPS), 6.95-6.84 (m, 2 H, C_{Ar}-H), 4.43 (dd, ^2J = 11.4 Hz, ^3J = 3.4 Hz, 1 H, C*H*HOR), 4.28 (dd, ^2J = 11.4 Hz, ^3J = 5.6 Hz, 1 H, CH*H*OR), 4.08-4.01 (m, 1 H, CHOTBDPS), 3.87 (s, 3 H, OMe), 3.67-3.53 (m, 2 H, CH_2OSiEt_3), 1.04 [s, 9 H, $SiC(CH_3)_3$], 0.85 [t, ^3J = 8.0 Hz, 9 H, $Si(CH_2CH_3)_3$], 0.47 [q, ^3J = 8.0 Hz, 6 H, $Si(CH_2CH_3)_3$].

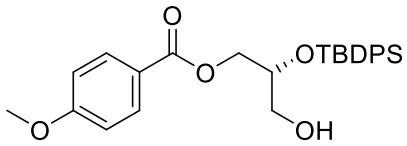
^{13}**C-NMR**: (101 MHz, $CDCl_3$, 300K) δ 166.2 (s, CO), 163.2 (s, COMe), 135.9 (d, C_{Ar}-H TBDPS), 135.8 (d, C_{Ar}-H TBDPS), 133.8 (s, C_{Ar} TBDPS), 133.8 (s, C_{Ar} TBDPS), 131.7 (d, C_{Ar}-H), 129.7 (d, C_{Ar}-H TBDPS), 129.6 (d, C_{Ar}-H TBDPS), 127.6 (d, C_{Ar}-H TBDPS), 127.6 (d, C_{Ar}-H TBDPS), 122.8 (s, C_{Ar}), 113.5 (d, C_{Ar}-H), 72.1 (d, CHOTBDPS), 66.1 (t, CH_2OR), 63.6 (t, CH_2OSiEt_3), 55.4 (q, OMe), 26.9 [q, $SiC(CH_3)_3$], 19.3 [s, $SiC(CH_3)_3$], 6.7 [q, $Si(CH_2CH_3)_3$], 4.2 [t, $Si(CH_2CH_3)_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2956 (m, C_{sp3}-H), 2911 (m, C_{sp3}-H), 2877 (m, C_{sp2}-H), 2859 (m, C_{sp2}-H), 1717 (vs, C=O), 1607 (s), 1256 (vs), 1103 (vs).

HRMS (ESI): *m/z* $[C_{33}H_{46}O_5Si_2 + H]^+$ calcd.: 579.2962; found: 579.2957.

$[C_{33}H_{46}O_5Si_2 + Na]^+$ calcd.: 601.2781; found: 601.2776.

Alcohol 136



136
$C_{27}H_{32}O_5Si$
464.63 g/mol

To a cold (0 °C) solution of silyl ether **135** (5.00 g, 8.64 mmol, 1.00 eq.) in THF (30 mL) was added HF · pyridine complex (1.04 mL, 30 wt.% HF, 932 mg, 34.5 mmol, 4.00 eq.). After 1.5 hours, the solution was poured into 200 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 100 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 4:1), alcohol **136** was obtained as a colorless oil (2.99 g, 74%).

TLC: R_f = 0.50 (pentane:diethyl ether = 1:1), [UV, CAM].

Specific rotation: $[\alpha]_D^{20} = +32.0$ (c = 1.00, $CHCl_3$).

^{1}H-NMR: (300 MHz, $CDCl_3$, 300K) δ 7.89-7.83 (m, 2 H, C_{Ar}-H), 7.74-7.63 (m, 4 H, C_{Ar}-H TBDPS), 7.50-7.30 (m, 6 H, C_{Ar}-H TBDPS), 6.92-6.83 (m, 2 H, C_{Ar}-H), 4.40 (dd, ^2J = 11.5 Hz, ^3J = 5.2 Hz, 1 H, C*H*HOR), 4.29 (dd, ^2J = 11.5 Hz, ^3J = 5.1 Hz, 1 H, CH*H*OR), 4.07 (*virt.* p, $^3J \approx {}^3J \approx$ 4.9 Hz, 1 H, C*H*OTBDPS), 3.86 (s, 3 H, OMe), 3.62 (dd, ^3J = 4.6 Hz, ^2J = 2.6 Hz, 2 H, CH_2OH), 1.08 [s, 9 H, $SiC(CH_3)_3$].

^{13}C-NMR: (75 MHz, $CDCl_3$, 300K) δ 166.4 (s, CO), 163.6 (s, COMe), 135.9 (d, C_{Ar}-H TBDPS), 133.5 (s, C_{Ar} TBDPS), 133.4 (s, C_{Ar} TBDPS), 131.9 (d, C_{Ar}-H), 130.2 (d, C_{Ar}-H TBDPS), 130.1 (d, C_{Ar}-H TBDPS), 128.0 (d, C_{Ar}-H TBDPS), 127.9 (d, C_{Ar}-H TBDPS), 122.4

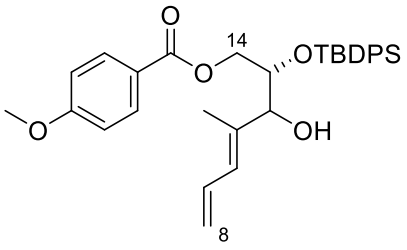
(s, C_{Ar}), 113.7 (d, C_{Ar}-H), 72.1 (d, CHOTBDPS), 65.1 (t, CH_2OR), 63.8 (t, CH_2OH), 55.6 (q, OMe), 27.1 [q, SiC(CH_3)$_3$], 19.5 [s, SiC(CH_3)$_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3480 (*br* m, OH), 3071 (w), 2957 (m, C_{sp3}-H), 2933 (m, C_{sp3}-H), 2893 (m, C_{sp2}-H), 2858 (m, C_{sp2}-H), 1714 (s, C=O), 1606 (s), 1257 (vs), 1104 (vs), 702 (s).

HRMS (ESI): *m/z* $[C_{27}H_{32}O_5Si + H]^+$ calcd.: 465.2097; found: 465.2097.

$[C_{27}H_{32}O_5Si + Na]^+$ calcd.: 487.1917; found: 487.1917.

Alcohol 137



137

$C_{32}H_{38}O_5Si$

530.74 g/mol

To a solution of primary alcohol **136** (5.17 g, 11.1 mmol, 1.00 eq.) in dichloromethane (500 mL) was added sodium bicarbonate (3.74 g, 44.5 mmol, 4.00 eq.) and *Dess-Martin* periodinane (9.43 g, 22.2 mmol, 2.00 eq.). After 60 minutes, the yellow suspension was poured into a mixture of 100 mL saturated aqueous sodium bicarbonate solution and 100 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the corresponding aldehyde as a yellow oil.

In parallel, mesylate **89** (9.68 g, 33.7 mmol, 3.00 eq.) was dissolved in diethyl ether and treated with potassium *tert*-butanolate (18.7 g, 166.8 mmol, 5.00 eq.) at 0 °C. After stirring for 15 minutes, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (250 mL). The layers were separated, and the aqueous layer was extracted with pentane (2 × 100 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure (p>400 mbar due to volatility) to yield the corresponding diene **84** as a yellow oil.

Chromium-(II)-chloride (20.5 g, 167 mmol, 15.0 eq.) and nickel-(II)-chloride (216 mg, 1.67 mmol, 0.15 eq.) were suspended in DMF (400 mL) and cooled to 0 °C. A solution of the

crude aldehyde and diene in DMF (100 mL) was added, which resulted in a deep green color of the suspension. After 10 minutes, the reaction was slowly warmed up to room temperature. Stirring was continued for one hour and the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (250 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 150 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 10:1 ⟶ 2:1), alcohol **137** was obtained as a yellowish oil (3.24 g, 55%).

TLC: R_f = 0.55 (pentane:diethyl ether = 1:2), [UV, CAM].

Diastereomeric ratio: d.r. = 2.3:1.

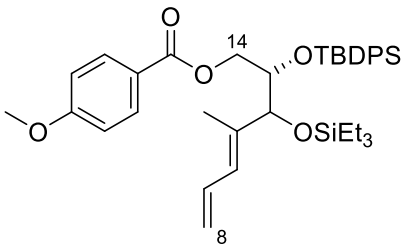
^{1}**H-NMR**: (500 MHz, $CDCl_3$, 300K) δ 7.78-7.74 (m, 2 H, C_{Ar}-H), 7.71-7.63 (m, 7 H, C_{Ar}-H), 7.48-7.27 (m, 10 H. C_{Ar}-H), 6.87-6.80 (m, 2 H, C_{Ar}-H), 6.56-6.46 (m, 1 H, H-9), 6.18 (d, ^3J = 11.0 Hz, 0.7 H, H-10$_A$), 6.14 (d, ^3J = 11.0 Hz, 0.3 H, H-10$_B$), 5.25-5.06 (m, 2 H, H-8), 4.40-4.28 (m, 2 H, H-14), 4.16-4.14 (m, 0.3 H, H-12$_B$), 4.11-4.09 (m, 1.4 H, H-12$_A$, H-13$_A$), 4.06 (q, ^3J = 5.0 Hz, 0.3 H, H-13$_B$), 3.86 (s, 3 H, OMe), 2.74 (d, ^3J = 5.7 Hz, 0.3 H, OH$_B$), 2.64 (d, ^3J = 2.6 Hz, 0.7 H, OH$_A$), 1.52 (d, ^3J = 1.4 Hz, 2 H, H-43$_A$), 1.50 (d, ^3J = 1.3 Hz, 1 H, H-43$_B$), 1.07 [s, 6 H, SiC(CH$_3$)$_3$]$_A$, 1.06 [s, 3 H, SiC(CH$_3$)$_3$]$_B$.

^{13}**C-NMR**: (101 MHz, $CDCl_3$, 300K) δ 166.5 (s, CO$_A$), 165.9 (d, CO$_B$), 163.4 (s, COMe), 136.5 (s, C-11$_B$), 136.0 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 135.5 (s, C-11$_A$), 133.4 (s, C_{Ar}), 133.0 (s, C_{Ar}), 132.4 (d, C-9), 131.9 (d, C_{Ar}-H), 130.2 (d, C_{Ar}-H), 129.9 (d, C_{Ar}-H), 128.0 (d, C-10$_B$), 127.0 (d, C-10$_A$), 122.5 (s, C_{Ar}), 122.4 (s, C_{Ar}), 117.6 (t, C-8$_B$), 117.5 (t, C-8$_A$), 113.6 (d, C_{Ar}-H), 77.3 (d, C-12$_A$), 76.8 (d, C-12$_B$), 73.1 (d, C-13$_A$), 72.5 (d, C-13$_B$), 65.1 (t, C-14), 55.5 (q, OMe), 27.1 [q, SiC(*C*H$_3$)$_3$]$_B$, 27.0 [q, SiC(*C*H$_3$)$_3$]$_A$, 19.6 [s, Si*C*(CH$_3$)$_3$]$_B$, 19.4 [s, Si*C*(CH$_3$)$_3$]$_A$, 13.5 (q, C-43$_A$), 13.2 (q, C-43$_B$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3491 (*br* m, OH), 3072 (w), 2958 (m, C_{sp3}-H), 2932 (m, C_{sp3}-H), 2895 (m, C_{sp2}-H), 2858 (m, C_{sp2}-H), 1714 (s, C=O), 1606 (s), 1257 (vs), 1104 (vs), 703 (s).

HRMS (ESI): *m/z* $[C_{32}H_{38}O_5Si + Na]^+$ calcd.: 553.2386; found: 553.2385.

TES protected fragment 138



138

$C_{38}H_{52}O_5Si_2$

645.00 g/mol

To a cold (0 °C) solution of alcohol **137** (1.36 g, 2.57 mmol, 1.00 eq.) in dichloromethane (20 mL) was added pyridine (622 µL, 610 mg, 7.71 mmol, 3.00 eq.) and triethylsilyl triflate (697 µL, 815 mg, 3.08 mmol, 1.20 eq.). After stirring for 40 minutes at 0 °C, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (20 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 50:1 ⟶ 20:1), silyl ether **138** was obtained as a colorless oil (1.43 g, 86%).

TLC: R_f = 0.75 (pentane:diethyl ether = 4:1), [UV, CAM].

Diastereomeric ratio: d.r. = 2:1.

^{1}**H-NMR**: (400 MHz, $CDCl_3$, 300K) δ 7.78-7.59 (m, 6 H, C_{Ar}-H), 7.45-7.17 (m, 6 H, C_{Ar}-H), 6.89-6.76 (m, 2 H, C_{Ar}-H), 6.63-6.47 (m, 1 H, H-9), 6.12 (d, ^3J = 10.8 Hz, 1 H, H-10), 5.24-5.01 (m, 2 H, H-8), 4.31-4.17 (m, 3 H, H-14, H-12), 4.11-4.00 (m, 0.3 H, H-13_B), 3.94 (dt, ^3J = 7.0 Hz, ^3J = 3.6 Hz, 0.7 H, H-13_A), 3.87 (s, 2 H, OMe_A), 3.85 (s, 1 H, OMe_B), 1.74 (s, 1 H, H-42_B), 1.59 (s, 2 H, H-42_A), 1.04 [s, 3 H, $SiC(CH_3)_3]_B$, 0.99 [s, 6 H, $SiC(CH_3)_3]_A$, 0.93-0.82 [m, 9 H, $Si(CH_2C\mathit{H}_3)_3$], 0.58-0.43 [m, 6 H, $Si(C\mathit{H}_2CH_3)_3$].

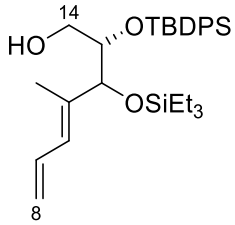
^{13}**C-NMR**: (101 MHz, $CDCl_3$, 300K) δ 166.2 (s, CO), 163.2 (s, COMe), 138.1 (s, C-11_A), 137.3 (s, C-11_B), 136.3 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 134.2 (s, C_{Ar}), 133.1 (s, C_{Ar}), 132.9 (d, C-9), 132.7 (s, C_{Ar}), 131.7 (d, C_{Ar}-H), 129.8 (d, C_{Ar}-H), 129.6 (d, C_{Ar}-H), 129.1 (d, C-10_A), 127.7 (d, C_{Ar}-H), 127.6 (d, C-10_B), 127.6 (d, C_{Ar}-H), 127.5 (d, C_{Ar}-H), 123.0 (d, C_{Ar}-H), 122.9 (d, C_{Ar}-H), 117.1 (t, C-8_A), 116.8 (t, C-8_B), 113.5 (d, C_{Ar}-H), 113.4 (d, C_{Ar}-H), 79.0 (d, C-12_A), 77.4 (d, C-12_B), 74.8 (d, C-13_A), 73.3 (d, C-13_B), 66.1 (t, C-14), 55.5 (q, OMe), 27.1 [q, $SiC(\mathit{C}H_3)_3]_B$,

27.0 [q, SiC(*C*H$_3$)$_3$]$_A$, 19.6 [s, Si*C*(CH$_3$)$_3$]$_B$, 19.5 [s, Si*C*(CH$_3$)$_3$]$_A$, 14.5 (q, C-43$_B$), 12.6 (q, C-43$_A$), 7.0 [q, Si(CH$_2$*C*H$_3$)$_3$]$_B$, 6.9 [q, Si(CH$_2$*C*H$_3$)$_3$]$_A$, 4.9 [t, Si(*C*H$_2$CH$_3$)$_3$]$_A$, 4.8 [t, Si(*C*H$_2$CH$_3$)$_3$]$_B$.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3073 (w), 2956 (m, C$_{sp3}$-H), 2877 (m, C$_{sp2}$-H), 2858 (m, C$_{sp2}$-H), 1717 (vs, C=O), 1606 (s), 1256 (vs), 1102 (vs), 702 (s).

HRMS (ESI): *m/z* [C$_{38}$H$_{52}$O$_5$Si$_2$ + Na]$^+$ calcd.: 667.3251; found: 667.3259.

Alcohol 139



139
C$_{30}$H$_{46}$O$_3$Si$_2$
510.87 g/mol

To a cold (–78 °C) solution of ester **138** (1.23 g, 1.91 mmol, 1.00 eq.) in dichloromethane (15 mL) was added di-*iso*-propylaluminiumhydrid (1M in dichloromethane, 9.54 mmol, 5.00 eq.). After stirring for two hours, the reaction was quenched by the addition of methanol (1 mL) and ethyl acetate (5 mL) and warmed up to room temperature. Saturated aqueous sodium potassium tartrate solution (30 mL) was added, and the resulting suspension was stirred for 20 minutes. The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 50 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 30:1 ⟶ 20:1), alcohol **139** was obtained as a colorless oil (907 mg, 93%)

TLC: R_f = 0.75 & 0.80 (pentane:diethyl ether = 4:1) [UV, CAM].

Diastereomeric ratio: d.r. = 2:1.

^{1}**H-NMR**: (300 MHz, CDCl$_3$, 300K) δ 7.79-7.61 (m, 4 H, C$_{Ar}$-H), 7.48-7.30 (m, 6 H, C$_{Ar}$-H), 6.60-6.41 (m, 1 H, H-9), 6.11 (d, ^3J = 11.2 Hz, 0.3 H, H-10$_B$), 6.05 (d, ^3J = 11.0 Hz, 0.7 H, H-10$_A$), 5.21-5.05 (m, 2 H, H-8), 4.20 (d, ^3J = 4.8 Hz, 0.3 H, H-12$_B$), 4.15 (d, ^3J = 6.5 Hz, 0.7 H,

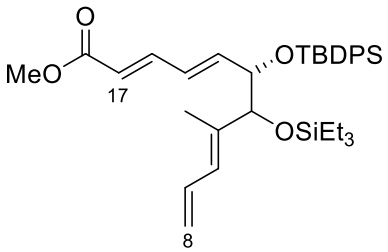
H-12$_A$), 3.93-3.86 (m, 0.3 H, H-13$_B$), 3.72-3.60 (m, 1.7 H, H-14a, H-13$_A$), 3.60-3.49 (m, 1 H, H-14b), 2.25 (dd, ^3J = 7.8 Hz, ^3J = 4.8 Hz, 0.7 H, OH$_A$), 2.17 (dd, ^3J = 7.6 Hz, ^3J = 4.5 Hz, 0.3 H, OH$_B$), 1.80-1.76 (m, 1 H, H-42$_B$), 1.44-1.39 (m, 2 H, H-42$_A$), 1.08 [s, 3 H, SiC(CH$_3$)$_3$]$_B$, 1.03 [s, 6 H, SiC(CH$_3$)$_3$]$_A$, 0.95-0.81 [m, 9 H, Si(CH$_2$C*H*$_3$)$_3$], 0.64-0.40 [m, 6 H, Si(C*H*$_2$CH$_3$)$_3$].

^{13}C-NMR: (101 MHz, CDCl$_3$, 300K) δ 137.8 (s, C-11), 136.1 (d, C$_{Ar}$-H), 135.8 (d, C$_{Ar}$-H), 134.2 (s, C$_{Ar}$), 132.6 (d, C-9), 129.8 (d, C$_{Ar}$-H), 129.0 (d, C-10), 127.9 (d, C$_{Ar}$-H), 127.8 (d, C$_{Ar}$-H), 127.7 (d, C$_{Ar}$-H), 127.6 (d, C$_{Ar}$-H), 117.1 (t, C-8), 80.9 (d, C-12$_A$), 78.5 (d, C-12$_B$), 75.4 (d, C-13$_B$), 73.9 (d, C-13$_A$), 64.4 (t, C-14), 27.1 [q, SiC(*C*H$_3$)$_3$]$_B$, 27.0 [q, SiC(*C*H$_3$)$_3$]$_A$, 19.3 [s, Si*C*(CH$_3$)$_3$], 14.6 (q, C-42$_B$), 12.2 (q, C-42$_A$), 6.8 [q, Si(CH$_2$*C*H$_3$)$_3$], 4.7 [t, Si(*C*H$_2$CH$_3$)$_3$]$_A$, 4.5 [t, Si(*C*H$_2$CH$_3$)$_3$]$_B$.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3507 (*br* m, OH), 2955 (s, C$_{sp3}$-H), 2933 (s, C$_{sp3}$-H), 2877 (s, C$_{sp2}$-H), 2859 (s, C$_{sp2}$-H), 1111 (vs), 702 (vs).

HRMS (ESI): *m/z* [C$_{30}$H$_{46}$O$_3$Si$_2$ + Na]$^+$ calcd.: 533.2883; found: 533.2877.

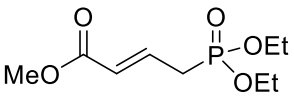
Ester 140



140

$C_{35}H_{50}O_4Si_2$

590.95 g/mol



128

To a solution of primary alcohol **139** (900 mg, 1.76 mmol, 1.00 eq.) in dichloromethane (20 mL) was added sodium bicarbonate (592 mg, 7.05 mmol, 4.00 eq.) and *Dess-Martin* periodinane (1.49 g, 3.52 mmol, 2.00 eq.). After 1.5 hours, the yellow suspension was poured into a mixture of 20 mL saturated aqueous sodium bicarbonate solution and 20 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the corresponding aldehyde as a yellow oil.

In parallel, a cold (0 °C) solution of di-*iso*-propylamine (522 µL, 3.70 mmol, 2.10 eq.) in THF (15 mL) was treated with *n*-butyllithium (2.5M in hexane, 3.70 mmol, 2.10 eq.). After stirring for 40 minutes, the solution was cooled to –60 °C, and a solution of phosphonate **128** (832 mg, 3.52 mmol, 2.00 eq.) in THF (5 mL) was added. The yellow solution was stirred for 20 minutes, and then the previously prepared aldehyde was added as a solution in THF (5 mL). Over the course of two hours, the reaction was warmed to –30 °C and then quenched by the addition of saturated aqueous ammonium chloride solution (20 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 1:0 ⟶ 20:1), ester **140** was obtained as a colorless oil (762 mg, 73%).

TLC: R_f = 0.85 (pentane:diethyl ether = 4:1) [UV, CAM].

Diastereomeric ratio: d.r. = 3:1.

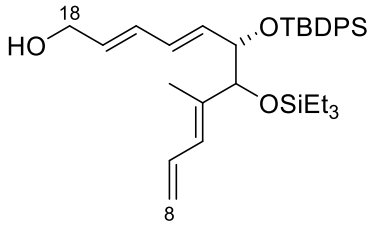
^{1}**H-NMR**: (500 MHz, $CDCl_3$, 300K) δ 7.74-7.57 (m, 4 H, C_{Ar}-H), 7.43-7.30 (m, 6 H, C_{Ar}-H), 7.13 (dd, ^3J = 15.3 Hz, ^3J = 10.0 Hz, 0.25 H, H-16$_B$), 7.07 (dd, ^3J = 15.3 Hz, ^3J = 11.1 Hz, 0.75 H, H-16$_A$), 6.55-6.46 (m, 1 H, H-9), 6.08-6.04 (m, 0.5 H, H-14$_B$, H-15$_B$), 6.00-5.90 (m, 1.75 H, H-10, H-14$_A$), 5.76 (dd, ^3J = 15.3 Hz, ^3J = 11.0 Hz, 0.75 H, H-15$_A$), 5.68 (d, ^3J = 15.4 Hz, 0.25 H, H-17$_B$), 5.63 (d, ^3J = 15.4 Hz, 0.75 H, H-17$_A$), 5.17-5.06 (m, 2 H, H-8), 4.32 (*virt.* t, $^3J \approx {}^3J$ = 5.0 Hz, 0.25 H, H-13$_B$), 4.07 (dd, ^3J = 7.4 Hz, ^3J = 6.2 Hz, 0.75 H, H-13$_A$), 3.97-3.93 (m, 1 H, H-12), 3.73 (s, 3 H, OMe), 1.65 (d, ^4J = 1.3 Hz, 0.75 H, H-43$_B$), 1.48 (d, ^4J = 1.3 Hz, 2.25 H, H-43$_A$), 1.07 [s, 3 H, $SiC(CH_3)_3]_B$, 1.01 [s, 6 H, $SiC(CH_3)_3]_A$, 0.86 [t, ^3J = 7.9 Hz, 6 H, $Si(CH_2CH_3)_3]_A$, 0.82 [t, ^3J = 7.9 Hz, 3 H, $Si(CH_2CH_3)_3]_B$, 0.50 [q, ^3J = 7.9 Hz, 4.5 H, $Si(CH_2CH_3)_3]_A$, 0.40 [q, ^3J = 7.9 Hz, 1.5 H, $Si(CH_2CH_3)_3]_B$.

