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Synthesis and Biological Evaluation of Gephyronic Acid Derivatives: Initial Steps towards the Identification of the Biological Target of Polyketide Inhibitors of Eukaryotic Protein Synthesis

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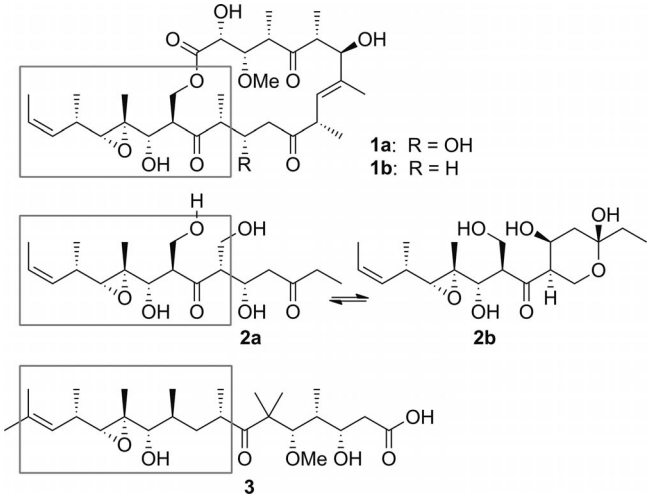
Coupled to the development of a total synthesis of gephyronic acid, a series of diastereomeric analogues and their precursors have been prepared by employing complementary aldol strategies for the key coupling step of fragments **4** and **5**. A biological evaluation revealed the importance of the epoxide for the cytotoxicity against L-929 (mouse fibroblast) and KB-3-1 (HeLa clone, human cervix carcinoma derived) cell lines. Moreover, variation of the configuration of the C3–C5 stereotriad and the C1 carboxylic acid were found to be important features. Improved activities compared with the natural product were observed when the carboxy terminus at C1 was replaced by a methyl ester or PMB-protected alcohol. Surprisingly, the derivatives (8*R*)-**17d** and (8*S*)-**16a** showed antibacterial activity against *Pseudomonas aeruginosa*.

Introduction

Complex natural products derived from marine or terrestrial organisms are interesting from both chemical and biological perspectives. For chemists, they provide challenging targets for total synthesis, which often require new synthetic methods or the novel orchestration of known procedures.[1] Furthermore, the chemical synthesis plays a decisive role in the elucidation of relative and absolute configurations when an X-ray crystal structure analysis is not possible.[2] For biologists, natural products or derivatives thereof are useful tools for the elucidation of biological mechanisms such as signal transduction or protein–protein interactions. In addition, natural products can serve as pharmacological lead structures for the development of new drug candidates.[3] Prominent examples are taxol,[4] epothilones,[5] and ecteinascidin-743.[6]

The structurally related polyketide natural products tedanolide (**1a**) and myriaporone 3/4 (**2a**,**b**) isolated from marine sources[7,8] and the myxobacterium *Archangium gephyra* strain Ar 3895 derived gephyronic acid[9] (**3**; Scheme 1) are promising bioactive compounds that have been found to be potent and selective eukaryotic protein synthesis inhibitors. Very recently, new tedanolide analogues, candidaspongiolide A and B from the sponge genus *Candidaspongia*, have been reported to inhibit melanoma cell growth.[10] Detailed structural information, synthetic approaches, and the general mode of action of tedanolides **1** and myriaporones 3/4 **2** are already known.[11–13] Structure–activity relationship (SAR) studies have identified the 60S large ribosomal subunit of *Saccharomyces cerevisiae* as



Scheme 1. Structurally related polyketide natural products tedanolide (**1a**), 13-deoxytedanolide (**1b**), myriaporone 3/4 (**2a**,**b**), and gephyronic acid (**3**).

