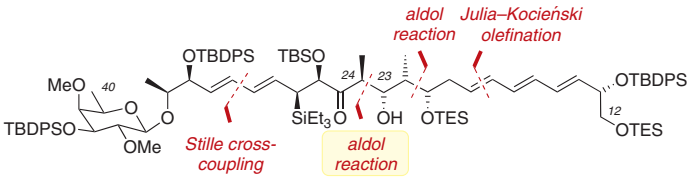
Synthesis S. Wienhold et al. Special Topic

Studies towards the Synthesis of (–)-Pulvomycin: Construction of the C12–C40 Segment by a Stereoselective Aldol Reaction

Sebastian Wienhold
Lukas Fritz
Tatjana Judt
Sabrina Hackl
Thomas Neubauer
Bastian Sauerer
Thorsten Bach*

Department Chemie and Catalysis Research Center (CRC), Technische Universität München, Lichtenbergstr. 4, 85747 Garching, Germany
thorsten.bach@ch.tum.de

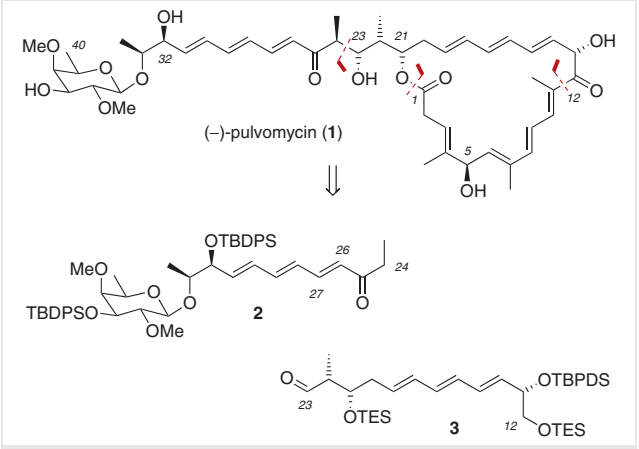
Published as part of the Special Issue
dedicated to Prof. Sarah Reisman, recipient of the 2019 Dr. Margaret Faul Women in Chemistry Award



Received: 19.03.2021
Accepted: 25.03.2021
Published online: 25.03.2021
DOI: 10.1055/a-1464-2576; Art ID: ss-2021-m0156-st

Abstract A convergent strategy was developed for the synthesis of the C12–C40 segment of (–)-pulvomycin. Key step was a diastereoselective aldol reaction between a chiral ethyl ketone representing the C24–C40 fragment and a chiral aldehyde representing the C12–C23 fragment. Both compounds were prepared from enantiomerically pure building blocks in a convergent fashion. The longest linear sequence commenced with a known D-fucose-derived glycosyl donor and entailed a total number of 16 steps. The desired *anti*-aldol product was obtained in a total yield of 5% over these steps and contains 12 out of 13 stereogenic centers present in the natural product.

Key words aldol reaction, alkenes, diastereoselectivity, natural products, polyketides, total synthesis



Scheme 1 Retrosynthetic disconnection of (–)-pulvomycin at the indicated positions leading to putative building blocks **2** (C24–C40 fragment) and **3** (C12–C23 fragment) for the natural product

The natural product (–)-pulvomycin (**1**) was isolated in 1957 by Zief et al. from an unidentified *Streptomyces* strain and its antibiotic activity towards gram positive bacteria was described.[1] In 1963, Akita et al. isolated a compound from *Streptomyces albosporeus* var. *labilomyceticus* which they named labilomycin and which was later shown to be identical to pulvomycin.[2] Akita et al. managed to decipher the structure of some subunits of the natural product including the carbohydrate (labilose) fragment but a complete structure assignment was impossible.[3] In 1978, it was shown that the antibiotic activity of pulvomycin was due to its binding to the bacterial elongation factor EF-Tu but the mode of binding remained unknown.[4] The complete structure of the compound except for the configuration at carbon atoms C32 and C33 was established in 1985 by thorough mass spectrometry and NMR analysis.[5] The biosynthesis of the polyketide was unraveled in 1995 by Priestley and Groeger.[6] In 2004, Parmeggiani and co-workers identified the binding site of pulvomycin at EF-Tu[7] and, two years later, they solved the crystal structure of the natural product in concert with EF-Tu and 5′-guanylyl imidodiphosphate (GDPNP).[8] Although it is undisputable that the unique binding mode of pulvomycin and its high potency against many bacteria make the compound a promising target for biological studies, its synthesis has remained elusive. Based on our interest in the chemistry of EF-Tu inhibitors[9] we have some time ago embarked on a total synthesis of pulvomycin. In an initial disconnection (Scheme 1) we identified three bonds, the retrosynthetic cleavage of which led to building blocks for the C1–C11 (not depicted), the C12–C23, and the C24–C40 segment. The C24–C40 segment **2** was

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previously described[10] and it was meant to undergo an aldol reaction with aldehyde **3** as one of the key steps. However, it turned out that trienone **2** was not only unstable upon storage but it also resisted the desired aldol reaction in extensive test experiments with simple aldehydes. In addition, we became concerned that the facial diastereoselectivity induced by the stereogenic centers of compound **3** might be insufficient to guarantee a high selectivity in the key aldol reaction. In this paper, we describe the preparation of aldehyde **3** and its successful aldol reaction with a C24–C40 building block which serves as a useful surrogate of compound **2**. Our synthetic efforts culminated in the stereoselective synthesis of the C12–C40 segment of pulvomycin.

When searching for potential alternative compounds to substitute trienone **2** as the C24–C40 fragment, we were guided by the desire (a) to introduce a stereogenic center at position C26 that induces a high diastereoselectivity in the aldol reaction step[11] and (b) to mask the double bond at C26/C27 by an entity that would at a later stage allow its diastereoselective formation.[12] There was literature precedence for *anti*-selective aldol reactions to occur from (O)-*E* enolates[13] which in turn were generated by treatment of ethyl ketones with a combination of a boron reagent (e.g. chlorodicyclohexylborane, Cy_2BCl)[14] and an amine base[15] or a magnesium base, such as 2,2,6,6-tetramethylpiperidin-1-ylmagnesium bromide (TMPMgBr).[16] If the substituent in the α-position to the ketone carbonyl group was a protected hydroxy group, diastereofacial control was achieved via a preferred Zimmerman–Traxler-type transition state[17] in which the bulky R^2 group points away from the aldehyde (Figure 1).[15a,16a] The enolate conformation is dictated by the 1,3-allylic strain[18] exerted by the enolate methyl group on the α-stereogenic center. The diastereofacial preference matches the less pronounced Felkin–Anh preference exerted by an α-methyl-substituted aldehyde.[19]

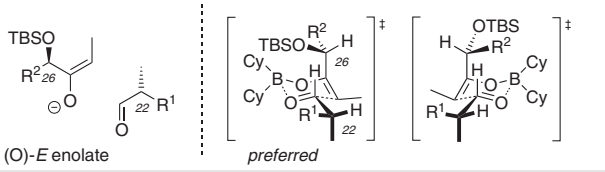


Figure 1 Control of the facial and simple diastereoselectivity in the reaction of an α-chiral aldehyde and an (O)-*E* enolate with an α-*tert*-butyldimethylsilyloxy (TBSO) substituent (see refs[15a,16a])

Adapted to our situation, it was desirable for the enolate component to display an α-stereogenic center with (*R*)-configuration at carbon atom C26. The stereogenic center would force an attack at the prostereogenic carbonyl group of the aldehyde to occur from the *Re* face. The configuration at carbon atom C22 in the aldehyde part could not be freely chosen but was determined by the configuration of this center in the natural product. A *syn*-stereospecific Peterson elimination[20] was considered to be a viable pathway to release the double bond C26/C27 in the desired (*E*)-configuration. To this end, it was required that the silyl group at carbon atom C27 was oriented *syn* to the TBSO group at the adjacent carbon atom.[12a] Based on these considerations, ketone **4** (Figure 2) appeared to be a suitable building block which promised a higher stability than **2**, a clean formation of the required (O)-*E* enolate, and a diastereoselective aldol reaction. Since the western part of the compound was unchanged as compared to **2**, it was envisaged that an access to the compound could be accomplished by a stereospecific Stille cross-coupling[21] that merges the respective olefin building blocks to the desired 1,3-diene.

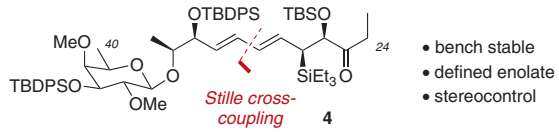
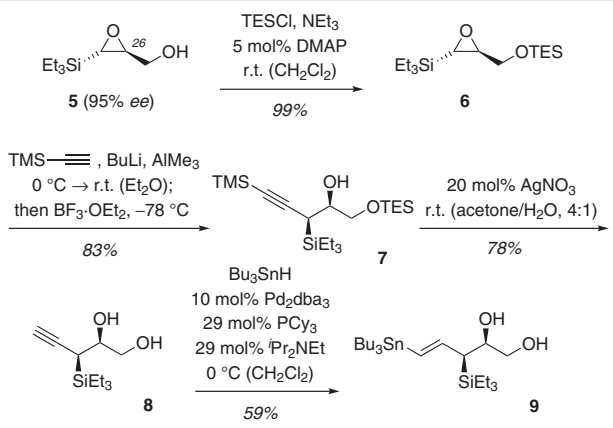


Figure 2 Ketone **4** as a surrogate for trienone **2** in a putative aldol reaction with aldehyde **3**

The synthesis of the C25–C29 segment of compound **4** commenced with the known epoxide **5** which was obtained by Sharpless epoxidation[22] from the respective (*E*)-configured allylic alcohol[23] (Scheme 2). Stereospecific S_N2-type ring opening of the epoxide required protection at the terminal hydroxy group. Two protective group strategies turned out to be viable, either employing the triethylsilyl (TES) group, as shown, or the tetrahydropyranyl (THP) group, as outlined in the Supporting Information (SI). TES protection proceeded smoothly employing triethylamine as stoichiometric base and 4-(dimethylamino)pyridine (DMAP) as catalyst.[24] Epoxide **6** was opened with an aluminum acetylide derived from trimethylsilyl (TMS) acetylene in the presence of boron trifluoride.[25]

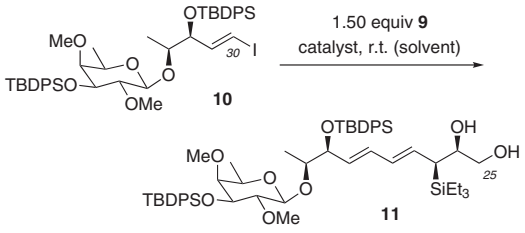


Scheme 2 Synthesis of alkenylstannane **9** from epoxide **5**, which is readily available by Sharpless epoxidation[22]

The release of the TMS group and the cleavage of the TES group in the presence of the elimination prone β-silylated alcohol **7** required careful optimization. Eventually, catalytic quantities of silver nitrate[26] in a 4:1 (v/v) mixture of acetone and water turned out to be ideal and delivered the desired diol **8** in 78% yield. An (*E*)-selective hydrostannylation of the free alkyne was accomplished with tributylstannane in the presence of catalytic quantities of tris(dibenzylideneacetone)dipalladium (Pd_2dba_3) and tricyclohexylphosphane (PCy_3).[27] The sterically encumbered phosphane ligand increases the regioselectivity by avoiding a stannylation at the internal carbon atom.[28] If palladium with a less bulky substituent, e.g. $Pd(PPh_3)_4$, was employed, the total yield decreased notably. Product **9** was free from any diastereoisomers and was to be coupled in the next step with an appropriate (*E*)-alkenyl iodide representing the western half of building block **4**. Previous studies had shown that iodide **10** can be readily obtained from an (*S*)-lactate-derived aldehyde and a D-fucose-derived glycosyl donor in nine steps.[10] By modifying the final two steps of the sequence (hydrostannylation and iodo-de-stannylation) an overall yield of 18% was achieved for the complete sequence. Optimization of the Stille cross-coupling between iodide **10** and stannane **9** commenced by using [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium [$PdCl_2$(dppf)] as the catalyst in DMF as the solvent[29] (Table 1, entry 1). The desired cross-coupling (62% yield) was accompanied by a notable Peterson elimination. Applying conditions described by Farina and Krishnan[30] did not facilitate a significant conversion (entry 2). A variation of the ligand in DMF as the solvent led to a successful cross-coupling in all cases (entries 3–5) but Peterson elimination was inevitable with PCy_3 and 1,2-bis(diphenylphosphino)ethane (dppe) as the ligand.[31] In the latter case (entry 4), the elimination went to completion (94% yield of the respective triene) and the desired product **11** was not observed. With 1,3-bis(diphenylphosphino)propane (dppp), diene **11** was obtained in 55% yield (entry 5). Eventually, a solvent variation helped to overcome the elimination issue.[32] While the use of $PdCl_2$(dppf) in dioxane gave no product (entry 6), acetonitrile turned out to be the solvent of choice (entry 7) delivering reproducibly high yields of the desired (*E*,*E*)-1,3-diene **11**.

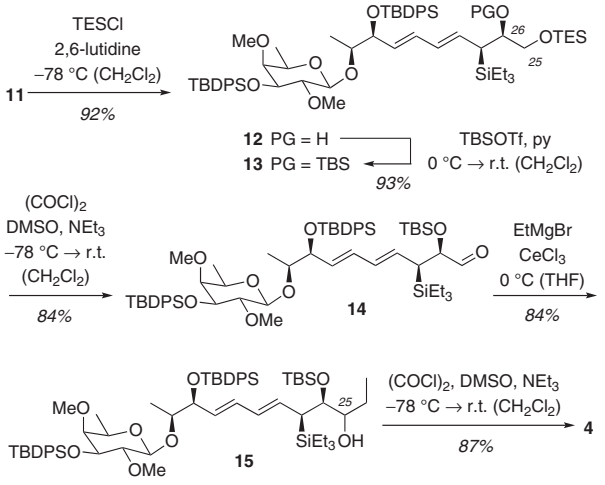
The conversion of diol **11** into fragment **4** commenced with a selective protection of the primary hydroxy group at the terminal carbon atom C25 (Scheme 3).[33] Treatment with TESCl in the presence of 2,6-lutidine furnished protected intermediate **12** which was taken into the second silyl protection step (PG = protecting group), now at carbon atom C26. The TBS group was installed by treatment with *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) in the presence of pyridine.[34] The known lability of the TES group under Swern oxidation conditions[35] allowed to convert compound **13** directly into aldehyde **14**. The ethyl group was favorably introduced via the ethyl cerium compound[36] and the sequence was completed by another Swern oxidation (**15** → **4**).

Table 1 Optimization of the Stille Cross-Coupling between Alkenyl Iodide **10** and Stannane **9**



Entry[a]	Catalyst	*t* [h]	Solvent	Yield [%][b]
1	20 mol% $PdCl_2$(dppf)	16	DMF	62[c]
2	10 mol% Pd_2dba_3 40 mol% P(2-furyl)$_3$	21	DMF	–[c]
3	10 mol% Pd_2dba_3 40 mol% PCy_3	16	DMF	69[c]
4	10 mol% Pd_2dba_3 20 mol% dppe	17	DMF	–[c]
5	10 mol% Pd_2dba_3 20 mol% dppp	21	DMF	55[c]
6	20 mol% $PdCl_2$(dppf)	16	dioxane	–[c]
7	20 mol% $PdCl_2$(dppf)	16	MeCN	88

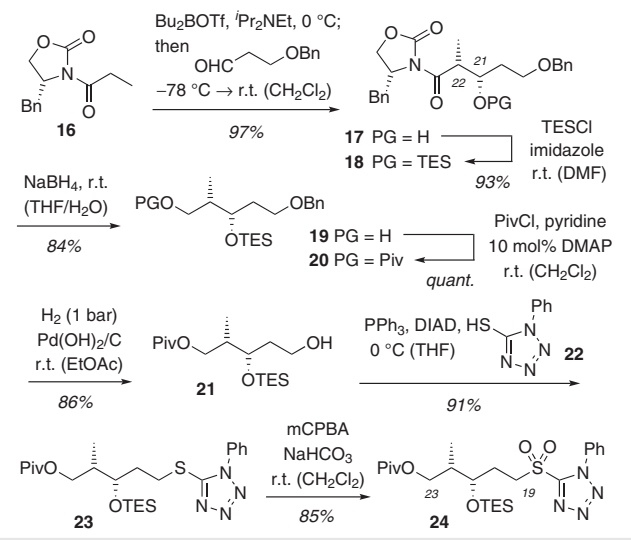
[a] The reaction was performed under exclusion of light by stirring the reaction mixture for the indicated period of time *t* at ambient temperature.
[b] Yield of isolated product after column chromatography.
[c] For additional information, see the narrative.



Scheme 3 Conversion of Stille cross-coupling product **11** into chiral ketone **4** (C24–C40 fragment)

The synthesis of the C12–C23 building block **3** followed a convergent synthesis strategy according to which the C19–C23 fragment was to be coupled with a C12–C18 aldehyde by an (*E*)-selective Julia–Kocieński olefination.[37] The two stereogenic centers were introduced by the Evans aldol

reaction[38] of *N*-propionyloxazolidinone **16** with 3-(benzyloxy)propanal.[39] The required (O)-*Z* enolate was generated by treatment of the CH-acidic fragment with dibutylboron triflate and Hünig's base.[40] Upon addition of the aldehyde the mixture was warmed to room temperature and the desired *syn*-aldol product **17** was obtained with perfect stereocontrol. After TES protection of the free hydroxy group at C21[41] the chiral auxiliary was reductively removed from compound **18**.[39e] Alcohol **19** was isolated in 84% yield and the chiral oxazolidinone was recovered in 91% yield (Scheme 4).