^{13}C-NMR: (126 MHz, $CDCl_3$, 300K) δ 167.7 (s, CO), 144.6 (d, C-16$_B$), 144.4 (d, C-16$_A$), 143.1 (d, C-14$_A$), 142.6 (d, C-14$_B$), 138.2 (s, C-11$_A$), 137.5 (s, C-11$_B$), 136.3 (d, C_{Ar}-H), 136.2 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 133.9 (s, C_{Ar}), 133.8 (s, C_{Ar}), 132.8 (d, C-9$_A$), 130.0 (d, C-15$_A$), 129.8 (d, C_{Ar}-H), 129.8 (d, C_{Ar}-H), 128.9 (d, C-10$_A$), 128.4 (d, C-15$_B$), 127.6 (d, C_{Ar}-H), 127.5 (d, C_{Ar}-H), 120.5 (d, C-17$_A$), 117.0 (t, C-8$_A$), 81.7 (d, 12$_A$), 76.1 (d, 13$_A$), 51.6 (q, OMe), 27.2 [q, $SiC(CH_3)_3]_B$, 27.1 [q, $SiC(CH_3)_3]_A$, 19.6 [s, $SiC(CH_3)_3]_B$, 19.5 [s, $SiC(CH_3)_3]_A$, 12.5 (q, C-43$_A$), 6.9 [q, $Si(CH_2CH_3)_3$], 4.9 [t, $Si(CH_2CH_3)_3]_A$, 4.7 [t, $Si(CH_2CH_3)_3]_B$.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2953 (m, C_{sp3}-H), 2877 (m, C_{sp2}-H), 2859 (m, C_{sp2}-H), 1721 (vs, C=O), 1111 (vs), 701 (vs).

HRMS (ESI): no ionization possible.

Alcohol 142



142
$C_{34}H_{50}O_3Si_2$
562.94 g/mol

To a cold (–78 °C) solution of ester **140** (760 mg, 1.29 mmol, 1.00 eq.) in dichloromethane (10 mL) was added di-*iso*-propylaluminiumhydrid (1M in dichloromethane, 6.43 mL, 6.43 mmol, 5.00 eq.). After stirring for four hours, the reaction was quenched by the addition of methanol (1 mL) and ethyl acetate (5 mL) and warmed up to room temperature. Saturated aqueous sodium potassium tartrate solution (20 mL) was added and the resulting suspension was stirred for 20 minutes. The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 6:1 ⟶ 3:1), alcohol **142** was obtained as a colorless oil (541 mg, 75%).

TLC: R_f = 0.25 (pentane:diethyl ether = 4:1), [UV, CAM].

Diastereomeric ratio: d.r. ≈ 4:1.

^{1}**H-NMR**: (500 MHz, $CDCl_3$, 300K) δ 7.74-7.57 (m, 4 H, C_{Ar}-H), 7.43-7.30 (m, 6H, C_{Ar}-H), 6.51 (dt, ^3J = 16.8 Hz, ^3J = 10.5 Hz, 1 H, H-9), 6.03 (ddt, ^3J = 15.1 Hz, ^3J = 9.9 Hz, ^4J = 1.5 Hz, 1 H, H-16), 5.06 (d, ^3J = 10.5 Hz, 1 H, H-10), 5.66-5.60 (m, 1 H, H-14_B, H-15), 5.59-5.52 (m, 1.75 H, H-14_A, H-17), 5.18-5.01 (m, 2 H, H-8), 4.25 (*virt.* t, $^3J \approx {}^3J$ = 5.8 Hz, 0.25 H, H-13_B), 4.14-4.10 (m, 2 H, H-18), 4.02 (dd, ^3J = 7.6 Hz, ^3J = 6.2 Hz, 0.75 H, H-13_A), 3.93 (d,

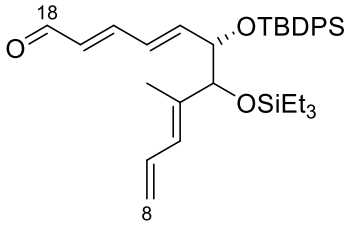
^3J = 5.4 Hz, 0.25 H, H-12$_B$), 3.92 (d, ^3J = 6.2 Hz, 0.75 H, H-12$_A$), 1.66 (d, ^3J = 1.3 Hz, 0.75 H, H-43$_B$), 1.50 (d, ^3J = 1.3 Hz, 2.25 H, H-43$_A$), 1.06 [s, 2 H, SiC(CH$_3$)$_3$]$_B$, 1.01 [s, 7 H, SiC(CH$_3$)$_3$]$_A$, 0.91-0.83 [m, 9 H, Si(CH$_2$C*H*$_3$)$_3$], 0.51 [q, ^3J = 8.0 Hz, 5 H, Si(C*H*$_2$CH$_3$)$_3$]$_A$, 0.41 [q, ^3J = 8.0 Hz, 1 H, Si(C*H*$_2$CH$_3$)$_3$]$_B$.

^{13}C-NMR: (126 MHz, CDCl$_3$, 300K) δ 138.8 (d, C-11$_A$), 136.4 (d, C$_{Ar}$-H), 136.3 (d, C$_{Ar}$-H), 136.2 (d, C$_{Ar}$-H), 134.9 (d, C$_{Ar}$-H), 134.5 (d, C-17$_A$), 134.3 (s, C$_{Ar}$), 134.1 (s, C$_{Ar}$), 133.0 (d, C-9$_A$), 131.8 (d, C-15$_A$), 131.5 (d, C-14$_A$), 131.1 (d, C-16$_A$), 129.8 (d, C$_{Ar}$-H), 129.6 (d, C$_{Ar}$-H), 129.5 (d, C$_{Ar}$-H), 128.6 (d, C-10$_A$), 127.9 (d, C$_{Ar}$-H), 127.6 (d, C$_{Ar}$-H), 127.5 (d, C$_{Ar}$-H), 127.4 (d, C$_{Ar}$-H), 116.6 (t, C-8), 81.9 (d, C-12), 76.7 (d, C-13), 63.6 (t, C-18), 27.2 [q, SiC(*C*H$_3$)$_3$], 19.5 [s, Si*C*(CH$_3$)$_3$], 12.5 (q, C-43), 7.0 [q, Si(CH$_2$*C*H$_3$)$_3$], 4.9 [t, Si(*C*H$_2$CH$_3$)$_3$]$_A$, 4.7 [t, Si(*C*H$_2$CH$_3$)$_3$]$_B$.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3324 (*br* m, OH), 2955 (s, C$_{sp3}$-H), 2932 (m, C$_{sp3}$-H), 2876 (m, C$_{sp2}$-H), 2858 (m, C$_{sp2}$-H), 1111 (vs), 701 (vs).

HRMS (ESI): no ionization possible.

Trienal 141



141
$C_{34}H_{48}O_3Si_2$
560.93 g/mol

To a solution of alcohol **142** (3.56 g, 6.34 mmol, 1.00 eq.) in dichloromethane (100 mL) was added manganese-(IV)-oxide (11.0 g, 127 mmol, 20.0 eq.) and the black suspension was stirred for 16 hours at room temperature. The suspension was filtered over Celite, and the solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 10:1), aldehyde **141** was obtained as a colorless oil (3.16 g, 89%).

TLC: R_f = 0.85 (pentane:diethyl ether = 4:1), [UV, KMnO$_4$].

Diastereomeric ratio: d.r. ≈ 4:1.

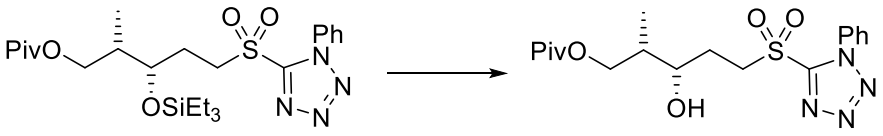
^{1}H-NMR: (300 MHz, $CDCl_3$, 300K) δ 9.48 (d, ^{3}J = 8.1 Hz, 1 H, CHO), 7.72-7.54 (m, 4 H, C_{Ar}-H), 7.45-7.28 (m, 6 H, C_{Ar}-H), 6.86 (dd, ^{3}J = 15.3, 10.7 Hz, 1 H, H-16), 6.61-6.43 (m, 1 H, H-9), 6.22-5.83 (m, 4 H, H-10, H-14, H-15, H-17), 5.21-5.03 (m, 2 H, H-8), 4.40-4.34 (m, 0.25 H, H-13_B), 4.13 (t, ^{3}J = 6.6 Hz, 0.75 H, H-13_A), 4.01-3.94 (m, 1 H, H-12), 1.67 (d, ^{3}J = 1.3 Hz, 0.6 H, H-43_B), 1.51 (d, ^{3}J = 1.3 Hz, 2.4 H, H-43_A), 1.08 [s, 2 H, $SiC(CH_3)_3]_B$, 1.03 [s, 7 H, $SiC(CH_3)_3]_A$, 0.92-0.82 [m, 9 H, $Si(CH_2C\mathit{H}_3)_3$], 0.57-0.37 [m, 6 H, $Si(C\mathit{H}_2CH_3)_3$].

^{13}C-NMR: (126 MHz, $CDCl_3$, 300K) δ 194.2 (d, CHO), 152.1 (d, C-16_B), 151.8 (d, C-16_A), 145.5 (d, C-14_A), 144.9 (d, C-14_B), 137.9 (s, C-11_A), 137.2 (s, C-11_B), 136.2 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 133.4 (d, C-9), 131.4 (d, C-17_A), 131.2 (d, C-17_B), 129.8 (d, C_{Ar}-H), 128.9 (d, C-15_A), 128.4 (d, C-15_B), 128.3 (d, C-10_B), 127.7 (d, C-10_A), 127.6 (d, C_{Ar}-H), 127.5 (d, C_{Ar}-H), 117.2 (t, C-8_A), 116.8 (t, C-8_B), 81.5 (d, C-12_A), 79.6 (d, C-12_B), 76.5 (d, C-13_B), 75.7 (d, C-13_A), 27.1 [q, $SiC(\mathit{C}H_3)_3]_B$, 27.0 [q, $SiC(\mathit{C}H_3)_3]_A$, 19.5 [q, $Si\mathit{C}(CH_3)_3]_B$, 19.4 [q, $Si\mathit{C}(CH_3)_3]_A$, 14.3 (q, C-43_B), 12.5 (q, C-43_A), 6.94 [q, $Si(CH_2\mathit{C}H_3)_3$], 4.80 [t, $Si(\mathit{C}H_2CH_3)_3]_A$, 4.59 [t, $Si(\mathit{C}H_2CH_3)_3]_B$.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2955 (m, C_{sp3}-H), 2934 (m, C_{sp3}-H), 2876 (m, C_{sp2}-H), 2859 (m, C_{sp2}-H), 1685 (vs, C=O), 1100 (vs), 700 (vs).

HRMS (ESI): *m/z* $[C_{34}H_{48}O_3Si_2 + H]^+$ calcd.: 561.3220; found: 561.3213.

Unprotected sulfone 148



12
$C_{24}H_{40}N_4O_5SSi$
524.75 g/mol

148
$C_{18}H_{26}N_4O_5S$
410.49 g/mol

To a solution of silyl ether **12** (9.93 g, 18.9 mmol, 1.00 eq.) in THF (90 mL) was added HF · pyridine complex (4.54 mL, 30 wt.% HF, 151 mmol, 8.00 eq.). After two hours, the solution was poured into 200 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 100 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash

column chromatography (silica, hexane:ethyl acetate = 1:0 ⟶ 0:1), alcohol **148** was obtained as a yellowish oil (7.41 g, 95%).

TLC: R_f = 0.25 (pentane:diethyl ether = 1:1), [UV, CAM].

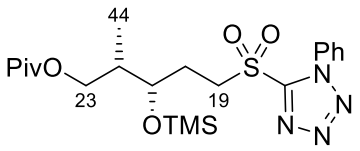
^{1}**H-NMR**: (300 MHz, $CDCl_3$, 300K) δ 7.75-7.52 (m, 5 H, C_{Ar}-H), 4.23 (dd, ^2J = 11.3 Hz, ^3J = 8.3 Hz, 1 H, C*H*HOPiv), 4.05-3.80 (m, 3 H, CH*H*OPiv, CH_2OS), 3.73 (dt, ^3J = 9.5 Hz, ^3J = 3.5 Hz, 1 H, CHOH), 2.17-2.06 (m, 2 H, CH_2), 1.99-1.82 (m, 1 H, CHMe), 1.20 [s, 9 H, $OCOC(CH_3)_3$], 0.94 (d, ^3J = 7.0 Hz, 3 H, CH_3).

^{13}C-NMR: (75 MHz, $CDCl_3$, 300K) δ 179.4 [s, O*C*OC(CH_3)], 153.7 (s, NCS), 133.2 (d, C_{Ar}), 131.6 (d, C_{Ar}-H), 129.9 (d, C_{Ar}-H), 125.3 (d, C_{Ar}-H), 69.4 (d, CHOH), 66.3 (t, CH_2OPiv), 53.9 (t, CH_2SO_2), 39.0 [s, OCO*C*(CH_3)], 38.5 (d, CHMe), 27.4 [q, OCOC(*C*H_3)], 27.2 (t, CH_2), 10.3 (q, CH_3).

Specific rotation: $[\alpha]_D^{20} = -20.0$ (*c* = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3491 (*br* m, OH), 2973 (m, C_{sp3}-H), 1724 (s, C=O), 1342 (s, S=O), 1154 (vs), 764 (s).

TMS protected sulfone 149



149

$C_{21}H_{34}N_4O_5SSi$

482.67 g/mol

To a cold (0 °C) solution of alcohol **148** (9.87 g, 24.0 mmol, 1.00 eq.) in dichloromethane (250 mL) was added triethylamine (16.7 mL, 12.2 g, 120 mmol, 5.00 eq.) and trimethylsilyl chloride (9.17 mL, 7.83 g, 72.0 mmol, 3.00 eq.). After stirring for 3.5 hours at room temperature, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (50 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 100 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column

chromatography (silica, pentane:diethyl ether = 4:1), silyl ether 149 was obtained as a colorless oil (10.3 g, 89%).

TLC: R_f = 0.4 (pentane:diethyl ether = 4:1), [UV, CAM].

Specific rotation: $[\alpha]_D^{20} = -4.00$ (c = 1.00, $CHCl_3$).

^{1}**H-NMR**: (400 MHz, C_6D_6, 300K) δ 7.38-7.29 (m, 2 H, C_{Ar}-H), 6.92-6.82 (m, 3 H, C_{Ar}-H), 3.98 (dd, ^3J = 11.0 Hz, ^2J = 6.5 Hz, 1 H, H-23a), 3.91 (dd, ^3J = 9.2 Hz, ^2J = 6.5 Hz, 1 H, H-23b), 3.72-3.66 (m, 1 H, H-21), 3.66-3.51 (m, 2 H, H-19), 2.11-2.03 (m, 2 H, H-20), 1.65-1.59 (m, 1 H, H-22), 1.18 [s, 9 H, $OCOC(CH_3)_3$], 0.74 (d, ^3J = 6.9 Hz, 3 H, H-44), 0.05 [s, 9 H, $Si(CH_3)_3$].

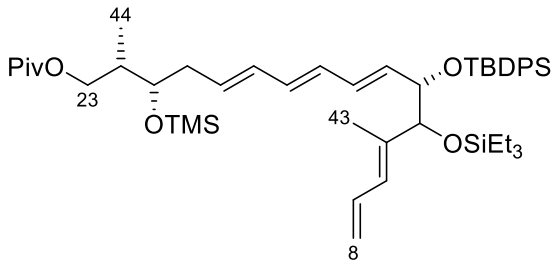
^{13}C-NMR: (101 MHz, C_6D_6, 300K) δ 177.2 [s, O*C*OC(CH_3)], 153.8 (s, SO_2CN), 133.2 (s, C_{Ar}), 130.6 (d, C_{Ar}-H), 129.2 (d, C_{Ar}-H), 124.8 (d, C_{Ar}-H), 70.9 (d, C-21), 65.4 (t, C-23), 53.0 (t, C-19), 38.5 [s, OCO*C*(CH_3)], 37.6 (d, C-22), 27.0 [q, OCOC(*C*H_3)], 26.9 (t, C-20), 11.2 (q, C-44), –0.1 [q, $Si(CH_3)_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2962 (s, C_{sp3}-H), 1727 (vs, C=O), 1344 (s, S=O), 1153 (vs), 842 (vs).

HRMS (ESI): *m/z* $[C_{21}H_{34}N_4O_5SSi + H]^+$ calcd.: 483.2094; found: 483.2098.

$[C_{21}H_{34}N_4O_5SSi + Na]^+$ calcd.: 505.1917; found: 505.1920.

Triene 150



150

$C_{48}H_{76}O_5Si_3$

817.39 g/mol

To a cold (–50 °C) solution of sulfone **149** (2.77 g, 5.75 mmol, 1.70 eq.) in THF (60 mL) was added KHMDS (0.5M in toluene, 13.5 mL, 6.77 mmol, 2.00 eq.) and the yellowish solution was stirred for 80 minutes. Subsequently, a solution of aldehyde **141** (1.90 g, 3.39 mmol,

1.00 eq.) in THF (15 mL) was added, and stirring was continued for one hour. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (100 mL) and water (50 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 100 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 30:1 ⟶ 1:1), triene **150** was obtained as a colorless oil (2.42 g, 88%).

TLC: R_f = 0.88 (pentane:diethyl ether = 4:1), [UV, CAM].

Diastereomeric ratio: d.r. = 4.5:1.

^{1}**H-NMR**: (500 MHz, C_6D_6, 300K) δ 7.92-7.76 (m, 4 H, C_{Ar}-H), 7.33-7.20 (m, 6 H, C_{Ar}-H), 6.64-6.55 (m, 1 H, H-9), 6.25 (d, ^3J = 11.1 Hz, 0.2 H, H-10_B), 6.21 (d, ^3J = 10.9 Hz, 0.8 H, H-10_A), 6.05-5.94 (m, 3 H, H-16, H-17, H-18), 5.91-5.84 (m, 1 H, H-14_B, H-15_A), 5.81-5.75 (m, 1 H, H-14_A, H-15_B), 5.52-5.42 (m, 1 H, H-19), 5.23-5.16 (m, 1 H, H-8a), 5.09-5.05 (m, 1 H, H-8b), 4.58-4.54 (m, 0.2 H, H-13_B), 4.32 (dd, ^3J = 7.8, ^3J = 6.5 Hz, 0.8 H, H-13_A), 4.18 (d, ^3J = 5.1 Hz, 0.2 H, H-12_B), 4.15 (d, ^3J = 6.5 Hz, 0.8 H, H-12_A), 4.08-4.03 (m, 2 H, H-23), 3.74 (td, ^3J = 6.6 Hz, ^3J = 3.0 Hz, 1 H, H-21), 2.26-2.12 (m, 2 H, H-20), 1.88-1.83 (m, 1 H, H-22), 1.81 (d, ^4J = 1.3 Hz, 0.66 H, H-43_B), 1.67 (d, ^4J = 1.4 Hz, 2.33 H, H-43_A), 1.22-1.18 [m, 18 H, OCOC(CH_3)$_3$, SiC(CH_3)$_3$], 0.98 [t, ^3J = 7.9 Hz, 9 H, Si($CH_2C\mathit{H}_3$)$_3$], 0.88 (d, ^3J = 6.9 Hz, 3 H, H-44), 0.62 [q, ^3J = 7.9 Hz, 5 H, Si($C\mathit{H}_2CH_3$)$_3$]$_A$, 0.54 [q, ^3J = 7.7 Hz, 1 H, Si($C\mathit{H}_2CH_3$)$_3$]$_B$, 0.11 (s, 9 H, TMS).

^{13}C-NMR: (126 MHz, C_6D_6, 300K) δ 177.6 [s, O*C*OC(CH_3)], 139.1 (s, C-11_A), 138.2 (s, C-11_B), 136.8 (d, C_{Ar}-H), 136.7 (d, C_{Ar}-H), 134.6 (s, C_{Ar}), 134.5 (s, C_{Ar}), 134.4 (d, C-15_B), 134.2 (d, C-14_A), 133.4 (d, C-15_A), 133.4 (d, C-9), 133.3 (d, C-17)*, 133.2 (d, C-16)*, 133.1 (d, C-18)*, 131.2 (d, C-19), 129.9 (d, C_{Ar}-H), 129.9 (d, C_{Ar}-H), 129.2 (d, C-10_A), 128.8 (d, C-10_B), 116.9 (d, C-8_A), 116.7 (d, C-8_B), 82.4 (d, C-12_A), 81.0 (d, C-12_B), 77.7 (d, C-13_B), 77.4 (d, C-13_A), 72.5 (d, C-21), 66.7 (t, C-23), 39.0 [s, OCO*C*(CH_3)], 38.9 (t, C-20), 37.7 (d, C-22), 27.4 [q, OCOC(*C*H_3), SiC(*C*H_3)$_3$], 19.7 [s, Si*C*(CH_3)$_3$], 14.5 (q, C-43_B), 12.6 (q, C-43_A), 10.5 (q, C-44), 7.2 [q, OSi($CH_2C\mathit{H}_3$)$_3$], 5.3 [t, Si($C\mathit{H}_2CH_3$)$_3$]$_A$, 5.1 [t, Si($C\mathit{H}_2CH_3$)$_3$]$_B$, 0.6 (q, TMS).

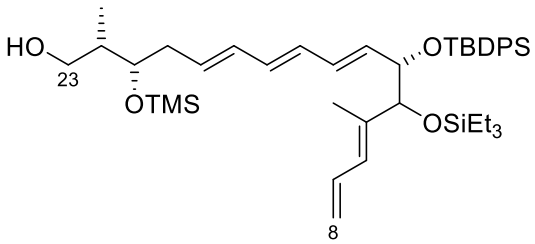
IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2957 (vs, C_{sp3}-H), 2877 (s, C_{sp2}-H), 1731 (vs, C=O), 1151 (s), 1111 (vs), 702 (vs).

HRMS (ESI): *m/z* $[C_{48}H_{76}O_5Si_3 + NH_4]^+$ calcd.: 834.5344; found: 834.5348.

$[C_{48}H_{76}O_5Si_3 + NH_4]^+$ calcd.: 839.4898; found: 839.4902.

*interchangeable signals.

Alcohol 152



152
$C_{43}H_{68}O_4Si_3$
733.27 g/mol

To a cold (–78 °C) solution of ester **150** (2.59 g, 3.17 mmol, 1.00 eq.) in dichloromethane (50 mL) was added di-*iso*-propylaluminiumhydride (1M in dichloromethane, 15.8 mL, 15.8 mmol, 5.00 eq.). After stirring for 40 minutes, the reaction was quenched by the addition of methanol (2 mL) and ethyl acetate (8 mL) and warmed up to room temperature. Saturated aqueous sodium potassium tartrate solution (100 mL) was added, and the resulting suspension was stirred for 20 minutes. The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 10:1 ⟶ 4:1), alcohol **152** was obtained as a colorless oil (2.15 g, 95%).

TLC: R_f = 0.20 (pentane:diethyl ether = 4:1), [UV, CAM].

Diastereomeric ratio: d.r. ≈ 3:1.