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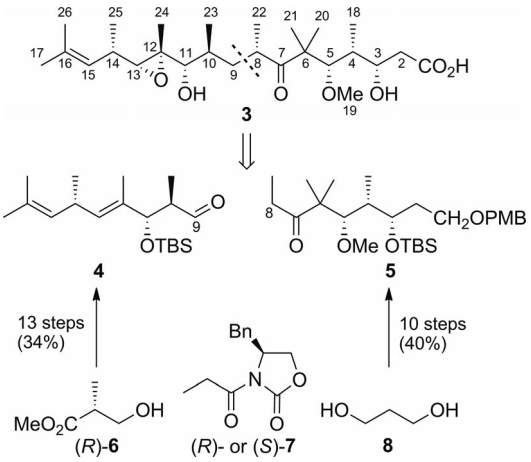
the 13-deoxytedanolide (**1b**) target[14] and myriaporone 3/4 **2** may potentially have the same mode of action.[15] In contrast, little is known about gephyronic acid (**3**), which shares parts of the southern hemisphere of the tedanolide family (Scheme 1). Recently, polyketide **3** was discussed as a pharmacophoric link to compounds **1** and **2** based on its proposed relative configuration.[16] A detailed NMR study resulted in a revision of the structure of **3**, including a full assignment of the relative and absolute stereochemistry,[17] which was finally confirmed by a convergent total synthesis.[18] Although the biological activity of gephyronic acid (**3**) is known, the specific target remains unidentified. Therefore we were interested in various diastereomers of gephyronic acid (**3**), which could serve as valuable tools for elucidating structure–property relationships. This should ultimately pave the way to identifying the target protein of **3**. Herein we report the synthetic routes to the diastereomers of gephyronic acid and its derivatives and discuss the results of the first SAR study.

Results and Discussion

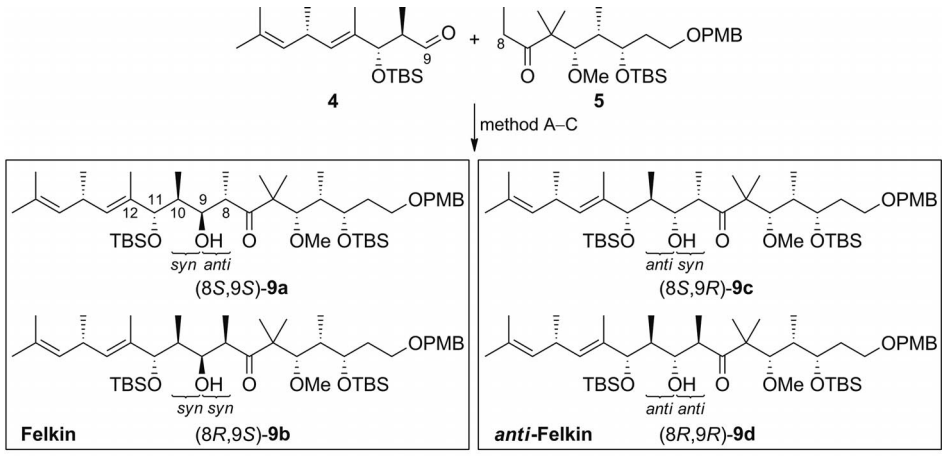
Synthesis of Gephyronic Acid Derivatives and Its Precursors

To gain access to diastereomers of gephyronic acid (**3**), we followed our previously established retrosynthetic strategy (Scheme 2).[18] Gephyronic acid (**3**) was traced back to building blocks **4** and **5**, which should be coupled by aldol reaction followed by deoxygenation and subsequent epoxidation as the key steps. Fragment **4** was obtained from Roche ester (*R*)-**6** and (*S*)-benzyloxazolidinone (*S*)-**7** in 13 steps and 34% overall yield by employing Evans *anti* aldol reaction[19] and two sequential Wittig reactions.[20] Fragment **5** was prepared from propane-1,3-diol (**8**) and (*R*)-benzyloxazolidinone (*R*)-**7** in 10 steps and 40% overall yield by Evans *syn* aldol[21] and Mukaiyama aldol reactions.[22]



Scheme 2. Key building blocks **4** and **5** of gephyronic acid (**3**); the numbering used for the NMR assignment is indicated.

The aldol coupling reaction between building blocks **4** and **5** turned out to be a critical step providing four possible diastereoisomers, the Felkin products (8*S*,9*S*)- and (8*R*,9*S*)-**9a**,**b** and the *anti*-Felkin products (8*S*,9*R*)- and (8*R*,9*R*)-**9c**,**d**, as shown in Scheme 3. Moreover, the product ratio could be controlled by using different coupling conditions. Under Mukaiyama conditions (method A), that is, treatment of ketone **5** with LDA followed by addition of TMSOTf to generate the enol-silane of **5** and subsequent addition of aldehyde **4** in the presence of $BF_3{\cdot}OEt_2$,[23] the Felkin/*anti*-Felkin selectivity was >95:5, yielding selectively the *syn*,*anti* diastereomer (8*S*,9*S*)-**9a** in 61% yield (*dr* > 95:5).[18,24] Upon generating the lithium enolate of **5** with LDA in THF followed by addition of HMPA and aldehyde