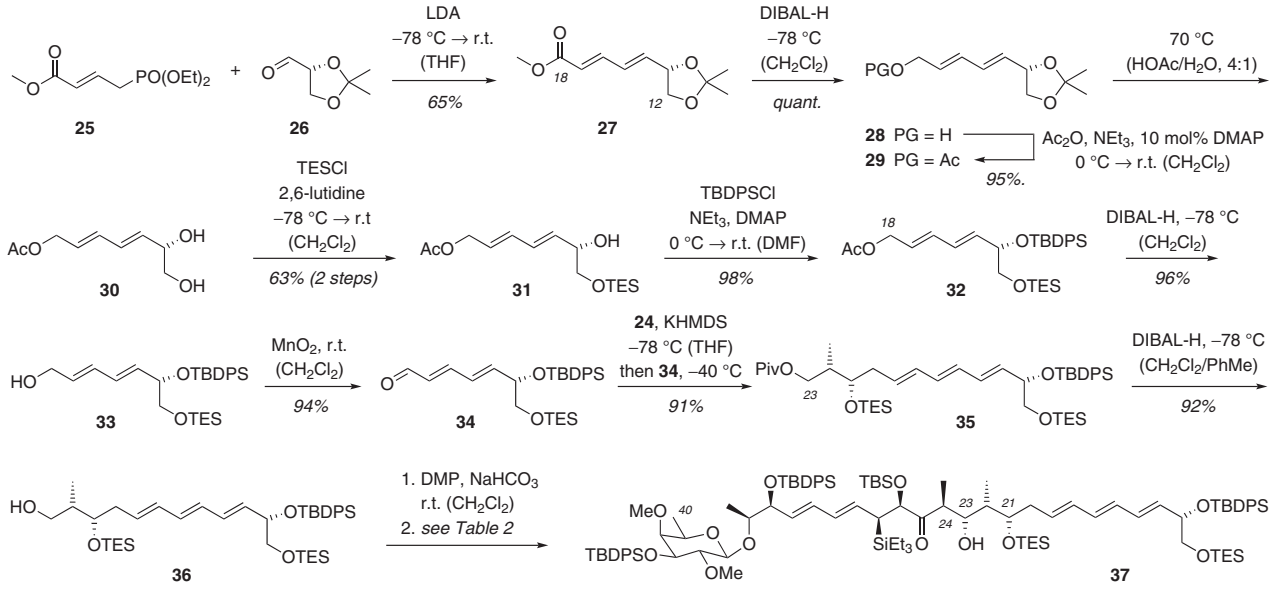


Scheme 4 Synthesis of 5-sulfonyltetrazole **24** from chiral, enantiomerically pure *N*-propionyloxazolidinone **16**

Since the outcome of the Evans aldol reaction is highly predictable and has been extensively verified[38] the absolute and relative configuration of alcohol **19** was not proven. Instead, the free primary hydroxy group was protected as pivalate **20**. The pivaloyl (Piv) protecting group was chosen to attain orthogonality with the other protecting groups of the molecule.[42] The removal of the benzyl group was performed by hydrogenolysis in the presence of Pearlman's catalyst and delivered alcohol **21**.[43] The subsequent transformation to the 5-sulfonyltetrazole **24** included a Mitsunobu reaction[44] with thiol **22** and an oxidation of intermediate **23** with *meta*-chloroperbenzoic acid (mCPBA).[45] Oxidation attempts with H_2O_2 and ammonium molybdate[46] induced an undesired cleavage of the TES ether at carbon atom C21.[47]

The assembly of the C12–C18 fragment required the introduction of the stereogenic center at C13 with (*S*)-configuration. Protected glyceraldehyde **26** was selected as a building block which is readily available from the chiral pool.[48] A vinylogous Horner–Wadsworth–Emmons reaction with phosphonate **25** delivered the known α,β,γ,δ-unsaturated ester **27**.[49] Reduction to alcohol **28**[50] was accomplished with diisobutylaluminum hydride (DIBAL-H) in dichloromethane. The terminal hydroxy group was temporarily protected with an acetyl group[51] before releasing the acetonide group from intermediate **29**.[52] The resulting diol **30** was selectively TES-protected at the primary position by treatment with TESCl and 2,6-lutidine.[33] In a subsequent step, the more robust TBDPS group was introduced to protect the free secondary alcohol **31**. The temporary acetyl protecting group at the C18 alcohol was released by reduction of the acetate **32** with DIBAL-H and the resulting alcohol **33** was oxidized to aldehyde **34** with manganese dioxide.[53] With this building block in hand the Julia–Kocieński olefination[37a] was performed employing potassium hexamethyldisilazanide (KHMDS) as the base. Deprotonation of the sulfone **24** was accomplished at –78 °C in THF as the solvent. After warming the reaction mixture to –40 °C, the aldehyde **34** was added as a solution in THF. The desired triene **35** was isolated as a mixture of diastereoisomers with the desired (*E*,*E*,*E*)-diastereoisomer prevailing. The diastereomeric ratio (d.r.) of **35** relative to its diastereoisomers was d.r. ≅ 90:10. In order to generate the aldehyde group at C18 of **3** for the key aldol reaction, the pivaloyl group was removed by reduction and the resulting alcohol **36** was oxidized with the Dess–Martin periodinane (DMP)[54] in dichloromethane (Scheme 5).

Attempts to generate the enolate from ketone **4** with a boron reagent and a weak amine base remained unsuccessful. Further deprotonation and optimization experiments were mainly performed with a TMP base.[16b,c,55] Table 2 shows a selection of the results and additional results are summarized in the Supporting Information. In the optimization experiments, both the aldol product and its *O*-borylated derivative[56] were isolated. The combined yield for the two products is given. Attempts to release the free aldol product from the borylated intermediate are described in the next paragraph. While the initial experiment to involve the resulting magnesium enolate directly in an aldol reaction[57] led to a mixture of diastereomeric aldol products combined with other impurities (entry 1), the reaction showed more promise if a transmetalation to boron was performed. The reaction with dibutylboron triflate already led to a major diastereoisomer but the d.r. was unsatisfactory (entry 2). Transmetalation to the bulkier dicyclohexylboron (Cy_2B) group gave mainly two diastereomeric products in a ratio of 78:22 (entry 3). The yield improved when the reaction was performed at 0 °C (entry 4) and a variation of the stoichiometry (entry 5) resulted in an acceptable yield of the aldol product. It was found that the base TMPMgBr which had to be freshly prepared in every reaction could be substituted by the commercially available TMPMgCl·LiCl complex (entry 6). In order to increase the diastereoselectivity of the aldol reaction a chiral boron fragment was installed at the enolate oxygen atom. (–)-Chlorodiisopinocampheylborane [(–)-Ipc_2BCl][14c,58] turned out to be the reagent of choice and delivered, to our delight, a single aldol



Scheme 5 Synthesis of aldehyde **3** starting from phosphonate **25** and protected glyceraldehyde **26**, and the product **37** of its aldol reaction with ketone **4**

product albeit in low yield (entry 7). The yield was improved when the reaction was warmed to room temperature once the addition of aldehyde was complete (entry 8). A decrease of the relative quantities for base, borane, and aldehyde **3** led to a decrease in yield (entry 9) but was more economical regarding the used aldehyde.

Several methods were probed to release the boron fragment from the product and it turned out that the use of 8-hydroxyquinoline in dichloromethane/methanol[59] was most efficient. No loss of aldol product was observed and it was possible (conditions of entry 9) to reproducibly isolate 40% of aldol product **37**. In addition, it was possible to re-isolate ketone **4** in 37% yield which in turn means that the yield based on conversion reached an acceptable value of 63%. The C12–C23 fragment was not recovered as aldehyde **3** but as alcohol **36** which can be explained by the known[58a] reductive properties of (–)-Ipc_2BCl. The recovery yield of the alcohol was 67% which compensated at least in part for the fact that the aldehyde was used in excess.

The relative configuration of product **37** was elucidated in two steps. In the first step, the relative configuration between the newly formed stereogenic centers at C23 and C24 was established. In the second step, the known absolute configuration at C21 was used as a handle to decipher the configuration at C23. Based on the assumption that ketone **4** forms the (O)-*E* enolate, the Zimmerman–Traxler

Table 2 Optimization of the Aldol Reaction between Chiral Ketone **4** and Aldehyde **3** (see Scheme 5)

Entry	**3** (equiv)	Base (equiv)	Borane (equiv)	Temp[a]	Yield[b] [%]	d.r.[c]
1	2.2	TMPMgBr (2.2)	–	0 °C	40	n.d.[d]
2	1.6	TMPMgBr (1.6)	Bu_2BOTf (1.6)	0 °C → r.t.	30	65:19:16
3	2.5	TMPMgBr (2.5)	Cy_2BCl (4.0)	–30 °C → 0 °C	27	78:22
4	2.0	TMPMgBr (2.0)	Cy_2BCl (3.0)	0 °C	43	89:11
5	1.8	TMPMgBr (2.4)	Cy_2BCl (2.5)	0 °C	49	86:14
6	1.8	TMPMgCl·LiCl (2.0)	Cy_2BCl (2.6)	0 °C	38	88:12
7	3.0	TMPMgCl·LiCl (1.8)	(–)-Ipc_2BCl (2.0)	0 °C	35	>95:5
8	3.0	TMPMgCl·LiCl (2.5)	(–)-Ipc_2BCl (2.5)	0 °C → r.t.	55	>95:5
9	2.5	TMPMgCl·LiCl (2.0)	(–)-Ipc_2BCl (2.0)	0 °C → r.t.	40	>95:5

[a] Temperature for enolization and addition of borane and aldehyde **3**. If the reaction mixture was warmed subsequently, the final temperature is given. All reactions were performed in THF as the solvent. For further details, see the Supporting Information.
[b] Yield as sum of free and *O*-borylated aldol product. For recovered ketone **4** and further details, see the Supporting Information.
[c] The diastereomeric ratio was determined by ^1H NMR analysis.
[d] n.d. = not determined.

transition state[17] (Figure 1) suggests formation of the *anti*-aldol product. The hydrogen bond between the β-hydroxy and the keto group of the aldol induces a preferred conformation in which the hydrogen atoms at the α- and β-carbon atoms are antiperiplanar for *anti*-aldol and synclinal for *syn*-aldol products. As a result, $^3J_{HH}$ coupling constants between these hydrogen atoms are large in *anti*- and small in *syn*-aldol products.[60] A second indication is the ^{13}C NMR chemical shift of the methyl group at the α-carbon atom which is larger in *anti*-aldol than in *syn*-aldol products.[61] Typical values from literature reports[62] are provided in Figure 3. In aldol product **37** the $^3J_{HH}$ coupling constant between α- and β-hydrogen atoms of the aldol subunit, corresponding to the hydrogen atoms in positions C24 and C23, was $^3J_{HH}$ = 9.7 Hz. The methyl group at C24 resonated at δ = 13.8 in the ^{13}C NMR spectrum. Both values are in perfect agreement with an *anti*-relationship of the methyl group at C23 and the hydroxy group at C24 substantiating the expected outcome of the aldol reaction, at least regarding the relative product configuration.

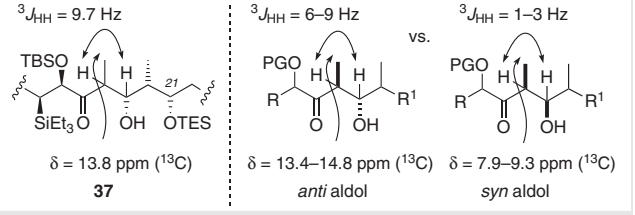


Figure 3 Proof of the relative configuration at the aldol bond C23 and C24 by NMR analysis. The product exhibits an *anti* configuration of the methyl group at C24 and the hydroxy group at C23.

The structure proof for the correct relative configuration of the newly formed stereogenic centers to the existing stereogenic centers was based on the known NMR data of 1,3-dioxanes that are obtained from 1,3-diols. Successive treatment of aldol product **37** with HF-pyridine[63] to release the TES group and with 2-methoxypropene to generate the dioxane ring[64] delivered product **38**. The C12 hydroxy group of **38** was protected as an acetone acetal and the dioxane ring was established between the two hydroxy groups at C21 and C23 (Figure 4).

The carbon atoms of the two methyl groups in the 1,3-dioxane ring (marked as •) resonate at distinctly different field if the dioxane is derived from a *syn*-1,3-diol.[65] The two equatorial groups R and R^1 stabilize a preferred ring conformer and avoid a change of position from axial to equatorial for the methyl group. In stark contrast, the dioxane ring derived from an *anti*-1,3-diol is conformationally flexible and the two methyl groups do not significant differ in their ^{13}C NMR resonance. For compound **38**, it was found that the axial methyl group displayed a ^{13}C NMR chemical shift of δ_1 = 19.4 and the equatorial methyl group resonated at δ_2 = 29.9. The results support the assumed absolute and relative configuration of aldol product **37** which bears twelve (out of 13) stereogenic centers required for the natural product.

In summary, a C12–C40 segment of (–)-pulvomycin has been assembled in a convergent and stereoselective fashion. The masked double bond at C26–C27 renders the compound stable towards degradation and isomerization. The envisaged Peterson elimination has been attempted with ketone **4** (tetrabutylammonium fluoride in THF) and delivered cleanly (*E*,*E*,*E*)-trienone **2**[10] in 81% yield. The completion of the total synthesis requires to attach a C1–C11 fragment at carbon atom C12 prior to macrocyclization. The proper handling of the protective groups will be of pivotal importance for a successful completion of the synthesis.

Thin-layer chromatography (TLC) was performed on silica-coated glass plates (silica gel 60 F254) with detection by UV (λ = 254 nm). Flash column chromatography (FCC) was performed on silica gel 60 (Merck, 230–400 mesh) with the indicated eluent. Common solvents for chromatography (pentane, Et_2O, EtOAc) were distilled prior to use. Solutions refer to saturated aqueous solutions unless otherwise stated. All melting points were determined using a *Büchi* M 565 melting point apparatus, with a range quoted to the nearest integer. IR spectra were recorded on a JASCO IR-4100 instrument (ATR). HRMS measurements were performed on a *Thermo Scientific* LTQ-FT Ultra or a high-resolution *Thermo Scientific* Exactive Plus Orbitrap mass spectrometer (ESI). ^1H, ^{13}C, and ^{19}F NMR spectra were recorded at 303 K either on a Bruker AVHD 300, AVHD 400, or AVHD 500 spectrometer. NMR spectra were calibrated to the respective residual solvent signals of $CDCl_3$ [δ (^1H) = 7.26, δ (^{13}C) = 77.16]. Apparent multiplets that occur as a result of the accidental equality of coupling constants to those of magnetically non-equivalent protons are marked as virtual (*virt.*). Assignments are based on COSY and HMBC experiments.

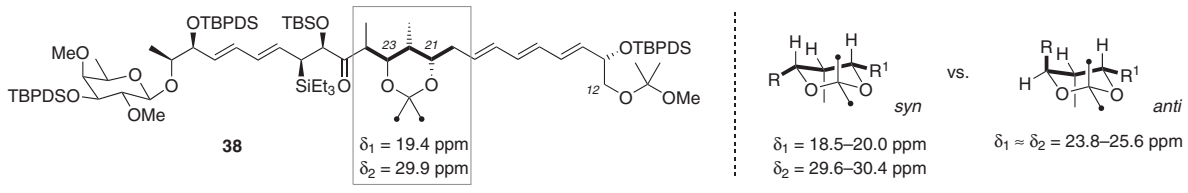


Figure 4 Proof of the relative configuration at carbon atoms C21 and C23. Dioxane **38** displays two magnetically non-equivalent methyl groups at the acetal carbon atom the ^{13}C NMR chemical shifts of which are significantly different. The chemical shift difference in turn stems from the stable chair conformation expected for an acetal derived from a 1,3-*syn*-diol.[65]

Silyl-Protected Epoxy Alcohol 6

To a solution of epoxide **5** (1.00 g, 5.31 mmol, 1.00 equiv) in CH_2Cl_2 (23 mL) were added NEt_3 (1.10 mL, 806 mg, 7.96 mmol, 1.50 equiv), DMAP (32.5 mg, 265 µmol, 5 mol%) and TESCl (1.07 mL, 960 mg, 6.37 mmol, 1.20 equiv). After stirring at r.t. for 3 h, sat. aq NH_4Cl solution (20 mL) was added. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O, 100:1), silyl-protected alcohol **6** was obtained as a colorless oil (1.59 g, 99%).

R_f = 0.82 (pentane/Et_2O, 20:1) [UV, $KMnO_4$].

IR (ATR): 2954 (s), 2912 (m), 2877 (s, C_{sp3}–H), 1459 (w, C–H), 1094 (vs), 1006 cm^{-1} (vs, C–O).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.57–0.66 [m, 12 H, Si(CH_2CH_3)$_3$, OSi(CH_2CH_3)$_3$], 0.96 [t, ^3J = 7.9 Hz, 9 H, OSi(CH_2CH_3)$_3$], 0.98 [t, ^3J = 7.9 Hz, 9 H, Si(CH_2CH_3)$_3$], 2.13 (d, ^3J = 3.6 Hz, 1 H, CH-27), 2.99 (*virt.* dt, ^3J = 5.4 Hz, $^3J \cong {}^3J$ = 3.5 Hz, 1 H, CH-26), 3.60 (dd, ^2J = 11.6 Hz, ^3J = 5.4 Hz, 1 H, C*H*H-25), 3.84 (dd, ^2J = 11.6 Hz, ^3J = 3.3 Hz, 1 H, CH*H*-25).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 2.0 [t, Si(CH_2CH_3)$_3$], 4.6 [t, OSi(CH_2CH_3)$_3$], 6.9 [q, OSi(CH_2CH_3)$_3$], 7.4 [q, Si(CH_2CH_3)$_3$], 47.0 (d, CH-27), 56.0 (d, CH-26), 65.9 (t, CH_2-25).

HRMS-ESI: *m*/*z* [$C_{15}H_{34}O_2Si_2$ + MeCN + H]$^+$ calcd: 344.2435; found: 344.2435.

TMS-Protected Alkynol 7

To a solution of trimethylsilylacetylene (19.2 mL, 13.2 g, 117 mmol, 3.00 equiv) in Et_2O (240 mL) were added BuLi (56.2 mL, 2.4 M in hexane, 135 mmol, 3.00 equiv) and $AlMe_3$ (65.2 mL, 2.0 M in hexane, 130 mmol, 2.90 equiv) at 0 °C. The reaction was warmed to r.t. and stirred for 1 h before epoxide **6** (13.6 g, 45.0 mmol, 2.00 equiv) was added as a solution in Et_2O (50 mL). After cooling to –78 °C, $BF_3{\cdot}OEt_2$ (11.4 mL, 12.8 g, 89.9 mmol, 2.00 equiv) was added and the mixture was stirred for 16 h at –78 °C. MeOH was added (138 mL) and the reaction was stirred at 0 °C for 1 h. Subsequently, aq pH 10 buffer (240 mL) was added, and stirring at 0 °C was continued for an additional 1 h. The layers were separated and the aqueous layer was extracted with Et_2O (2 × 250 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O, 100:1 → 50:1), alkyne **7** was obtained as a colorless oil (15.0 g, 83%).