^{1}**H-NMR**: (500 MHz, C_6D_6, 300K) δ 7.93-7.76 (m, 4 H, C_{Ar}-H), 7.30-7.21 (m, 6 H, C_{Ar}-H), 6.66-6.50 (m, 1 H, H-9), 6.25 (d, ^3J = 11.0 Hz, 0.25 H, H-10$_B$), 6.21 (d, ^3J = 10.8 Hz, 0.75 H, H-10$_A$), 6.09-5.94 (m, 3 H, H-16, H-17, H-18), 5.94-5.84 (m, 1 H, H-14$_B$, H-15$_A$), 5.79 (dd, ^3J = 15.2 Hz, ^3J = 7.8 Hz, 0.75 H, H-14$_A$), 5.55-5.44 (m, 1 H, H-19), 5.24-5.15 (m, 1 H, H-8a), 5.10-5.01 (m, 1 H, H-8b), 4.56 (ddd, ^3J = 6.6 Hz, ^3J = 5.1 Hz, ^4J = 1.2 Hz, 0.25 H, H-13$_B$), 4.32 (dd, ^3J = 7.8 Hz, ^3J = 6.4 Hz, 0.75 H, H-13$_A$), 4.18 (d, ^3J = 5.1 Hz, 0.25 H, H-12$_B$), 4.15 (d,

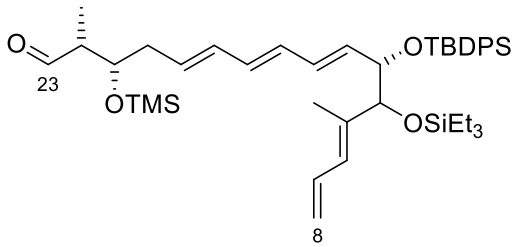
^3J = 6.4 Hz, 0.75 H, H-12$_A$), 3.81 (ddd, ^3J = 7.3 Hz, ^3J = 5.9 Hz, ^3J = 3.1 Hz, 1 H, H-21), 3.45 (*virt.* t, ^3J = 9.3 Hz, 1 H, H-23a), 3.34-3.29 (m, 1 H, H-23b), 2.33-2.11 (m, 2 H, H-20), 1.81 (d, ^4J = 1.3 Hz, 0.7 H, 43$_B$), 1.67 (d, ^4J = 1.3 Hz, 2.3 H, 43$_A$), 1.64-1.58 (m, 1 H, H-22), 1.24 [s, 2 H, SiC(CH$_3$)$_3$]$_B$, 1.21 [s, 7 H, SiC(CH$_3$)$_3$]$_A$, 0.98 [t, ^3J = 7.9 Hz, 9 H, Si(CH$_2$C*H*$_3$)$_3$], 0.80 (d, ^3J = 6.9 Hz, 3 H, H-44), 0.61 [q, ^3J = 7.9 Hz, 5 H, Si(C*H*$_2$CH$_3$)$_3$]$_A$, 0.54 [q, ^3J = 7.7 Hz, 1 H, Si(C*H*$_2$CH$_3$)$_3$]$_B$, 0.11 (s, 9 H, TMS).

^{13}C-NMR: (126 MHz, C_6D_6, 300K) δ 139.1 (d, C-11$_A$), 138.2 (d, C-11$_B$), 136.7 (d, C$_{Ar}$-H), 136.7 (d, C$_{Ar}$-H), 134.6 (s, C$_{Ar}$), 134.5 (s, C$_{Ar}$), 134.1 (d, C-14$_A$), 133.5 (d, C-15$_A$, C-9), 133.3 (d, C-16)*, 133.2 (d, C-17)*, 131.8 (d, C-19), 131.0 (d, C-18)*, 129.2 (d, C-10$_A$), 128.8 (d, C-10$_B$), 116.9 (t, C-8$_A$), 116.7 (t, C-8$_B$), 82.4 (d, C-12$_A$), 81.0 (d, C-12$_B$), 77.8 (d, C-13$_B$), 77.5 (d, C-13$_A$), 73.6 (d, C-21), 65.6 (t, C23), 40.3 (d, C-22), 38.4 (t, C-20), 27.4 [q, SiC(*C*H$_3$)$_3$], 19.7 [s, Si*C*(CH$_3$)$_3$], 14.5 (q, C-43$_A$), 12.6 (q, C-43$_B$), 10.9 (q, C-44), 7.2 [q, Si(CH$_2$*C*H$_3$)$_3$], 5.3 [t, Si(*C*H$_2$CH$_3$)$_3$]$_A$, 5.1 [t, Si(*C*H$_2$CH$_3$)$_3$]$_B$, 0.5 (q, TMS).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3409 (*br* m, OH), 2956 (s, C$_{sp3}$-H), 2877 (m, C$_{sp2}$-H), 2859 (m, C$_{sp2}$-H), 1110 (vs), 996 (vs), 702 (vs).

HRMS (ESI): *m/z* [C$_{43}$H$_{68}$O$_4$Si$_3$ + NH$_4$]$^+$ calcd.: 750.4769; found: 750.4768.

Aldeyhde 161



161

$C_{43}H_{66}O_4Si_3$

731.25 g/mol

To a solution of primary alcohol **152** (1.76 g, 2.40 mmol, 1.00 eq.) in dichloromethane (25 mL) was added sodium bicarbonate (806 mg, 9.60 mmol, 4.00 eq.) and *Dess-Martin* periodinane (1.53 g, 3.60 mmol, 1.50 eq.). After one hour, the yellow suspension was poured into a mixture of 50 mL saturated aqueous sodium bicarbonate solution and 50 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 25 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure.

Following flash column chromatography (silica, pentane:diethyl ether = 20:1), aldehyde **161** was obtained as a colorless oil (1.31 g, 75%).

TLC: R_f = 0.80 (pentane:diethyl ether = 4:1), [UV, CAM].

Diastereomeric ratio: d.r. ≈ 4:1.

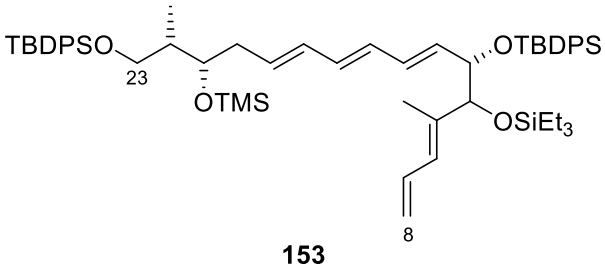
^{1}**H-NMR**: (400 MHz, C_6D_6, 300K) δ 9.49-9.41 (m, 1 H, CHO), 7.93-7.74 (m, 4 H, C_{Ar}-H), 7.33-7.19 (m, 6 H, C_{Ar}-H), 6.66-6.52 (m, 1 H, H-9), 6.22 (d, ^3J = 11.0 Hz, 1 H, H-10), 6.06-5.86 (m, 3 H, H-16-18), 5.83 (d, ^3J = 7.7 Hz, 0.8 H, H-14$_A$), 5.80 (d, ^3J = 7.8 Hz, 0.2 H, H-15$_B$), 5.40-5.29 (m, 1 H, H-19), 5.19 (d, ^3J = 16.9 Hz, 1 H, H-8a), 5.07 (d, ^3J = 10.1 Hz, 1 H, H-8b), 4.58 (t, ^3J = 5.9 Hz, 0.2 H, H-13$_B$), 4.33 (t, ^3J = 7.0 Hz, 0.8 H, H-13$_A$), 4.19 (d, ^3J = 5.2 Hz, 0.2 H, H-12$_B$), 4.15 (d, ^3J = 6.4 Hz, 0.8 H, H-12$_A$), 4.03-3.92 (m, 1 H, H-21), 2.21-2.02 (m, 2 H, H-20), 1.99-1.94 (m, 1 H, H-22), 1.82 (s, 0.6 H, H-43$_B$), 1.67 (s, 2.4 H, H-43$_A$), 1.24 [s, 2 H, SiC(CH$_3$)$_3$]$_B$, 1.21 [s, 7 H, SiC(CH$_3$)$_3$]$_A$, 1.02-0.94 [m, 12 H, Si(CH$_2$*C*H$_3$)$_3$, C-44], 0.67-0.49 [m, 6H, Si(C*H*$_2$CH$_3$)$_3$], 0.06 (s, 3 H, TMS$_B$), 0.04 (s, 5 H, TMS$_A$).

^{13}C-NMR: (101 MHz, C_6D_6, 300K) δ 202.9 (s, CHO), 139.0 (s, C-11), 136.7 (d, C_{Ar}-H), 136.6 (d, C_{Ar}-H), 134.6 (d, C-14*), 134.5 (d, C-15*), 133.8 (d, C-16**), 133.2 (d, C-9), 132.8 (d, C-17**), 131.5 (d, C-18**), 130.2 (d, C-19), 129.2 (d, C-10), 116.9 (t, C-8), 82.4 (d, C-12), 77.4 (d, C-13), 71.5 (d, C-21), 51.2 (d, C-22), 39.1 (t, C-20), 27.4 [q, SiC(*C*H$_3$)$_3$], 19.7 [s, Si*C*(CH$_3$)$_3$], 12.6 (q, C-43$_B$), 7.6 (q, C-44), 7.2 [q, Si(CH$_2$*C*H$_3$)$_3$], 5.3 [t, Si(*C*H$_2$CH$_3$)$_3$], 0.5 (q, TMS).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2955 (s, C_{sp3}-H), 2877 (m, C_{sp2}-H), 2859 (m, C_{sp2}-H), 1727 (s, C=O), 1109 (vs), 702 (vs).

HRMS (ESI): *m/z* [$C_{43}H_{66}O_4Si_3$ + Na]$^+$ calcd.: 753.4167; found: 753.4165.

TBDPS protected fragment 153



153

$C_{59}H_{86}O_4Si_4$

971.67 g/mol

To a cold (0 °C) solution of alcohol **152** (311 mg, 424 µmol, 1.00 eq.) in dichloromethane (10 mL) was added imidazole (72.0 mg, 1.06 mmol, 2.50 eq.), 4-(dimethylamino)-pyridine (5.2 mg, 42.0 µmol, 0.10 eq.) and *tert*-butyldiphenylsilyl chloride (220 µL, 233 mg, 847 µmol, 2.00 eq). After stirring for one hour, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution (10 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 1:0 ⟶ 20:1), silyl ether **153** was obtained as a colorless oil (381 mg, 392 µmol, 93%).

TLC: R_f = 0.80 (pentane:diethyl ether = 4:1) [UV, CAM].

Diastereomeric ratio: d.r. ≈ 4:1.

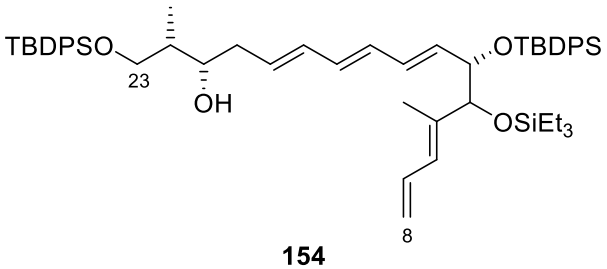
^{1}**H-NMR**: (500 MHz, C_6D_6) δ 7.94-7.73 (m, 8 H, C_{Ar}-H), 7.32-7.20 (m, 12 H, C_{Ar}-H), 6.65-6.54 (m, 1 H, H-9), 6.26 (d, ^3J = 11.1 Hz, 0.2 H, H-10$_B$), 6.21 (d, ^3J = 10.9 Hz, 0.8 H, H-10$_A$), 6.06-5.95 (m, 3 H, H-16, H-17, H-18), 5.94-5.84 (m, 1 H, H-14$_B$, H-15$_A$), 5.78 (dd, ^3J = 15.1 Hz, ^3J = 7.9 Hz, 0.8 H, H-14$_A$), 5.61-5.51 (m, 1 H, H-19), 5.24-5.15 (m, 1 H, H-8a), 5.10-5.02 (m, 1 H, H-8b), 4.56 (ddd, ^3J = 6.5 Hz, ^3J = 5.0 Hz, ^4J = 1.2 Hz, 0.2 H, H-13$_B$), 4.33 (dd, ^3J = 7.9 Hz, ^3J = 6.4 Hz, 0.8 H, H-13$_A$), 4.19 (d, ^3J = 5.0 Hz, 0.2 H, H-12$_B$), 4.15 (d, ^3J = 6.4 Hz, 0.8 H, H-12$_A$), 4.02-3.94 (m, 1 H, H-21), 3.80-3.72 (m, 1 H, H-23a), 3.65-3.57 (m, 1 H, H-23b), 2.31-2.20 (m, 2 H, H-20), 1.86-1.78 (m, 1.7 H, H-22, H-43$_B$), 1.68 (d, ^4J = 1.4 Hz, 2.2 H, H-43$_A$), 1.25 [s, 2.5 H, SiC(CH$_3$)$_3$]$_B$, 1.21 [s, 15.5 H, SiC(CH$_3$)$_3$]$_A$, 1.01-0.92 [m, 12 H, OSi(CH$_2$C*H*$_3$)$_3$, H-44], 0.62 [q, ^3J = 7.9 Hz, 5 H, Si(C*H*$_2$CH$_3$)$_3$]$_A$, 0.54 [q, ^3J = 7.7 Hz, 1 H, Si(C*H*$_2$CH$_3$)$_3$]$_B$, 0.13 (s, 9 H, TMS).

^{13}C-NMR: (101 MHz, C_6D_6) δ 139.1 (s, C-11), 136.8 (d, C_{Ar}-H), 136.7 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 134.6 (d, C_{Ar}), 134.6 (d, C_{Ar}), 134.4 (d, C_{Ar}), 134.3 (d, C_{Ar}), 134.0 (d, C-14$_A$), 133.6 (d, C-15), 133.4 (d, C-18)*, 133.3 (d, C-9)*, 133.1 (d, C-17)*, 131.9 (d, C-19), 130.9 (d, C-16), 130.1 (d, C_{Ar}-H), 130.0 (d, C_{Ar}-H), 129.9 (d, C_{Ar}-H), 129.9 (d, C_{Ar}-H), 129.2 (d, C-10$_A$), 116.9 (t, C-8), 82.5 (d, C-12$_A$), 77.5 (d, C-13$_A$), 72.5 (d, C-21), 66.7 (t, C-23), 40.8 (d, C-22), 39.2 (t, C-20), 27.5 [q, SiC(*C*H$_3$)$_3$], 27.2 [q, SiC(*C*H$_3$)$_3$], 19.7 [s, Si*C*(CH$_3$)$_3$], 19.6 [s, Si*C*(CH$_3$)$_3$], 12.7 (q, C-43), 11.0 (q, C-44), 7.2 [q, Si(CH$_2$*C*H$_3$)$_3$], 5.3 [t, Si(*C*H$_2$CH$_3$)$_3$]$_A$, 5.1 [t, Si(*C*H$_2$CH$_3$)$_3$]$_B$, 0.7 (q, TMS).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3072 (w, C_{sp2}-H), 3049 (w, C_{sp2}-H), 2956 (m, C_{sp3}-H), 2933 (m, C_{sp3}-H), 2877 (m, C_{sp2}-H), 2858 (m, C_{sp2}-H), 1111 (vs), 701 (vs).

HRMS (ESI): no ionization possible.

Alcohol 154



154
$C_{56}H_{78}O_4Si_3$
899.49 g/mol

To a cold (–20 °C) solution of silyl ether **153** (250 mg, 257 µmol, 1.00 eq.) in THF (5 mL) was added HF · pyridine complex (134 µL, 30 wt% HF, 5.15 mmol, 20.0 eq.). After one hour, an additional 50 µL HF · pyridine complex (7.00 eq.) was added, and stirring was continued for one hour. The solution was poured into 30 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 15 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 1:0 ⟶ 10:1), alcohol **154** was obtained as a colorless oil (223 g, 248 µmol, 96%).

TLC: R_f = 0.45 (pentane:diethyl ether = 4:1) [UV, CAM].

Diastereomeric ratio: d.r. ≈ 4:1.

^{1}H-NMR: (500 MHz, C_6D_6) δ 7.94-7.73 (m, 8 H, C_{Ar}-H), 7.31-7.18 (m, 12 H, C_{Ar}-H), 6.64 - 6.54 (m, 1 H, H-9), 6.26 (d, ^{3}J = 11.0 Hz, 0.2 H, H-10_B), 6.21 (d, ^{3}J = 10.9 Hz, 0.8 H, H-10_A), 6.09-5.95 (m, 3 H, H-16, H-17, H-18), 5.94-5.87 (m, 1 H, H-14_B, H-15_A), 5.81 (dd, ^{3}J = 15.0 Hz, ^{3}J = 7.8 Hz, 0.8 H, H-14_A), 5.58 (dt, ^{3}J = 13.6 Hz, ^{3}J = 7.2 Hz, 1 H, H-19), 5.23-5.16 (m, 1 H, H-8a), 5.08-5.03 (m, 1 H, H-8b), 4.57 (ddd, ^{3}J = 6.6 Hz, ^{3}J = 5.1 Hz, ^{4}J = 1.2 Hz, 0.2 H, H-13_B), 4.35 (dd, ^{3}J = 7.8 Hz, ^{3}J = 6.2 Hz, 0.8 H, H-13_A), 4.19 (d, ^{3}J = 5.1 Hz, 0.2 H, H-12_B), 4.6 (d, ^{3}J = 6.1 Hz, 0.8 H, H-12_A), 3.84-3.77 (m, 1 H, H-21), 3.72-3.61 (m, 2 H, H-23), 2.28-2.18 (m, 1 H, H-20a), 2.14-2.04 (m, 1 H, H-20b), 1.98-1.92 (m, 1 H, OH), 1.83 (d, ^{4}J = 1.3 Hz, 0.7 H, H-43_B), 1.67 (d, ^{4}J = 1.3 Hz, 2.3 H, H-43_A), 1.64-1.58 (m, 1 H, H-22), 1.25 [s, 2 H, $C_{12}OSiC(CH_3)_3]_B$, 1.21 [s, 7 H, $C_{12}OSiC(CH_3)_3]_A$, 1.16 [s, 9 H, $C_{23}OSiC(CH_3)_3$], 1.01-0.95 [m, 9 H, $Si(CH_2CH_3)_3$], 0.91-0.88 (m, 3 H, H-44), 0.62 [q, ^{3}J = 7.9 Hz, 5 H, $Si(CH_2CH_3)_3]_A$, 0.53 [q, ^{3}J = 7.9 Hz, 1 H, $Si(CH_2CH_3)_3]_B$.

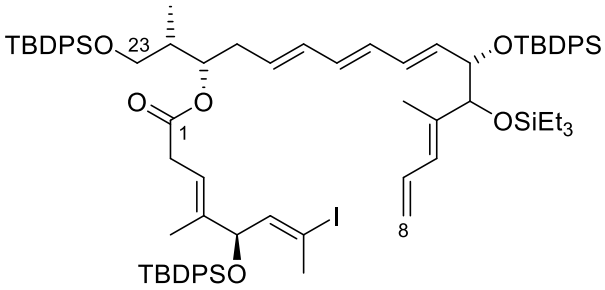
^{13}C-NMR: (126 MHz, C_6D_6) δ 139.1 (s, C-11_A), 138.2 (s, C-11_B), 136.7 (d, C_{Ar}-H), 136.6 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 134.0 (d, C-14), 133.9 (s, C_{Ar}), 133.8 (s, C_{Ar}), 133.5 (d, C-15)*, 133.4 (d, C-17)*, 133.3 (d, C-18)*, 133.1 (d, C-9)*, 131.8 (d, C-19), 130.9 (d, C-16), 129.9 (d, C_{Ar}-H), 129.9 (d, C_{Ar}-H), 129.1 (d, C-10_A), 128.8 (d, C-10_B), 116.9 (t, C-8_A), 116.7 (t, C-8_B), 82.5 (d, C-12_A), 81.0 (d, C-12_B), 77.8 (d, C-13_B), 77.5 (d, C-13_A), 72.7 (d, C-21), 68.2 (t, C-23), 39.8 (d, C-22), 38.8 (t, C-20), 27.4 [q, $C_{12}OSiC(CH_3)_3$], 27.1 [q, $C_{23}OSiC(CH_3)_3$], 19.8 [s, $C_{12}OSiC(CH_3)_3]_B$, 19.7 [s, $C_{12}OSiC(CH_3)_3]_A$, 19.5 [s, $C_{23}OSiC(CH_3)_3$], 14.4 (q, C-43_B), 12.7 (q, C-43_A), 10.5 (q, C-44), 7.2 [q, $Si(CH_2CH_3)_3$], 5.3 [t, $Si(CH_2CH_3)_3]_A$, 5.1 [t, $Si(CH_2CH_3)_3]_B$.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3517 (*br* w, OH), 3071 (w, C_{sp2}-H), 3015 (w, C_{sp2}-H), 2957 (s, C_{sp3}-H), 2932 (m, C_{sp3}-H), 2876 (m, C_{sp2}-H), 1427 (m), 1111 (vs), 701 (vs).

HRMS (ESI): *m/z* $[C_{56}H_{78}O_4Si_3 + NH_4]^+$ calcd.: 916.5552; found: 916.5563.

$[C_{56}H_{78}O_4Si_3 + Na]^+$ calcd.: 921.5106; found: 921.5111.

Diene 155



155

$C_{81}H_{107}IO_6Si_4$

1415.99 g/mol

To a cold (0 °C) solution of carboxylic acid **38** (367 mg, 686 µmol, 1.70 eq.) in toluene (10 mL) was added triethylamine (190 µL, 139 mg, 1.37 mmol, 3.40 eq.), followed by 2,4,6-trichlorobenzoyl chloride (107 µL, 167 mg, 686 µmol, 1.70 eq.). After stirring for 20 minutes, a solution of alcohol **154** (363 mg, 404 µmol, 1.00 eq.) in toluene (10mL) and 4-(dimethylamino)-pyridine (49.3 mg, 404 µmol, 1.00 eq.) was added. While stirring for one hour at 0 °C, the solution turned into an orange suspension. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (30 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 30 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 1:0 ⟶ 10:1), ester **155** was obtained as a colorless oil (444 mg, 313 µmol, 78%).

TLC: R_f = 0.40 (pentane:diethyl ether = 20:1) [UV, CAM].

Diastereomeric ratio: d.r. ≈ 4:1.

^{1}**H-NMR**: (400 MHz, C_6D_6) δ 7.92-7.73 (m, 12 H, C_{Ar}-H), 7.32-7.20 (m, 18 H, C_{Ar}-H), 6.67-6.53 (m, 1 H, H-9), 6.39 (d, ^3J = 8.7 Hz, 0.8 H, H-6_A), 6.34 (d, ^3J = 8.3 Hz, 0.2 H, H-6_B), 6.25 (d, ^3J = 11.3 Hz, 0.2 H, H-10_B), 6.21 (d, ^3J = 10.9 Hz, 0.8 H, H-10_A), 6.08-5.91 (m, 4 H, H-16-18), 5.89-5.78 (m, 2 H, H-3, H-14), 5.55-5.38 (m, 2 H, H-19, H-21), 5.25-5.15 (m, 1 H, H-8a), 5.10-5.04 (m, 1 H, H-8b), 4.68 (d, ^3J = 8.8 Hz, 0.8 H, H-5_A), 4.62-4.55 (m, 0.4 H, H-5_B, H-13_B), 4.33 (t, ^3J = 6.8 Hz, 0.8 H, H-13_A), 4.19-4.14 (m, 1 H, H-12), 3.66-3.52 (m, 2 H, H-23), 2.97-2.83 (m, 2 H, H-2), 2.47-2.35 (m, 1 H, H-20a), 2.34-2.23 (m, 1 H, H-20b), 2.00-1.89 (m, 1 H, H-22), 1.82 (s, 0.7 H, H-43_B), 1.71 (d, ^4J = 1.5 Hz, 3 H, H-42), 1.67 (s, 2.3 H, H-43_A), 1.46 (s, 2.3 H, H-41_A), 1.38 (s, 0.7 H, H-41_B), 1.21 [s, 9 H, $SiC(CH_3)_3$], 1.21 [s, 9 H, $SiC(CH_3)_3$], 1.16

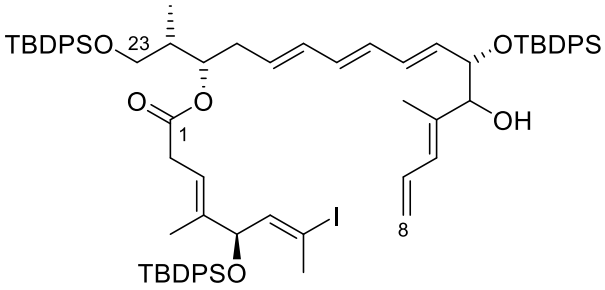
[s, 9 H, SiC(CH_3)$_3$], 1.02-0.87 [m, 12 H, Si($CH_2C\mathit{H}_3$)$_3$, H-44], 0.63 [q, ^3J = 7.9 Hz, 5 H, Si($C\mathit{H}_2CH_3$)$_3$]$_A$, 0.53 [q, ^3J = 8.0 Hz, 1 H, Si($C\mathit{H}_2CH_3$)$_3$]$_B$.