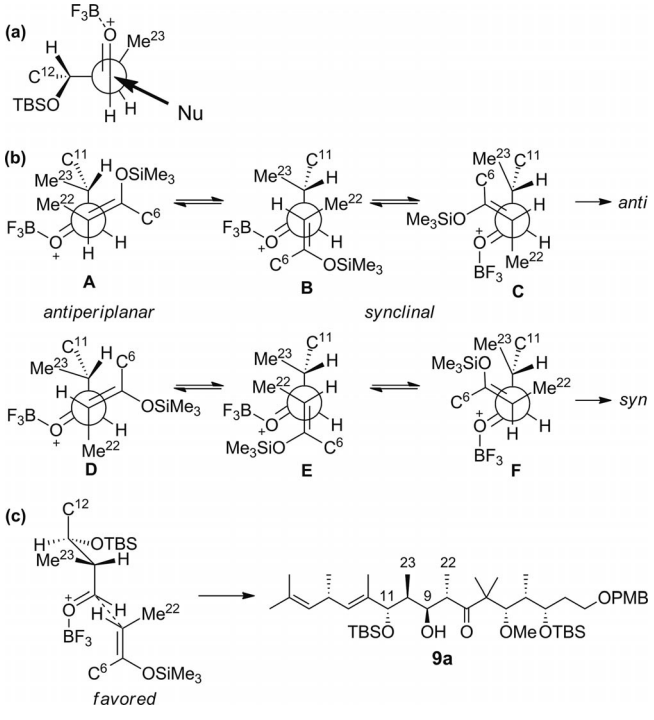


	Felkin : *anti*-Felkin	Compound ratio	Yield [%]
Method A: LDA, HMPA, TMSOTf, $BF_3{\cdot}OEt_2$	>95 : 5	**9a** *dr* >95 : 5	61 (**9a**)
Method B: LDA, HMPA	<1 : 99	**9c** : **9d** = 89 : 11	12 (**9c**)
Method C: $TiCl_4$, NEt_3	6 : 94	**9c** : **9d** = 16 : 84	61 (**9d**)

Scheme 3. Coupling of fragments **4** and **5** by aldol reaction to yield the possible diastereoisomers **9**. Reagents and conditions: Method A: (1) **5** (3 equiv.), LDA, THF, –50 °C; (2) HMPA; (3) TMSOTf, – 78 °C; (4) **4** (1 equiv.), CaH_2 (1 equiv.), $BF_3{\cdot}OEt_2$ (3.3 equiv.), CH_2Cl_2, –95 °C; Method B: (1) **5** (1 equiv.), LDA, THF, –50 °C; (2) HMPA (3 equiv.), –95 °C, **4** (1.1 equiv.); Method C: **5** (3 equiv.), $TiCl_4$ (2.9 equiv.), NEt_3, CH_2Cl_2, –78 °C, **4** (1 equiv.), –78 °C.

4 (method B), the formation of *anti*-Felkin products dominated (Felkin/*anti*-Felkin, <1:99) with (8*S*,9*R*)-**9c** as the major product (**9c/9d** = 89:11), albeit with a poor yield of 12%. Alternatively, treatment of ketone **5** with $TiCl_4$ in the presence of NEt_3 followed by reaction with aldehyde **4** (method C) resulted in a similar Felkin/*anti*-Felkin selectivity (6:94) but a reversed **9c/9d** ratio of 16:84 (Scheme 3). The diastereomers (8*S*,9*R*)-**9c** and (8*R*,9*R*)-**9d** were isolated in 8 and 61% yields, respectively. Thus, precursors **9a**,**c** and **9d** with *anti* and *syn* orientation at C8–C10 were accessible depending on the method.