R_f = 0.73 (pentane/Et_2O, 20:1) [$KMnO_4$].

IR (ATR): 3549 (w), 2954 (vs), 2912 (s), 2877 (vs, C_{sp3}–H), 1459 (w, C–H), 1094 (vs), 1006 cm^{-1} (vs, C–O).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.11 [s, 9 H, Si(CH_3)$_3$], 0.57–0.68 [m, 6 H, OSi(CH_2CH_3)$_3$], 0.69–0.77 [m, 6 H, Si(CH_2CH_3)$_3$], 0.95–1.03 [m, 18 H, Si(CH_2CH_3)$_3$, OSi(CH_2CH_3)$_3$], 2.06 (d, ^3J = 9.5 Hz, 1 H, CH-27), 2.57 (d, ^3J = 4.6 Hz, 1 H, OH), 3.61 (dd, ^2J = 9.8 Hz, ^3J = 6.7 Hz, 1 H, C*H*H-25), 3.74–3.83 (m, 1 H, CH-26), 3.90 (dd, ^2J = 9.8 Hz, ^3J = 2.9 Hz, 1 H, CH*H*-25).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 0.3 [q, Si(CH_3)$_3$], 3.5 [t, Si(CH_2CH_3)$_3$], 4.6 [t, OSi(CH_2CH_3)$_3$], 6.9 [q, OSi(CH_2CH_3)$_3$], 7.7 [q, Si(CH_2CH_3)$_3$], 22.3 (d, CH-27), 66.8 (t, CH_2-25), 72.3 (d, CH-26), 86.7 (s, C-29), 106.3 (s, C-28).

HRMS-ESI: *m*/*z* [$C_{20}H_{44}O_2Si_3$ + H]$^+$ calcd: 401.2722; found: 401.2721.

Pentyne-1,2-diol 8

The reaction was carried out in a brown glass flask. To a solution of alkyne **7** (10.3 g, 25.7 mmol, 1.00 equiv) in acetone (200 mL) was added a solution of $AgNO_3$ (873 mg, 5.14 mmol, 0.20 equiv) in water (46 mL). The suspension was stirred for 18 h at r.t. and was then poured into sat. aq NaCl solution (70 mL). The layers were separated and the aqueous layer was extracted with EtOAc (4 × 25 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 2:1 → 1:1), diol **8** was obtained as a colorless oil (4.29 g, 78%).

R_f = 0.45 (pentane/Et_2O, 1:2) [$KMnO_4$].

IR (ATR): 3372 (br s), 3313 (vs, O–H), 2953 (vs), 2912 (s), 2876 (vs, C_{sp3}–H), 2099 (w, C≡C), 1458 (m), 1416 (m, O–H), 1239 (m), 1017 (vs, C–O), 720 cm^{-1} (vs).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.68–0.77 [m, 6 H, Si(CH_2CH_3)$_3$], 1.00 [t, ^3J = 7.7 Hz, 9 H, Si(CH_2CH_3)$_3$], 2.06 (d, ^4J = 2.9 Hz, 1 H, CH-29), 2.10–2.15 (m, 2 H, CH-27, CH-26–O*H*), 2.44 (d, ^3J = 6.1 Hz, 1 H, CH_2-25–O*H*), 3.66–3.74 (m, 1 H, C*H*H-25), 3.81–3.89 (m, 2 H, CH*H*-25, CH-26).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 3.3 [t, Si(CH_2CH_3)$_3$], 7.6 [q, Si(CH_2CH_3)$_3$], 21.8 (d, CH-27), 66.5 (t, CH_2-25), 71.3 (d, CH-29), 72.1 (d, CH-26), 83.0 (s, C-28).

HRMS-ESI: *m*/*z* [$C_{11}H_{22}O_2Si$ – H_2O]$^+$ calcd: 196.1294; found: 196.1279.

Stannylated Pentene-1,2-diol 9

The reaction was carried out in a brown glass flask. To a solution of $Pd_2dba_3{\cdot}CHCl_3$ (2.75 g, 2.66 mmol, 0.10 equiv) in CH_2Cl_2 (200 mL) were added $PCy_3{\cdot}HBF_4$ (2.87 g, 7.78 mmol, 0.29 equiv) and $^iPr_2NEt$ (2.65 mL, 2.01 g, 15.6 mmol, 0.58 equiv). The red solution was stirred for 1 h at r.t. A solution of alkynediol **8** (5.70 g, 26.6 mmol, 1.00 equiv) in CH_2Cl_2 (40 mL) was added and the reaction was cooled to 0 °C. Subsequently, Bu_3SnH (9.86 mL, 10.8 g, 37.2 mmol, 1.40 equiv) was added and the reaction was stirred for another 15 h at 0 °C. The reaction was quenched by the addition of sat. aq NH_4Cl solution (300 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (4 × 250 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 5:1), stannane **9** was obtained as a colorless oil (7.93 g, 59%).

R_f = 0.57 (pentane/Et_2O, 1:1) [UV, $KMnO_4$].

IR (ATR): 3364 (br m, O–H), 2954 (vs), 2925 (vs), 2873 (s, C_{sp3}–H), 1584 (w, C=C), 1458 (m, C_{sp3}–H), 1417 (w, O–H), 1376 (w, C_{sp3}–H), 1239 (w, C–O), 1089 (m), 1017 cm^{-1} (m, C–O).

^1H NMR (500 MHz, $CDCl_3$): δ = 0.63 [q, ^3J = 7.9 Hz, 6 H, Si(CH_2CH_3)$_3$], 0.84–0.87 {m, 6 H, Sn[$CH_2(CH_2)_2CH_3$]$_3$}, 0.89 {t, ^3J = 7.3 Hz, 9 H, Sn[$(CH_2)_3CH_3$]$_3$}, 0.96 [t, 9 H, ^3J = 7.9 Hz, Si(CH_2CH_3)$_3$], 1.30 {*virt.* h, $^3J \cong {}^3J$ = 7.3 Hz, 6 H, Sn[$(CH_2)_2CH_2CH_3$]$_3$}, 1.45–1.51 [m, 6 H, Sn($CH_2CH_2CH_2CH_3$)$_3$], 1.85 (br s, 1 H, CH_2-25–O*H*), 2.01 (br s, 1 H, CH-26–O*H*), 2.06 (*virt.* t, $^3J \cong {}^3J$ = 9.0 Hz, 1 H, CH-27), 3.45 (ddd, ^2J = 11.0 Hz, ^3J = 7.8, 4.5 Hz, 1 H, C*H*H-25), 3.72 (ddd, ^2J = 11.0 Hz, ^3J = 7.2, 2.9 Hz, 1 H, CH*H*-25), 3.90 (dddd, ^3J = 9.0 Hz, 7.8, 6.2, 2.9 Hz, 1 H, CH-26), 5.74–5.84 (m, 2 H, CH-28, CH-29).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 3.5 [t, Si(CH_2CH_3)$_3$], 7.8 [q, Si(CH_2CH_3)$_3$], 9.7 {t, Sn[$CH_2(CH_2)_2CH_3$]$_3$}, 13.9 {q, Sn[$(CH_2)_3CH_3$]}, 27.4 {t, Sn[$(CH_2)_2CH_2CH_3$]$_3$}, 29.4 [t, Sn($CH_2CH_2CH_2CH_3$)$_3$], 42.6 (d, CH-27), 67.1 (t, CH_2-25), 72.8 (d, CH-26), 128.9 (d, CH-29), 146.0 (d, CH-28).

Glycoside Diol Fragment 11

The reaction was carried out in a brown glass flask. To a solution of $PdCl_2$(dppf) (392 mg, 535 µmol, 0.20 equiv) in MeCN (10 mL) was added a solution of stannane **9** (2.03 g, 4.01 mmol, 1.50 equiv) in MeCN (15 mL). Vinyl iodide **10** (2.35 g, 2.68 mmol, 1.00 equiv) was added and the reaction was stirred at r.t. for 16 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica, pentane/Et_2O 2:1 → 1:1), to afford diol **11** as a yellowish oil (2.27 g, 88%).

R_f = 0.27 (pentane/Et_2O, 1:1) [UV, $KMnO_4$].

IR (ATR): 3436 (br w, O–H), 3071 (w), 3049 (w, C_{Ar}–H), 2956 (s), 2931 (vs), 2875 (s), 2857 (s, C_{sp3}–H), 1734 (w), 1652 (w), 1589 (w, C=C), 1461 (m, C_{Ar}=C_{Ar}), 1426 (m, O–H), 1109 (vs), 1059 cm^{-1} (s, C–O).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.63 [q, ^3J = 7.7 Hz, 6 H, Si(CH_2CH_3)$_3$], 0.98 [t, ^3J = 7.7 Hz, 9 H, Si(CH_2CH_3)$_3$], 1.03 (d, ^3J = 6.5 Hz, 3 H, CH_3-40), 1.05 [s, 9 H, C(CH_3)$_3$], 1.08 [s, 9 H, C(CH_3)$_3$], 1.11 (d, ^3J = 6.4 Hz, 3 H, CH_3-34), 1.81 (br s, 1 H, CH_2-25-O*H*), 1.97 (dd, ^3J = 10.7, 9.1 Hz, 1 H, CH-27), 2.08 (br s, 1 H, CH-26-O*H*), 2.68 (d, ^3J = 3.0 Hz, 1 H, CH-38), 2.89 (q, ^3J = 6.5 Hz, 1 H, CH-39), 3.12 (dd, ^3J = 9.7, 7.7 Hz, 1 H, CH-36), 3.16 (s, 3 H, CH-36–OC*H*$_3$), 3.36–3.43 (m, 1 H, C*H*H-25), 3.40 (s, 3 H, CH-38–OC*H*$_3$), 3.45–3.53 (m, 3 H, CH-33, CH-35, CH-37), 3.66 (dd, ^2J = 10.9 Hz, ^3J = 2.9 Hz, 1 H, CH*H*-25), 3.81–3.86 (m, 1 H, CH-26), 4.25–4.28 (m, 1 H, CH-32), 5.34 (dd, ^3J = 14.4, 10.7 Hz, 1 H, CH-28), 5.57 (dd, ^3J = 15.0, 6.1 Hz, 1 H, CH-31), 5.88 (dd, ^3J = 14.4, 10.4 Hz, 1 H, CH-29), 6.00 (dd, ^3J = 15.0, 10.4 Hz, 1 H, CH-30), 7.27–7.46 (m, 12 H, CH_{Ar}), 7.58–7.64 (m, 4 H, CH_{Ar}), 7.71–7.75 (m, 4 H, CH_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 3.5 [t, Si(*C*H_2CH$_3$)$_3$], 7.7 [q, Si(CH_2*C*H$_3$)$_3$], 15.7 (q, CH_3-34), 16.7 (q, CH_3-40), 19.5 [s, *C*(CH$_3$)$_3$], 19.6 [s, *C*(CH$_3$)$_3$], 27.2 [q, C(*C*H$_3$)$_3$], 36.4 (d, CH-27), 60.4 (q, CH-36–O*C*H$_3$), 62.1 (q, CH-38–O*C*H$_3$), 67.0 (t, CH_2-25), 69.8 (d, CH-39), 73.2 (d, CH-26), 74.3 (d, CH-32), 76.3 (d, CH-37), 77.8 (d, CH-33), 81.0 (d, CH-36), 82.1 (d, CH-38), 103.2 (d, CH-35), 127.4 (d, CH_{Ar}), 127.5 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 127.7 (d, CH_{Ar}), 128.9 (d, CH-31), 129.5 (d, CH_{Ar}), 129.6 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 129.8 (d, CH_{Ar}), 130.5 (d, CH-29), 130.8 (d, CH-28), 132.0 (d, CH-30), 134.1 (s, C_{Ar}), 134.3 (s, C_{Ar}), 134.3 (s, C_{Ar}), 134.5 (s, C_{Ar}), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}), 136.2 (d, CH_{Ar}), 136.3 (d, CH_{Ar}).

HRMS-ESI: *m*/*z* [$C_{56}H_{82}O_8Si_3$ + NH_4]$^+$ calcd: 984.5656; found: 984.5662.

TES-Protected Glycoside Fragment 12

A solution of diol **11** (2.22 g, 2.30 mmol, 1.00 equiv) in CH_2Cl_2 (35 mL) was cooled to –78 °C. 2,6-Lutidine (1.07 mL, 986 mg, 9.20 mmol, 4.00 equiv) and TESCl (771 µL, 693 mg, 4.60 mmol, 2.00 equiv) were added. After stirring for 17 h, the reaction was quenched by addition of sat. aq NH_4Cl solution (90 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (4 × 100 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 20:1 → 5:1), silyl-protected alcohol **12** was obtained as a colorless oil (2.29 g, 92%).

R_f = 0.54 (pentane/Et_2O, 5:1) [UV, $KMnO_4$].

IR (ATR): 3567 (w, O–H), 3069 (w), 3052 (w, C_{Ar}–H), 2954 (s), 2932 (s), 2910 (m), 2875 (m), 2857 (m, C_{sp3}–H), 1461 (m, C_{Ar}=C_{Ar}), 1427 (m, O–H), 1369 (m), 1112 cm^{-1} (vs, C–O).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.57–0.67 [m, 12 H, Si(CH_2CH_3)$_3$], 0.95 [t, ^3J = 8.0 Hz, 9 H, OSi(CH_2CH_3)$_3$], 0.98 [t, ^3J = 8.0 Hz, 9 H, CHSi(CH_2CH_3)$_3$], 1.03 (d, ^3J = 6.4 Hz, 3 H, CH_3-40), 1.06 [s, 9 H, C(CH_3)$_3$], 1.08 [s, 9 H, C(CH_3)$_3$], 1.12 (d, ^3J = 6.4 Hz, 3 H, CH_3-34), 1.93 (*virt.* t, $^3J \cong {}^3J$ = 10.3 Hz, 1 H, CH-27), 2.60 (d, ^3J = 3.8 Hz, 1 H, OH), 2.67 (d, ^3J = 2.9 Hz, 1 H, CH-38), 2.87 (q, ^3J = 6.4 Hz, 1 H, CH-39), 3.11 (dd, ^3J = 9.6, 7.7 Hz, 1 H, CH-36), 3.17 (s, 3 H, CH-36–OC*H*$_3$), 3.30 (dd, ^2J = 9.9 Hz, ^3J = 7.4 Hz, 1 H, C*H*H-25), 3.39 (s, 3 H, CH-38–OC*H*$_3$), 3.43–3.52 (m, 3 H, CH-33, CH-35, CH-37), 3.63 (dd, ^2J = 9.9 Hz, ^3J = 2.9 Hz, 1 H, CH*H*-25), 3.75–3.80 (m, 1 H, CH-26), 4.25–4.27 (m, 1 H, CH-32), 5.36 (dd, ^3J = 15.0, 10.3 Hz, 1 H, CH-28), 5.55 (dd, ^3J = 15.2, 6.3 Hz, 1 H, CH-31), 5.85 (dd, ^3J = 15.0, 10.4 Hz, 1 H, CH-29), 6.00 (dd, ^3J = 15.2, 10.4 Hz, 1 H, CH-30), 7.27–7.45 (m, 12 H, CH_{Ar}), 7.60–7.65 (m, 4 H, CH_{Ar}), 7.72–7.75 (m, 4 H, CH_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 3.6 [t, CHSi(*C*H_2CH$_3$)$_3$], 4.5 [t, OSi(*C*H_2CH$_3$)$_3$], 6.9 [q, OSi(CH_2*C*H$_3$)$_3$], 7.8 [q, CHSi(CH_2*C*H$_3$)$_3$], 15.6 (q, CH_3-34), 16.7 (q, CH_3-40), 19.4 [s, *C*(CH$_3$)$_3$], 19.6 [s, *C*(CH$_3$)$_3$], 27.2 [q, C(*C*H$_3$)$_3$], 35.6 (d, CH-27), 60.4 (q, CH-36–O*C*H$_3$), 62.1 (q, CH-38–O*C*H$_3$), 67.2 (t, CH_2-25), 69.7 (d, CH-39), 72.9 (d, CH-26), 74.3 (d, CH-32), 76.3 (d, CH-37), 77.6 (d, CH-33), 80.9 (d, CH-36), 82.1 (d, CH-38), 103.0 (d, CH-35), 127.4 (d, CH_{Ar}), 127.5 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 128.0 (d, CH-31), 129.5 (d, CH-29), 129.5 (d, CH_{Ar}), 129.6 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 132.0 (d, CH-28), 132.5 (d, CH-30), 134.1 (s, C_{Ar}), 134.2 (s, C_{Ar}), 134.4 (s, C_{Ar}), 134.6 (s, C_{Ar}), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}), 136.2 (d, CH_{Ar}), 136.3 (d, CH_{Ar}).

HRMS-ESI: *m*/*z* [$C_{62}H_{96}O_8Si_4$ + NH_4]$^+$ calcd: 1098.6521; found: 1098.6532.

TBS-Protected Glycoside Fragment 13

A solution of alcohol **12** (2.29 g, 2.12 mmol, 1.00 equiv) in CH_2Cl_2 (23 mL) was cooled to –78 °C. Pyridine (2.05 mL 2.01 g, 25.4 mmol, 12.0 equiv) and TBSOTf (2.92 mL, 3.36 g, 12.7 mmol, 6.00 equiv) were added successively. The reaction was stirred for 22 h while warming up to r.t. Subsequently, sat. aq NH_4Cl solution (70 mL) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 20:1), silyl-protected diol **13** was obtained as a colorless oil (2.36 g, 93%).

R_f = 0.74 (pentane/Et_2O, 5:1), [UV, $KMnO_4$].