^{13}C-NMR: (101 MHz, C_6D_6) δ 170.6 (s, CO_B), 170.0 (s, CO_A), 142.5 (d, C-6), 139.0 (s, C-11), 138.8 (s, C-4), 136.7 (d, C_{Ar}-H), 136.6 (d, C_{Ar}-H), 136.3 (d, C_{Ar}-H), 136.2 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 134.5-133.2 (m, C-9, C-14-18), 130.1 (d, C_{Ar}-H), 129.7 (d, C-19), 129.1 (d, C-10), 118.1 (d, C-3), 116.8 (t, C-8), 96.9 (s, C-7), 82.5 (d, C-12), 77.6 (d, C-13), 75.7 (d, C-5), 73.4 (d, C-21), 65.9 (t, C-23), 38.6 (d, C-22), 35.9 (t, C-20), 33.8 (t, C-2), 27.9 (q, C-42), 27.4 [q, SiC($\mathit{C}H_3$)$_3$], 27.1 [q, SiC($\mathit{C}H_3$)$_3$], 27.1 [q, SiC($\mathit{C}H_3$)$_3$], 19.7 [s, SiC(CH_3)$_3$], 19.6 [s, SiC(CH_3)$_3$], 19.5 [s, SiC(CH_3)$_3$], 12.8 (q, C-43), 12.4 (q, C-41), 11.4 (q, C-44), 7.2 [q, Si($CH_2\mathit{C}H_3$)$_3$], 5.3 [t, Si($\mathit{C}H_2CH_3$)$_3$]$_A$, 5.1 [t, Si($\mathit{C}H_2CH_3$)$_3$]$_B$.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3071 (w, C_{sp2}-H), 3048 (w, C_{sp2}-H), 2957 (m, C_{sp3}-H), 2932 (m, C_{sp3}-H), 2876 (m, C_{sp2}-H), 2858 (m, C_{sp2}-H), 1735 (m, C=O), 1427 (m), 1111 (vs), 701 (vs).

HRMS (ESI): no ionization possible.

Alcohol 156



156
$C_{75}H_{93}IO_6Si_3$
1301.72 g/mol

To a solution of silyl ether **155** (188 mg, 133 µmol, 1.00 eq.) in THF (5 mL) was added HF · pyridine complex (73.0 µL, 30 wt% HF, 2.82 mmol, 21.0 eq.). After 30 minutes, an additional 100 µL HF · pyridine complex (28 eq.) was added, and stirring was continued for two hours. Additional 200 µL HF · pyridine complex (54 eq.) were added, and stirring was continued for one hour. The solution was poured into 30 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 15 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced

pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 1:0 ⟶ 10:1), alcohol **156** was obtained as a colorless oil (132 g, 101 µmol, 76%).

TLC: R_f = 0.65 (pentane:diethyl ether = 4:1).

Diastereomeric ratio: d.r. ≈ 4:1.

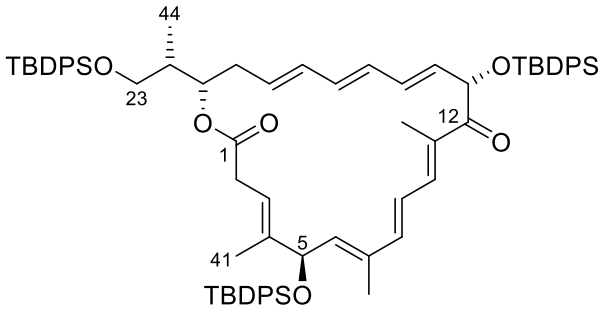
^{1}**H-NMR**: (400 MHz, C_6D_6) δ 7.82-7.72 (m, 12 H, C_{Ar}-H), 7.30-7.19 (m, 18 H, C_{Ar}-H), 6.59-6.48 (m, 1 H, H-9), 6.42-6.23 (m, 2 H, H-6, H-10), 6.10-5.91 (m, 4 H, H-15-18), 5.91-5.80 (m, 1 H, H-3), 5.75 (dd, ^3J = 14.9 Hz, ^3J = 7.3 Hz, 1 H, H-14), 5.58-5.50 (m, 1 H, H-19), 5.48-5.42 (m, 1 H, H-21), 5.20-5.09 (m, 1 H, H-8a), 5.06-4.99 (m, 1 H, H-8b), 4.68 (d, ^3J = 9.1 Hz, 1 H, H-5), 4.42-4.33 (m, 1 H, H-13), 4.12 (s, 0.8 H, H-12$_A$), 4.06 (s, 0.2 H, H-12$_B$), 3.65-3.53 (m, 2 H, H-23), 2.94-2.87 (m, 2 H, H-2), 2.47-2.37 (m, 1 H, H-20a), 2.34-2.25 (m, 1 H, H-20b), 2.22 (d, ^3J = 2.9 Hz, 1 H, OH), 2.00-1.88 (m, 1 H, H-22), 1.71 (s, 3 H, H-42), 1.57 (s, 0.7 H, H-43$_B$), 1.48 (s, 2.3 H, H-43$_A$), 1.45 (s, 3 H, H-41), 1.20 [s, 9 H, SiC(CH$_3$)$_3$], 1.17 [s, 9 H, SiC(CH$_3$)$_3$], 1.16 [s, 9 H, SiC(CH$_3$)$_3$].

^{13}C-NMR: (126 MHz, C_6D_6) δ 170.8 (s, C-1), 142.5 (d, C-6), 138.8 (s, C-4), 136.5 (s, C-11), 136.4 (d, C_{Ar}-H), 136.3 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 134.1 (d, C-18)*, 133.8 (d, C-15)*, 133.5 (d, C-16)*, 133.0 (d, C-9), 131.2 (d, C-14), 131.1 (d, C-17)*, 130.2 (d, C-19), 130.14 (d, C_{Ar}-H), 130.11 (d, C_{Ar}-H), 127.6 (d, C-10), 118.1, (d, C-3) 116.9 (t, C-8), 96.9 (s, C-7), 79.6 (d, C-12), 76.8 (d, C-13), 75.7 (d, C-5), 73.4 (d, C-21), 65.8 (t, C-23), 38.7 (d, C-22), 35.8 (t, C-20), 33.6 (t, C-2), 27.9 (q, C-42), 27.4 [q, C_{13}OSiC(CH$_3$)$_3$]$_B$, 27.3 [q, C_{13}OSiC(CH$_3$)$_3$]$_A$, 27.2 [q, SiC(CH$_3$)$_3$], 27.1 [q, SiC(CH$_3$)$_3$], 19.7 [q, Si*C*(CH$_3$)$_3$], 19.6 [q, Si*C*(CH$_3$)$_3$], 19.5 [q, Si*C*(CH$_3$)$_3$], 13.4 (q, C-43), 12.5 (q, C-41), 11.5 (q, C-44).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3566 (*br* w, OH), 3071 (w, C_{sp2}-H), 3015 (w, C_{sp2}-H), 2959 (m, C_{sp3}-H), 2857 (m, C_{sp2}-H), 1735 (m, C=O), 1427 (m), 1111 (vs), 701 (vs).

HRMS (ESI): *m/z* [$C_{75}H_{93}IO_6Si_3$ + NH_4]$^+$ calcd.: 1318.5668; found: 1318.5662.

TBDPS protected macrolactone 159



159
$C_{75}H_{90}O_6Si_3$
1171.79 g/mol

To a solution of alcohol **156** (22.0 mg, 17.0 µmol, 1.00 eq.) in dichloromethane (2 mL) was added sodium bicarbonate (4.26 mg, 51.0 µmol, 3.00 eq.) and *Dess-Martin* periodinane (10.8 mg, 25.0 µmol, 1.50 eq.). After one hour, the colorless suspension was poured into a mixture of 2 mL saturated aqueous sodium bicarbonate solution, and 2 mL saturated aqueous sodium thiosulfate solution. The layers were separated, and the aqueous layer was extracted with diethyl ether (2 × 3 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the corresponding ketone as a yellow oil (R_f = 0.75, pentane:diethyl ether = 4:1). The oil was dissolved in DMF (2 mL) and sodium bicarbonate (14.1 mg, 169 µmol, 10.0 eq.), tetrabutylammonium iodide (6.24 mg, 17.0 µmol, 1.00 eq.) and palladium-(II)-acetate (4.93 mg, 22.0 µmol, 1.30 eq.) were added. After stirring for two hours at room temperature, the reaction was quenched by the addition of Celite. The solvent was removed under a high vacuum using an external cooling trap. Following flash column chromatography (silica, pentane:diethyl ether = 10:1), macrolactone **159** was obtained as a yellowish oil (1.60 mg, 8%).

TLC: R_f = 0.60 (pentane:diethyl ether = 4:1).

^{1}**H-NMR**: (500 MHz, C_6D_6) δ 7.85-7.76 (m, 12 H, C_{Ar}-H), 7.29-7.20 (m, 18 H, C_{Ar}-H), 6.87-6.81 (m, 1 H, H-10), 6.36 (dd, ^3J = 9.3, 5.5 Hz, 1 H, H-3), 6.16.08 (m, 2 H, H-8, H-9), 5.96 (d, ^3J = 9.7 Hz, 1 H, H-16), 5.93 (d, ^3J = 9.7 Hz, 1 H, H-15), 5.77-5.65 (m, 3 H, H-17-19), 5.64-5.60 (m, 2 H, H-13, H-14), 5.60-5.56 (m, 2 H, H-6, H-21), 4.77 (d, ^3J = 9.2 Hz, 1 H, H-5), 3.63-3.53 (m, 2 H, H-23), 2.98 (dd, ^2J = 17.0, ^3J = 9.3 Hz, 1 H, H-2a), 2.83 (dd, ^2J = 17.0, ^3J = 5.5 Hz, 1 H, H-2b), 2.27-2.17 (m, 2 H, H-20), 1.85 (d, ^3J = 1.1 Hz, 3 H, H-43), 1.83-1.76 (m, 1 H, H-22), 1.35 [s, 9 H, $SiC(CH_3)_3$], 1.23 [s, 9 H, $SiC(CH_3)_3$], 1.22 [s, 9 H, $SiC(CH_3)_3$],

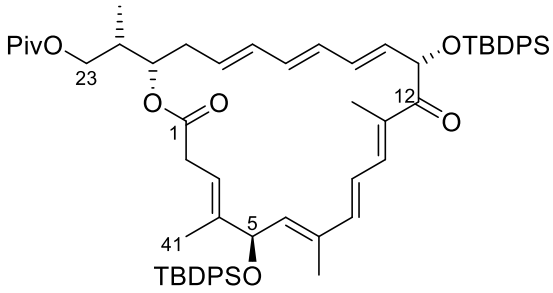
1.17 (d, ^4J = 1.4 Hz, 3 H, H-41), 1.14 (d, ^4J = 1.1 Hz, 3 H, H-42), 0.89 (d, ^3J = 7.0 Hz, 3 H, H-44).

^{13}C-NMR: (126 MHz, C_6D_6) δ 196.4 (s, C-12), 171.2 (s, C-1), 145.4 (d, C-8), 141.9 (d, C-10), 139.2 (d, C-6), 139.4 (s, C-4), 136.7 (d, C_{Ar}-H), 136.8 (d, C_{Ar}-H), 136.5 (d, C_{Ar}-H), 136.9 (d, C_{Ar}-H), 136.4 (d, C_{Ar}-H), 136.2 (d, C_{Ar}-H), 136.8 (d, C_{Ar}-H), 134.8 (d, C-16), 132.4 (d, C-18), 132.6 (d, C-19), 132.0 (s, C-11), 131.5 (d, C-14), 130.2 (d, C_{Ar}-H), 130.5 (d, C_{Ar}-H), 129.4 (d, C-16), 123.0 (d, C-9), 117.6 (d, C-3), 78.4 (d, C-13), 73.4 (d, C-5, C-21), 65.8 (t, C-23), 40.5 (d, C-22), 36.7 (t, C-20), 33.1 (t, C-2), 27.2 [q, SiC(CH$_3$)$_3$], 27.1 [q, SiC(CH$_3$)$_3$], 19.9 [s, SiC(CH$_3$)$_3$], 19.7 [s, SiC(CH$_3$)$_3$], 19.5 [s, SiC(CH$_3$)$_3$], 14.4 (q, C-41), 12.2 (q, C-42, C-44), 12.1 (q, C-43).

Specific rotation: $[\alpha]_D^{20} = -58.0$ (c = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2957 (vs) 2928 (vs) 2857 (vs) (C_{sp3}-H), 1737 (m, CO), 1675 (m, COOR), 1428 (w), 1111 (vs), 702 (vs).

Macrolactone 92



92

$C_{64}H_{80}O_7Si_2$

1017.51 g/mol

To a solution of alcohol **93** (89.0 mg, 78.0 µmol, 1.00 eq.) in dichloromethane (4 mL) was added sodium bicarbonate (26.0 mg, 31.0 µmol, 4.00 eq.) and *Dess-Martin* periodinane (65.8 mg, 155 µmol, 2.00 eq.). After one hour, the colorless suspension was poured into a mixture of 8 mL saturated aqueous sodium bicarbonate solution, and 8 mL saturated aqueous sodium thiosulfate solution. The layers were separated, and the aqueous layer was extracted with diethyl ether (2 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the corresponding ketone as a yellow oil (R_f = 0.5, pentane:diethyl ether = 4/1). The oil was dissolved in DMF (3 mL)

and potassium phosphate (32.9 mg, 155 µmol, 2.00 eq.) and palladium-(II)-acetate (17.4 mg, 78.0 µmol, 1.00 eq.) were added. After stirring for three hours at room temperature, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution. The layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 1:0 ⟶ 10:1), macrolactone **92** was obtained as a yellowish oil (16.3 mg, 21%).

TLC: R_f = 0.40 (pentane:diethyl ether = 4:1).

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.74-7.62 (m, 8 H, C_{Ar}-H), 7.48-7.28 (m, 12 H, C_{Ar}-H), 6.76 (d, ^3J = 10.0 Hz, 1 H, H-10), 6.22-6.11 (m, 2 H, H-8, H-9), 6.02-5.98 (m, 2 H, H-17, H-18), 5.99-5.91 (m, 1 H, H-16), 5.88 (t, ^3J = 7.2 Hz, 1 H, H-3), 5.78 (dd, ^3J = 15.2 Hz, ^3J = 10.0 Hz, 1 H, H-15), 5.63-5.56 (m, 1 H, H-19), 5.49 (dd, ^3J = 15.2 Hz, ^3J = 9.5 Hz, 1 H, H-14), 5.39 (d, ^3J = 9.2 Hz, 1 H, H-6), 5.31 (d, ^3J = 9.5 Hz, 1 H, H-13), 5.21 (ddd, ^3J = 11.0 Hz, ^3J = 4.5 Hz, ^3J = 2.4 Hz, 1 H, H-21), 4.61 (d, ^3J = 9.2 Hz, 1 H, H-5), 4.00 (dd, ^2J = 11.1, ^3J = 6.8 Hz, 1 H, H-23a), 3.91 (dd, ^2J = 11.1, ^3J = 6.1 Hz, 1 H, H-23b), 2.99 (d, ^3J = 7.4 Hz, 2 H, H-2), 2.46-2.40 (m, 1 H, H-20a), 2.38-2.30 (m, 1 H, H-20b), 2.11-1.99 (m, 1 H, H-22), 1.75 (s, 3 H, H-43), 1.32 (s, 3 H, H-41), 1.26 (s, 3 H, H-42), 1.23 [s, 9 H, $OCOC(CH_3)_3$], 1.07 [s, 9 H, $SiC(CH_3)_3$], 0.98 (d, ^3J = 7.0 Hz, 3 H, H-44).

^{13}**C-NMR**: (126 MHz, $CDCl_3$) δ 197.4 (s, C-12), 178.7 [s, $OCOC(CH_3)$], 171.9 (s, C-1), 145.8 (d, C-8), 142.4 (d, C-10), 140.0 (d, C-6), 139.7 (s, C-4), 136.2 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.0 (d, C-15), 135.9 (d, C_{Ar}-H), 134.4 (d, C-18**), 133.8 (s, C_{Ar}), 133.8 (s, C_{Ar}), 133.7 (s, C_{Ar}), 133.5 (s, C_{Ar}), 132.3 (s, C-7), 132.2 (d, C-17**), 132.1 (d, C-19), 131.6 (s, C-11), 130.9 (d, C-14), 129.8 (d, C_{Ar}-H), 129.7 (d, C_{Ar}-H), 129.6 (d, C-16), 127.7 (d, C_{Ar}-H), 127.6 (d, C_{Ar}-H), 127.5 (d, C_{Ar}-H), 122.5 (d, C-9), 116.4 (d, C-3), 77.6 (d, C-13), 73.2 (d, C-21), 72.8 (d, C-5), 65.6 (t, C-23), 39.0 [s, $OCOC(CH_3)$], 36.9 (t, C-22), 35.8 (t, C-20), 33.1 (t, C-2), 27.3 [q, $OCOC(CH_3)$], 27.0 [q, $SiC(CH_3)_3$], 19.5 [s, $SiC(CH_3)_3$], 19.4 [s, $SiC(CH_3)_3$], 14.7 (q, C-41), 12.3 (q, C-42*), 12.1 (q, C-44*), 12.0 (q, C-43).

Specific rotation: $[\alpha]_D^{20} = -106$ (c = 1.00, $CHCl_3$).

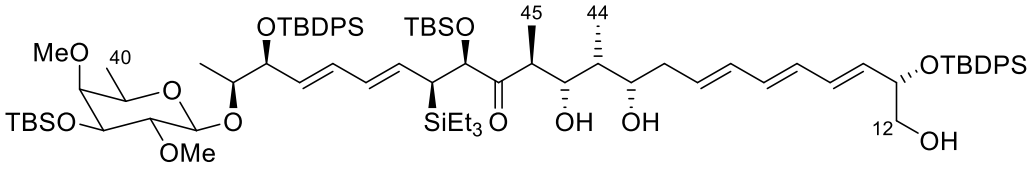
IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3071 (w), 3049 (w, sp^2-CH), 2959 (s, sp^3-CH), 2931 (s, sp^3-CH), 2858 (s, sp^3-CH), 1731 (vs), 1675 (s), 1112 (vs), 703 (vs).

HRMS (ESI): $[C_{64}H_{80}O_7Si_2 + H]^+$ calcd.: 1017.5514; found: 1017.5521.

$[C_{64}H_{80}O_7Si_2 + NH_4]^+$	calcd.: 1034.5780;	found: 1034.5785.
$[C_{64}H_{80}O_7Si_2 + Na]^+$	calcd.: 1039.5334;	found: 1039.5338.

11.4. C1-C40 fragment

Triol 119



119
$C_{83}H_{132}O_{12}Si_5$
1462.38 g/mol

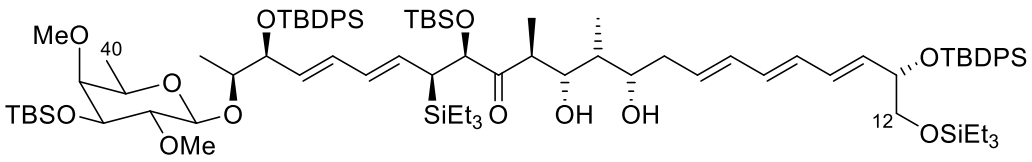
Aldol product **18** (1.54 g, 913 µmol, 1.00 eq.) was added to a cold solution of dichloromethane (7.5 mL), methanol (7.5 mL), and formic acid (750 µL). After two hours, further 3 mL formic acid was added. After two hours, the reaction was quenched by the addition of a saturated aqueous sodium bicarbonate solution (25 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 3:1 ⟶ 2:1), triol **119** was obtained as a colorless foam (635 mg, 434 µmol, 48%).

TLC: R_f = 0.75 (pentane:diethyl ether = 1:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.74-7.59 (m, 8 H, C_{Ar}-H), 7.46-7.30 (m, 12 H, C_{Ar}-H), 6.17-5.94 (m, 5 H, H-15-18, H-30), 5.88 (dd, ^3J = 14.9, 10.5 Hz, 1 H, H-29), 5.70-5.54 (m, 3 H, H-14, H-19, H-31), 5.39 (dd, ^3J = 15.1, 10.7 Hz, 1 H, H-28), 4.33 (d, ^3J = 3.4 Hz, 1 H, H-26), 4.29 (q, ^3J = 5.7 Hz, 2 H, H-13, H-32), 4.02-3.97 (m, 1 H, H-23), 3.92-3.85 (m, 1 H, H-21), 3.55 (m, 5 H, H-33, H-35, C_{38}-OMe), 3.52-3.45 (m, 1 H, H-12), 3.33 (s, 3 H, C_{36}-OMe), 3.30 (dd, ^3J = 9.5, 3.1 Hz, 1 H, H-37), 3.20-3.14 (m, 1 H, H-24), 3.09 (q, ^3J = 6.5 Hz, 1 H, H-39), 3.01-2.93 (m, 2 H, H-36, H-38), 2.38-2.31 (m, 1 H, H-20b), 2.27-2.21 (m, 1 H, H-20a), 2.17 (dd, ^3J = 10.7, 3.5 Hz, 1 H, H-27), 1.61 (d, ^3J = 7.1 Hz, 1 H, H-22), 1.17 (d, ^3J = 6.5 Hz, 1 H, H-40), 1.15 (d, ^3J = 6.4 Hz, 1 H, H-34), 1.07 [s, 9 H, $SiC(CH_3)_3$ TBDPS], 1.06 [s, 9 H, $SiC(CH_3)_3$ TBDPS], 0.97-0.92 [m, 9 H, $Si(CH_2C\mathit{H}_3)_3$], 0.91 (m, 6 H, H-44, H-45), 0.90 [s, 9 H, $SiC(CH_3)_3$ TBS], 0.64 [*virt.* qd, ^3J = 7.8, 1.6 Hz, 6 H, $Si(C\mathit{H}_2CH_3)_3$], 0.09 (s, 3 H, $SiCH_3$), 0.08 (s, 3 H, $SiCH_3$), 0.07 (s, 6 H, $SiCH_3$).

The analytical data obtained matched those reported in the literature.[30]

Diol 120



120

$C_{89}H_{146}O_{12}Si_6$

1576.65 g/mol

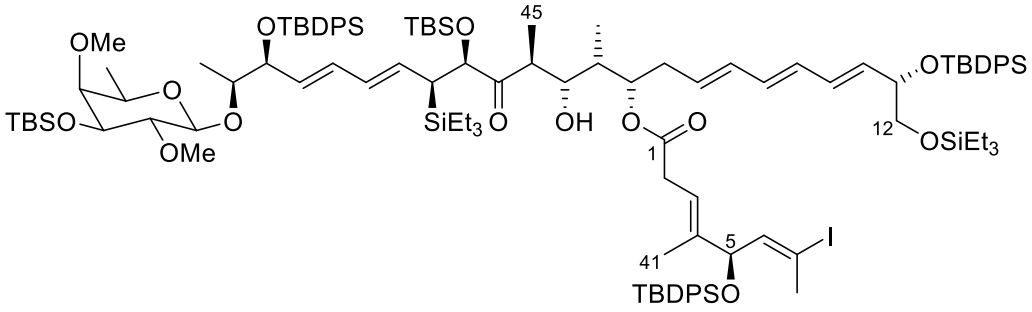
To a cold (0 °C) solution of triol **119** (183 mg, 125 µmol, 1.00 eq.) in dichloromethane (5 mL) was added 2,6-lutidine (30 µL, 26.8 mg, 250 µmol, 2.00 eq.) and TESCl (26 µL, 23.6 mg, 157 µmol, 1.20 eq.). After four hours, the reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (25 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 10:1 ⟶ 4:1), diol **120** was obtained as a colorless oil (187 mg, 119 µmol, 95%).