However, the *anti* selectivity was surprising for a Mukaiyama aldol reaction.[25] Comparison of the coupling constants, $^3J_{(8\text{-H},9\text{-H})}$ = 9.8 Hz and $^3J_{(9\text{-H},10\text{-H})}$ = 1.4 Hz, with structurally related compounds revealed the *anti* configuration at C8/C9.[23] The monodentate Lewis acid $BF_3{\cdot}OEt_2$ rules out a chelation model. The resulting more positively charged transition state (see Scheme 4a) increases the dipolar moment and this should explain the better selectivity that is obtained compared with lithium enolate. From the *anti* aldehyde **4**, facial selectivity is dictated by a merged 1,2- and 1,3-asymmetric induction. The *anti* relationship between the methyl C23 and the TBS-protected ether reinforces the selectivity of the nucleophilic attack, as depicted in Scheme 4a. The C11 substituent is oriented *anti* to the C10–C=O bond and the polarized C11–OTBS and the carbonyl have opposed dipoles. The methyl C23 is placed *syn* to the carbonyl moiety to give the Felkin product **9a** as shown in Scheme 4.



Scheme 4. Proposed transition states for coupling by the Mukaiyama aldol reaction.

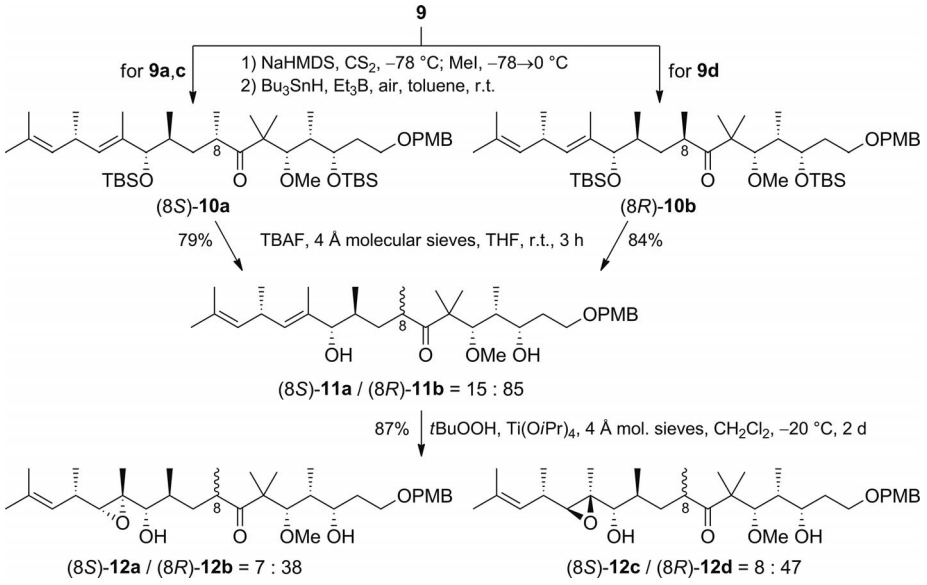
The staggered Newman projections for the reaction with the *Z*-silyl enol ether are summarized in Scheme 4b to give a potential explanation for the selectivity of the *anti* Mukaiyama aldol. Orientations **C** and **E** are disfavored due to the parallel dipole–dipole interactions of the aldehyde and the carbon–oxygen bond. **C** is further disfavored due to the steric interactions between the two fragments represented by C6 and C11 as in projection **D**. The synclinal transition state **F** can also be eliminated due to the steric interaction between the *gem*-dimethyl moiety at C6 and the methyl C23. The remaining orientations **A** and **B** both lead to the *syn*,*anti* product **9a**, however, preference is given to the synclinal **B** due to the antiperiplanar position of the side-chains and the unfavorable *syn*-pentane interaction between methyl groups C22 and C23 in **A**. To summarize, an alternative representation of the proposed transition state is shown in Scheme 4c.

The necessary deoxygenation of the C9 secondary alcohol in **9** under Barton–McCombie conditions[18,26] yielded derivatives (8*S*)-**10a** and (8*R*)-**10b** (Scheme 5).

Although precursors (8*S*,9*S*)-**9a** and (8*S*,9*R*)-**9c** gave the same deoxygenation product (8*S*)-**10a**, the two-step reaction of **9a** occurred without any problems to provide **10a** in 85% yield,[18] whereas the deoxygenation of **9c** was accompanied by a competitive retro-aldol reaction, decreasing the yield of the intermediate xanthogenate. Subsequent radical fragmentation gave selectively **10a** (55% total yield). Partial retro-aldolization was also observed for (8*R*,9*R*)-**9d**, which was deoxygenated to (8*R*)-**10b** in 60% yield over two steps. In this case, traces of a potential cyclopentane product, stemming from the formation of the radical intermediate and cyclization of the C12/C13 internal olefin, were found. The cyclization turned out to be faster yielding a 65:35 mixture of the deoxypropionate **10b** and the cyclopentane product when 1.5 equiv. of $HSnBu_3$ were used (see the Supporting Information). The formation of this byproduct was reduced by increasing the amount of tri-*n*-butyltin hydride up to 7 equiv.