IR (ATR): 3073 (w), 3048 (w, C_{Ar}–H), 2954 (s), 2929 (vs), 2878 (s), 2856 (s, C_{sp3}–H), 1463 (m, C_{Ar}=C_{Ar}), 1254 (w), 1113 (vs), 1063 cm^{-1} (s, C–O).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.03 [s, 3 H, Si(CH_3)], 0.04 [s, 3 H, Si(CH_3)], 0.58 [q, ^3J = 7.9 Hz, 6 H, OSi(CH_2CH_3)$_3$*], 0.60 [q, ^3J = 7.9 Hz, 6 H, CHSi(CH_2CH_3)$_3$*], 0.86 [s, 9 H, C(CH_3)$_3$], 0.95 [t, ^3J = 7.9 Hz, 9 H, OSi(CH_2CH_3)$_3$*], 0.95 [t, ^3J = 7.9 Hz, 9 H, CHSi(CH_2CH_3)$_3$*], 1.01 (d, ^3J = 6.3 Hz, 3 H, CH_3-40), 1.05 [s, 9 H, C(CH_3)$_3$], 1.07 [s, 9 H, C(CH_3)$_3$], 1.10 (d, ^3J = 6.5 Hz, 3 H, CH_3-34), 2.08 (dd, ^3J = 11.0, 3.6 Hz, 1 H, CH-27), 2.65 (d, ^3J = 3.0 Hz, 1 H, CH-38), 2.85 (q, ^3J = 6.3 Hz, 1 H, CH-39), 3.10 (dd, ^3J = 9.6, 7.7 Hz, 1 H, CH-36), 3.18 (s, 3 H, CH-36–OC*H*$_3$), 3.38 (s, 3 H, CH-38–OC*H*$_3$), 3.40–3.45 (m, 2 H, CH-33, CH-35), 3.46–3.53 (m, 3 H, CH_2-25, CH-37), 3.83–3.88 (m, 1 H, CH-26), 4.23–4.25 (m, 1 H, CH-32), 5.54 (dd, ^3J = 15.3, 11.5 Hz, 1 H, CH-31), 5.52–5.59 (m, 1 H, CH-28), 5.84 (dd, ^3J = 14.9, 10.5 Hz, 1 H, CH-29), 6.05 (dd, ^3J = 15.3, 10.5 Hz, 1 H, CH-30), 7.27–7.45 (m, 12 H, CH_{Ar}), 7.60–7.65 (m, 4 H, CH_{Ar}), 7.71–7.74 (m, 4 H, CH_{Ar}); * interchangeable assignment.

^{13}C NMR (101 MHz, $CDCl_3$): δ = –4.2 [q, Si(CH_3)], –4.2 [q, Si(CH_3)], 3.7 [t, CHSi(*C*H_2CH$_3$)$_3$], 4.5 [t, OSi(*C*H_2CH$_3$)$_3$], 7.0 [q, OSi(CH_2*C*H$_3$)$_3$], 7.9 [q, CHSi(CH_2*C*H$_3$)$_3$], 15.7 (q, CH_3-34), 16.7 (q, CH_3-40), 18.4 [s, *C*(CH$_3$)$_3$], 19.4 [s, *C*(CH$_3$)$_3$], 19.6 [s, *C*(CH$_3$)$_3$], 26.2 [q, C(*C*H$_3$)$_3$], 27.2 [q, C(*C*H$_3$)$_3$], 37.1 (d, CH-27), 60.5 (q, CH-36–O*C*H$_3$), 62.1 (q, CH-38–O*C*H$_3$), 66.6 (t, CH_2-25), 69.7 (d, CH-39), 74.3 (d, CH-32), 76.3 (d, CH-37), 76.4 (d, CH-26), 77.6 (d, CH-33), 80.9 (d, CH-36), 82.1 (d, CH-38), 103.0 (d, CH-35), 127.4 (d, CH_{Ar}*), 127.5 (d, CH_{Ar}*), 127.6 (d, CH_{Ar}, CH-31*), 129.5

(d, CH_{Ar}*), 129.6 (d, CH-29*), 129.6 (d, CH_{Ar}*), 129.7 (d, CH_{Ar}*), 129.7 (d, CH_{Ar}*), 132.8 (d, CH-30), 133.4 (d, CH-28), 134.1 (s, C_{Ar}), 134.2 (s, C_{Ar}), 134.4 (s, C_{Ar}), 134.6 (s, C_{Ar}), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}), 136.2 (d, CH_{Ar}), 136.3 (d, CH_{Ar}); * interchangeable assignment.

HRMS-ESI: *m/z* $[C_{68}H_{110}O_8Si_5 + NH_4]^+$ calcd: 1212.7385; found: 1212.7413.

α-Silyloxyaldehyde 14

Oxalyl chloride (746 µL, 1.10 g, 8.69 mmol, 4.40 equiv) was added dropwise to a cold solution (–78 °C) of DMSO (1.24 mL, 1.36 g, 17.4 mmol, 8.80 equiv) in CH_2Cl_2 (10 mL). After 50 min, a solution of TES-protected alcohol **13** (2.36 g 1.98 mmol, 1.00 equiv) in CH_2Cl_2 (10 mL) was added slowly over the course of 10 min. The solution was warmed to –30 °C and stirred for 1.5 h. Subsequently, the reaction was cooled back to –78 °C and NEt_3 (4.11 mL, 3.00 g, 29.6 mmol, 15.0 equiv) was added. The mixture was warmed up to r.t. over the course of 1 h and then poured into sat. aq NH_4Cl solution (220 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 200 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 15:1 → 5:1), aldehyde **14** was obtained as a colorless oil (1.76 g, 84%).

R_f = 0.53 (pentane/Et_2O, 5:1), [UV, $KMnO_4$].

IR (ATR): 3069 (w), 3048 (w, C_{Ar}–H), 2955 (s), 2929 (vs), 2858 (s, C_{sp3}–H), 1735 (m, C=O), 1463 (m, C_{Ar}=C_{Ar}), 1112 (vs), 1065 cm^{-1} (s, C–O).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.06 [s, 3 H, $Si(CH_3)$], 0.06 [s, 3 H, $Si(CH_3)$], 0.59 [q, ^3J = 8.0 Hz, 6 H, $Si(CH_2CH_3)_3$], 0.92 [s, 9 H, $C(CH_3)_3$], 0.95 [t, ^3J = 8.0 Hz, 9 H, $Si(CH_2CH_3)_3$], 1.02 (d, ^3J = 6.4 Hz, 3 H, CH_3-40), 1.05 [s, 9 H, $C(CH_3)_3$], 1.08 [s, 9 H, $C(CH_3)_3$], 1.10 (d, ^3J = 6.4 Hz, 3 H, CH_3-34), 2.22 (dd, ^3J = 10.7, 4.7 Hz, 1 H, CH-27), 2.66 (d, ^3J = 3.0 Hz, 1 H, CH-38), 2.87 (q, ^3J = 6.4 Hz, 1 H, CH-39), 3.11 (dd, ^3J = 9.6, 7.7 Hz, 1 H, CH-36), 3.18 (s, 3 H, CH-36–OCH_3), 3.39 (s, 3 H, CH-38–OCH_3), 3.41–3.44 (m, 2 H, CH-33, CH-35), 3.47–3.51 (m, 1 H, CH-37), 4.12 (dd, ^3J = 4.7, 1.8 Hz, 1 H, CH-26), 4.24–4.27 (m, 1 H, CH-32), 5.51 (dd, ^3J = 15.0, 10.7 Hz, 1 H, CH-28), 5.59 (dd, ^3J = 15.2, 6.0 Hz, 1 H, CH-31), 5.91 (dd, ^3J = 15.0, 10.5 Hz, 1 H, CH-29), 6.05 (dd, ^3J = 15.2, 10.5 Hz, 1 H, CH-30), 7.28–7.45 (m, 12 H, CH_{Ar}), 7.59–7.64 (m, 4 H, CH_{Ar}), 7.71–7.74 (m, 4 H, CH_{Ar}), 9.55 (d, ^3J = 1.8 Hz, 1 H, CH-25).

^{13}C NMR (101 MHz, $CDCl_3$): δ = –4.4 [q, $Si(CH_3)$], –4.3 [q, $Si(CH_3)$], 3.6 [t, $Si(CH_2CH_3)_3$], 7.7 [q, $Si(CH_2CH_3)_3$], 15.8 (q, CH_3-34), 16.7 (q, CH_3-40), 18.4 [s, $C(CH_3)_3$], 19.5 [s, $C(CH_3)_3$], 19.6 [s, $C(CH_3)_3$], 26.1 [q, $C(CH_3)_3$], 27.2 [q, $C(CH_3)_3$], 27.2 [q, $C(CH_3)_3$], 36.0 (d, CH-27), 60.5 (q, CH-36–OCH_3), 62.1 (q, CH-38–OCH_3), 69.7 (d, CH-39), 74.2 (d, CH-32), 76.3 (d, CH-37), 77.7 (d, CH-33), 80.7 (d, CH-26), 80.9 (d, CH-36), 82.1 (d, CH-38), 103.2 (d, CH-35), 127.4 (d, CH_{Ar}), 127.5 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 129.2 (d, CH-31), 129.5 (d, CH_{Ar}), 129.6 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 129.8 (d, CH_{Ar}), 130.3 (d, CH-29), 131.2 (d, CH-28), 132.0 (d, CH-30), 134.0 (s, C_{Ar}), 134.2 (s, C_{Ar}), 134.4 (s, C_{Ar}), 134.5 (s, C_{Ar}), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}), 136.2 (d, CH_{Ar}), 136.3 (d, CH_{Ar}), 203.6 (d, CH-25).

HRMS-ESI: *m/z* $[C_{62}H_{94}O_8Si_4 + NH_4]^+$ calcd: 1096.6364; found: 1096.6380.

Dienyl Alcohol 15

$CeCl_3$ (609 mg, 2.47 mmol, 2.00 equiv) was added to a solution of aldehyde **14** (1.33 g, 1.24 mmol, 1.00 equiv) in THF (25 mL) and cooled to 0 °C. EtMgBr solution (9.88 mL, 1.0 M in THF, 9.88 mmol, 8.00 equiv) was added over the course of 40 min and the mixture was stirred for 1.5 h at 0 °C. Subsequently, the reaction was quenched by addition of sat. aq NH_4Cl solution (50 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 50 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 10:1 → 5:1), alcohol **15** was obtained as a colorless oil (1.15 g, 84%).

d.r. [**15** (A)/*epi*-**15** (B)] ≈ 5:1.

R_f = 0.36 (pentane/Et_2O, 5:1), [UV, $KMnO_4$].

IR (ATR): 3069 (w), 3048 (w, C_{Ar}–H), 2953 (m), 2931 (s), 2876 (m), 2857 (m, C_{sp3}–H), 1731 (w), 1666 (w, C=C), 1459 (m), 1427 (m, C_{Ar}=C_{Ar}), 1112 (vs), 1061 (s, C–O), 740 cm^{-1} (s).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.07 [s, 3 H, $Si(CH_3)$], 0.09 [s, 3 H, $Si(CH_3)$], 0.63 [q, ^3J = 7.9 Hz, 6 H, $Si(CH_2CH_3)_3$], 0.89 [s, 9 H, $C(CH_3)_3$], 0.93 (dd, ^3J = 11.2, 7.6 Hz, 3 H, CH_3-45), 0.96 [t, ^3J = 7.9 Hz, 9 H, $Si(CH_2CH_3)_3$], 1.03 (d, ^3J = 6.5 Hz, 3 H, CH_3-40), 1.05 [s, 9 H, $C(CH_3)_3$], 1.07 [s, 9 H, $C(CH_3)_3$], 1.07–1.09 (m, 0.45 H, CH_3-34$_B$), 1.12 (d, ^3J = 6.4 Hz, 2.55 H, CH_3-34$_A$), 1.32–1.38 (m, 1 H, CHH-24), 1.54–1.59 (m, 1 H, CHH-24), 1.67 (d, ^3J = 4.5 Hz, 1 H, OH), 2.19 (dd, ^3J = 10.8, 4.5 Hz, 0.85 H, CH-27$_A$), 2.24–2.28 (m, 0.15 H, CH-27$_B$), 2.65 (d, ^3J = 2.9 Hz, 0.15 H, CH-38$_B$), 2.68 (d, ^3J = 3.0 Hz, 0.85 H, CH-38$_A$), 2.82–2.86 (m, 0.15 H, CH-39$_B$), 2.88 (q, ^3J = 6.5 Hz, 0.85 H, CH-39$_A$), 3.11 (dd, ^3J = 9.6, 7.7 Hz, 1 H, CH-36), 3.16 (s, 2.55 H, CH-36–O$CH_{3\text{-}A}$), 3.20 (s, 0.45 H, CH-36–O$CH_{3\text{-}B}$), 3.37–3.41 (m, 0.3 H, CH-33$_B$, CH-35$_B$), 3.39 (s, 0.45 H, CH-38–O$CH_{3\text{-}B}$), 3.40 (s, 2.55 H, CH-38–O$CH_{3\text{-}A}$), 3.46–3.51 (m, 3.7 H, CH-25, CH-33$_A$, CH-35$_A$, CH-37), 3.81 (*virt.* t, $^3J \cong {}^3J$ = 4.5 Hz, 1 H, CH-26), 4.25 (dd, ^3J = 6.3, 3.7 Hz, 0.85 H, CH-32$_A$), 4.36 (*virt.* t, $^3J \cong {}^3J$ = 4.7 Hz, 0.15 H, CH-32$_B$), 5.51–5.54 (m, 1.15 H, CH-28$_B$, CH-31), 5.57 (dd, ^3J = 14.9, 10.8 Hz, 0.85 H, CH-28$_A$), 5.83 (dd, ^3J = 14.9, 10.4 Hz, 1 H, CH-29), 6.02 (dd, ^3J = 15.3, 10.4 Hz, 1 H, CH-30), 7.28–7.45 (m, 12 H, CH_{Ar}), 7.59–7.65 (m, 4 H, CH_{Ar}), 7.71–7.75 (m, 4 H, CH_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = –4.3 [q, $Si(CH_3)$], –3.4 [q, $Si(CH_3)$], 3.9 [t, $Si(CH_2CH_3)_{3\text{-}A}$], 4.2 [t, $Si(CH_2CH_3)_{3\text{-}B}$], 7.7 [q, $Si(CH_2CH_3)_{3\text{-}B}$], 8.0 [q, $Si(CH_2CH_3)_{3\text{-}A}$], 10.5 (q, CH_3-45), 15.7 (q, CH_3-34), 16.7 (q, CH_3-40), 18.4 [s, $C(CH_3)_3$], 19.4 [s, $C(CH_3)_3$], 19.6 [s, $C(CH_3)_3$], 26.2 [q, $C(CH_3)_3$], 26.3 (t, CH_2-24), 27.2 [q, $C(CH_3)_3$], 36.2 (d, CH-27), 60.4 (q, CH-36–OCH_3), 62.1 (q, CH-38–OCH_3), 69.8 (d, CH-39), 74.4 (d, CH-32), 76.3 (d, CH-37), 76.6 (d, CH-25), 77.4 (d, CH-33), 78.0 (d, CH-26), 80.9 (d, CH-36), 82.1 (d, CH-38), 103.0 (d, CH-35), 127.4 (d, CH_{Ar}*), 127.5 (d, CH_{Ar}*), 127.6 (d, CH_{Ar}*), 127.6 (d, CH_{Ar}*), 127.8 (d, CH-31*), 129.5 (d, CH_{Ar}#), 129.6 (d, CH_{Ar}#), 129.7 (d, CH_{Ar}#), 129.7 (d, CH_{Ar}#), 129.8 (d, CH-29#), 132.8 (d, CH-30), 133.3 (d, CH-28), 134.2 (s, C_{Ar}), 134.3 (s, C_{Ar}), 134.4 (s, C_{Ar}), 134.6 (s, C_{Ar}), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}), 136.2 (d, CH_{Ar}), 136.3 (d, CH_{Ar}); *,# interchangeable assignments.

HRMS-ESI: *m/z* $[C_{64}H_{100}O_8Si_4 + NH_4]^+$ calcd: 1126.6834; found: 1126.6846.

α-Siloxy Ketone 4

Oxalyl chloride (49.1 µL, 72.7 mg, 572 µmol, 4.40 equiv) was added dropwise to a cold solution (–78 °C) of DMSO (81.4 µL, 89.5 mg, 1.15 mmol, 8.80 equiv) in CH_2Cl_2 (600 µL). After 30 min, a solution of alcohol **15** (144 mg, 1.98 mmol, 1.00 equiv) in CH_2Cl_2 (1.0 mL) was added and the mixture was stirred for 1 h. Subsequently, NEt_3 (217 µL, 198 mg, 1.95 mmol, 15.0 equiv) was added and the reaction was warmed up to r.t. The mixture was poured into sat. aq NH_4Cl solution (5 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 15:1), ketone **4** was obtained as a colorless oil (125 mg, 87%).

R_f = 0.57 (pentane/Et_2O, 5:1), [UV, $KMnO_4$].

IR (ATR): 3073 (w), 3048 (w, C_{Ar}–H), 2953 (s), 2931 (s), 2876 (m), 2857 (s, C_{sp3}–H), 1713 (m, C=O), 1472 (m), 1463 (m), 1427 (m, C_{Ar}=C_{Ar}), 1112 (vs), 1083 (vs), 1065 cm^{-1} (s, C–O).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.01 [s, 3 H, Si(CH_3)], 0.05 [s, 3 H, Si(CH_3)], 0.61 [q, ^3J = 8.0 Hz, 6 H, Si(CH_2CH_3)$_3$], 0.91 [s, 9 H, C(CH_3)$_3$], 0.95 [t, ^3J = 8.0 Hz, 9 H, Si(CH_2CH_3)$_3$], 0.95–0.99 (m, 3 H, CH_3-45), 1.02 (d, ^3J = 6.4 Hz, 3 H, CH_3-40), 1.05 [s, 9 H, C(CH_3)$_3$], 1.08 [s, 9 H, C(CH_3)$_3$], 1.11 (d, ^3J = 6.4 Hz, 3 H, CH_3-34), 2.09 (dd, ^3J = 11.1, 5.8 Hz, 1 H, CH-27), 2.43 (dd, ^2J = 18.6 Hz, ^3J = 7.3 Hz, 1 H, C*H*H-24), 2.49 (dd, ^2J = 18.6 Hz, ^3J = 7.3 Hz, 1 H, CH*H*-24), 2.66 (d, ^3J = 3.0 Hz, 1 H, CH-38), 2.87 (q, ^3J = 6.4 Hz, 1 H, CH-39), 3.11 (dd, ^3J = 9.6, 7.7 Hz, 1 H, CH-36), 3.17 (s, 3 H, CH-36–OC*H*$_3$), 3.39 (s, 3 H, CH-38–OC*H*$_3$), 3.42 (d, ^3J = 7.7 Hz, 1 H, CH-35), 3.42–3.46 (m, 1 H, CH-33), 3.49 (dd, ^3J = 9.6, 3.0 Hz, 1 H, CH-37), 4.19 (d, ^3J = 5.8 Hz, 1 H, CH-26), 4.22–4.25 (m, 1 H, CH-32), 5.32 (dd, ^3J = 14.9, 11.1 Hz, 1 H, CH-28), 5.56 (dd, ^3J = 15.3, 6.2 Hz, 1 H, CH-31), 5.85 (dd, ^3J = 14.9, 10.5 Hz, 1 H, CH-29), 6.01 (dd, ^3J = 15.3, 10.5 Hz, 1 H, CH-30), 7.27–7.47 (m, 12 H, CH_{Ar}), 7.58–7.64 (m, 4 H, CH_{Ar}), 7.71–7.74 (m, 4 H, CH_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$): δ = –4.6 [q, Si(CH_3)], –4.4 [q, Si(CH_3)], 3.3 [t, Si(CH_2CH_3)$_3$], 7.4 (q, CH_3-45), 7.8 [q, Si(CH_2CH_3)$_3$], 15.7 (q, CH_3-34), 16.7 (q, CH_3-40), 18.3 [s, *C*(CH_3)$_3$], 19.4 [s, *C*(CH_3)$_3$], 19.6 [s, *C*(CH_3)$_3$], 26.0 [q, C(CH_3)$_3$], 27.2 [q, C(*C*H_3)$_3$], 27.2 [q, C(CH_3)$_3$], 31.5 (t, CH_2-24), 38.4 (d, CH-27), 60.5 (q, CH-36–O*C*H_3), 62.1 (q, CH-38–O*C*H_3), 69.7 (d, CH-39), 74.2 (d, CH-32), 76.2 (d, CH-37), 77.6 (d, CH-33), 80.4 (d, CH-26), 80.9 (d, CH-36), 82.1 (d, CH-38), 103.0 (d, CH-35), 127.4 (d, CH_{Ar}), 127.5 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 128.7 (d, CH-31), 129.5 (d, CH_{Ar}), 129.6 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 130.5 (d, CH-29), 130.8 (d, CH-28), 132.2 (d, CH-30), 134.0 (s, C_{Ar}), 134.2 (s, C_{Ar}), 134.3 (s, C_{Ar}), 134.5 (s, C_{Ar}), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}), 136.2 (d, CH_{Ar}), 136.3 (d, CH_{Ar}), 213.8 (s, C-25).