TLC: R_f = 0.80 (pentane:diethyl ether = 1:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.73-7.54 (m, 8 H, C_{Ar}-H), 7.46-7.29 (m, 12 H, C_{Ar}-H), 6.18-5.99 (m, 5 H, H-15-18, H-30), 5.88 (dd, ^3J = 14.9, 10.4 Hz, 1 H, H-29), 5.68 (dd, ^3J = 14.9, 6.5 Hz, 1 H, H-14), 5.65-5.57 (m, 2 H, H-19, H-31), 5.40 (dd, ^3J = 15.0, 10.7 Hz, 1 H, H-28), 4.33 (d, ^3J = 3.4 Hz, 1 H, H-26), 4.29 (*virt*. t, ^3J = 5.3 Hz, 1 H, H-32), 4.21 (*virt*. q, ^3J = 6.4 Hz, 1 H, H-13), 4.01 (d, ^3J = 9.2 Hz, 1 H, H-23), 3.88 (t, ^3J = 7.0 Hz, 1 H, H-21), 3.61-3.51 (m, 6 H, H-12b, H-33, H-35, C_{38}-OMe), 3.39 (dd, ^3J = 9.8, 6.9 Hz, 1 H, H-12a), 3.33 (s, 3 H, C_{36}-OMe), 3.29 (dd, ^3J = 9.5, 3.1 Hz, 1 H, H-37), 3.16 (dd, ^3J = 9.4, 7.2 Hz, 1 H, H-24), 3.08 (q, ^3J = 6.2 Hz, 1 H, H-39), 2.98 (d, ^3J = 3.1 Hz, 1 H, H-38), 2.96-2.91 (m, 1 H, H-36), 2.39-2.31 (m, 1 H. H-20b), 2.27-2.20 (m, 1 H, H-20a), 2.17 (dd, ^3J = 10.7, 3.4 Hz, 1 H, H-27), 1.63 (s, 1 H. H-22), 1.17 (d, ^3J = 6.2 Hz, 3 H, H-40), 1.15 (d, ^3J = 6.5 Hz, 3 H, H-34), 1.07-1.04 (m, 18 H, $SiC(CH_3)_3$ TBDPS), 0.97-0.92 [m, 9 H, $C_{27}OSi(CH_2CH_3)_3$], 0.91-0.90 (m, 24 H, H-44, H-45, 2x $SiC(CH_3)_3$ TBS), 0.84 [t, ^3J = 7.9 Hz, 9 H, $C_{12}OSi(CH_2CH_3)_3$], 0.63 [qd, ^3J = 7.9, 1.7 Hz, 6 H $C_{27}OSi(CH_2CH_3)_3$], 0.44 [q, ^3J = 7.9 Hz, 6 H, $C_{12}OSi(CH_2CH_3)_3$], 0.09 (s, 3 H, $SiCH_3$), 0.07 (s, 3 H, $SiCH_3$), 0.06 (s, 6 H, $SiCH_3$).

The analytical data obtained matched those reported in the literature.[30]

Ester 121



121
$C_{114}H_{175}IO_{14}Si_7$
2093.14

To a cold (0 °C) solution of carboxylic acid **38** (108 mg, 203 µmol, 1.20 eq.) in toluene (5 mL) was added triethylamine (56 µL, 41.0 mg, 405 µmol, 1.20 eq.) and 2,4,6-trichlorobenzoyl chloride (32 µL, 49.4 mg, 203 µmol, 1.20 eq.). After ten minutes, a solution of diol **120** (266 mg, 169 µmol, 1.00 eq.) in toluene (3 mL) and DMAP (20.6 mg, 169 µmol, 1.00 eq.) was added. After two hours, the reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (25 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 1:0 ⟶ 4:1), ester **121** was obtained as a colorless oil (225 mg, 108 µmol, 64%). 74.9 mg of the starting material was reisolated (47.5 µmol, 28%).

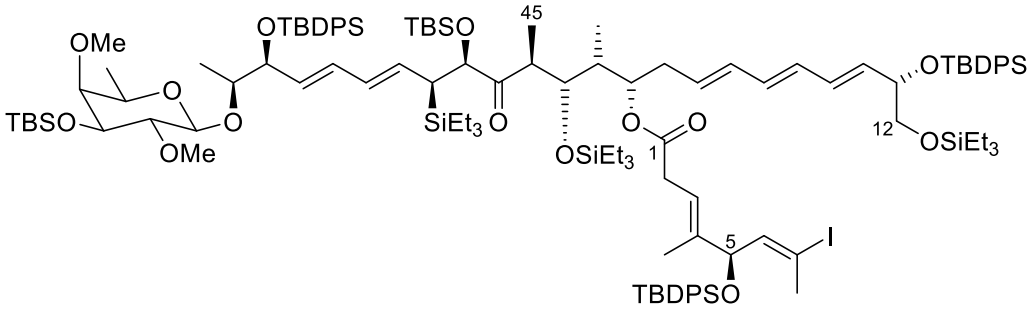
TLC: R_f = 0.75 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.79-7.60 (m, 12 H, C_{Ar}-H), 7.46-7.30 (m, 18 H, C_{Ar}-H), 6.14 (dq, ^3J = 8.8 Hz, ^4J = 1.8 Hz, 1 H, H-6), 6.10-5.98 (m, 5 H, H-15-16, H-30), 5.88 (dd, ^3J = 14.8, 10.5 Hz, 1 H, H-29), 5.67 (dd, ^3J = 14.2, 6.4 Hz, 1 H, H-14), 5.64-5.50 (m, 3 H, H-3, H-19, H-31), 5.39 (dd, ^3J = 15.0, 10.5 Hz, 1 H, H-28), 4.99 (dt, ^3J = 12.2, 6.8 Hz, 1 H, H-21), 4.56 (d, ^3J = 8.8 Hz, 1 H, H-5), 4.34-4.26 (m, 2 H, H-26, H-32), 4.21 (*virt*. q, $^3J \approx {}^3J$ = 6.3 Hz, 1 H, H-13), 3.88 (s, 1 H, H-23), 3.61-3.58 (m, 1 H, H-35), 3.55 (s, 3 H, C_{38}-OMe), 3.54-3.51 (m, 2 H, H-12a, H-33), 3.42-3.37 (m, 4 H, C_{36}-OMe, H-12b), 3.30 (dd, ^3J = 9.5, 3.0 Hz, 1 H, H-37), 3.17 (q, ^3J = 7.7 Hz, 1 H, H-24), 3.09 (q, ^3J = 6.3 Hz, 1 H, H-39), 3.03-2.93 (m, 4 H, H-2, H-36, H-38), 2.54-2.45 (m, 1 H, H-20a), 2.42-2.34 (m, 1 H, H-20b), 2.24 (d, ^3J = 5.2 Hz, 1 H, OH), 2.19-2.14 (m, 1 H, H-27), 1.85-1.78 (m, 4 H, H-22, H-42), 1.58-1.56 (m, 3 H, H-41), 1.18-1.16 (m,

3 H, H-40), 1.15-1.13 (m, 3 H, H-34), 1.09-1.02 [m, 27 H, $SiC(CH_3)_3$ TBDPS], 0.94 [t, ^3J = 7.5 Hz, 9 H, $C_{27}OSi(CH_2CH_3)_3$], 0.91-0.89 [m, 18 H, $SiC(CH_3)_3$ TBS], 0.87 (s, 6 H, H-44, H-45), 0.84 [t, ^3J = 7.9 Hz, 9 H, $C_{12}OSi(CH_2CH_3)_3$], 0.63 [q, ^3J = 7.5 Hz, 6 H, $C_{27}OSi(CH_2CH_3)_3$], 0.45 [q, ^3J = 7.9 Hz, 6 H, $C_{12}OSi(CH_2CH_3)_3$], 0.11-0.05 (m, 12 H, $SiCH_3$).

The analytical data obtained matched those reported in the literature.[30]

Silyl protected fragment 122



122
$C_{120}H_{189}IO_{14}Si_8$
2207.40 g/mol

To a cold (0 °C) solution of alcohol **121** (211 mg, 101 µmol, 1.00 eq.) in dichloromethane (5 mL) was added TESOTf (68 µL, 80.0 mg, 302 µmol, 3.00 eq.). After three hours, the reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (25 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 20:1), silyl protected fragment **122** was obtained as a colorless oil (138 mg, 62.5 µmol, 62%).

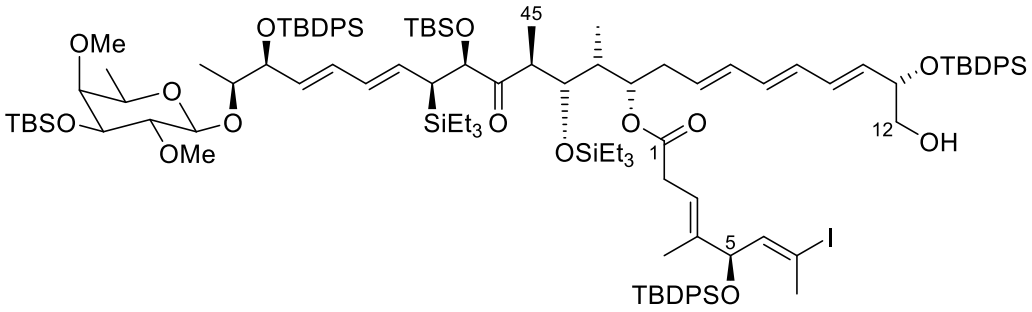
TLC: R_f = 0.85 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.81-7.54 (m, 12 H, C_{Ar}-H), 7.46-7.28 (m, 18 H, C_{Ar}-H), 6.20-5.96 (m, 6 H, H-6, H-15-H-18, H-30), 5.87 (t, ^3J = 12.6 Hz, 1 H, H-29), 5.50-5.70 (m, 3 H, H-3, H-19, H-31), 5.28 (t, ^3J = 13.1 Hz, 1 H, H-28), 5.01-4.90 (m, 1 H, H-21), 4.55 (d, ^3J = 8.8 Hz, 1 H, H-5), 4.32-4.26 (m, 1 H, H-32), 4.25-4.18 (m, 2 H, H-13, H-26), 4.11 (d, ^3J = 11.1 Hz, 1 H, H-23), 3.63-3.44 (m, 6 H, H-12b, H-33, C38-OMe, H-35), 3.43-3.24 (m, 6 H, H-37, C_{36}-OMe, H-24, H-12a), 3.15-3.03 (m, 2 H, H-2b, H-39), 3.03-2.91 (m, 3 H, H-2a, H-36, H-38),

2.69-2.59 (m, 1 H, H-20b), 2.31-2.19 (m, 1 H, H-20a), 2.07 (d, ^3J = 11.4 Hz, 1 H, H-27), 1.79 (m, 4 H, H-42, H-22), 1.57-1.55 (m, 3 H, H-41), 1.16 (t, ^3J = 4.2 Hz, 1 H, H-40), 1.12 (d, ^3J = 5.9 Hz, 1 H, H-34), 1.05-0.87 [m, 63 H, SiC(CH_3)$_3$ TBS/TBDPS, $C_{23/27}$OSi(CH_2CH_3)$_3$], 0.88-0.80 [m, 9 H, C_{12}OSi(CH_2CH_3)$_3$], 0.81-0.76 (m, 6 H, H-44, H-45), 0.71-0.63 (m, 6 H, C_{27}OSi(CH_2CH_3)$_3$], 0.63-0.56 (m, 6 H, C_{23}OSi(CH_2CH_3)$_3$], 0.44 [q, ^3J = 8.5 Hz, 6 H, C_{12}OSi(CH_2CH_3)$_3$], 0.10 (s, 6 H, $SiCH_3$), 0.06 (s, 6 H, $SiCH_3$).

The analytical data obtained matched those reported in the literature.[30]

Alcohol 123



123
$C_{114}H_{175}IO_{14}Si_7$
2093.14 g/mol

To a cold (0 °C) solution of silyl protected fragment **122** (135 mg, 61.0 µmol, 1.00 eq.) in THF (3 mL) and diethyl ether (3 mL) was added HF · pyridine (60 µL, 2.45 mmol, 40.0 eq.). After one hour, the reaction was quenched by the addition of a saturated aqueous sodium bicarbonate solution (25 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 10:1 ⟶ 4:1), alcohol **123** was obtained as a colorless oil (111 mg, 53.0 µmol, 87%).

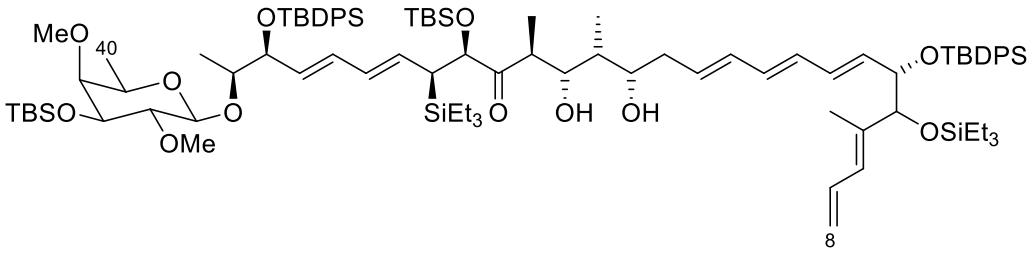
TLC: R_f = 0.25 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.73-7.54 (m, 12 H, C_{Ar}-H), 7.47-7.29 (m, 18 H, C_{Ar}-H), 6.13 (dq, ^3J = 8.8 Hz, ^4J = 1.4 Hz, 1 H, H-6), 6.11-5.91 (m, 5 H, H-15-18, H-30), 5.87 (dd, ^3J = 14.7, 10.5 Hz, 1 H, H-29), 5.65-5.52 (m, 4 H, H-3, H-14, H-19, H-31), 5.27 (dd, ^3J = 14.9, 10.9 Hz,

1 H, H-28), 4.94 (ddd, ^3J = 10.6, 7.8, 3.3 Hz, 1 H, H-21), 4.55 (d, ^3J = 8.8 Hz, 1 H, H-5), 4.32-4.25 (m, 2 H, H-13, H-32), 4.22 (d, ^3J = 3.0 Hz, 1 H, H-26), 4.11 (dd, ^3J = 9.2, 1.4 Hz, 1 H, H-23), 3.55 (s, 3 H, C_{38}-OMe), 3.54-3.50 (m, 4 H, H-12, H-33, H-35), 3.37-3.34 (m, 1 H, H-24), 3.32 (s, 3 H, C_{36}-OMe), 3.29 (dd, ^3J = 9.6, 3.2 Hz, 1 H, H-37), 3.10-3.05 (m, 1 H, H-2b, H-39), 3.03-2.93 (m, 3 H, H-2a, H-36, H-38), 2.69-2.60 (m, 1 H, H-20b), 2.32-2.21 (m, 1 H, H-20a), 2.06 (dd, ^3J = 10.9, 3.1 Hz, 1 H, H-27), 1.81-1.79 (m, 3 H, H-42), 1.79-1.78 (m, 1 H, H-22), 1.58-1.56 (m, 3 H, H-41), 1.16 (d, ^3J = 6.3 Hz, 3 H, H-40), 1.13 (d, ^3J = 6.4 Hz, 3 H, H-34), 1.07 [s, 9 H, $SiC(CH_3)_3$ TBDPS], 1.04 [s, 9 H, $SiC(CH_3)_3$ TBDPS], 1.03 [s, 9 H, $SiC(CH_3)_3$ TBDPS], 1.00-0.91 [m, 18 H, 2x $Si(CH_2CH_3)_3$], 0.90 [m, 18 H, $SiC(CH_3)_3$ TBS], 0.80 (d, ^3J = 6.7 Hz, 3 H, H-44), 0.78 (d, ^3J = 7.1 Hz, 3 H, H-45), 0.70-0.65 [m, 6 H, $C_{27}OSi(CH_2CH_3)_3$], 0.63-0.57 [m, 6 H, $C_{23}OSi(CH_2CH_3)_3$], 0.10 (s, 6 H, $SiCH_3$), 0.06 (s, 6 H, $SiCH_3$).

The analytical data obtained matched those reported in the literature.[30]

Diol 163



163

$C_{94}H_{152}O_{12}Si_6$

1642.75 g/mol

To a cold (0 °C) solution of ketone **11** (900 mg, 915 µmol, 1.00 eq.) in THF (10 mL) was added tetramethylpiperidinylmagnesium chloride lithium chloride complex (0.80 M in THF, 2.29 mL, 1.83 mmol, 2.00 eq.). After three hours, (–)-B-chlorodi-*iso*-campheylborane (980 µL, 1.37 mmol, 1.50 eq.) was added. After two hours, aldehyde **161** (1.67 g, 2.29 mmol, 2.50 eq.) was added as a solution in THF (3 mL). The reaction was warmed to room temperature over the course of 18 hours and then quenched by the addition of saturated aqueous sodium potassium tartrate solution (50 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 100 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column

chromatography (silica, pentane:diethyl ether = 10:1 ⟶ 4:1), 2.14 g of an inseparable mixture of aldol product **162**, ketone **11** and aldehyde **161** as well as 519 mg of alcohol **152** (709 µmol) were isolated. The mixture was dissolved in methanol (33 mL) and dichloromethane (7 mL) and 8-hydroxychinoline (853 mg, 5.88 mmol, 6.43 eq.) was added. After stirring for 2.5 hours at room temperature, a 10% copper-(II)-sulfate solution was added (80 mL). The green suspension was filtered over Celite and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 100 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 30:1⟶ 10:1), aldehyde **161** (181 mg), as well as 809 mg of an inseparable mixture of ketone 11 and aldol product 162, were isolated. The mixture was dissolved in THF (5 mL) and added to a cold (–25 °C) solution of HF · pyridine complex (35wt.%, 612 µL, 23.5 mmol, 50.0 eq.) in THF (10 mL). After one hour, the reaction was poured into saturated aqueous sodium bicarbonate solution (100 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 8:1), diol **163** was obtained as a colorless oil (389 mg, 237 µmol, 26%). Additionally, ketone **11** was reisolated (261 mg, 265 µmol, 29%). The yield of the diol based on reisolated ketone is 36% over three steps.

TLC: R_f = 0.25 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$, 300K) δ 7.72-7.56 (m, 8 H, C_{Ar}-H), 7.43-7.27 (m, 12 H, C_{Ar}-H), 6.51 (dt, ^3J = 16.8, 10.5 Hz, 1 H, H-9), 6.14-6.02 (m, 1 H, H-18), 6.06 (dd, ^3J = 15.3, 10.5 Hz, 1 H, H-30), 6.00-5.85 (m, 3 H, H-10, H-16, H-17), 5.89 (dd, ^3J = 15.1, 10.5 Hz, 1 H, H-29), 5.67-5.57 (m, 3 H, H-15, H-19, H-31), 5.53 (dd, ^3J = 15.3, 7.8 Hz, 1 H, H-14), 5.41 (dd, ^3J = 14.9, 10.6 Hz, 1 H, H-28), 5.13 (dd, ^3J = 16.8 Hz, ^2J = 2.2 Hz, 1 H, H-8a), 5.06 (dd, ^3J = 10.1, ^2J = 2.2 Hz, 1 H, H-8b), 4.34 (d, ^3J = 3.4 Hz, 1 H, H-26), 4.30 (dd, ^3J = 6.4, 4.3 Hz, 1 H, H-32), 4.25 (*virt.* t, $^3J \approx {}^3J$ = 5.7 Hz, 0.2 H, H-13$_B$), 4.05-3.99 (m, 1.8 H, H-13$_A$, H-23), 3.95-3.85 (m, 2 H, H-12, H-21), 3.60 (dd, ^3J = 7.9 Hz, ^4J = 2.6 Hz, 1 H, H-35), 3.58-3.56 (m, 1 H, H-33), 3.56 (s, 3 H, OMe), 3.34 (s, 3 H, OMe), 3.30 (dd, ^3J = 9.5, 3.1 Hz, 1 H, H-37), 3.18-3.15 (m, 1 H, H-24), 3.10 (q, ^3J = 6.4 Hz, 1 H, H-39), 3.00-2.94 (m, 2 H, H-36, H-38), 2.37-2.30 (m, 1 H, H-20a), 2.26-2.22 (m, 1 H, H-20b), 2.19 (dd, ^3J = 10.7, 3.3 Hz, 1 H, H-27), 1.66-1.60 (m, 2 H, H-22, H-43$_B$), 1.50 (d, ^4J = 1.4 Hz, 2 H, H-43$_A$), 1.17 (d, ^3J = 6.5 Hz, 3 H, H-40), 1.16 (d, ^3J = 6.5

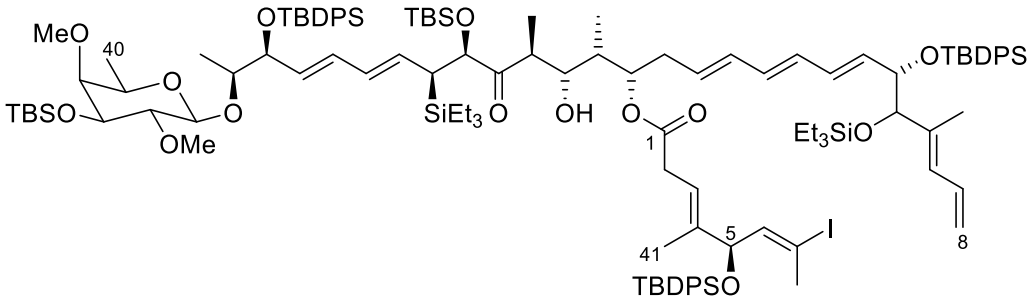
Hz, 3 H, H-34), 1.06 [s, 9 H, TBDPS SiC(CH_3)$_3$], 1.00 [s, 9 H, TBDPS SiC(CH_3)$_3$], 0.95 [t, ^3J = 8.0 Hz, 9 H, Si($CH_2C\mathit{H}_3$)$_3$], 0.93-0.90 [m, 24 H, H-44, H-45, TBS SiC(CH_3)$_3$], 0.86 [t, ^3J = 8.0 Hz, 9 H, Si($CH_2C\mathit{H}_3$)$_3$], 0.67-0.61 [m, 6 H, C_{27}OSi($C\mathit{H}_2CH_3$)$_3$], 0.53-0.46 [m, 5 H, C_{12}OSi($C\mathit{H}_2CH_3$)$_3$]$_A$, 0.40 [q, ^3J = 8.0 Hz, 1 H, C_{12}OSi($C\mathit{H}_2CH_3$)$_3$]$_B$, 0.12-0.06 [m, 12 H, TBS Si(CH_3)$_2$].