Removal of the TBS groups in **10** was found to be rather capricious. Both under acidic (MeCN/48% HF 20:1) and neutral conditions (TASF in DMF) only a complex product mixture was obtained. The desilylation with $3HF{\cdot}NEt_3$ and NEt_3 in MeCN failed completely and after reaction for 7 d, starting reagent **10** was reisolated almost quantitatively. Finally, the use of TBAF and 4 Å molecular sieves in THF at room temperature yielded the desilylated products **11a**,**b**, albeit as a chromatographically inseparable 15:85 mixture of diastereomers (8*S*)-**11a** and (8*R*)-**11b**, regardless of the starting material (8*S*)-**10a** or (8*R*)-**10b** (Scheme 5). Presumably, epimerization at C8 occurred under the reaction conditions with the unnaturally configured diastereomer (8*R*)-**11b** as the main product.

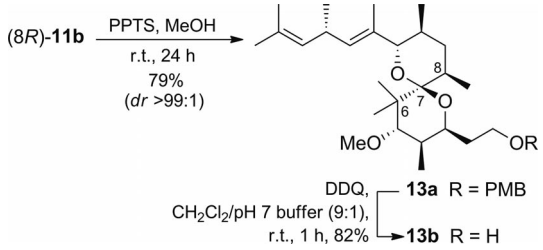
The epoxidation of **11a/b** (15:85) with *m*CPBA under the conditions reported for tedanolides **1**[11,20a] and myriaporones **2**[13a] resulted in a mixture of oxidation products, whereas no conversion was observed in the classic Sharpless asymmetric epoxidation with diethyl D-(–)-tartrate [(–)-DET]. Presumably the 1,4-*syn*-allylic alcohol **11** in combination with (–)-DET represents a mismatched case. However, under identical conditions without DET the mixture



Scheme 5. Deoxygenation of coupling products **9**[18] followed by desilylation and epoxidation of diol **11**.

of **11a/b** was epoxidized chemo- and regioselectively to derivatives **12** in 87% yield. The diastereomers were separated to give (8*S*)-**12a** and (8*R*)-**12b** in yields of 5 and 34% together with (8*S*)-**12c** and (8*R*)-**12d** in yields of 6 and 42%, respectively (Scheme 5).

The 1,3-*syn* relationship of the methyl groups at C8 and C10 in **11b** was confirmed by the NMR coupling constants of the bicyclic acetal **13b**, which was obtained from **11b** by acid-catalyzed acetalization and subsequent oxidative removal of the PMB group (Scheme 6).[27]



Scheme 6. Acid-catalyzed acetalization of diol (8*R*)-**11b**.

Cleavage of the PMB ether in **12** and subsequent oxidation should accomplish the synthesis of gephyronic acid (**3**). However, oxidative PMB ether cleavage led to acetal formation instead of the required primary alcohol. To overcome this problem and to avoid undesired epimerization during the desilylation of derivatives **10**, the order of the sequence was changed (Scheme 7).