HRMS-ESI: *m*/*z* [$C_{64}H_{98}O_8Si_4$ + NH_4]$^+$ calcd: 1124.6677; found: 1124.6690.

Evans Aldol Product 17

A solution of oxazolidinone **16** (40.8 g, 175 mmol, 1.00 equiv) in CH_2Cl_2 (700 mL) was cooled to 0 °C and Bu_2BOTf (210 mL, 1.0 M in CH_2Cl_2, 210 mmol, 1.20 equiv) was added over the course of 30 min. Subsequently, ^{i}Pr$_2$NEt (41.6 mL, 31.6 g, 245 mmol, 1.40 equiv) was added over the course of 10 min. The solution was stirred a further 10 min and then cooled to –78 °C. A solution of 3-(benzyloxy)propanal (33.6 g, 205 mmol, 1.17 equiv) in CH_2Cl_2 (70 mL) was added over the course of 10 min and the reaction was stirred for 2 h at –78 °C and 1.5 h at 0 °C. Subsequently, the reaction was quenched by addition of aq pH 7 buffer (225 mL) and MeOH (325 mL). After stirring for 30 min, MeOH (450 mL) and H_2O_2 (30%, 225 mL) were added and stirring was continued for 30 min at r.t. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 250 mL). The organic layers were combined, washed with sat. aq $NaHCO_3$ solution (280 mL) and sat. aq NaCl solution (390 mL), and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was purified with flash column chromatography (silica, pentane/Et_2O 1:1 → 0:1), to afford alcohol **17** as a colorless oil (67.2 g, 97%).

R_f = 0.10 (pentane/Et_2O, 1:1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.29 (d, ^3J = 7.0 Hz, 3 H, CH_3-44), 1.75 (dddd, ^2J = 14.3 Hz, ^3J = 6.6, 4.7, 3.0 Hz, 1 H, C*H*H-20), 1.88 (dddd, ^2J = 14.3 Hz, ^3J = 9.4, 7.3, 4.8 Hz, 1 H, CH*H*-20), 2.78 (dd, ^2J = 13.4 Hz, ^3J = 9.5 Hz, 1 H, CHC*H*HAr), 3.26 (dd, ^2J = 13.4 Hz, ^3J = 3.4 Hz, 1 H, CHCH-*H*Ar), 3.31 (d, ^3J = 2.4 Hz, 1 H, OH), 3.59–3.73 (m, 2 H, CH_2OCO), 3.80–3.87 (m, 1 H, CH-22), 4.16–4.21 (m, 3 H, CH_2-19, CH-21), 4.52 (s, 2 H, OCH_2Ar), 4.68 (ddt, ^3J = 9.5, 6.8, 3.4 Hz, 1 H, CHN), 7.19–7.21 (m, 2 H, CH_{Ar}), 7.26–7.36 (m, 8 H, CH_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 11.3 (q, CH_3-44), 33.9 (t, CH_2-20), 38.0 (t, $CHCH_2$Ar), 42.7 (d, CH-22), 55.4 (d, CHN), 66.3 (t, CH_2-19), 68.5 (t, *C*H_2OCO), 70.6 (d, CH-21), 73.4 (t, OCH_2Ar), 127.5 (d, CH_{Ar}), 127.8 (d, CH_{Ar}), 127.8 (d, CH_{Ar}), 128.6 (d, CH_{Ar}), 129.1 (d, CH_{Ar}), 129.6 (d, CH_{Ar}), 135.3 (s, C_{Ar}), 138.2 (s, C_{Ar}), 153.2 (s, OCO), 176.8 (s, C-23).

The analytical data matched those reported in the literature.[66]

TES-Protected Aldol Product 18

To a solution of alcohol **17** (10.0 g, 25.2 mmol, 1.00 equiv) in DMF (40 mL) were added imidazole (15.4 g, 226 mmol, 9.00 equiv), DMAP (307 mg, 2.52 mmol, 0.10 equiv), and TESCl (10.6 mL, 9.48 g, 62.9 mmol, 2.50 equiv) successively. The solution was stirred for 24 h at r.t. and then quenched by addition of sat. aq NH_4Cl solution (40 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 45 mL). The combined organic layers were washed with sat. aq NaCl solution, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure and the residue was purified with flash column chromatography (silica, pentane/Et_2O 10:1 → 5:1), to afford silyl ether **18** as a colorless oil (11.9 g, 93%).

R_f = 0.29 (pentane/Et_2O, 5:1) [UV, $KMnO_4$].

IR (ATR): 3086 (w), 3063 (w), 3033 (w, C_{Ar}–H), 2978 (m), 2954 (m), 2937 (m), 2912 (m), 2875 (m, C_{sp3}–H), 1780 (vs), 1695 (s, C=O), 1455 (m), 1383 (m), 1208 (s), 1106 (vs, C–O), 741 (vs), 699 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.59 [q, ^3J = 7.9 Hz, 6 H, OSi(CH_2)$_3$], 0.95 [t, ^3J = 7.9 Hz, 9 H, OSi(CH_2CH_3)$_3$], 1.25 (d, ^3J = 6.9 Hz, 3 H, CH_3-44), 1.84–1.98 (m, 2 H, CH_2-20), 2.73 (dd, ^2J = 13.3 Hz, ^3J = 9.6 Hz, 1 H, CH-C*H*HAr), 3.23 (dd, ^2J = 13.3 Hz, ^3J = 3.2 Hz, 1 H, CHCH*H*Ar), 3.52 (ddd, ^2J = 9.4 Hz, ^3J = 6.6, 5.6 Hz, 1 H, C*H*H-19), 3.63 (*virt.* dt, ^2J = 9.4 Hz, ^3J ≅ ^3J = 6.2 Hz, 1 H, CH*H*-19), 3.78 (*virt.* t, ^3J ≅ ^3J = 8.3 Hz, 1 H, C*H*HOCO), 3.89 (*virt.* p, ^3J ≅ ^3J = 6.9 Hz, 1 H, CH-22), 4.03 (dd, ^3J = 9.0 Hz, ^3J = 2.1 Hz, 1 H, CH*H*OCO), 4.15 (dt, ^3J = 6.8, 5.1 Hz, 1 H, CH-21), 4.43 (d, ^2J = 11.8 Hz, 1 H, OC*H*HAr), 4.48 (d, ^2J = 11.8 Hz, 1 H, OCH*H*Ar), 4.50–4.55 (m, 1 H, CHN), 7.18–7.34 (m, 10 H, CH_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 5.2 [t, OSi(CH_2)$_3$], 7.1 [q, OSi(CH_2CH_3)$_3$], 13.8 (q, CH_3-44), 35.4 (t, CH_2-20), 37.9 (t, $CHCH_2$Ar), 43.4 (d, CH-22), 55.6 (d, CHN), 66.0 (t, CH_2OCO), 66.5 (t, CH_2-19), 71.3 (d, CH-21), 73.1 (t, OCH_2Ar), 127.4 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 127.8 (d, CH_{Ar}), 128.4 (d, CH_{Ar}), 129.0 (d, CH_{Ar}), 129.6 (d, CH_{Ar}), 135.6 (s, C_{Ar}), 138.7 (s, C_{Ar}), 153.0 (s, OCO), 175.7 (s, C-23).

HRMS-ESI: *m*/*z* [$C_{29}H_{41}NO_5Si$ + H]$^+$ calcd: 512.2827; found: 512.2829.

TES/Benzyl-Protected Pentanol 19

Silyl ether **18** (78.8 g, 154 mmol, 1.00 equiv) was dissolved in THF (3.45 L) and a solution of $NaBH_4$ (29.1 g, 770 mmol, 5.00 equiv) in water (950 mL) was slowly added at 0 °C. The reaction was stirred for 20 h at r.t. and then quenched by careful addition of sat. aq NH_4Cl solution (1.0 L). The layers were separated and the aqueous layer was extracted with EtOAc (6 × 600 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 20:1 → 1:1 → EtOAc), alcohol **19** was obtained as a colorless oil (43.6 g, 84%). Additionally, oxazolidinone (24.9 g, 140 mmol, 91%) was re-isolated.

R_f = 0.32 (pentane/Et_2O, 2:1) [UV, $KMnO_4$].

IR (ATR): 3430 (br m, O–H), 2955 (vs), 2912 (s), 2875 (vs, C_{sp3}–H), 1455 (m), 1413 (w, C–H), 1363 (w), 1239 (w), 1092 (vs), 1048 (vs), 1017 (vs, C–O), 733 cm^{-1} (vs).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.61 [q, ^3J = 7.9 Hz, 6 H, OSi(CH_2)$_3$], 0.82 (d, ^3J = 7.0 Hz, 3 H, CH_3-44), 0.96 [t, ^3J = 7.9 Hz, 9 H, OSi(CH_2CH_3)$_3$], 1.74–1.86 (m, 2 H, CH_2-20), 1.97 (dqdd, ^3J = 8.5, 7.0, 4.9, 3.6 Hz, 1 H, CH-22), 2.76 (br s, 1 H, OH), 3.50–3.58 (m, 3 H, CH_2-19, C*H*H-23), 3.70 (ddd, ^2J = 11.3 Hz, ^3J = 8.5, 2.9 Hz, 1 H, CH*H*-23), 3.98 (dt, ^3J = 7.9, 3.6 Hz, 1 H, CH-21), 4.48 (d, ^2J = 12.0 Hz, 1 H, OC*H*HAr), 4.52 (d, ^2J = 12.0 Hz, 1 H, OC*H*HAr), 7.26–7.37 (m, 5 H, CH_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 5.2 [t, OSi(CH_2)$_3$], 7.0 [q, OSi(CH_2CH_3)$_3$], 12.5 (q, CH_3-44), 32.6 (t, CH_2-20), 40.1 (d, CH-22), 66.1 (t, CH_2-23), 67.3 (t, CH_2-19), 73.2 (t, OCH_2Ar), 73.3 (d, CH-21), 127.7 (d, CH_{Ar}), 127.8 (d, CH_{Ar}), 128.5 (d, CH_{Ar}), 138.6 (s, C_{Ar}).

HRMS-ESI: *m*/*z* [$C_{19}H_{34}O_3Si$ + H]$^+$ calcd: 339.2350; found: 339.2351.

Piv/TES/Benzyl-Protected Pentanol 20

To a solution of alcohol **19** (43.6 g, 129 mmol, 1.00 equiv) in CH_2Cl_2 (436 mL) was added pyridine (31.2 mL, 30.5 g, 386 mmol, 3.00 equiv), DMAP (1.57 g, 12.9 mmol, 0.10 equiv), and pivaloyl chloride (23.8 mL, 23.3 g, 193 mmol, 1.50 equiv). The reaction was stirred for 16.5 h at r.t. and then quenched by addition of sat. aq NH_4Cl solution (200 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 200 mL). The combined organic layers were dried (Na_2SO_4) and filtered. The solvent was removed under reduced pressure and the residue was purified with flash column chromatography (silica, pentane/Et_2O 30:1 → 10:1), to afford pivalate **20** as a colorless oil (11.9 g, quant.).

R_f = 0.43 (pentane/Et_2O, 10:1) [UV, $KMnO_4$].

IR (ATR): 3033 (w, C_{Ar}–H), 2957 (vs), 2912 (m), 2876 (s, C_{sp3}–H), 1730 (vs, C=O), 1481 (m), 1456 (m, C–H), 1283 (m), 1155 (vs), 1101 (s), 1051 (m, C–O), 735 cm^{-1} (vs).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.59 [q, ^3J = 8.0 Hz, 6 H, OSi(CH_2)$_3$], 0.89 (d, ^3J = 6.9 Hz, 3 H, CH_3-44), 0.94 [t, ^3J = 8.0 Hz, 9 H, OSi(CH_2CH_3)$_3$], 1.19 [s, 9 H, C(CH_3)$_3$], 1.70–1.77 (m, 1 H, C*H*H-20), 1.78–1.84 (m, 1 H, CH*H*-20), 1.89 (*virt.* qd, $^3J \cong {}^3J$ = 6.8, ^3J = 3.2 Hz, 1 H, CH-22), 3.50 (t, ^3J = 6.6 Hz, 2 H, CH_2-19), 3.93–3.96 (m, 1 H, CH-21), 3.97–4.04 (m, 2 H, CH_2-23), 4.47 (d, ^2J = 11.9 Hz, 1 H, OC*H*HAr), 4.50 (d, ^2J = 11.9 Hz, 1 H, OC*H*HAr), 7.27–7.29 (m, 1 H, CH_{Ar}), 7.31–7.36 (m, 4 H, CH_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 5.3 [t, OSi(CH_2)$_3$], 7.1 [q, OSi(CH_2CH_3)$_3$], 11.3 (q, CH_3-44), 27.4 [q, C(CH_3)$_3$], 34.5 (t, CH_2-20), 38.0 (d, CH-22), 38.9 [s, *C*(CH_3)$_3$], 66.5 (t, CH_2-23), 67.3 (t, CH_2-19), 69.9 (d, CH-21), 73.1 (t, OCH_2Ar), 127.6 (d, CH_{Ar}), 127.7 (d, CH_{Ar}), 128.5 (d, CH_{Ar}), 138.6 (s, C_{Ar}), 178.7 (s, COO).

HRMS-ESI: *m*/*z* [$C_{24}H_{42}O_4Si$ + H]$^+$ calcd: 423.2925; found: 423.2929.

Piv/TES-Protected Pentanol 21

Pd(OH)$_2$/C (686 mg, 20 wt%) was added to a solution of pivalate **20** (5.50 g, 13.0 mmol, 1.00 equiv) in EtOAc (91 mL). The reaction flask was flushed with argon and then exchanged for a H_2 atmosphere (1 atm). After stirring for 23.5 h at r.t. the reaction flask was again flushed with argon and the mixture was filtered over Celite. The solvent was removed under reduced pressure and the residue was purified with flash column chromatography (silica, pentane/EtOAc 5:1), to afford alcohol **21** as a colorless oil (3.74 g, 86%).

R_f = 0.73 (pentane/EtOAc, 2:1) [$KMnO_4$].

IR (ATR): 3447 (br m, O–H), 2957 (vs), 2913 (s), 2878 (s, C_{sp3}–H), 1732 (vs), 1713 (s, C=O), 1481 (m), 1460 (m, C–H), 1285 (s), 1159 (vs), 1035 (s), 1008 (s, C–O), 742 cm^{-1} (vs).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.62 [q, ^3J = 7.9 Hz, 6 H, OSi(CH_2)$_3$], 0.93 (d, ^3J = 6.9 Hz, 3 H, CH_3-44), 0.96 [t, ^3J = 7.9 Hz, 9 H, OSi(CH_2CH_3)$_3$], 1.20 [s, 9 H, C(CH_3)$_3$], 1.66–1.80 (m, 2 H, CH_2-20), 1.84 (br s, 1 H, OH), 1.91–1.99 (m, 1 H, CH-22), 3.7–3.8 (m, 2 H, CH_2-19), 3.93 (ddd, ^3J = 7.5, 4.9, 4.0 Hz, 1 H, CH-21), 3.97 (dd, ^2J = 10.8 Hz, ^3J = 6.9 Hz, 1 H, C*H*H-23), 4.06 (dd, ^2J = 10.8 Hz, ^3J = 5.8 Hz, 1 H, CH*H*-23).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 5.2 [t, OSi(CH_2)$_3$], 7.0 [q, OSi(CH_2CH_3)$_3$], 12.3 (q, CH_3-44), 27.4 [q, C(CH_3)$_3$], 36.1 (t, CH_2-20), 38.2 (d, CH-22), 39.0 [s, *C*(CH_3)$_3$], 60.5 (t, CH_2-19), 66.2 (t, CH_2-23), 71.8 (d, CH-21), 178.7 (s, COO).

HRMS-ESI: *m*/*z* [$C_{17}H_{36}O_4Si$ + H]$^+$ calcd: 333.2456; found: 333.2456.

Piv/TES-Protected Thioether 23

To a cold solution (0 °C) of alcohol **21** (3.74 g, 11.2 mmol, 1.00 equiv) in THF (130 mL) were added 1-phenyl-1*H*-tetrazole-5-thiol (**22**; 3.02 g, 16.9 mmol, 1.51 equiv), DIAD (3.41 g, 16.9 mmol, 1.50 equiv), and PPh_3 (4.42 g, 16.9 mmol, 1.50 equiv). After stirring for 3 h, the reaction was quenched by addition of sat. aq $NaHCO_3$ solution (150 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 150 mL) and the combined organic layers were dried (Na_2SO_4) and filtered. The solvent was removed under reduced pressure and the residue was purified with flash column chromatography (silica, pentane/Et_2O 10:1 → 5:1), to afford thioether **23** as a colorless oil (5.04 g, 91%).