^{13}C-NMR: (126 MHz, $CDCl_3$, 300K) δ 216.5 (s, C-25$_B$), 216.3 (s, C-25$_A$), 138.9 (s, C-11$_A$), 138.1 (s, C-11$_B$), 136.4 (d, C_{Ar}-H), 136.3 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.1 (C_{Ar}-H), 134.4 (d, C-14), 134.3 (s, C_{Ar}), 134.2 (C_{Ar}), 134.1 (C_{Ar}), 134.0 (d, C-17), 133.6 (d, C-18), 133.1 (d, C-9), 132.6 (d, C-15), 132.5 (d, C-30), 132.3 (d, C-28), 131.4 (d, C-16), 130.3 (d, C-29), 130.1 (d, C-19), 129.7 (d, C_{Ar}-H), 129.6 (d, C_{Ar}-H), 129.5 (d, C_{Ar}-H), 129.5 (d, C_{Ar}-H), 128.6 (d, C-10), 128.5 (d, C-31), 127.6 (d, C_{Ar}-H), 127.5 (d, C_{Ar}-H), 127.5 (d, C_{Ar}-H), 127.3 (d, C_{Ar}-H), 116.5 (t, C-8$_A$), 116.2 (t, C-8$_B$), 102.7 (d, C-35), 82.7 (d, C-36), 81.9 (d, C-12), 81.1 (d, C-38), 80.6 (d, C-26), 78.5 (d, C-23), 77.1 (d, C-13$_B$, C-33), 76.7 (d, C-13$_A$), 76.2 (d, C-21), 75.9 (d, C-37), 74.1 (d, C-32), 69.8 (d, C-39), 62.2 (q, OMe), 60.9 (q, OMe), 44.7 (d, C-24), 39.0 (t, C-20), 38.2 (d, C-27), 37.2 (d, C-22), 27.2 [q, TBDPS SiC($\mathit{C}H_3$)$_3$], 27.1 [q, TBDPS SiC($\mathit{C}H_3$)$_3$], 26.0 [q, TBS SiC($\mathit{C}H_3$)$_3$], 25.9 [q, TBS SiC($\mathit{C}H_3$)$_3$], 19.4 [s, TBDPS SiC(CH_3)$_3$], 19.4 [s, TBDPS SiC(CH_3)$_3$], 18.3 [s, TBS SiC(CH_3)$_3$], 16.6 (q, C-40), 15.5 (q, C-34), 13.3 (q, C-45), 12.5 (q, C-43), 7.9 [q, C_{27}OSi($CH_2\mathit{C}H_3$)$_3$], 6.9 [q, C_{12}OSi($CH_2\mathit{C}H_3$)$_3$], 4.9 [t, C_{12}OSi($\mathit{C}H_2CH_3$)$_3$]$_A$, 4.8 [t, C_{12}OSi($\mathit{C}H_2CH_3$)$_3$]$_B$, 4.7 (q, C-44), 3.4 [t, C_{27}OSi($\mathit{C}H_2CH_3$)$_3$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3469 (*br* w, OH), 3072 (vw, C_{sp2}-H), 2953 (m, C_{sp3}-H), 2931 (m, C_{sp3}-H), 2876 (m, C_{sp2}-H), 2857 (m, C_{sp2}-H), 1719 (w, C=O), 1462 (m), 1112 (vs), 1078 (vs), 733 (vs), 700 (vs).

HRMS (ESI): *m/z* [$C_{94}H_{152}O_{12}Si_6$ + Na + ^{13}C]$^+$ calcd.: 1664.9831; found: 1664.9808.

Ester 165



165

$C_{119}H_{181}IO_{14}Si_7$

2159.24 g/mol

To a cold (–30 °C) solution of carboxylic acid **38** (370 mg, 693 µmol, 2.50 eq.) in toluene (10 mL) was added triethylamine (192 µL, 140 mg, 1.39 mmol, 5.00 eq.), followed by 2,4,6-trichlorobenzoyl chloride (87 µL, 135 mg, 554 µmol, 2.00 eq.). After stirring for ten minutes, a solution of alcohol **163** (455 mg, 277 µmol, 1.00 eq.) in toluene (10 mL) and 4-(dimethylamino)-pyridine (33.9 mg, 277 µmol, 1.00 eq.) was added. While stirring for two hours at –30°C, the solution turned into an orange suspension. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution. The layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 25 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 8:1), ester **165** was obtained as a colorless oil (369 mg, 171 µmol, 62%). 16% of the alcohol were reisolated (73%brsm).

TLC: R_f = 0.70 (pentane:diethyl ether = 4:1), [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$, 300K) δ 7.71-7.57 (m, 12 H, C_{Ar}-H), 7.44-7.27 (m, 18 H, C_{Ar}-H), 6.51 (dt, ^3J = 16.8, 10.5 Hz, 1 H, H-9), 6.14 (dq, ^3J = 9.2 Hz, ^4J = 1.1 Hz, 1 H, H-6), 6.10-6.00 (m, 2 H, H-30, H-15), 5.98-5.84 (m, 4 H, H-10, H-16, H-17, H-29), 5.65-5.56 (m, 3 H, H-3, H-18, H-31), 5.55-5.47 (m, 2 H, H-14, H-19), 5.40 (dd, ^3J = 15.0, 10.5 Hz, 1 H, H-28), 5.15-5.04 (m, 2 H, H-8), 5.02-4.96 (m, 1 H, H-21), 4.56 (d, ^3J = 8.8 Hz, 1 H, H-5), 4.33-4.27 (m, 2 H, H-26, H-32), 4.06-3.98 (m, 1 H, H-13), 3.93-3.85 (m, 2 H, H-12, H-23), 3.62-3.58 (m, 1 H, H-35), 3.55 (s, 4 H, OMe, H-33), 3.33 (m, 3 H, OMe), 3.30 (dd, ^3J = 9.5, 3.1 Hz, 1 H, H-37), 3.21-3.13 (m, 1 H, H-24), 3.09 (q, ^3J = 6.5 Hz, 1 H, H-39), 3.02-2.94 (m, 4 H, H-2, H-36, H-38), 2.53-2.43 (m, 1 H, H-20a), 2.41-2.33 (m, 1 H, H-20b), 2.23 (d, ^3J = 5.2 Hz, 1 H, C_{23}-

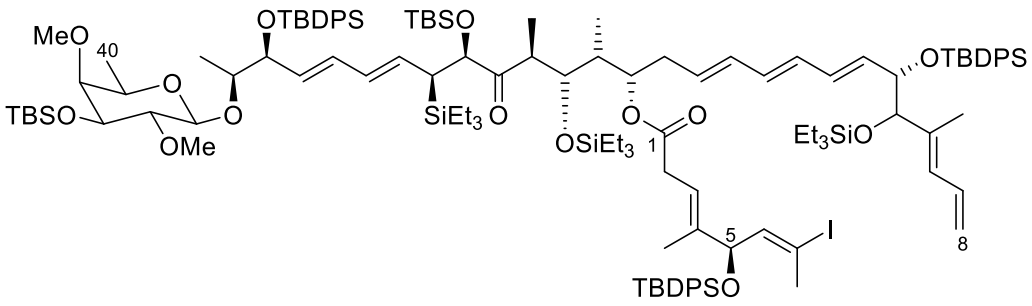
OH), 2.17 (dd, ^{3}J = 10.5, 3.3 Hz, 1 H, H-27), 1.83-1.78 (m, 4 H, H-42, H-22), 1.64 (s, 0.6 H, H-43$_B$), 1.56 (s, 3 H, H-41), 1.51-1.48 (m, 2.4 H, H-43$_A$), 1.17 (d, ^{3}J = 6.5 Hz, 3 H, H-40), 1.14 (d, ^{3}J = 6.5 Hz, 3 H, H-34), 1.07-1.03 [m, 18 H, TBDPS SiC(CH$_3$)$_3$], 1.00 [s, 9 H, TBDPS SiC(CH$_3$)$_3$], 0.96-0.92 [m, 9 H, Si(CH$_2$C*H*$_3$)$_3$], 0.91-0.89 [m, 18 H, TBS SiC(CH$_3$)$_3$], 0.90-0.82 [m, 15 H, Si(CH$_2$C*H*$_3$)$_3$, H-44, H-45], 0.66-0.59 [m, 6 H, C$_{27}$OSi(C*H*$_2$CH$_3$)$_3$], 0.53-0.46 [m, 6 H, C$_{12}$OSi(C*H*$_2$CH$_3$)$_3$]$_A$, 0.40 [q, ^{3}J = 7.9 Hz, 6 H, C$_{12}$OSi(C*H*$_2$CH$_3$)$_3$]$_B$, 0.11-0.06 (m, 12 H, TBS CH$_3$).

^{13}C-NMR: (126 MHz, CDCl$_3$, 300K) δ 216.1 (s, C-25), 171.4 (s, C-1), 142.1 (d, C-6), 138.9 (s, C-4), 138.8 (s, C-11), 136.4 (d, C$_{Ar}$-H), 136.2 (d, C$_{Ar}$-H), 136.1 (d, C$_{Ar}$-H), 136.1 (d, C$_{Ar}$-H), 136.0 (d, C$_{Ar}$-H), 135.9 (d, C$_{Ar}$-H), 134.0 (d, C-14), 133.7 (d, C-15), 133.0 (d, C-9), 132.7 (d, C-30), 132.4 (d, C-28), 132.1 (d, C-16)*, 131.4 (d, C-17)*, 130.3 (d, C-29), 129.8 (d, C$_{Ar}$-H), 129.8 (d, C$_{Ar}$-H), 129.6 (d, C$_{Ar}$-H), 129.5 (d, C$_{Ar}$-H), 128.7 (d, C-19)**, 128.6 (d, C-31)**, 128.5 (d, C-10), 127.7 (d, C$_{Ar}$-H), 127.7 (d, C$_{Ar}$-H), 127.6 (d, C$_{Ar}$-H), 127.4 (d, C$_{Ar}$-H), 127.3 (d, C$_{Ar}$-H), 117.1 (d, C-3), 116.5 (t, C-8), 102.8 (d, C-35), 96.6 (s, C-7), 82.7 (d, C-36), 81.9 (d, C-12), 81.1 (d, C-38), 80.7 (d, C-26), 77.0 (d, C-33), 76.8 (d, C-13), 76.3 (c, C-21), 75.9 (d, C-37), 75.2 (d, C-5), 74.1 (d, C-32), 73.5 (d, C-23), 69.8 (d, C-39), 62.2 (q, OMe), 60.9 (q, OMe), 44.7 (d, C-24), 38.0 (d, C-27), 37.4 (d, C-22), 35.7 (t, C-20), 33.7 (t, C-2), 27.9 (q, C-42), 27.2 [q, TBDPS SiC(*C*H$_3$)$_3$], 27.2 [q, TBDPS SiC(*C*H$_3$)$_3$], 27.0 [q, TBDPS SiC(*C*H$_3$)$_3$], 26.0 [q, TBS SiC(*C*H$_3$)$_3$], 26.0 [q, TBS SiC(*C*H$_3$)$_3$], 19.5 [s, TBDPS Si*C*(CH$_3$)$_3$], 19.5 [s, TBDPS Si*C*(CH$_3$)$_3$], 19.4 [s, TBDPS Si*C*(CH$_3$)$_3$], 18.3 [s, TBS Si*C*(CH$_3$)$_3$], 16.6 (q, C-40), 15.6 (q, C-34), 14.3 (q, C-43$_B$), 13.6 (q, C-45), 12.7 (q, C-41), 12.5 (q, C-43$_A$), 8.2 (q, C-44), 7.9 [q, C$_{27}$OSi(CH$_2$*C*H$_3$)$_3$], 6.9 [q, C$_{12}$OSi(CH$_2$*C*H$_3$)$_3$], 4.9 [t, C$_{12}$OSi(*C*H$_2$CH$_3$)$_3$]$_A$, 4.7 [t, C$_{12}$OSi(*C*H$_2$CH$_3$)$_3$]$_B$, 3.5 [t, C$_{27}$OSi(*C*H$_2$CH$_3$)$_3$], –4.1 (q, TBS CH$_3$), –4.4 (q, TBS CH$_3$), –4.6 (q, TBS CH$_3$), –4.6 (q, TBS CH$_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3500 (*br* vw, OH), 2954 (s, C$_{sp3}$-H), 2931 (s, C$_{sp3}$-H), 2858 (s, C$_{sp2}$-H), 1732 (m, C=O), 1472 (m), 1428 (m), 1112 (vs), 702 (vs).

HRMS (ESI): *m/z* [C$_{119}$H$_{181}$IO$_{14}$Si$_7$ + Na + ^{13}C]$^+$ calcd.: 2182.0846; found: 2182.0825.

Silyl protected fragment 166



166
$C_{125}H_{195}IO_{14}Si_8$
2273.51 g/mol

To a cold (–30°C) solution of triethylsilyl trifluormethanesulfonate (136 µL, 159 mg, 603 µmol, 4.00 eq.) in dichloromethane (6 mL) was added 2,6-lutidine (412 µL, 404 mg, 3.77 mmol, 25.0 eq.), followed by alcohol **165** (326 mg, 151 µmol, 1.00 eq.). After stirring for 2.5 hours, the reaction was quenched by the addition of saturated aqueous ammonium chloride solution. The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 15:1), silyl-protected fragment **166** was obtained as a colorless oil (312 mg, 91%).

TLC: R_f = 0.85 (pentane:diethyl ether = 4:1), [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$, 300K) δ 7.73-7.54 (m, 12 H, C_{Ar}-H), 7.42-7.29 (m, 18 H, C_{Ar}-H), 6.50 (dt, ^3J = 17.0, 10.6 Hz, 1 H, H-9), 6.20-6.12 (m, 1 H, H-6), 6.09-5.83 (m, 6 H, H-10, H-15, H-16, H-17, H-29, H-30), 5.65-5.56 (m, 3 H, H-3, H-18, H-31), 5.55-5.47 (m, 2 H, H-14, H-19), 5.28 (dd, ^3J = 14.8, 10.9 Hz, 1 H, H-28), 5.12 (d, ^3J = 17.6 Hz, 1 H, H-8a), 5.06 (d, ^3J = 9.0 Hz, 1 H, H-8b), 4.94 (t, ^3J = 9.1 Hz, 1 H, H-21), 4.56 (d, ^3J = 8.7 Hz, 1 H, H-5), 4.32-4.20 (m, 2 H, H-27, H-32), 4.11 (d, ^3J = 9.4 Hz, 1 H, H-23), 4.02 (dd, ^3J = 7.9, 6.1 Hz, 1 H, H-13), 3.93-3.88 (m, 1 H, H-12), 3.61-3.57 (m, 1 H, H-35), 3.55 (s, 3 H, OMe), 3.53 (dd, ^3J = 6.6, 4.3 Hz, 1 H, H-33), 3.36 (s, 1 H, H-24), 3.33 (s, 3 H, OMe), 3.31-3.27 (m, 1 H, H-37), 3.08 (q, ^3J = 6.4 Hz, 1 H, H-39), 3.02-2.92 (m, 4 H, H-2, H-36, H-38), 2.68-2.57 (m, 1 H, H-20a), 2.27-2.19 (m, 1 H, H-20b), 2.08 (dd, ^3J = 11.0, 3.3 Hz, 1 H, H-27), 1.81-1.77 (m, 3 H, H-42), 1.76-1.71 (m, 1 H, H-22), 1.64 (s, 0.6 H, H-43_B), 1.57 (s, 3 H, H-41), 1.50 (s, 2.4 H, H-43_A), 1.16 (d, ^3J = 6.3 Hz, 3 H, H-40), 1.13 (d, ^3J = 6.5 Hz, 3 H, H-34), 1.06-1.02 [m, 18 H, TBDPS

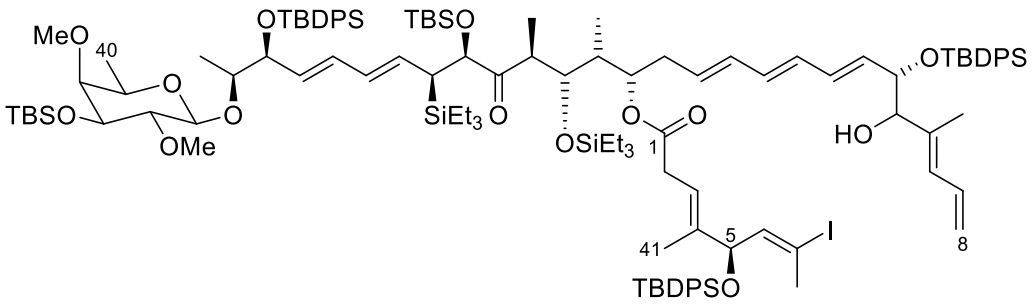
SiC(CH_3)$_3$], 1.02-0.99 [m, 9 H, TBDPS SiC(CH_3)$_3$], 0.99-0.93 [m, 18 H, $C_{23/27}$OSi($CH_2C\mathit{H}_3$)$_3$], 0.90 [s, 18 H, TBS SiC(CH_3)$_3$], 0.88-0.83 [m, 9 H, C_{12}OSi($CH_2C\mathit{H}_3$)$_3$], 0.83-0.78 (m, 6 H, H-44, H-45), 0.71-0.63 [m, 6 H, C_{23}OSi($C\mathit{H}_2CH_3$)$_3$], 0.63-0.57 [m, 6 H, C_{27}OSi($C\mathit{H}_2CH_3$)$_3$], 0.53-0.46 [m, 5 H, C_{12}OSi($C\mathit{H}_2CH_3$)$_3]_A$, 0.40 [q, ^3J = 7.9 Hz, 1 H, C_{12}OSi($C\mathit{H}_2CH_3$)$_3]_B$, 0.12-0.09 [m, 6 H, TBS Si(CH_3)$_2$], 0.07 [m, 6 H, TBS Si(CH_3)$_2$].

^{13}C-NMR: (126 MHz, $CDCl_3$, 300K) δ 215.3 (s, C-25), 171.1 (s, C-1), 142.1 (d, C-6), 138.9 (s, C-4), 138.8 (s, C-11), 136.3 (d, C_{Ar}-H), 136.2 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 135.9 (d, C_{Ar}-H), 133.9 (d, C-14), 133.6 (d, C-15), 133.1 (d, C-9), 132.7 (d, C-30), 132.3 (d, C-28), 132.2 (d, C-16), 131.7 (d, C-17), 131.2 (d, C-29), 129.8 (d, C_{Ar}-H), 129.7 (d, C_{Ar}-H), 129.5 (d, C_{Ar}-H), 128.8 (d, C-19), 128.6 (d, C-31), 128.3 (d, C-10), 127.7 (d, C_{Ar}-H), 127.6 (d, C_{Ar}-H), 127.3 (d, C_{Ar}-H), 117.3 (d, C-3), 116.5 (t, C-8), 102.8 (d, C-35), 96.5 (s, C-7), 82.7 (d, C-36), 81.9 (d, C-12), 81.1 (d, C-38), 80.7 (d, C-26), 76.8 (d, C-33), 76.8 (d, C-13), 75.9 (d, C-37), 75.2 (d, C-5), 73.9 (d, C-32), 72.7 (d, C-23), 69.8 (d, C-39), 62.2 (q, OMe), 60.9 (q, OMe), 45.6 (d, C-24), 39.5 (d, C-27), 39.1 (d, C-22), 36.4 (t, C-20), 33.7 (t, C-2), 27.9 (q, C-42), 27.2 [q, TBDPS SiC($\mathit{C}H_3$)$_3$], 27.1 [q, TBDPS SiC($\mathit{C}H_3$)$_3$], 26.9 [q, TBDPS SiC($\mathit{C}H_3$)$_3$], 26.0 [q, TBS SiC($\mathit{C}H_3$)$_3$], 25.9 [q, TBS SiC($\mathit{C}H_3$)$_3$], 19.5 [s, TBDPS SiC(CH_3)$_3$], 19.4 [s, TBDPS SiC(CH_3)$_3$], 18.3 [s, TBS SiC(CH_3)$_3$], 18.2 [s, TBS SiC(CH_3)$_3$], 16.6 (q, C-40), 15.6 (q, C-34), 14.3 (q, C-43$_B$), 12.8 (q, C-45), 12.6 (q, C-41), 12.5 (q, C-43$_A$), 9.3 (q, C-44), 7.9 [q, C_{23}OSi($CH_2\mathit{C}H_3$)$_3$], 7.2 [q, C_{27}OSi($CH_2\mathit{C}H_3$)$_3$], 6.9 [q, C_{12}OSi($CH_2\mathit{C}H_3$)$_3$], 5.7 [t, C_{27}OSi($\mathit{C}H_2CH_3$)$_3$], 4.9 [t, C_{12}OSi($\mathit{C}H_2CH_3$)$_3$], 3.5 [t, C_{23}OSi($\mathit{C}H_2CH_3$)$_3$], –3.8 (q, TBS CH_3), –4.4 (q, TBS CH_3), –4.6 (q, TBS CH_3), –4.8 (q, TBS CH_3).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3072 (*br* vw, OH), 2954 (s, C_{sp3}-H), 2932 (s, C_{sp3}-H), 2877 (s, C_{sp2}-H), 2858 (s, C_{sp2}-H), 1734 (m, C=O), 1462 (m), 1428 (m), 1111 (vs), 1079 (vs), 734 (vs), 701 (vs).

HRMS (ESI): *m/z* [$C_{125}H_{195}IO_{14}Si_8$ + Na + ^{13}C]$^+$ calcd.: 2295.1677; found: 2295.1628.

Cyclization precursor 124



124
$C_{119}H_{181}IO_{14}Si_7$
2159.24 g/mol

a) *Via Nozaki-Hiyama* reaction from alcohol **123**

To a solution of primary alcohol **123** (30.0 mg, 14.0 µmol, 1.00 eq.) in dichloromethane (2 mL) was added sodium bicarbonate (4.80 mg, 57.0 µmol, 4.00 eq.) and *Dess-Martin* periodinane (12.2 mg, 29.0 µmol, 2.00 eq.). After two hours, the yellow suspension was poured into a mixture of 5 mL saturated aqueous sodium bicarbonate solution and 5 mL saturated aqueous sodium thiosulfate solution and extracted with diethyl ether (2 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the aldehyde as a yellow oil. Chromium-(II)-chloride (36.3 mg, 295 µmol, 21.0 eq.) and nickel-(II)-chloride (0.36 mg, 3.02 µmol, 21.0 mol%) were suspended in DMF (1 mL) and cooled to 0 °C. A solution of vinyl iodide **84** (27.8 mg, 143 µmol, 10.0 eq.) and previously prepared aldehyde in DMF (1 mL) was added. The dark green solution was stirred for 30 minutes and then poured into a mixture of cold (0 °C) saturated aqueous ammonium chloride solution (20 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (5 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 7:1), alcohol **166** was obtained as a yellowish oil (16.2 mg, <7.50 µmol, <50%).

b) *Via* deprotection of silyl protected fragment **166**

The reaction was performed in a teflon flask. To a cold (–30°C) solution of HF · pyridine complex (285 µL, 30 wt.% HF, 10.9 mmol, 80.0 eq.) in THF (12 mL) was added silyl ether **166** (312 mg, 137 mmol, 1.00 eq.). After 24 hours, the reaction was warmed to –20°C and stirred for three days. 150 µL HF · pyridine complex was added, and stirring was continued for 24 hours. The clear solution was poured into 50 mL saturated aqueous sodium bicarbonate solution (violent gas evolution) and extracted with diethyl ether (3 × 20 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 8:1), alcohol **166** was obtained as a colorless foam (205 mg, 69%). 18% of the starting material was reisolated.

TLC: R_f = 0.50 (pentane:diethyl ether = 4:1), [UV, CAM].

Diastereomeric ratio: d.r. = 1:1 (Route a); 2.3:1 (Route b).

Melting point: 70 °C.