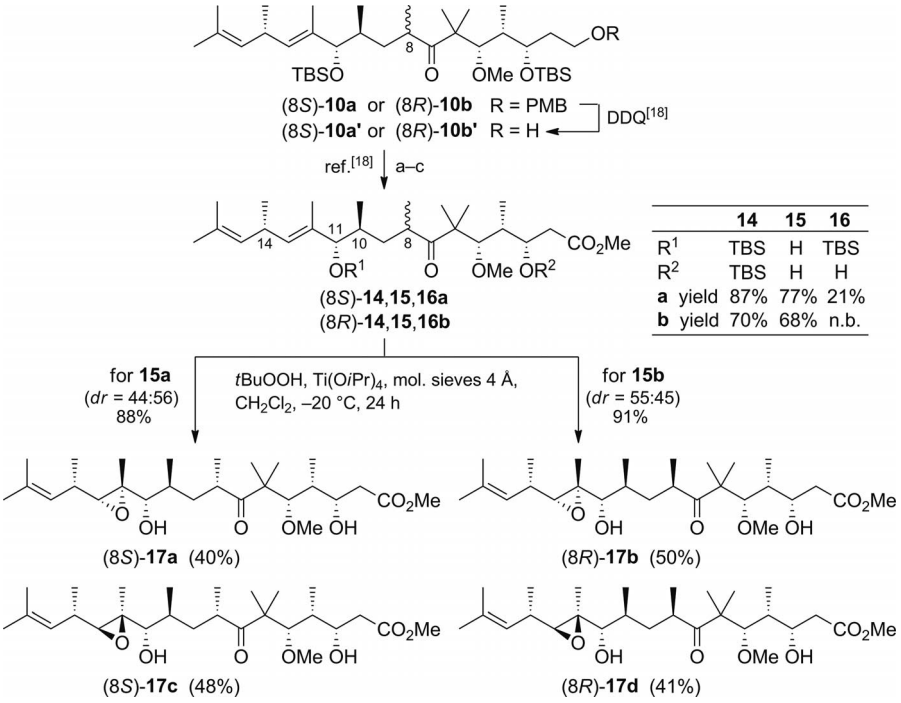
As previously described,[18] deprotection of compounds **10a** and **10b** with DDQ followed by successive Swern and Pinnick oxidation as well as esterification gave the methyl esters (8*S*)-**14a**[18] and (8*R*)-**14b** in yields of 87 and 70%, respectively. Again, desilylation caused some problems. In contrast to precursors **10**, which were desilylated with TBAF, the removal of the TBS groups in **14** was achieved by employing $3HF{\cdot}NEt_3$ in the presence of NEt_3 in MeCN at room temperature.[20a] After reaction for 7 d, the desired products (8*S*)-**15a**[18] or (8*R*)-**15b** were isolated in yields of 77 and 68% together with the C3 monodeprotected derivatives **16a** and **16b**. The latter could be separated and converted under these conditions into diols **15**, thus increasing their total yield (e.g., 89% for **15a**). Applying the epoxidation conditions described for **11a**,**b**, diol (8*S*)-**15a** afforded the desired epoxide (8*S*)-**17a** and diastereomer (8*S*)-**17c** in 88% yield (*dr* = 44:56).[18] Thus, the stereogenic centers at C11 and C14 do not exert any control on the incoming electrophile. Under the same conditions, compound (8*R*)-**15b** was epoxidized to the respective derivatives (8*R*)-**17b** and (8*R*)-**17d** in 91% yield with a diastereomeric ratio of 55:45 (Scheme 7).

Following this synthetic strategy, additional diastereoisomers of gephyronic acid (**3**) were accessible (Scheme 8).

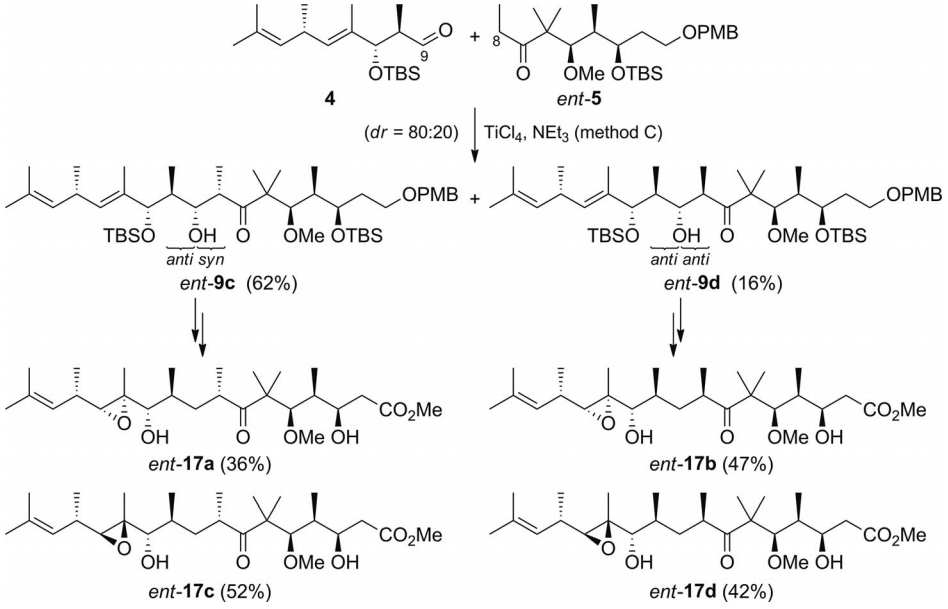
The coupling of aldehyde **4** and ketone *ent*-**5**, which was obtained from **8** and (*S*)-benzyloxazolidinone (*S*)-**7** as previously published,[18,21a,28] under the conditions of method C ($TiCl_4$, NEt_3) yielded the *anti*-Felkin products *ent*-(8*S*,9*R*)-**9c** and *ent*-(8*R*,9*R*)-**9d**. According to the procedures described above, derivatives *ent*-**9c**,**d** were converted into the methyl esters *ent*-**17a**,**c** and *ent*-**17b**,**d** in yields of 88 and 89%, respectively.