R_f = 0.75 (pentane/Et_2O, 1:1) [UV, $KMnO_4$].

IR (ATR): 2958 (vs), 2911 (s), 2877 (s, C_{sp3}–H), 1728 (vs, C=O), 1501 (m, C–H), 1283 (s), 1156 (vs, C–O), 744 cm^{-1} (vs).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.59 [q, ^3J = 7.9 Hz, 6 H, OSi(CH_2)$_3$], 0.91 (d, ^3J = 7.9 Hz, 3 H, CH_3-44), 0.94 [t, ^3J = 7.9 Hz, 9 H, OSi(CH_2CH_3)$_3$], 1.17 [s, 9 H, C(CH_3)$_3$], 1.90–1.98 (m, 2 H, C*H*H-20, CH-22), 2.04 (dddd, ^2J = 14.0 Hz, ^3J = 8.6, 6.6, 5.4 Hz, 1 H, CH*H*-20), 3.35–3.44 (m, 2 H, CH_2-19), 3.89 (ddd, ^3J = 7.2, 5.4, 3.4 Hz, 1 H, CH-21), 3.97 (dd, ^2J = 10.8 Hz, ^3J = 6.6 Hz, 1 H, C*H*H-23), 4.06 (dd, ^2J = 10.8 Hz, ^3J = 6.4 Hz, 1 H, CH*H*-23), 7.51–7.59 (m, 5 H, CH_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 5.3 [t, OSi(CH_2)$_3$], 7.1 [q, OSi(CH_2CH_3)$_3$], 11.6 (q, CH_3-44), 27.3 [q, C(CH_3)$_3$], 30.1 (t, CH_2-19), 33.5 (t, CH_2-20), 37.8 (d, CH-22), 38.9 [s, *C*(CH_3)$_3$], 66.0 (t, CH_2-23), 71.6 (d, CH-21), 124.0 (d, CH_{Ar}), 129.9 (d, CH_{Ar}), 130.2 (d, CH_{Ar}), 133.9 (s, C_{Ar}), 154.2 (s, OCNN), 178.7 (s, COO).

HRMS-ESI: *m*/*z* [$C_{24}H_{40}N_4O_3SSi$ + H]$^+$ calcd: 493.2663; found: 493.2666.

Piv/TES-Protected Sulfone 24

To a solution of thioether **23** (36.5 g, 74.2 mmol, 1.00 equiv) in CH_2Cl_2 (1.4 L) were added $NaHCO_3$ (62.3 g, 742 mmol, 10.0 equiv) and mCPBA (77 wt%, 99.7 g, 445 mmol, 6.00 equiv). The colorless suspension was stirred for 24 h at r.t., before sat. aq sodium sulfite solution (1 M, 145 mL) was added. After separation of the layers, the aqueous layer was extracted with CH_2Cl_2 (3 × 250 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 10:1 → 3:1), alcohol **24** was obtained as a colorless oil (33.0 g, 85%).

R_f = 0.24 (pentane/Et_2O, 5:1), 0.74 (CH_2Cl_2/THF, 80:1) [UV, $KMnO_4$].

IR (ATR): 2959 (vs), 2912 (s), 2878 (s, C_{sp3}–H), 1728 (vs, C=O), 1346 (s), 1154 (vs, C–O), 770 cm^{-1} (vs).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.62 [q, ^3J = 8.0 Hz, 6 H, OSi(CH_2)$_3$], 0.94–0.98 (m, 3 H, CH_3-44), 0.96 [t, ^3J = 8.0 Hz, 9 H, OSi(CH_2CH_3)$_3$], 1.19 [s, 9 H, C(CH_3)$_3$], 1.93 (*virt.* qd, $^3J \cong {}^3J$ = 6.5 Hz, ^3J = 4.1 Hz, 1 H, CH-22), 2.06–2.18 (m, 2 H, CH_2-20), 3.74 (ddd, ^2J = 14.4 Hz, ^3J = 10.5, 5.4 Hz, 1 H, C*H*H-19), 3.82 (ddd, ^2J = 14.4 Hz, ^3J = 10.6, 5.7 Hz, 1 H, CH*H*-

19), 3.90 (dt, ^3J = 7.3, 4.6 Hz, 1 H, CH-21), 3.98 (dd, ^2J = 11.0 Hz, ^3J = 6.2 Hz, 1 H, C*H*H-23), 4.05 (dd, ^2J = 11.0 Hz, ^3J = 6.0 Hz, 1 H, CH*H*-23), 7.59–7.64 (m, 3 H, CH_{Ar}), 7.69–7.71 (m, 2 H, CH_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 5.2 [t, $OSi(CH_2)_3$], 7.1 [q, $OSi(CH_2CH_3)_3$], 12.1 (q, CH_3-44), 26.6 (t, CH_2-20), 27.3 [q, $C(CH_3)_3$], 38.1 (d, CH-22), 39.0 [s, $C(CH_3)_3$], 53.3 (t, CH_2-19), 65.5 (t, CH_2-23), 71.4 (d, CH-21), 125.1 (d, CH_{Ar}), 129.9 (d, CH_{Ar}), 131.6 (d, CH_{Ar}), 133.1 (s, C_{Ar}), 153.5 (s, OCNN), 178.5 (s, COO).

HRMS-ESI: *m*/*z* $[C_{24}H_{40}N_4O_5SSi + H]^+$ calcd: 525.2561; found: 525.2564.

Methyl Dienoate 27

A solution of $^iPr_2NH$ (18.8 mL, 13.6 g, 134 mmol, 1.10 equiv) in THF (540 mL) was cooled to –78 °C and BuLi (53.6 mL, 2.5 M in hexane, 134 mmol, 1.10 equiv) was added dropwise. After stirring for 30 min at 0 °C, the solution was cooled back to –78 °C and phosphonate **25**[67] (28.8 g, 122 mmol, 1.00 equiv) was added as a solution in THF (20 mL). Stirring was continued for 20 min, before a solution of aldehyde **26** (22.2 g, 170 mmol, 1.40 equiv) in THF (20 mL) was added. The reaction was slowly warmed to 0 °C over the course of 15 h and then quenched by the addition of sat. aq NH_4Cl solution (250 mL). After separation of the layers, the aqueous layer was extracted with Et_2O (3 × 200 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 10:1 → 5:1), dienoate **27** was obtained as a colorless oil (16.8 g, 65%).

R_f = 0.66 (pentane/Et_2O, 1:1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.40 (s, 3 H, CCH_3), 1.44 (s, 3 H, CCH_3), 3.63 (dd, ^2J = 8.2 Hz, ^3J = 7.4 Hz, 1 H, C*H*H-12), 3.75 (s, 3 H, OCH_3), 4.14 (dd, ^2J = 8.2 Hz, ^3J = 6.4 Hz, 1 H, CH*H*-12), 4.58–4.63 (m, 1 H, CH-13), 5.91 (d, ^3J = 15.4 Hz, 1 H, CH-17), 6.06 (*virt.* ddt, ^3J = 15.3 Hz, ^3J = 6.9 Hz, $^4J \cong {}^4J$ = 0.8 Hz, 1 H, CH-14), 6.42 (*virt.* ddt, ^3J = 15.2 Hz, ^3J = 11.1 Hz, $^4J \cong {}^4J$ = 0.9 Hz, 1 H, CH-15), 7.27 (ddd, ^3J = 15.4, 11.0 Hz, ^4J = 0.7 Hz, 1 H, CH-16).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 26.0 (q, CCH_3), 26.7 (q, CCH_3), 51.8 (q, OCH_3), 69.4 (t, CH_2-12), 76.1 (d, CH-13), 110.0 (s, $C(CH_3)_2$), 122.2 (d, CH-17), 130.1 (d, CH-15), 139.2 (d, CH-14), 143.5 (d, CH-16), 167.3 (s, C-18).

The analytical data obtained matched those reported in the literature.[49]

Acetal-Protected Pentadienol 28

DIBAL-H (150 mL, 1.0 M in CH_2Cl_2, 150 mmol, 2.20 equiv) was slowly added to a cold (–78 °C) solution of ester **27** (14.4 g, 68.0 mmol, 1.00 equiv) in CH_2Cl_2 (141 mL) over the course of 10 min. After stirring for 16 h, sat. aq potassium sodium tartrate solution (400 mL) was added and the mixture was warmed to r.t. while stirring. Water (200 mL) was added and the layers were separated. The aqueous layer was extracted with EtOAc (3 × 200 mL) and the combined organic layers were dried (Na_2SO_4) and filtered. After removal of the solvent under reduced pressure, alcohol **28** was obtained as a colorless oil (12.5 g, quant.) and used without further purification.

R_f = 0.32 (pentane/Et_2O, 1:1) [UV, $KMnO_4$].

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 3 H, CCH_3), 1.43 (s, 3 H, CCH_3), 3.59 (*virt.* t, $^2J \cong {}^3J$ = 8.0 Hz, 1 H, C*H*H-12), 4.09 (dd, ^2J = 8.1 Hz, ^3J = 6.0 Hz, 1 H, CH*H*-12), 4.19 (*virt.* t, $^3J \cong {}^3J$ = 5.4 Hz, 2 H, CH_2-18), 4.54 (ddd, ^3J = 8.0, 7.1, 6.0 Hz, 1 H, CH-13), 5.65 (*virt.* dd, ^3J = 14.3 Hz, $^3J \cong {}^3J$ = 7.5 Hz, 1 H, CH-17), 5.87 (*virt.* dt, ^3J = 14.7 Hz, $^3J \cong {}^3J$ = 5.8 Hz, 1 H, CH-14), 6.22–6.35 (m, 2 H, CH-15, CH-16).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 26.0 (q, CCH_3), 26.8 (q, CCH_3), 63.3 (t, CH_2-18), 69.6 (t, CH_2-12), 76.1 (d, CH-13), 109.5 (s, $C(CH_3)_2$), 130.1 (d, CH-15), 130.6 (d, CH-14), 132.7 (d, CH-17), 133.5 (d, CH-16).

The analytical data matched those reported in the literature.[50]

Acetal-Protected Pentadienyl Acetate 29

To a cold (0 °C) solution of alcohol **28** (12.5 g, 68.0 mmol, 1.00 equiv) in CH_2Cl_2 (81 mL) was added NEt_3 (18.8 mL, 13.8 g, 136 mmol, 2.00 equiv), Ac_2O (7.71 mL, 8.33 g, 81.6 mmol, 1.20 equiv), and DMAP (1.25 g, 10.2 mmol, 0.15 equiv) successively. After stirring for 15 min at 0 °C, the reaction was warmed to r.t. and stirring was continued for 16 h. The reaction was quenched by the addition of sat. aq NH_4Cl solution (160 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 200 mL) and the combined organic layers were dried (Na_2SO_4) and filtered. The solvent was removed under reduced pressure and the residue was purified with flash column chromatography (silica, pentane/Et_2O 2:1), to afford acetate **29** as a colorless oil (14.6 g, 95%).

R_f = 0.65 (pentane/Et_2O, 1:1) [UV, $KMnO_4$].

IR (ATR): 2987 (w), 2515 (m), 2159 (m), 2160 (m), 2026 (w), 1738 (s), 1222 (s), 1056 cm^{-1} (s, C–O).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 3 H, CCH_3), 1.43 (s, 3 H, CCH_3), 2.07 (s, 3 H, CH_3CO), 3.59 (*virt.* t, $^2J \cong {}^3J$ = 7.9 Hz, 1 H, C*H*H-12), 4.09 (dd, ^2J = 8.2 Hz, ^3J = 6.2 Hz, 1 H, CH*H*-12), 4.54 (*virt.* q, $^3J \cong {}^3J$ = 7.2 Hz, 1 H, CH-13), 4.59 (d, *J* = 6.0 Hz, 2 H, CH_2-18), 5.67–5.72 (m, 1 H, CH-17), 5.75–5.82 (m, 1 H, CH-14), 6.24–6.33 (m, 2 H, CH-15, CH-16).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 21.1 (q, CH_3CO), 26.0 (q, CCH_3), 26.8 (q, CCH_3), 64.6 (t, CH_2-18), 69.6 (t, CH_2-12), 76.7 (d, CH-13), 109.6 (s, $C(CH_3)_2$), 128.0 (d, CH-17), 131.9 (d, CH-15), 132.1 (d, CH-14), 133.0 (d, CH-16), 170.8 (s, CO).

HRMS-ESI: *m*/*z* $[C_{12}H_{18}O_4 + H]^+$ calcd: 226.1200; found: 226.1196.

Acetyl-Protected Heptadienol 30

Acetate **29** (14.6 g, 64.6 mmol, 1.00 equiv) was dissolved in a mixture of HOAc (55.8 mL) and water (15.4 mL) and heated on the rotary evaporator at 480 mbar and 70 °C for 4 h. Subsequently, the solvents were removed under reduced pressure. In order to remove traces of water and HOAc, the residue was dissolved in toluene (150 mL) and the solvent was again removed under reduced pressure. The diol **30** was used without further purification in the next step.

Acetyl/TES-Protected Heptadienol 31

Crude diol **30** was dissolved in CH_2Cl_2 (500 mL) and 2,6-lutidine (14.9 mL, 13.8 g, 129 mmol, 2.00 equiv) and TESCl (11.9 mL, 10.7 g, 71.1 mmol, 1.10 equiv) were added at –78 °C. The solution was stirred for 19 h while warming up to r.t. After addition of sat. aq NH_4Cl solution (400 mL) the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 200 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 5:1 → 1:1), alcohol **31** was obtained as a colorless oil (12.1 g, 63%, 2 steps).

R_f = 0.20 (pentane/Et_2O, 4:1) [UV, $KMnO_4$].

IR (ATR): 3453 (w, O–H), 3408 (w, O–H), 2953 (s, C_{sp3}–H), 2911 (m, C_{sp3}–H), 2876 (m, C_{sp2}–H), 1739 (s, C=O), 1227 (m), 990 (m), 727 cm^{-1} (m).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.61 [q, ^3J = 7.9 Hz, 6 H, $OSi(CH_2)_3$], 0.96 [t, ^3J = 7.9 Hz, 9 H, $OSi(CH_2CH_3)_3$], 2.06 (s, 3 H, CH_3CO), 2.66 (br s, 1 H, OH), 3.42 (dd, ^2J = 10.0 Hz, ^3J = 7.9 Hz, 1 H, C*H*H-12), 3.64 (dd, ^2J = 10.0

Hz, ^3J = 3.7 Hz, 1 H, CH*H*-12), 4.22 (*virt.* t, $^3J \cong {}^3J$ = 16.8 Hz, 1 H, CH-13), 4.59 (d, ^3J = 6.4 Hz, 2 H, CH_2-18), 5.69 (dd, ^3J = 14.7, 6.0 Hz, 1 H, CH-14), 5.76 (dt, ^3J = 14.6, 6.4 Hz, 1 H, CH-17), 6.27 (dd, ^3J = 14.6, 10.6 Hz, 1 H, CH-16), 6.33 (dd, ^3J = 14.7, 10.6 Hz, 1 H, CH-15).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 4.5 [t, $OSi(CH_2)_3$], 6.8 [q, $OSi(CH_2CH_3)_3$], 21.1 (q, CH_3CO), 64.7 (t, CH_2-18), 66.8 (t, CH_2-12), 72.5 (d, CH-13), 127.2 (d, CH-17), 130.7 (d, CH-15), 133.0 (d, CH-14), 133.7 (d, CH-16), 170.9 (s, CO).

HRMS-ESI: *m*/*z* $[C_{15}H_{28}O_4Si + Na]^+$ calcd: 323.1655; found: 323.1649.

Acetyl/TES/TBDPS-Protected Heptadienol 32

To a cold solution (0 °C) of alcohol **31** (15.7 g, 52.4 mmol, 1.00 equiv) in DMF (120 mL) were added TBDPSCl (20.4 mL, 21.6 g, 78.6 mmol, 1.50 equiv), NEt_3 (14.5 mL, 10.6 g, 105 mmol, 2.00 equiv), and DMAP (6.40 g, 52.4 mmol, 1.00 equiv). After warming to r.t., the reaction was stirred for 17 h and then quenched by addition of sat. aq NH_4Cl solution (280 mL). After separation of the layers, the aqueous layer was extracted with Et_2O (3 × 200 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 20:1), diene **32** was obtained as a colorless oil (27.7 g, 98%).

R_f = 0.67 (pentane/Et_2O, 4:1) [UV, $KMnO_4$].

IR (ATR): 2954 (s, C_{sp3}–H), 2876 (s, C_{sp2}–H), 2665 (w), 1739 (s, C=O), 1057 (w), 1016 (w), 990 (m), 727 (m), 671 cm^{-1} (w).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.45 [q, ^3J = 7.9 Hz, 6 H, $OSi(CH_2)_3$], 0.84 [t, ^3J = 7.9 Hz, 9 H, $OSi(CH_2CH_3)_3$], 1.07 [s, 9 H, $C(CH_3)_3$-TBDPS], 2.07 (s, 3 H, CH_3CO), 3.38 (dd, ^2J = 9.8 Hz, ^3J = 7.0 Hz, 1 H, C*H*H-12), 3.51–3.54 (m, 1 H, CH*H*-12), 4.22 (*virt.* q, $^3J \cong {}^3J$ = 6.2 Hz, 1 H, CH-13), 4.57 (dd, ^3J = 6.5 Hz, ^3J = 1.2 Hz, 2 H, CH_2-18), 5.62 (dd, ^3J = 15.1, 6.5 Hz, 1 H, CH-14), 5.76 (dt, ^3J = 15.3, 5.9 Hz, 1 H, CH-17), 6.06 (dd, ^3J = 15.3, 10.6 Hz, 1 H, CH-16), 6.20 (dd, ^3J = 15.1, 10.6 Hz, 1 H, CH-15), 7.32–7.44 (m, 6 H, CH_{Ar}), 7.62–7.73 (m, 4 H, CH_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 4.4 [t, $OSi(CH_2)_3$], 6.8 [q, $OSi(CH_2CH_3)_3$], 19.5 [s, $C(CH_3)_3$-TBDPS], 21.1 (q, CH_3CO), 27.2 [q, $C(CH_3)_3$-TBDPS], 64.9 (t, CH_2-18), 67.2 (t, CH_2-12), 74.3 (d, CH-13), 126.1 (d, CH-14), 127.6 (d, CH_{Ar}), 129.6 (d, CH_{Ar}*), 129.7 (d, CH_{Ar}*), 129.7 (d, CH_{Ar}*), 129.8 (d, CH-16*), 134.0 (s, C_{Ar}), 134.2 (d, CH-15), 134.3 (s, C_{Ar}), 135.7 (d, CH-17), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}), 170.9 (s, CO); * interchangeable assignment.