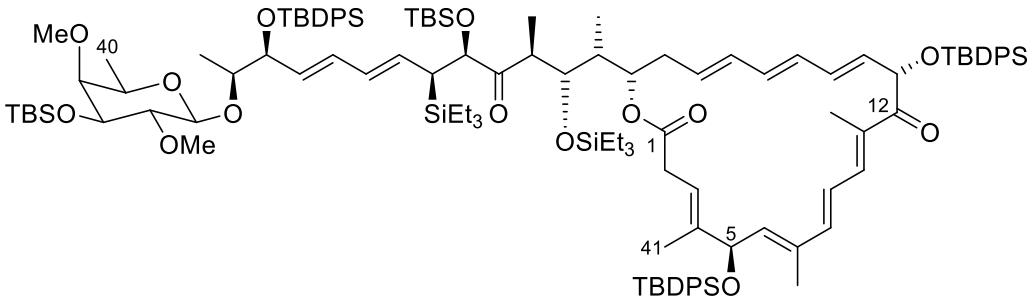
^{1}**H-NMR**: (500 MHz, $CDCl_3$, 300K) δ 7.73-7.57 (m, 12 H, C_{Ar}-H), 7.46-7.28 (m, 18 H, C_{Ar}-H), 6.53-6.40 (m, 1 H, H-9), 6.15-6.12 (m, 1 H, H-6), 6.10-5.97 (m, 5 H, H-30, H-15, H-16, H-17, H-18), 5.87 (dd, ^3J = 14.9, 10.6 Hz, 1 H, H-29), 5.66-5.49 (m, 4 H, H-3, H-14, H-19, H-31), 5.28 (dd, ^3J = 14.8, 10.9 Hz, 1 H, H-28), 5.13 (d, ^3J = 16.8 Hz, 1 H, H-8a), 5.07-5.02 (m, 1 H, H-8b), 4.95 (t, ^3J = 8.5 Hz, 1 H, H-21), 4.56 (d, ^3J = 8.9 Hz, 1 H, H-5), 4.33-4.28 (m, 1 H H-32), 4.27-4.20 (m, 1.6 H, H-26, H-13$_A$), 4.16-4.08 (m, 1.4 H, H-23, H-13$_B$), 3.94 (s, 0.7 H, H-12$_A$), 3.89 (s, 0.3 H, H-12$_B$), 3.61-3.57 (m, 1 H, H-35), 3.55 (s, 3 H, OMe), 3.54-3.51 (m, 1 H, H-33), 3.39-3.34 (m, 1 H, H-24), 3.33 (s, 3 H, OMe), 3.29 (dd, ^3J = 9.5, 3.1 Hz, 1 H, H-37), 3.08 (q, ^3J = 6.4 Hz, 1 H, H-39), 3.02-2.94 (m, 4 H, H-2, H-36, H-38), 2.68-2.60 (m, 1 H, H-10a), 2.35 (d, ^3J = 2.6 Hz, 0.3 H, OH$_B$), 2.30 (d, ^3J = 2.8 Hz, 0.8 H, OH$_A$), 2.27-2.22 (m, 1 H, H-20b), 2.07 (dd, ^3J = 11.2, 2.9 Hz, 1 H, H-27), 1.84-1.77 (m, 3 H, H-42), 1.77-1.70 (m, 1 H, H-22), 1.57 (s, 3 H, H-41), 1.51 (s, 0.6 H, H-43$_B$), 1.46-1.42 (m, 2.4 H, H-43$_A$), 1.16 (d, ^3J = 6.4 Hz, 3 H, H-40), 1.13 (d, ^3J = 6.4 Hz, 3 H, H-34), 1.07 [s, 9 H, TBDPS SiC(CH$_3$)$_3$], 1.05 [s, 9 H, TBDPS SiC(CH$_3$)$_3$], 1.03 [s, 9 H, TBDPS SiC(CH$_3$)$_3$], 1.00-0.93 [m, 18 H, C$_{23/27}$OSi(CH$_2$C*H*$_3$)$_3$], 0.91-0.88 [m, 18 H, TBS SiC(CH$_3$)$_3$], 0.83-0.77 (m, 6 H, H-44, H-45), 0.71-0.63 [m, 6 H, C$_{23}$OSi(C*H*$_2$CH$_3$)$_3$], 0.63-0.56 [m, 6 H, C$_{27}$OSi(C*H*$_2$CH$_3$)$_3$], 0.11-0.09 (m, 6 H, TBS CH$_3$), 0.09-0.05 (m, 6 H, TBS CH$_3$).

^{13}C-NMR: (126 MHz, $CDCl_3$, 300K) δ 215.4 (s, C-25), 171.2 (s, C-1), 142.2 (d, C-6), 138.8 (s, C-4), 136.2 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.1 (d, C_{Ar}-H), 136.0 (d, C_{Ar}-H), 135.9 (s, C-11), 133.6 (d, C-15), 133.5 (d, C-16)*, 133.4 (d, C-17)*, 133.2 (d, C-18), 132.6 (d, C-9), 132.3 (d, C-30), 131.7 (d, C-28), 130.9 (d, C-29), 130.3 (d, C-14), 130.0 (d, C-19), 129.9 (d, C_{Ar}-H), 129.8 (d, C_{Ar}-H), 129.7 (d, C_{Ar}-H), 129.6 (d, C_{Ar}-H), 128.3 (d, C-31), 127.9 (d, C_{Ar}-H), 127.7 (d, C_{Ar}-H), 127.7 (d, C_{Ar}-H), 127.7 (d, C_{Ar}-H), 127.4 (d, C_{Ar}-H), 127.1 (d, C-10), 117.3 (d, C-3), 117.1 (t, C-8), 102.8 (d, C-35), 96.6 (s, C-7), 82.8 (d, C-36), 81.1 (d, C-38), 80.6 (d, C-26), 79.0 (d, C-12), 77.0 (d, C-33), 76.0 (d, C-13), 75.9 (d, C-37), 75.3 (d, C-5), 74.9 (d, C-21), 73.9 (d, C-32), 72.6 (d, C-23), 69.8 (d, C-39), 62.2 (q, OMe), 60.9 (q, OMe), 45.7 (d, C-24), 39.7 (d, C-27), 39.1 (d, C-22), 36.3 (t, C-20), 33.7 (t, C-2), 27.9 (q, C-42), 27.2 [q, TBDPS SiC(CH$_3$)$_3$], 27.2 [q, TBDPS SiC(CH$_3$)$_3$], 27.0 [q, TBDPS SiC(CH$_3$)$_3$], 26.1 [q, TBS SiC(CH$_3$)$_3$], 25.9 [q, TBS SiC(CH$_3$)$_3$], 19.5 [s, TBDPS SiC(CH$_3$)$_3$], 19.5 [s, TBDPS SiC(CH$_3$)$_3$], 18.3 [s, TBS SiC(CH$_3$)$_3$], 18.2 [s, TBS SiC(CH$_3$)$_3$], 16.6 (q, C-40), 15.6 (q, C-34), 13.4 (q, C-43), 12.8 (q, C-45), 12.6 (q, C-41), 9.3 (q, C-44), 8.0 [q, C_{23}OSi(CH$_2$$CH_3$)$_3$], 7.3 [q, C_{27}OSi(CH$_2$$CH_3$)$_3$], 5.7 [t, C_{27}OSi(CH$_2CH_3$)$_3$], 3.6 [t, C_{23}OSi(CH$_2CH_3$)$_3$], –3.8 [q, TBS Si(CH$_3$)$_2$], –4.4 [q, TBS Si(CH$_3$)$_2$], –4.6 [q, TBS Si(CH$_3$)$_2$], –4.8 [q, TBS Si(CH$_3$)$_2$].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3504 (*br* vw, OH), 3072 (w, C_{sp2}-H), 2954 (m, C_{sp3}-H), 2031 (m), 2247 (vw), 1718 (m, C=O), 1427 (m), 1170 (m), 1111 (s), 907 (vs).

HRMS (ESI): *m/z* [$C_{119}H_{181}IO_{14}Si_7$ + Na + ^{13}C]$^+$ calcd.: 2181.0812; found: 2181.0786.

Silyl protected macrocycle 126



126

$C_{119}H_{178}O_{14}Si_7$

2029.31 g/mol

To a solution of alcohol **124** (15.7 mg, 7.27 µmol, 1.00 eq.) in dichloromethane (2.5 mL) was added sodium bicarbonate (2.44 mg, 29.0 µmol, 4.00 eq.) and *Dess-Martin* periodinane (4.62 mg, 11.0 µmol, 1.50 eq.). After 1.5 hours, the colorless suspension was poured into a mixture of 2 mL saturated aqueous sodium bicarbonate solution, and 2 mL saturated aqueous sodium thiosulfate solution. The layers were separated, and the aqueous layer was extracted with diethyl ether (2 × 3 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to yield the corresponding ketone as a yellow oil (R_f = 0.75, pentane:diethyl ether = 4:1). The oil was dissolved in DMF (2.5 mL), and potassium phosphate (3.09 mg, 15.0 µmol, 2.00 eq.), triethylamine (2.0 µL, 1.47 mg, 15.0 µmol, 2.00 eq.) and palladium-(II)-acetate (2.12 mg, 9.46 µmol, 1.30 eq.) were added. After stirring for two hours at room temperature, QuadraPure^{TM} TU (250 mg) was added, and stirring was continued for ten minutes. The suspension was filtered over Celite, and the solvent was removed under a high vacuum using an external cooling trap. Following flash column chromatography (silica, pentane:diethyl ether = 9:1), macrolactone **126** was obtained as a yellowish oil (7.10 mg, 3.49 µmol, 48%).

TLC: R_f = 0.32 (pentane:diethyl ether = 4:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, C_6D_6, 300K) δ 7.87-7.76 (m, 12 H, C_{Ar}-H), 7.33-7.19 (m, 18 H, C_{Ar}-H), 6.86-6.82 (m, 1 H, H-10), 6.44-6.35 (m, 2 H, H-3, H-30), 6.16 (dd, ^3J = 14.8, 10.4 Hz, 1 H, H-29), 6.11-6.8 (m, 2 H, H-8, H-9), 6.03-5.98 (m, 1 H, H-14), 5.98-5.88 (m, 4 H, H-15, H-16, H-17, H-31), 5.80-5.75 (m, 1 H, H-19), 5.73 (d, ^3J = 11.3 Hz, 1 H, H-18), 5.64 (dd, ^3J = 7.3 Hz, ^4J = 3.0 Hz, 1 H, H-13), 5.62-5.56 (m, 2 H, H-6, H-28), 5.51-5.41 (td, ^3J = 10.7, 1.9 Hz, 1 H, H-21), 4.79 (d, ^3J = 9.2 Hz, 1 H, H-5), 4.61 (dd, ^3J = 6.7, 4.1 Hz, 1 H, H-32), 4.49 (d,

^{3}J = 3.3 Hz, 1 H, H-26), 4.37 (d, ^{3}J = 9.2 Hz, 1 H, H-23), 3.98-3.89 (m, 2 H, H-33, H-35), 3.66-3.58 (m, 1 H, H-24), 3.52 (s, 3 H, OMe), 3.50 (s, 3 H, OMe), 3.45-3.41 (m, 2 H, H-36 H-37), 3.12 (dd, ^{2}J = 16.6 Hz, ^{3}J = 9.3 Hz, 1 H, H-2a), 3.05 (q, ^{3}J = 6.6 Hz, 1 H, H-39), 3.00 (dd, ^{2}J = 16.6 Hz, ^{3}J = 5.7 Hz, 1 H, H-2b), 2.92-2.90 (m, 1 H, H-38), 2.82 (*br*. d, ^{2}J = 15.9 Hz, 1 H, H-20a), 2.29 (dd, ^{3}J = 11.0, 3.4 Hz, 1 H, H-27), 2.22-2.12 (m, 1 H, H-20b), 1.84 (s, 4 H, H-43, H-22), 1.44 (d, ^{3}J = 6.3 Hz, 3 H, H-34), 1.25 (s, 3 H, H-41), 1.23-1.19 [m, 27 H, TBDPS SiC(CH_3)$_3$], 1.16-1.11 [m, 21 H, $C_{23/27}$OSi($CH_2C\mathit{H}_3$)$_3$, H-42], 1.10 (d, ^{3}J = 6.8 Hz, 3 H, H-44), 1.04 [m, 9 H, TBS SiC(CH_3)$_3$], 1.01 [m, 9 H, TBS SiC(CH_3)$_3$], 1.00-0.97 (m, 3 H, H-45), 0.93-0.80 [m, 12 H, $C_{23/27}$OSi($C\mathit{H}_2CH_3$)$_3$], 0.22 (s, 3 H, TBS CH_3), 0.21 (s, 3 H, TBS CH_3), 0.17 (s, 3 H, TBS CH_3), 0.16 (s, 3 H, TBS CH_3).

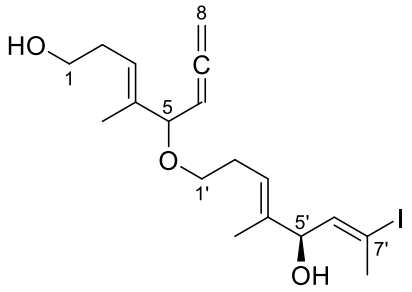
^{13}C-NMR: (126 MHz, C_6D_6, 300K) δ 215.2 (d, C-25), 196.4 (s, C-12), 171.3 (s, C-1), 145.2 (d, C-8), 141.9 (d, C-10), 139.7 (s, C-4), 139.6 (d, C-6), 136.7 (d, C_{Ar}-H), 136.5 (d, C_{Ar}-H), 136.5 (d, C_{Ar}-H), 136.4 (d, C_{Ar}-H), 136.3 (d, C_{Ar}-H), 136.3 (d, C_{Ar}-H), 136.2 (d, C-14), 134.5 (d, C-15)*, 134.4 (d, C-16)*, 134.3 (d, C-17)*, 133.1 (d, C-30), 132.8 (s, C-7), 132.3 (d, C-28), 132.0 (s, C-11), 131.8 (d, C-19), 131.4 (d, C-29), 130.1 (d, C_{Ar}-H), 130.1 (d, C-18), 130.1 (d, C_{Ar}-H), 130.0 (d, C_{Ar}-H), 129.9 (d, C_{Ar}-H), 129.1 (d, C-31), 123.1 (d, C-9), 117.4 (d, C-3), 103.3 (d, C-35), 83.1 (d, C-38), 81.6 (d, C-36), 80.8 (d, C-26), 78.3 (d, C-13), 77.1 (d, C-33), 76.5 (d, C-37), 75.2 (d, C-32), 74.8 (d, C-21), 73.4 (d, C-5), 73.0 (d, C-23), 70.0 (d, C-39), 61.9 (q, OMe), 61.1 (q, OMe), 46.2 (d, C-24), 40.6 (d, C-27, C-22), 37.1 (t, C-20), 33.4 (t, C-2), 27.3 [q, TBDPS SiC($\mathit{C}H_3$)$_3$], 27.2 [q, TBDPS SiC($\mathit{C}H_3$)$_3$], 27.1 [q, TBDPS SiC($\mathit{C}H_3$)$_3$], 26.2 [q, TBS SiC($\mathit{C}H_3$)$_3$], 25.9 [q, TBS SiC($\mathit{C}H_3$)$_3$], 19.9 [s, TBDPS SiC(CH_3)$_3$], 19.7 [s, TBDPS SiC(CH_3)$_3$], 19.4 [s, TBDPS SiC(CH_3)$_3$], 18.5 [s, TBS SiC(CH_3)$_3$], 18.3 [s, TBS SiC(CH_3)$_3$], 16.9 (q, C-40), 16.3 (q, C-34), 14.4 (q, C-41), 13.1 (q, C-45), 12.2 (q, C-42), 12.2 (q, C-43), 9.7 (q, C-44), 8.3 [q, Si($CH_2\mathit{C}H_3$)$_3$], 7.5 [q, Si($CH_2\mathit{C}H_3$)$_3$], 6.1 [t, Si($\mathit{C}H_2CH_3$)$_3$], 4.0 [t, Si($\mathit{C}H_2CH_3$)$_3$], –3.8 (q, TBS CH_3), –4.1 (q, TBS CH_3), –4.6 (q, TBS CH_3), –4.7 (q, TBS CH_3).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2953 (s, C_{sp3}-H), 2927 (vs, C_{sp3}-H), 2856 (s, C_{sp2}-H), 1729 (m, C=O), 1671 (s, C=C), 1096 (vs), 703 (vs).

HRMS (ESI): *m/z* [$C_{119}H_{178}O_{14}Si_7$ + Na + ^{13}C]$^{+}$ calcd.: 2051.1533; found: 2051.1512.

11.5. Deprotection

Allene 168



168
$C_{18}H_{27}IO_3$
418.32 g/mol

To a solution of silyl-protected fragment **36** (1.34 g, 2.11 mmol, 1.00 eq.) in THF (15 mL) was added TBAF (1M in THF, 8.43 mL, 8.43 mmol, 4.00 eq.). After 1.5 hours, the reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (50 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 1:2 ⟶ 0:1), allene **168** was obtained as a colorless oil (284 mg, 32%).

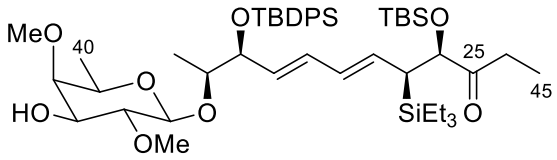
TLC: R_f = 0.25 (pentane:diethyl ether = 1:4) [$KMnO_4$].

^{1}**H-NMR**: (300 MHz, $CDCl_3$) δ 6.22 (dq, ^3J = 8.5 Hz, ^4J = 1.5 Hz, 1 H, H-6‘), 5.52 (tq, ^3J = 7.3 Hz, ^4J = 1.3 Hz, 2 H, H-3, H-3‘), 5.25 (td, ^3J = 6.6, 6.0 Hz, 1 H, H-6), 4.91 (dd, ^4J = 6.6 Hz, ^5J = 2.7 Hz, 2 H, H-8), 4.74-4.66 (m, 1 H, H-5‘), 4.63-4.56 (m, 1 H, H-5), 3.72-3.62 (m, 4 H, H-1, H-1‘), 2.48 (d, ^3J = 1.5 Hz, 3 H, H-42), 2.40-2.28 (m, 4 H, H-2, H-2‘), 2.04 (d, ^3J = 4.4 Hz, 1 H, $C_{5'}$-OH), 1.70-1.63 (m, 7 H, H-41, H-41‘, C_1-OH).

^{13}**C-NMR**: (75 MHz, $CDCl_3$) δ 207.3 (s, C-7), 141.8 (d, C-6’), 139.3 (s, C-4)*, 138.4 (s, C-4’)*, 122.4 (d, C-3)$^{\#}$, 122.3 (d, C-3’)$^{\#}$, 98.0 (s, C-7’), 93.8 (d, C-6), 78.2 (t, C-8), 74.8 (d, C-5), 74.5 (d, C-5’), 62.3 (t, C-1, C-1’), 31.3 (t, C-2)”, 31.2 (t, C-2’)”, 28.6 (q, C-42), 12.7 (q, C-41)$^{\#\#}$, 12.4 (q, C-41’)$^{\#\#}$.

$^{\#}$, $^{\#\#}$, *, “ interchangeable signals.

Partially deprotected C24-C40 fragment 172



172
$C_{48}H_{80}O_8Si_3$
869.42 g/mol

To a solution of silyl-protected fragment **11** (15.5 mg, 16.0 µmol, 1.00 eq.) in THF (2 mL) was added HF · pyridine (41 µL, 1.57 mmol, 100 eq.). After 30 min, another 100 µL HF · pyridine (3.82 mmol, 240 eq.) was added, and stirring was continued for 40 hours at room temperature. The reaction was quenched by the addition of a saturated aqueous sodium bicarbonate solution (10 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 5:1 ⟶ 0:1), triene **171** was obtained as a colorless oil (7.10 mg, 52%).

TLC: R_f = 0.30 (pentane:diethyl ether = 1:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.73-7.59 (m, 4 H, C_{Ar}-H), 7.46-7.30 (m, 6 H, C_{Ar}-H), 6.00 (*virt*. t, $^3J \approx {}^3J \approx$ 13.0 Hz, 1 H, H-30), 5.86 (*virt.* t, $^3J \approx {}^3J \approx$ 12.4 Hz, 1 H, H-29), 5.67-5.54 (m, 1 H, H-31), 5.33 (*virt.* t, $^3J \approx {}^3J \approx$ 12.5 Hz, 1 H, H-28), 4.30-4.21 (m, 1 H, H-32), 4.16 (d, ^3J = 5.1 Hz, 1 H, H-26), 3.66-3.62 (m, 1 H, H-35), 3.59-3.54 (m, 4 H, OMe, H-33), 3.45-3.42 (m, 3 H, OMe), 3.31 (d, ^3J = 10.6 Hz, 1 H, H-37), 3.19 (s, 1 H, H-38), 3.17-3.12 (m, 1 H, H-39), 2.97 (*virt.* t, $^3J \approx {}^3J \approx$ 9.8 Hz, 1 H, H-36), 2.58-2.37 (m, 2 H, H-24), 2.13-2.04 (m, 1 H, H-27), 1.24-1.20 (m, 3 H, H-40), 1.19-1-14 (m, 3 H, H-34), 1.08-1.05 [m, 9 H, TBDPS $SiC(CH_3)_3$], 0.99-0.92 [m, 12 H, H-45, $Si(CH_2C\mathit{H}_3)_3$], 0.92-0.88 [m, 9 H, TBS $SiC(CH_3)_3$], 0.60 (q, ^3J = 9.5 Hz, 6 H, $Si(C\mathit{H}_2CH_3)_3$), 0.09-0.02 [m, 6 H, $Si(CH_3)_2$].

^{13}**C-NMR**: (126 MHz, $CDCl_3$) δ 213.7 (s, C-25), 136.1 (d, C_{Ar}-H), 134.9 (s, C_{Ar}), 134.3 (s, C_{Ar}), 132.8 (d, C-30), 131.1 (d, C-28), 130.3 (d, C-29), 129.8 (d, C_{Ar}-H), 129.7 (d, C_{Ar}-H), 128.3 (d, C-31), 127.6 (d, C_{Ar}-H), 127.5 (d, C_{Ar}-H), 102.2 (d, C-35), 81.4 (d, C-38), 81.3 (d, C-36), 80.4 (d, C-26), 77.0 (d, C-33), 74.2 (d, C-37), 74.1 (d, C-32), 70.3 (d, C-39), 62.4 (q, OMe), 61.1 (q, OMe), 38.4 (d, C-27), 31.3 (t, C-24), 27.1 [q, TBDPS $SiC(\mathit{C}H_3)_3$], 26.0 [q, TBS $SiC(\mathit{C}H_3)_3$], 19.4 [s, TBDPS $Si\mathit{C}(CH_3)_3$], 18.3 [s, TBDPS $Si\mathit{C}(CH_3)_3$], 16.6 (q, C-40), 15.6 (q, C-34), 7.80

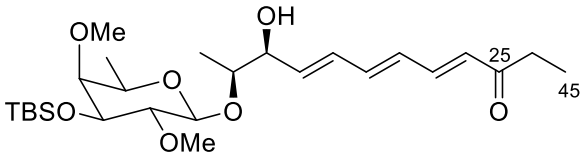
[q, Si(CH_2CH_3)$_3$], 7.37 (q, C-45), 3.32 [t, Si(CH_2CH_3)$_3$], –4.38 [q, Si(CH_3)$_2$], –4.60 [q, Si(CH_3)$_2$].

Specific rotation: $[\alpha]_D^{20} = +44.0$ (c = 1.00, $CHCl_3$).

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3481 (w, OH), 2954 (vs) 2933 (vs) 2877 (vs) (C_{sp3}-H), 1715 (m, CO), 1111 (vs).

HRMS (ESI): *m/z* $[C_{48}H_{80}O_8Si_3 + NH_4]^+$ calcd. 886.5505; found: 886.5489.

TBS protected C24-C40 fragment 171



171
$C_{26}H_{46}O_7Si$
498.73 g/mol

To a cold (0 °C) solution of silyl protected fragment **11** (26.0 mg, 26.0 µmol, 1.00 eq.) in THF (3 mL) was added acetic acid (15 µL, 15.9 mg, 264 µmol, 10.0 eq.) and TBAF (1M in THF, 264 µL, 264 µmol, 10.0 eq.). After two hours, the reaction was warmed to ambient temperature and stirred for 20 hours. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (5 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 5:1 ⟶ 0:1), triene **171** was obtained as a colorless oil (3.4 mg, 26%).