HRMS-ESI: *m*/*z* $[C_{31}H_{46}O_4Si_2 + Na]^+$ calcd: 561.2827; found: 561.2830.

TES/TBDPS-Protected Heptadienol 33

To a cold (–78 °C) solution of acetate **32** (23.7 g, 44.0 mmol, 1.00 equiv) in CH_2Cl_2 (600 mL) was added DIBAL-H (74.8 mL, 1.0 M solution in CH_2Cl_2, 74.8 mmol, 1.70 equiv). After stirring for 16 h, the reaction was quenched by addition of sat. aq potassium sodium tartrate solution (500 mL). After warming up to r.t., the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (1 × 200 mL) and Et_2O (3 × 250 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 9:1 → 3:1), alcohol **33** was obtained as a colorless oil (21.0 g, 96%).

R_f = 0.59 (pentane/Et_2O, 1:1) [UV, $KMnO_4$].

IR (ATR): 3349 (br s, O–H), 2954 (s, C_{sp3}–H), 2876 (s, C_{sp2}–H), 2535 (w), 1078 (w), 987 cm^{-1} (m).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.46 [q, ^3J = 8.0 Hz, 6 H, $OSi(CH_2)_3$], 0.85 [t, ^3J = 8.0 Hz, 9 H, $OSi(CH_2CH_3)_3$], 1.07 [s, 9 H, $OSiC(CH_3)_3$], 1.26 (t, ^3J = 5.9 Hz, 1 H, OH), 3.40 (dd, ^2J = 9.8 Hz, ^3J = 7.0 Hz, 1 H, C*H*H-12), 3.54 (dd, ^2J = 9.8 Hz, ^3J = 5.8 Hz, 1 H, CH*H*-12), 4.16 (*virt.* t, $^3J \cong {}^3J$ = 5.5 Hz, 2 H, CH_2-18), 4.22 (*virt.* q, $^3J \cong {}^3J$ = 6.2 Hz, 1 H, CH-13), 5.67–5.74 (m, 2 H, CH-14, CH-17), 6.05 (dd, ^3J = 15.4, 10.5 Hz, 1 H, CH-16), 6.17 (dd, ^3J = 15.2, 10.5 Hz, 1 H, CH-15), 7.32–7.43 (m, 6 H, CH_{Ar}), 7.63–7.65 (m, 2 H, CH_{Ar}), 7.68–7.70 (m, 2 H, CH_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 4.4 [t, $OSi(CH_2)_3$], 6.8 [q, $OSi(CH_2CH_3)_3$], 19.5 [s, $OSiC(CH_3)_3$], 27.2 [q, $OSiC(CH_3)_3$], 63.6 (t, CH_2-12), 67.3 (t, CH_2-18), 74.4 (d, CH-13), 127.6 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 130.1 (d, CH-16), 131.3 (d, CH-15), 131.6 (d, CH-14), 134.1 (s, C_{Ar}), 134.4 (s, C_{Ar}), 134.6 (d, CH-17), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}).

HRMS-ESI: *m*/*z* $[C_{29}H_{44}O_3Si_2 + Na]^+$ calcd: 519.2721; found: 519.2723.

Heptadienal 34

MnO_2 (21.3 g, 246 mmol, 20.0 equiv) was added to a solution of alcohol **33** (6.10 g, 12.3 mmol, 1.00 equiv) in CH_2Cl_2 (140 mL) at r.t. After stirring for 24 h, the black suspension was filtered over Celite and the solvent was removed under reduced pressure to afford aldehyde **34** as a colorless oil (5.69 g, 94%).

R_f = 0.60 (pentane/Et_2O, 4:1) [UV, $KMnO_4$].

IR (ATR): 2954 (s, C_{sp3}–H), 2876 (s, C_{sp2}–H), 1684 (s, C=O), 1104 (w), 1007 (w), 958 (w), 700 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.46 [q, ^3J = 7.9 Hz, 6 H, $OSi(CH_2)_3$], 0.85 [t, ^3J = 7.9 Hz, 9 H, $OSi(CH_2CH_3)_3$], 1.09 [s, 9 H, $OSiC(CH_3)_3$], 1.26 (t, ^3J = 5.9 Hz, 1 H, OH), 3.43 (dd, ^2J = 9.7 Hz, ^3J = 7.5 Hz, 1 H, C*H*H-12), 3.58 (dd, ^2J = 9.7 Hz, ^3J = 5.6 Hz, 1 H, CH*H*-12), 4.32 (*virt.* dt, ^3J = 7.3 Hz, $^3J \cong {}^3J$ = 5.4 Hz, 1 H, CH-13), 5.03 (dd, ^3J = 15.3, 8.0 Hz, 1 H, CH-17), 6.27 (dd, ^3J = 15.4, 5.0 Hz, 1 H, CH-14), 6.36 (dd, ^3J = 15.4, 10.3 Hz, 1 H, CH-15), 7.02 (dd, ^3J = 15.3, 10.3 Hz, 1 H, CH-16), 7.32–7.44 (m, 6 H, CH_{Ar}), 7.61–7.63 (m, 2 H, CH_{Ar}), 7.67–7.69 (m, 2 H, CH_{Ar}), 9.50 (d, ^3J = 8.0 Hz, 1 H, CH-18).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 4.4 [t, $OSi(CH_2)_3$], 6.8 [q, $OSi(CH_2CH_3)_3$], 19.5 [s, $OSiC(CH_3)_3$], 27.1 [q, $OSiC(CH_3)_3$], 66.7 (t, CH_2-12), 73.9 (d, CH-13), 127.8 (d, CH_{Ar}), 128.3 (d, CH-15), 130.0 (d, CH_{Ar}), 130.0 (d, CH_{Ar}), 131.7 (d, CH-17), 133.6 (s, C_{Ar}), 133.8 (s, C_{Ar}), 136.0 (d, CH_{Ar}), 145.7 (d, CH-14), 151.9 (d, CH-16), 194.0 (d, CH-18).

HRMS-ESI: *m*/*z* $[C_{29}H_{42}O_3Si_2 + Na]^+$ calcd: 517.2565; found: 517.2565.

Protected Triene 35

Sulfone **24** (3.57 g, 6.80 mmol, 1.16 equiv) was dissolved in THF (100 mL), cooled to –78 °C and KHMDS (21.1 mL, 0.5 M solution in toluene, 10.6 mmol, 1.80 equiv) was added slowly. After 30 min, the solution was warmed to –40 °C and a solution of aldehyde **34** (2.90 g, 5.86 mmol, 1.00 equiv) in THF (30 mL) was added. The reaction was stirred for 19 h and then quenched by addition of sat. aq NH_4Cl solution (150 mL). After warming to r.t., the layers were separated and the aqueous layer was extracted with Et_2O (3 × 150 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following double flash column chromatography (1. silica, pentane/Et_2O 100:1, 2. silica, pentane/$CHCl_3$ 1:1), triene **35** was obtained as a colorless oil (4.23 g, 91%).

R_f = 0.85 (pentane/Et_2O, 4:1) [UV, $KMnO_4$, CAM]

IR (ATR): 2956 (vs), 2935 (s), 2911 (s), 2877 (s, C_{sp3}–H), 2859 (m), 1731 (vs, C=O), 1460 (m, C=C), 1112 (vs, C–O), 997 cm^{-1} (vs).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.45 [q, ^3J = 8.0 Hz, 6 H, $OSi(CH_2)_3$-12], 0.58 [q, ^3J = 7.8 Hz, 6 H, $OSi(CH_2)_3$-21], 0.84 [t, ^3J = 8.0 Hz, 9 H, $OSi(CH_2CH_3)_3$-12], 0.89 (d, ^3J = 6.9 Hz, 3 H, CH_3-44), 0.95 [t, ^3J = 7.8 Hz, 9 H, $OSi(CH_2CH_3)_3$-21], 1.06 [s, 9 H, $OSiC(CH_3)_3$], 1.20 [s, 9 H, $COC(CH_3)_3$], 1.87 (*virt.* qd, $^3J \cong {}^3J$ = 6.8 Hz, ^3J = 3.0 Hz, 1 H, CH-22), 2.23–2.33 (m, 2 H, CH_2-20), 3.40 (dd, ^2J = 9.8 Hz, ^3J = 6.9 Hz, 1 H, C*H*H-

12), 3.54 (dd, ^2J = 9.8 Hz, ^3J = 5.9 Hz, 1 H, CH*H*-12), 3.79 (td, ^3J = 6.6, 3.0 Hz, 1 H, CH-21), 3.93–4.00 (m, 2 H, CH_2-23), 4.21 (*virt.* q, $^3J \cong {}^3J$ = 6.3 Hz, 1 H, CH-13), 5.58 (dt, ^3J = 14.8, 7.3 Hz, 1 H, CH-19), 5.67 (dd, ^3J = 14.7, 6.6 Hz, 1 H, CH-14), 5.98–6.09 (m, 4 H, CH-15, CH-16, CH-17, CH-18), 7.31–7.43 (m, 6 H, CH_{Ar}), 7.63–7.65 (m, 2 H, CH_{Ar}), 7.68–7.70 (m, 2 H, CH_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 4.4 [t, OSi(CH_2)$_3$-12], 5.2 [t, OSi(CH_2)$_3$-21], 6.9 [q, OSi(CH_2*C*H$_3$)$_3$-12], 7.1 [q, OSi(CH_2*C*H$_3$)$_3$-21], 10.6 (q, CH_3-44), 19.5 [s, OSi*C*(CH$_3$)$_3$], 27.2 [q, OSiC(*C*H$_3$)$_3$], 27.4 [q, COC(*C*H$_3$)$_3$], 37.2 (d, CH-22), 38.6 (t, CH_2-20), 38.9 [s, CO*C*(CH$_3$)$_3$], 66.7 (t, CH_2-23), 67.3 (t, CH_2-12), 72.2 (d, CH-21), 74.6 (d, CH-13), 127.5 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 129.6 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 130.6 (d, CH-19), 131.1 (d, CH-15), 131.2 (d, CH-16*), 132.5 (d, CH-18), 132.8 (d, CH-17*), 133.8 (d, CH-14), 134.1 (s, C_{Ar}), 134.4 (s, C_{Ar}), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}), 178.6 (s, CO); * interchangeable assignment.

HRMS-ESI: *m/z* [$C_{46}H_{76}O_5Si_3$ + Na]$^+$ calcd: 815.4893; found: 815.4884.

Trienol 36

To a cold (–78 °C) solution of triene **35** (1.38 g, 1.73 mmol, 1.00 equiv) in CH_2Cl_2 (58 mL) and toluene (58 mL) was added DIBAL-H (8.67 mL, 1.0 M in CH_2Cl_2, 8.67 mmol, 5.00 equiv). After 2 h, the reaction was quenched by addition of sat. aq potassium sodium tartrate solution (75 mL). After warming up to r.t., the layers were separated and the aqueous layer was extracted with EtOAc (3 × 200 mL). The organic layers were combined, washed with sat. aq NaCl solution (1 × 100 mL), dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 10:1 → 5:1), alcohol **36** was obtained as a colorless oil (1.13 g, 92%).

R_f = 0.31 (pentane/Et_2O, 4:1) [UV, $KMnO_4$, CAM].

IR (ATR): 3435 (br m, O–H), 2955 (vs), 2933 (vs), 2877 (s), 2858 (s, C_{sp3}–H), 1740 (m), 1693 (s), 1415 (s, C=C), 1113 (vs), 998 cm^{-1} (vs, C–O).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.46 [q, ^3J = 8.0 Hz, 6 H, OSi(CH_2)$_3$-12], 0.61 [q, ^3J = 7.9 Hz, 6 H, OSi(CH_2)$_3$-21], 0.85 [t, ^3J = 8.0 Hz, 9 H, OSi(CH_2*CH*$_3$)$_3$-12], 0.85 (d, ^3J = 7.0 Hz, 3 H, CH_3-44), 0.96 [t, ^3J = 7.9 Hz, 9 H, OSi(CH_2*CH*$_3$)$_3$-21], 1.07 [s, 9 H, OSiC(CH$_3$)$_3$], 1.89–1.96 (m, 1 H, CH-22), 2.31 (*virt.* t, $^3J \cong {}^3J$ = 6.9 Hz, 2 H, CH_2-20), 2.51 (dd, ^3J = 6.0, 4.3 Hz, 1 H, OH), 3.41 (dd, ^2J = 9.8 Hz, ^3J = 6.9 Hz, 1 H, C*H*H-12), 3.53–3.57 (m, 2 H, CH*H*-12, C*H*H-23), 3.68 (ddd, ^2J = 10.6 Hz, ^3J = 8.1, 4.3 Hz, 1 H, CH*H*-23), 3.86 (td, ^3J = 6.5, 3.1 Hz, 1 H, CH-21), 4.21 (*virt.* q, $^3J \cong {}^3J$ = 6.4 Hz, 1 H, CH-13), 5.61 (dd, ^3J = 14.9, 7.5 Hz, 1 H, CH-19), 5.67 (dd, ^3J = 14.9, 6.4 Hz, 1 H, CH-14), 5.98–6.08 (m, 4 H, CH-15, CH-16, CH-17, CH-18), 7.31–7.42 (m, 6 H, CH_{Ar}), 7.63–7.65 (m, 2 H, CH_{Ar}), 7.68–7.70 (m, 2 H, CH_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 4.4 [t, OSi(CH_2)$_3$-12], 5.2 [t, OSi(CH_2)$_3$-21], 6.8 [q, OSi(CH_2*C*H$_3$)$_3$-12], 7.0 [q, OSi(CH_2*C*H$_3$)$_3$-21], 11.7 (q, CH_3-44), 19.5 [s, OSi*C*(CH$_3$)$_3$], 27.2 [q, OSiC(*C*H$_3$)$_3$], 37.0 (t, CH_2-20), 39.8 (d, CH-22), 66.3 (t, CH_2-23), 67.3 (t, CH_2-12), 74.7 (d, CH-13), 75.6 (d, CH-21), 127.5 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 129.6 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 131.0 (d, CH-19), 131.1 (d, CH-15*), 131.3 (d, CH-16*), 132.4 (d, CH-17*), 132.9 (d, CH-18*), 133.8 (d, CH-14), 134.2 (s, C_{Ar}), 134.9 (s, C_{Ar}), 136.1 (d, CH_{Ar}), 136.2 (d, CH_{Ar}); * interchangeable assignment.

HRMS-ESI: *m/z* [$C_{41}H_{68}O_4Si_3$ + NH_4]$^+$ calcd: 726.4764; found: 726.4762.

Trienal 3

To a solution of alcohol **36** (2.45 g, 3.45 mmol, 1.00 equiv) in CH_2Cl_2 (100 mL) was added $NaHCO_3$ (1.16 g, 13.8 mmol, 4.00 equiv) and Dess–Martin periodinane (2.93 g, 6.91 mmol, 2.00 equiv). The suspension was stirred for 1.5 h at r.t. and then diluted with pentane (100 mL). After filtration over Celite, the organic layer was washed twice with a mixture of $NaHCO_3$ solution (40 mL) and $Na_2S_2O_3$ solution (40 mL). The combined aqueous layers were extracted with a mixture of pentane/Et_2O (10:1, 50 mL). The organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 30:1 → 15:1), aldehyde **3** was obtained as a colorless oil (2.22 g, 91%).

R_f = 0.81 (pentane/Et_2O, 4:1) [UV, $KMnO_4$, CAM].

IR (ATR): 2955 (vs), 2932 (vs), 2912 (s), 2876 (s), 2858 (s, C_{sp3}–H), 1729 (s, C=O), 1428 (m, C=C), 1106 (vs), 998 cm^{-1} (vs, C–O).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.45 [q, ^3J = 7.9 Hz, 6 H, OSi(CH_2)$_3$-12], 0.58 [q, ^3J = 7.8 Hz, 6 H, OSi(CH_2)$_3$-21], 0.85 [t, ^3J = 7.9 Hz, 9 H, OSi(CH_2*CH*$_3$)$_3$-12], 0.94 [t, ^3J = 7.8 Hz, 9 H, OSi(CH_2*CH*$_3$)$_3$-21], 1.07 [s, 9 H, OSiC(CH$_3$)$_3$], 1.09 (d, ^3J = 7.0 Hz, 3 H, CH_3-44), 2.33 (*virt.* t, $^3J \cong {}^3J$ = 7.1 Hz, 2 H, CH_2-20), 2.42–2.47 (m, 1 H, CH-22), 3.40 (dd, ^2J = 9.8 Hz, ^3J = 6.9 Hz, 1 H, C*H*H-12), 3.54 (dd, ^2J = 9.8 Hz, ^3J = 5.8 Hz, 1 H, CH*H*-12), 4.19–4.23 (m, 2 H, CH-13, CH-21), 5.58 (dd, ^3J = 15.1, 7.5 Hz, 1 H, CH-19), 5.69 (dd, ^3J = 14.9, 6.2 Hz, 1 H, CH-14), 5.99–6.06 (m, 3 H, CH-15, CH-16, CH-17), 6.07–6.13 (m, 1 H, CH-18), 7.31–7.43 (m, 6 H, CH_{Ar}), 7.63–7.65 (m, 2 H, CH_{Ar}), 7.68–7.70 (m, 2 H, CH_{Ar}), 9.74 (d, ^3J = 1.0 Hz, 1 H, CH-23).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 4.4 [t, OSi(CH_2)$_3$-12], 5.2 [t, OSi(CH_2)$_3$-21], 6.8 [q, OSi(CH_2*C*H$_3$)$_3$-12], 7.0 [q, OSi(CH_2*C*H$_3$)$_3$-21], 7.7 (q, CH_3-44), 19.5 [s, OSi*C*(CH$_3$)$_3$], 27.2 [q, OSiC(*C*H$_3$)$_3$], 38.8 (t, CH_2-20), 51.3 (d, CH-22), 67.3 (t, CH_2-12), 71.9 (d, CH-21), 74.6 (d, CH-13), 127.6 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 129.4 (d, CH-19), 129.6 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 131.1 (d, CH-15*), 131.7 (d, CH-16*), 132.1 (d, CH-17*), 133.7 (d, CH-18), 134.2 (d, CH-14), 134.2 (s, C_{Ar}), 134.2 (s, C_{Ar}), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}), 205.1 (d, CH-23); * interchangeable assignment.

HRMS-ESI: *m/z* [$C_{41}H_{66}O_4Si_3$ + H]$^+$ calcd: 707.4342; found: 707.4340.

Aldol Product 37

To a cold (0 °C) solution of ketone **4** (890 mg, 803 µmol, 1.00 equiv) in THF (5.5 mL) was added TMPMgCl·LiCl (2.11 mL, 0.76 M solution in THF/toluene, 1.61 mmol, 2.00 equiv) over the course of 6 min. The orange solution was stirred for 2.5 h and then (–)-*B*-chlorodiisopinocampheylborane (1.15 mL, 50–65% in heptane, 1.61 mmol, 2.00 equiv) was added. After stirring for 2 h, a solution of aldehyde **3** (1.42 g, 2.01 mmol, 2.50 equiv) in THF (5.5 mL) was added. The solution was stirred for 17 h while warming up to r.t. and then sat. aq potassium sodium tartrate solution (50 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (5 × 50 mL). The combined organic layers were washed with sat. aq NaCl solution (1 × 50 mL) and the aqueous layer was again extracted with EtOAc (1 × 50 mL). All organic layers were combined, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 30:1 → 5:1), a mixture of aldol **37**, diisopinocampheylboron aldol adduct, ketone **4**, and alcohol **36** was isolated as a colorless oil.

The mixture was dissolved in CH_2Cl_2 (25 mL) and MeOH (25 mL) and 8-hydroxyquinoline (350 mg, 2.41 mmol, 3.00 equiv) was added. After stirring at r.t. for 2.5 h, a further 350 mg 8-hydroxyquinoline (2.41 mmol, 3.00 equiv) and CH_2Cl_2 (25 mL) were added, and stirring at r.t. was continued for 20 h. Subsequently, sat. aq NH_4Cl solution (25 mL)

was added, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (4 × 25 mL) and Et_2O (1 × 25 mL). The combined organic layers were dried (Na_2SO_4) and filtered. After removal of the solvent under reduced pressure, the residue was purified with flash column chromatography (silica, pentane/Et_2O 25:1 → 1:5), to afford aldol **37** as a colorless foam (679 mg, 40%). Ketone **4** (331 mg, 37%) and alcohol **36** (953 mg, 67%) were re-isolated.

R_f = 0.45 (pentane/Et_2O, 7:1), [UV, $KMnO_4$, CAM].

IR (ATR): 3510 (br w, O–H), 3072 (w), 3049 (w, $C_{Ar–H}$), 2955 (s), 2931 (s), 2876 (m), 2858 (m, C_{sp3}–H), 1725 (w, C=O), 1462 (m, C=C), 1112 (vs), 1080 (vs), 998 (s, C–O), 822 cm^{-1} (s).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.04 [s, 3 H, OSi(CH_3)], 0.10 [s, 3 H, OSi(CH_3)], 0.45 [q, ^3J = 8.0 Hz, 6 H, CH_2-12–OSi(CH_2CH_3)$_3$], 0.59–0.66 [m, 12 H, CH-21–OSi(CH_2CH_3)$_3$, CH-27–Si(CH_2CH_3)$_3$], 0.82–0.83 (m, 3 H, CH_3-45), 0.84 [t, ^3J = 8.0 Hz, 9 H, CH_2-12–OSi(CH_2CH_3)$_3$], 0.87–0.88 (m, 3 H, CH_3-44), 0.91 [s, 9 H, OSiC(CH_3)$_3$-TBS], 0.93 [t, ^3J = 8.0 Hz, 9 H, CH-27–Si(CH_2CH_3)$_3$], 0.96 [t, ^3J = 8.0 Hz, 9 H, CH-21–OSi(CH_2CH_3)$_3$], 1.02 (d, ^3J = 6.5 Hz, 3 H, CH_3-40), 1.04 [s, 9 H, OSiC(CH_3)$_3$-TBDPS], 1.06 [s, 9 H, OSiC(CH_3)$_3$-TBDPS], 1.07 [s, 9 H, OSiC(CH_3)$_3$-TBDPS], 1.11 (d, ^3J = 6.6 Hz, 3 H, CH_3-34), 1.62–1.64 (m, 1 H, CH-22), 2.32–2.38 (m, 3 H, CH_2-20, CH-27), 2.65 (d, ^3J = 3.0 Hz, 1 H, CH-38), 2.86 (q, ^3J = 6.5 Hz, 1 H, CH-39), 3.04 (br s, 1 H, OH), 3.04–3.08 (m, 1 H, CH-24), 3.10 (dd, ^3J = 9.7, 7.6 Hz, 1 H, CH-36), 3.17 (s, 3 H, CH-36–OCH_3), 3.38 (s, 3 H, CH-38–OCH_3), 3.38–3.41 (m, 1 H, C*H*H-12), 3.43 (d, ^3J = 7.6 Hz, 1 H, CH-35), 3.44–3.46 (m, 1 H, CH-33), 3.49 (dd, ^3J = 9.7, 3.0 Hz, 1 H, CH-37), 3.53 (dd, ^2J = 9.7 Hz, ^3J = 5.9 Hz, 1 H, CH*H*-12), 3.91–3.95 (m, 2 H, CH-21, CH-23), 4.19–4.24 (m, 2 H, CH-13, CH-32), 4.34 (d, ^3J = 2.8 Hz, 1 H, CH-26), 5.52–5.58 (m, 3 H, CH-19, CH-28, CH-31), 5.68 (dd, ^3J = 14.7, 6.3 Hz, 1 H, CH-14), 5.87 (dd, ^3J = 15.0, 10.5 Hz, 1 H, CH-29), 5.99–6.11 (m, 5 H, CH-15, CH-16, CH-17, CH-18, CH-30), 7.26–7.45 (m, 18 H, CH_{Ar}), 7.59–7.64 (m, 6 H, CH_{Ar}), 7.68–7.74 (m, 6 H, CH_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$): δ = –4.6 [q, OSi(CH_3)], –4.2 [q, OSi(CH_3)], 3.3 [t, CH-27–Si(CH_2CH_3)$_3$], 4.4 [t, CH_2-12–OSi(CH_2CH_3)$_3$], 5.4 [t, CH-21–OSi(CH_2CH_3)$_3$], 6.9 [q, CH_2-12–OSi(CH_2CH_3)$_3$], 7.0 [q, CH-21–OSi(CH_2CH_3)$_3$], 8.0 [q, CH-27–Si(CH_2CH_3)$_3$], 13.8 (q, CH_3-45), 14.3 (q, CH_3-44), 15.6 (q, CH_3-34), 16.7 (q, CH_3-40), 18.4 [s, OSi*C*(CH_3)$_3$-TBS], 19.4 [s, OSi*C*(CH_3)$_3$-TBDPS], 19.5 [s, OSi*C*(CH_3)$_3$-TBDPS], 19.6 [s, OSi*C*(CH_3)$_3$-TBDPS], 26.1 [q, OSiC(*C*H_3)$_3$-TBS], 27.2 [q, OSiC(*C*H_3)$_3$-TBDPS], 27.2 [q, OSiC(CH_3)$_3$-TBDPS], 27.2 [q, OSiC(*C*H_3)$_3$-TBDPS], 36.5 (d, CH-27), 36.6 (d, CH-22), 38.8 (t, CH_2-20), 44.5 (d, CH-24), 60.5 (q, CH-36–OCH_3), 62.1 (q, CH-38–OCH_3), 67.3 (t, CH_2-12), 69.7 (d, CH-39), 74.3 (d, CH-32), 74.5 (d, CH-13), 76.2 (d, CH-37), 77.4 (d, CH-21[a]), 77.6 (d, CH-23[a]), 77.8 (d, CH-33[a]), 80.9 (d, CH-36), 81.1 (d, CH-26), 82.1 (d, CH-38), 102.9 (d, CH-35), 127.4 (d, CH_{Ar}), 127.5 (d, CH_{Ar}), 127.5 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 127.9 (d, CH-31), 129.4 (d, CH-19[b]), 129.5 (d, CH-29[b]), 129.6 (d, CH_{Ar}), 129.6 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 131.1 (d, CH-15[c]), 131.3 (d, CH-16[cd]), 132.3 (d, CH-17[d]), 132.8 (d, CH-18[d]), 133.2 (d, CH-30[d]), 133.9 (d, CH-14[e]), 133.9 (d, CH-28[e]), 133.9 (s, C_{Ar}[e]), 134.0 (s, C_{Ar}), 134.1 (s, C_{Ar}), 134.1 (s, C_{Ar}), 134.4 (s, C_{Ar}), 134.5 (s, C_{Ar}), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}), 136.1 (d, CH_{Ar}), 136.2 (d, CH_{Ar}), 136.3 (d, CH_{Ar}), 214.7 (s, C-25); [a–e] interchangeable assignments.

HRMS-ESI: *m*/*z* [$C_{105}H_{164}O_{12}Si_7$ + NH_4]$^+$ calcd: 1831.0946; found: 1831.1003.

Acetal-Protected Aldol Product 38

To a cold (0 °C) solution of aldol product **37** (40.0 mg, 22.0 µmol, 1.00 equiv) in THF (700 µL) were added pyridine (7.0 µL, 7.0 mg, 44 µmol, 4.00 equiv) and HF-pyridine (70 wt%/30 wt%, 10.4 µL, 11.4 mg, 44.0 µmol, 2.00 equiv). After 3 and 5 h, further pyridine (7.0 µL, 7.0 mg, 44 µmol, 4.00 equiv) and HF-pyridine (70 wt%/30 wt%, 10.4 µL, 11.4 mg, 44.0 µmol, 2.00 equiv) were added. The reaction was warmed to r.t. and stirred for an additional 1 h and then quenched by addition of sat. aq $NaHCO_3$ solution (3 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with sat. aq NaCl solution, dried (Na_2SO_4), and filtered. The solvent was removed under reduced pressure. Following flash column chromatography (silica, pentane/Et_2O 3:1), the desired triol was obtained as a colorless oil (25.6 mg, 73%).

The triol was dissolved in acetone (500 µL) and PPTS (4.2 mg, 16.8 µmol, 1.00 equiv) and 2-methoxypropene (18.1 mg, 251 µmol, 15.0 equiv) were added. The solution was stirred for 1.5 h at r.t. and then quenched by the addition of sat. aq $NaHCO_3$ solution (2 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and filtered. After removal of the solvent under reduced pressure, the residue was purified with flash column chromatography (silica, pentane/Et_2O 10:1 → 7:1), to afford acetal-protected aldol product **38** as a colorless oil (17.4 mg, 64%). The methoxy acetal at C_{12} turned out to be labile upon column chromatography.

R_f = 0.54 (pentane/Et_2O, 3:1), [UV, $KMnO_4$, CAM].

IR (ATR): 2956 (m), 2927 (s), 2856 (m, C_{sp3}–H), 1724 (m, C=O), 1260 (s), 1111 cm^{-1} (vs, C–O).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.07 [s, 3 H, OSi(CH_3)], 0.12 [s, 3 H, OSi(CH_3)], 0.63 [*virt.* qd, ^3J = 7.9, 3.4 Hz, 6 H, Si(CH_2CH_3)$_3$], 0.81 (d, ^3J = 7.0 Hz, 3 H, CH_3-45), 0.84 (d, ^3J = 6.8 Hz, 3 H, CH_3-44), 0.90 [s, 9 H, OSiC(CH_3)$_3$-TBS], 0.96 [t, ^3J = 7.9 Hz, 9 H, Si(CH_2CH_3)$_3$], 1.02 (d, ^3J = 6.4 Hz, 3 H, CH_3-40), 1.04 [s, 9 H, OSiC(CH_3)$_3$-TBDPS], 1.07 [s, 18 H, 2 OSiC(CH_3)$_3$-TBDPS], 1.11 (d, ^3J = 6.5 Hz, 3 H, CH_3-34), 1.18 [s, 3 H, O(CH_3)C(CH_3)OMe], 1.20 [s, 3 H, O(CH_3)C(CH_3)OMe], 1.31 [s, 3 H, O(CH_3)C(CH_3)O], 1.34 [s, 3 H, O(CH_3)C(CH_3)O], 1.40–1.43 (m, 1 H, CH-22), 2.15–2.21 (m, 2 H, C*H*H-20, CH-27), 2.31–2.37 (m, 1 H, CH*H*-20), 2.66 (d, ^3J = 3.0 Hz, 1 H, CH-38), 2.86 (q, ^3J = 6.4 Hz, 1 H, CH-39), 3.02 (s, 3 H, OCMe$_2$OCH_3), 3.09 (dd, ^3J = 9.7, 7.7 Hz, 1 H, CH-36), 3.15 (s, 3 H, CH-36–OCH_3), 3.19 (*virt.* dd, $^3J \cong {}^3J$ = 10.2, 7.1 Hz, 1 H, CH-24), 3.23 (dd, ^3J = 9.4, 5.9 Hz, 1 H, C*H*H-12), 3.34 (dd, ^3J = 9.4, 6.4 Hz, 1 H, CH*H*-12), 3.38 (s, 3 H, CH-38–OCH_3), 3.44 (d, ^3J = 7.7 Hz, 1 H, CH-35), 3.46–3.48 (m, 1 H, CH-33), 3.49 (dd, ^3J = 9.7, 3.0 Hz, 1 H, CH-37), 3.91 (td, ^3J = 7.1, 2.1 Hz, 1 H, CH-21), 4.06 (dd, ^3J = 10.2, 2.1 Hz, 1 H, CH-23), 4.21–4.23 (m, 1 H, CH-32), 4.24 (d, ^3J = 3.4 Hz, 1 H, CH-26), 4.31 (*virt.* q, $^3J \cong {}^3J$ = 6.2 Hz, 1 H, CH-13), 5.48 (dd, ^3J = 14.9, 10.4 Hz, 1 H, CH-28), 5.52 (dd, ^3J = 15.2, 6.5 Hz, 1 H, CH-31), 5.60 (*virt.* dd, ^3J = 13.8 Hz, $^3J \cong {}^3J$ = 7.2 Hz, 1 H, CH-19), 5.67 (dd, ^3J = 14.9, 6.2 Hz, 1 H, CH-14), 5.85 (dd, ^3J = 14.9, 10.5 Hz, 1 H, CH-29), 5.99 (dd, ^3J = 15.2, 10.5 Hz, 1 H, CH-30), 6.02–6.08 (m, 3 H, CH-15, CH-16, CH-17), 6.09–6.14 (m, 1 H, CH-18), 7.27–7.45 (m, 18 H, CH_{Ar}), 7.59–7.66 (m, 6 H, CH_{Ar}), 7.70–7.74 (m, 6 H, CH_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$): δ = –4.7 [q, OSi(CH_3)], –4.1 [q, OSi(CH_3)], 3.7 [t, Si(CH_2CH_3)$_3$], 4.8 (q, CH_3-44), 8.0 [q, Si(CH_2CH_3)$_3$], 12.1 (q, CH_3-45), 15.5 (q, CH_3-34), 16.7 (q, CH_3-40), 18.3 [s, OSi*C*(CH_3)$_3$-TBS], 19.4 [q, O(*C*H_3)C(CH_3)O], 19.5 [s, OSi*C*(CH_3)$_3$-TBDPS], 19.5 [s, OSi*C*(CH_3)$_3$-TBDPS], 19.6 [s, OSi*C*(CH_3)$_3$-TBDPS], 24.4 [q, O(*C*H_3)C(CH_3)OMe], 24.4 [q, O(CH_3)C(*C*H_3)OMe], 26.0 [q, OSiC(*C*H_3)$_3$-TBS], 27.2 [q, 2 OSiC(*C*H_3)$_3$-TBDPS], 27.2 [q, OSiC(*C*H_3)$_3$-TBDPS], 29.9 [q, O(CH_3)C(*C*H_3)O], 31.7 (d, CH-22), 36.5 (t, CH_2-20), 36.9 (d, CH-27), 41.9 (d, CH-24), 48.5 (q, OCMe$_2$OCH_3), 60.5 (q, CH-36–OCH_3), 62.1 (q, CH-38–OCH_3), 65.5 (t, CH_2-12), 69.7 (d, CH-39), 73.1 (d, CH-21), 73.2 (d, CH-13), 74.3 (d, CH-32), 75.9 (d, CH-23), 76.2 (d, CH-37), 77.4 (d, CH-33), 80.9 (d, CH-26), 80.9 (d, CH-36), 82.1 (d, CH-38), 99.0 (s, O*C*Me$_2$O), 100.0 (s, O*C*Me$_2$OMe), 102.7 (d, CH-35), 127.4 (d, CH_{Ar}), 127.4 (d, CH_{Ar}), 127.5 (d, CH_{Ar}), 127.5 (d, CH_{Ar}), 127.6 (d, CH_{Ar}), 127.7 (d, CH_{Ar}), 127.7 (d, CH-31), 129.5 (d,

CH_{Ar}), 129.6 (d, CH_{Ar}), 129.6 (d, CH_{Ar}), 129.6 (d, CH_{Ar}), 129.7 (d, CH_{Ar}), 129.8 (d, CH_{Ar}), 130.0 (d, CH-19[a]), 130.0 (d, CH-29[a]), 131.0 (d, CH-15[b]), 131.0 (d, CH-16[bc]), 132.7 (d, CH-17[bc]), 132.8 (d, CH-18[c]), 133.0 (d, CH-30), 133.3 (d, CH-28), 133.6 (d, CH-14), 134.1 (s, C_{Ar}), 134.1 (s, C_{Ar}), 134.1 (s, C_{Ar}), 134.4 (s, C_{Ar}), 134.4 (s, C_{Ar}), 134.5 (s, C_{Ar}), 136.1 (d, CH_{Ar}), 136.1 (d, 2 C, 2 CH_{Ar}), 136.2 (d, 2 C, 2 CH_{Ar}), 136.3 (d, CH_{Ar}), 213.8 (s, C-25); [a–c] interchangeable assignments.

HRMS-ESI: *m*/*z* $[C_{100}H_{148}O_{13}Si_5 + NH_4]^+$ calcd: 1642.9529; found: 1642.9554.

Conflict of Interest

The authors declare no conflict of interest.

Funding Information

Financial support by the Deutsche Forschungsgemeinschaft (Ba 1372/18) is gratefully acknowledged. S.W. was supported by a Ph.D. fellowship of the Fonds der Chemischen Industrie, T.N. was the recipient of a Ph.D. scholarship by the Studienstiftung des Deutschen Volkes.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/a-1464-2576.

Primary Data

Primary data for this article are available online at https://zenodo.org/record/4637081 and can be cited using the following DOI: 10.5281/zenodo.4637081.

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