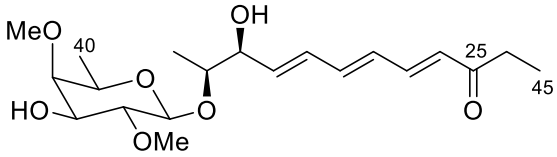
TLC: R_f = 0.25 (pentane:diethyl ether = 1:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.18 (dd, ^3J = 15.4, 11.2 Hz, 1 H, H-27), 6.59 (dd, ^3J = 14.8, 10.9 Hz, 1 H, H-29), 6.47 (ddd, ^3J = 15.2, 11.0 Hz, ^4J = 1.3 Hz, 1 H, H-30), 6.31 (dd, ^3J = 14.8, 11.1 Hz, 1 H, H-28), 6.18 (d, ^3J = 15.5 Hz, 1 H, H-26), 5.84 (dd, ^3J = 15.1, 6.3 Hz, 1 H, H-31), 4.39 (d, ^3J = 7.9 Hz, 1 H, H-35), 4.06 (ddd, ^3J = 8.0, 6.2 Hz, ^4J = 1.1 Hz, 1 H, H-32), 3.61 (s, 3 H, C_{36}OMe), 3.59 (s, 4 H, H-37, C_{38}OMe), 3.54-3.51 (m, 1 H, H-33), 3.49-3.45 (m, 1 H, H-

39), 3.29 (dd, ^{3}J = 9.6, 7.9 Hz, 1 H, H-38), 3.08 (dd, ^{3}J = 3.0 Hz, ^{4}J = 0.9 Hz, 1 H, H-36), 2.58 (q, ^{3}J = 7.4 Hz, 1 H, H-24), 1.30-1.22 (m, 6 H, H-34, H-40), 1.12 (t, ^{3}J = 7.3 Hz, 3 H, H-45), 0.94 [s, 9 H, $SiC(CH_3)_3$], 0.12 [s, 3 H, $Si(CH_3)_2$], 0.10 [s, 3 H, $Si(CH_3)_2$].

MS (ESI): *m/z* = 521 (100) $[M+Na]^+$, 522 (20) $[M+Na+\ ^{13}C]^+$, 523 (10) $[M+Na+\ 2\ ^{13}C]^+$, 1020 (10) $[2M+Na]^+$.

Deprotected C24-C40 fragment 167



167
$C_{20}H_{32}O_7$
384.47 g/mol

a) *Via* treatment of ketone **11** with TBAF

To a cold (0 °C) solution of silyl protected fragment **11** (26.0 mg, 26.0 µmol, 1.00 eq.) in THF (3 mL) was added TBAF (1M in THF, 264 µL, 264 µmol, 10.0 eq.). After two hours, the reaction was warmed to ambient temperature and stirred for 20 hours. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (5 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, hexane:ethyl acetate = 5:1 ⟶ 0:1), triene **167** was obtained as a colorless oil (3.4 mg, 26%).

b) *Via* treatment of partially deprotected fragment **172** with buffered TBAF

To a cold (0 °C) solution of silyl protected fragment **172** (26.0 mg, 26.0 µmol, 1.00 eq.) in THF (3 mL) was added acetic acid (15 µL, 15.9 mg, 264 µmol, 10.0 eq.) and TBAF (1M in THF, 264 µL, 264 µmol, 10.0 eq.). After two hours, the reaction was warmed to ambient temperature and stirred for 20 hours. The reaction was quenched by the addition of a saturated aqueous ammonium chloride solution (5 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column

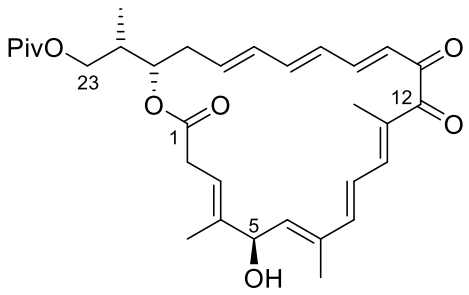
chromatography (silica, hexane:ethyl acetate = 5:1 ⟶ 0:1), triene **167** was obtained as a colorless oil (3.4 mg, 26%).

TLC: R_f = 0.10 (pentane:diethyl ether = 1:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 7.18 (dd, ^3J = 15.4, 11.1 Hz, 1 H, H-27), 6.59 (dd, ^3J = 14.8, 10.8 Hz, 1 H, H-29), 6.47 (ddd, ^3J = 15.0, 11.0, 1.3 Hz, 1 H, H-30), 6.32 (dd, ^3J = 14.9, 11.1 Hz, 1 H, H-28), 6.19 (d, ^3J = 15.5 Hz, 1 H, H-26), 5.85 (dd, ^3J = 15.1, 6.3 Hz, 1 H, H-31), 4.39 (d, ^3J = 7.9 Hz, 1 H, H-35), 4.07 (*virt*. t, $^3J \approx {}^3J$ = 7.8 Hz, 1 H, H-32), 3.67 (s, 3 H, C_{36}-OMe), 3.62 (s, 3 H, C_{38}-OMe), 3.63-3.59 (m, 1 H, H-37), 3.52-3.58 (m, 2 H, H-33, H-39), 3.28 (d, ^3J = 3.7 Hz, 1 H, H-38), 3.18 (dd, ^3J = 9.5, 7.8 Hz, 1 H, H-36), 2.58 (q, ^3J = 7.4 Hz, 2 H, H-24), 1.34 (d, ^3J = Hz, 3 H, H-40), 1.25 (d, ^3J = 6.3 Hz, 3 H, H-34), 1.11 (t, ^3J = 7.4 Hz, 3 H, H-45).

The analytical data match those reported in the literature.[30]

Diketone 170



170
$C_{32}H_{42}O_7$
538.68 g/mol

To a solution of macrocycle **92** (8.9 mg, 8.75 µmol, 1.00 eq.) in THF (2 mL) was added acetic acid (2.50 µL, 2.60 mg, 44.0 mmol, 5.00 eq.), followed by TBAF (1M in THF, 44 µL, 44 µmol, 5.00 eq.). The colorless solution was stirred for five hours at room temperature. Another 2.5 µL (2.60 mg, 44.0 mmol, 5.00 eq.) acetic acid and TBAF (1M in THF, 44 µL, 44 µmol, 5.00 eq.) were added, and stirring was continued for two hours. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (5 mL). The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure.

Following flash column chromatography (silica, hexane:ethyl acetate = 5:1 ⟶ 0:1), diketone **170** was obtained as a colorless oil (2.70 mg, 57%).

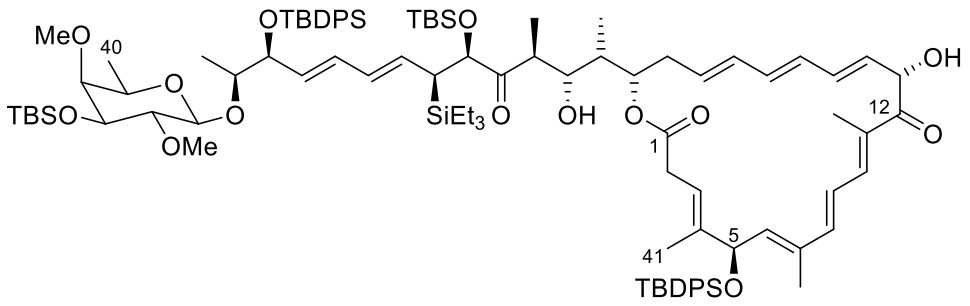
TLC: R_f = 0.10 (pentane:diethyl ether = 1:1) [UV, CAM].

^{1}**H-NMR**: (500 MHz, $CDCl_3$) δ 6.91 (d, ^3J = 11.0 Hz, 1 H, H-15), 6.88 (d, ^3J = 10.4 Hz, 1 H, H-10), 6.62-6.53 (m, 2 H, H-8, H-9), 6.42 (dd, ^3J = 15.0, 10.6 Hz, 1 H, H-17), 6.35-6.27 (m, 2 H, H-14, H-16), 6.23 (dd, ^3J = 15.2, 10.6 Hz, 1 H, H-18), 5.85 (dt, ^3J = 15.2, 7.5 Hz, 1 H, H-19), 5.68 (d, ^3J = 9.0 Hz, 1 H, H-6), 5.48 (t, *virt.* $^3J \approx {}^3J \approx$ 7.2 Hz, 1 H, H-3), 5.07 (dt, ^3J = 9.9, 3.9 Hz, 1 H, H-21), 4.83 (d, ^3J = 9.0 Hz, 1 H, H-5), 4.00 (dd, ^3J = 11.2, 6.1 Hz, 1 H, H-23a), 3.94 (dd, ^3J = 11.2, 6.0 Hz, 1 H, H-23b), 3.12 (dd, ^3J = 17.4, 7.7 Hz, 1 H, H-2a), 3.00 (dd, ^3J = 17.4, 6.6 Hz, 1 H, H-2b), 2.48-2.32 (m, 2 H, H-20), 2.10-2.05 (d, ^3J = 6.1 Hz, 1 H, H-22), 2.01 (s, 3 H, H-43), 1.91 (s, 3 H, H-42), 1.71 (s, 3 H, H-41), 1.24-1.17 [m, 9 H, $OCOC(CH_3)_3$], 0.99 (d, ^3J = 6.9 Hz, 3 H, H-44).

^{13}C-NMR: (126 MHz, $CDCl_3$) δ 198.2 (s, C-13), 197.5 (s, C-12), 178.6 [s, $OCOC(CH_3)_3$], 171.5 (s, C-1), 149.9 (d, C-15), 149.0 (d, C-10), 147.5 (d, C-8), 142.9 (d, C-17), 139.9 (s, C-4), 139.7 (d, C-6), 136.9 (d, C-19), 134.6 (s, C-7), 133.5 (s, C-11), 132.6 (d, C-18), 129.2 (d, C-16), 128.5 (d, C-14), 123.2 (d, C-19), 117.7 (d, C-3), 75.2 (d, C-21), 71.7 (d, C-5), 65.4 (t, C-23), 39.0 [s, $OCOC(CH_3)_3$], 37.2 (d, C-22), 34.5 (t, C-20), 32.9 (t, C-2), 27.3 [s, $OCOC(CH_3)_3$], 14.9 (q, C-41), 12.8 (q, C-42), 12.6 (q, C-44), 10.7 (q, C-43).

MS (ESI): *m/z* = 561 (100) $[M+Na]^+$, 562 (30) $[M+Na+ {}^{13}C]^+$, 563 (20) $[M+Na+ 2 {}^{13}C]^+$, 1100 (10) $[2M+Na]^+$.

Partially deprotected macrocycle 174



174
$C_{97}H_{146}O_{14}Si_5$
1676.65 g/mol

To a solution of HF · pyridine complex (90 µL) in THF (1.5 mL) was added silyl protected macrocycle **126** (7.0 mg, 3.44 µmol, 1.00 eq.) as a solution in THF (1.5 mL). After stirring for ten hours at room temperature, the reaction was quenched by the addition of 5 mL saturated aqueous sodium bicarbonate solution. The layers were separated, and the aqueous layer was extracted with diethyl ether (4 × 4 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane:diethyl ether = 4:1 ⟶ 1:1), diol **174** was obtained as a colorless oil (1.7 mg, 29%).

TLC: R_f = 0.50 (pentane:diethyl ether = 1:1), [UV, CAM].

^{1}**H-NMR**: (500 MHz, C_6D_6, 300K) δ 7.87-7.70 (m, 8 H, C_{Ar}-H), 7.31-7.19 (m, 12 H, C_{Ar}-H), 7.06 (d, ^3J = 11.1 Hz, 1 H, H-10), 6.42-6.33 (m, 2 H, H-3, H-30), 6.30 (d, ^3J = 15.0 Hz, 1 H, H-8), 6.22-6.12 (m, 3 H, H-9, H-15, H-29), 6.07 (dd, ^3J = 15.0, 10.3 Hz, 1 H, H-17), 5.94 (dd, ^3J = 15.3, 6.8 Hz, 1 H, H-31), 5.86 (dd, ^3J = 14.6, 10.3 Hz, 1 H, H-18), 5.79 (dd, ^3J = 15.0, 10.7 Hz, 1 H, H-16), 5.76-5.72 (dd, ^3J = 15.2, 4.6 Hz, 1 H, H-28), 5.70 (d, ^3J = 9.0 Hz, 1 H, H-6), 5.68-5.62 (ddd, ^3J = 14.6, 9.6, 4.1 Hz, 1 H, H-19), 5.41-5.31 (m, 2 H, H-14, H-21), 5.17 (dd, ^3J = 9.9, 4.8 Hz, 1 H, H-13), 4.81 (d, ^3J = 9.0 Hz, 1 H, H-5), 4.65-4.59 (m, 2 H, H-32, C_{13}-OH), 4.50 (d, ^3J = 3.4 Hz, 1 H, H-26), 4.08-4.02 (dd, ^3J = 9.2, 1.8 Hz, 1 H, H-23), 3.98-3.92 (m, 3 H, H-33, H-35, C_{23}-OH), 3.53 (s, 3 H, OMe), 3.50 (s, 3 H, OMe), 3.47-3.40 (m, 2 H, H-36, H-37), 3.32 (dq, ^3J = 9.2, 7.0 Hz, 1 H, H-24), 3.13-3.02 (m, 2 H, H-39, H-2a), 2.94 (dd, ^2J = 16.9 Hz, ^3J = 5.5 Hz, 1 H, H-2b), 2.92-2.89 (dd, ^3J = 2.8, 1.1 Hz, 1 H, H-38), 2.41-2.36 (m, 2 H, H-27, H-20a), 2.28-2.20 (*virt*. dt, ^2J = 16.1 Hz, $^3J \approx {}^3J \approx$ 10.4 Hz, 1 H, H-20b), 1.85 (d, ^4J = 1.1 Hz, 3 H, H-43), 1.76-1.69 (m, 1 H, H-22), 1.45 (d, ^3J = 6.4 Hz, 3 H, H-34), 1.23 [s, 12 H, H-41,

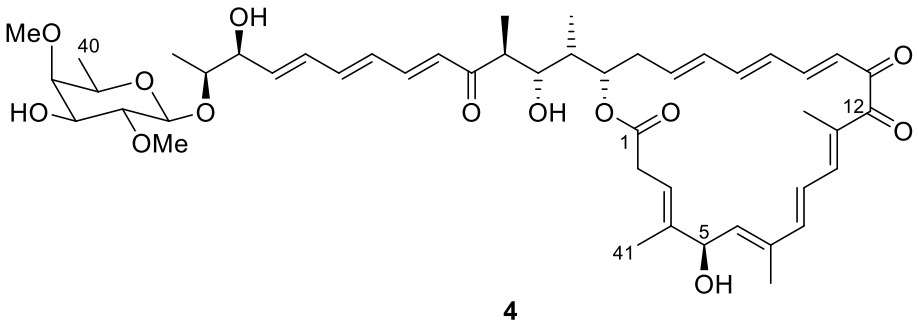
TBDPS SiC(CH_3)$_3$], 1.21 [s, 12 H, H-40, TBDPS SiC(CH_3)$_3$], 1.18-1.17 (m, 3 H, H-42), 1.11 [t, ^3J = 7.9 Hz, 9 H, Si(CH_2CH_3)$_3$], 1.04 [s, 12 H, H-44, TBS SiC(CH_3)$_3$], 1.01 [s, 9 H, TBS SiC(CH_3)$_3$], 0.94 (d, ^3J = 7.0 Hz, 3 H, H-45), 0.85 [q, ^3J = 7.9 Hz, 6 H, Si(CH_2CH_3)$_3$], 0.22 (s, 3 H, TBS CH_3), 0.17 (s, 3 H, TBS CH_3), 0.16 (s, 3 H, TBS CH_3), 0.13 (s, 3 H, TBS CH_3).

^{13}C-NMR*: 146.6 (d, C-8), 144.9 (d, C-10), 140.7 (d, C-6), 135.5 (d, C-15), 133.7 (d, C-17), 132.7 (d, C-28), 132.6 (d, C-30), 132.2 (d, C-18), 132.0 (d, C-14), 131.8 (d, C-19), 130.2 (d, C-9), 129.4 (d, C-16), 128.8 (d, C-31), 122.2 (d, C-29), 117.3 (d, C-3), 102.8 (d, C-33), 82.7 (d, C-38), 81.2 (d, C-36), 80.5 (d, C-26), 76.6 (d, C-35), 76.0 (d, C-37), 75.5 (d, C-13, C-21), 75.0 (d, C-32), 73.3 (d, C-23), 72.9 (d, C-5), 69.4 (d, C-39), 61.3 (q, OMe), 60.4 (q, OMe), 44.5 (d, C-24), 38.6 (d, C-22), 38.3 (d, C-27), 36.2 (t, C-20), 33.2 (t, C-2), 27.1 [q, TBDPS SiC(CH_3)$_3$], 26.8 [q, TBDPS SiC(CH_3)$_3$], 26.0 [q, TBS SiC(CH_3)$_3$], 25.8 [q, TBS SiC(CH_3)$_3$], 19.4 [s, TBDPS SiC(CH_3)$_3$], 18.2 [s, TBS SiC(CH_3)$_3$], 16.3 (q, C-40), 15.7 (q, C-34), 13.8 (q, C-41), 13.1 (q, C-45), 11.5 (q, C-42), 11.1 (q, C-43), 7.6 [q, Si(CH_2CH_3)$_3$], 3.5 [t, Si(CH_2CH_3)$_3$], –4.4 [q, Si(CH_3)$_2$], –4.9 [q, Si(CH_3)$_2$].

MS (ESI): *m/z* = 1699 (100%, M+Na^+), 1698 (60%), 1701 (40%).

*extracted from HSQC data

Pulvomycin D (4)



4

$C_{47}H_{64}O_{13}$

837.02 g/mol

To a solution of HF triethylamine complex (300 µL, 250 eq.) in THF (2 mL) was added silyl protected macrocycle **126** (16.6 mg, 8.18 µmol, 1.00 eq.) as a solution in THF (2 mL). After stirring for six days at 40 °C, the reaction was poured into 15 mL saturated aqueous sodium bicarbonate solution. The layers were separated, and the aqueous layer was extracted with diethyl ether (4 × 4 mL). The combined organic layers were dried over sodium sulfate and filtered. The solvent was removed under reduced pressure to obtain a yellow oil. The crude material was dissolved in acetonitrile (2 mL) and added to a mixture of TBAF (1M in THF, 1.58 mL, 1.58 mmol, 210 eq.), acetic acid (90 µL, 90.8 mg, 1.51 mmol, 200 eq.), and acetonitrile (1 mL). After stirring at room temperature for 18 hours, the reaction was quenched by the addition of 15 mL saturated aqueous ammonium chloride solution. The layers were separated, and the aqueous layer was extracted with diethyl ether (5 × 4 mL). The combined organic layers were washed with saturated aqueous sodium bicarbonate solution (1 × 4 mL), dried over sodium sulfate, and filtered. The solvent was removed under reduced pressure to obtain a yellow oil. The crude material was purified using semi-preparative reversed-phase HPLC (Kromasil C18, water/acetonitrile). Pulvomycin D (**4**) was obtained as a yellow solid.

TLC: R_f = 0.50 (ethyl acetate) [UV, CAM].

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3394 (*br* vs, OH), 2962 (s) 2931 (s) 2876 (s) (C_{sp3}-H), 1724 (s) 1649 (s) 1601 (s) (C=O), 1082 (vs), 1111 (vs).

HRMS (ESI): *m/z* $[C_{47}H_{64}O_{13} + Na]^+$ calcd.: 859.4245; found: 859.4241.

Table 22. Comparison of synthetic and natural Pulvomycin D.[21]

Position	natural (600 MHz) δ_H, mult (*J* in Hz)	synthetic (500 MHz) δ_H, mult (*J* in Hz)
1	-	-
2a	3.15, dd (17.8, 8.0)	3.18, dd (17.8, 8.3)
2b	3.04, dd (17.8, 6.0)	3.05, dd (17.8, 6.0)
3	5.42, t (6.9)	5.40, t (7.2)
4	-	-
5	4.82, d (9.0)	4.82, d (9.2)
6	5.74, d (9.0)	5.74, dq (9.1, 1.2)
7	-	-
8*	6.71, m	6.72, m
9	6.71, m	6.72, m
10	6.99, d (11.0)	6.99, d (10.7)
11	-	-
12	-	-
13	-	-
14	6.30, d (15.0)	6.30, d (16.1)
15	7.00, dd (15.0, 11.0)	7.00, dd (15.9, 10.7)
16	6.41, dd (15.0, 11.0)	6.53-6.41, m
17	6.57, dd (15.0, 11.0)	6.58, dd (14.7, 10.5)
18	6.34, m	6.34, m
19	5.98, dt (15.0, 11.0)	5.98, *virt*. dt (15.4, 7.7)
20a	2.41, m	2.41, m
20b	2.56, m	2.56, m
21	5.07, ddd (10.0, 7.0, 2.5)	5.07, m
22	1.83, ddd (10.0, 7.0, 2.5)	1.83, m
23	3.92, dd (9.0, 2.5)	3.92, dd (9.0, 2.6)
24	3.09, dq (9.0, 7.0)	3.10, dd (9.0, 7.0)
25	-	-
26	6.32, d (15.0)	6.34, m
27	7.34, dd (15.0, 11.0)	7.34, dd (14.9, 10.9)
28	6.43, dd (15.0, 11.0)	6.53-6.41, m
29	6.77, dd (15.0, 11.0)	6.78, dd (14.9, 10.8)
30	6.49, dd (15.0, 11.0)	6.53-6.41, m
31	6.06, dd (15.0, 6.0)	6.06, dd (15.2, 6.1)
32	4.31, dd (5.5, 5.5)	4.21, t (5.6)

33	3.76, dq (6.5, 6.0)	3.77, dq (6.3)
34	1.10, d (6.5)	1.19, d (6.4)
35	4.39, d (8.0)	4.39, dd (7.8, 1.5)
36	3.10, dd (10.0, 8.0)	3.10, dd (9.8, 7.7)
37	3.54, dd (10.0, 3.5)	3.54, dd (10.8, 4.0)
38	3.26, dd (3.5, 0.5)	3.26, d (3.3)
39	3.58, m	3.6, m
40	1.25, d (6.5)	1.26, d (6.4)
41	1.70, s	1.71, s
42	1.89, s	1.9, d (1.2)
43	2.00, s	2.00, d (1.2)
44	0.96, d (7.0)	0.96, m
45	0.96, d (7.0)	0.96, m
46	3.58, s	3.59, s
47	3.56, s	3.57, s

12. Abbreviations

Ac	acetyl
ATR	attenuated total reflection
Bn	benzyl
br	broad
Calcd	calculated
CAM	Cer ammonium molybdate
CBS	*Corey-Bakshi-Shibata*
COSY	correlated spectroscopy
d.r.	diastereomeric ratio
DMAP	4-dimethylaminopyridine
DMF	dimethylformamide
DMSO	dimethylsulfoxide
DMP	*Dess-Martin* periodinane
ee	enantiomeric excess
EF-Tu	elongation factor thermal unstable
ESI	electron spray ionization
equiv	equivalents
Et_2O	diethyl ether
EtOAc	ethyl acetate
Et	ethyl
GTP	guanosine triphosphate
h	hour
HMBC	heteronuclear multiple bond correlation
HPLC	high pressure liquid chromatography
HSQC	heteronuclear single quantum coherence
HWE	*Horner-Wadsworth-Emmons*
HRMS	High resolution mass spectrometry
i	*iso*
Ipc	diisopinocampheyl
IR	infrared
m	*meta*

min	minute
MeOH	methanol
Ms	mesyl
n.c.	no conversion
$NaHCO_3$	sodium bicarbonate
NMR	nuclear magnetic resonance
OAc	acetate
OTf	triflate
p	*para*
Ph	phenyl
ppm	parts per million
PPTS	pyridinium-*para*-toluenesulfonate
Piv	pivaloyl
Quant	quantitative
r.t.	room temperature
Rf	retention factor
t	tertiary
t	time
T	temperature
TBAF	tetrabutylammonium fluoride
tBu	tetrabutyl
THF	tetrahydrofuran
TLC	thin-layer chromatography
TMS	trimethylsilyl
TES	triethysilyl
TBDPS	*tert*-butyldiphenylsilyl
TBS	*tert*-butyldimethylsilyl
TIPS	tri-*iso*-propyl
TMP	2,2,6,6-tetramethylpiperidinyl

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