Biological Studies of Gephyronic Acid Derivatives

The ability of a set of 19 derivatives to inhibit the proliferation of mammalian tumor cell lines was investigated in an MTT assay.[29] The assay measures the metabolic activity of cells grown in a 96-well plate after 5 days and allows IC_{50} values to be determined from concentration-dependent activity curves. The results are summarized in Table 1. Surprisingly, (8*S*)-**17a** and (8*S*)-**12a** exhibited the highest activity with IC_{50} values of 1.4–6.3 $ng\,mL^{-1}$ and are 5- to 15-fold more potent than the naturally occurring gephyronic acid (**3**) in this assay, which demonstrates the influence of functionalization at the C1 terminus (Table 1, Entries 1, 8, and 9). Variation at C12–C13 in diastereomer (8*R*)-**11b** with



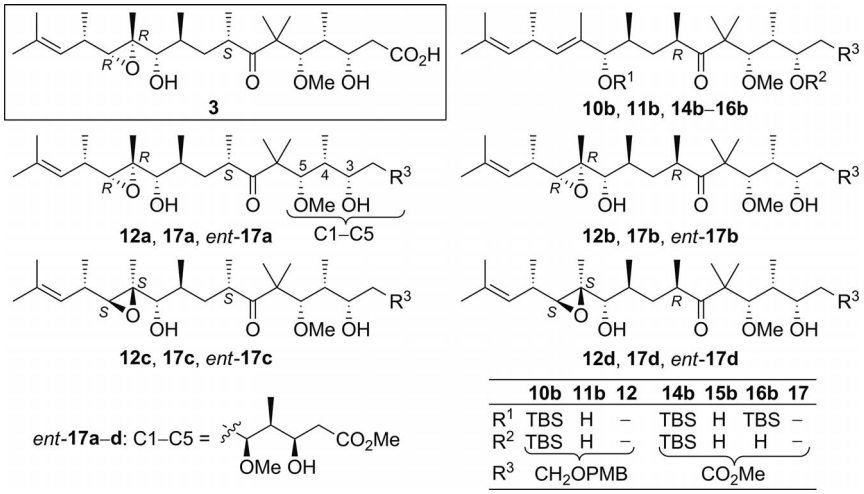
Scheme 7. Synthesis of derivatives **17** in analogy to ref.[18] Reagents and conditions: (a) $(COCl)_2$ (2 equiv.), DMSO (3 equiv.), NEt_3 (6 equiv.), CH_2Cl_2, –78 °C → r.t.; (b) (1) $NaClO_2$ (2.5 equiv.), KH_2PO_4 (7 equiv.), 2-methyl-2-butene (4.5 equiv.), *t*BuOH/H_2O (3:1), r.t., 1 h; (2) $TMSCHN_2$ (2 equiv.), CH_2Cl_2/MeOH (4:1), r.t., 1 h; (c) 3HF·NEt_3, NEt_3, MeCN, r.t., 7 d.



Scheme 8. Synthesis of diastereomers *ent*-**17a**–**d**.

a C=C bond instead of an epoxide led to reduced potency against the L-929 cell line compared with its congener (8*R*)-**12b** (Table 1, Entries 4 and 14). The least active (IC_{50} > 40 μg mL^{-1}) in the series of C12–C13 unsaturated analogues in this assay were products **9**, **10b**, and **14b** with TBS-protecting groups on the secondary alcohols at C3 and C11 (Table 1, Entries 2, 3, and 5). The correct absolute and relative stereochemistry turned out to be crucial for antitumor activity. Inversion of the configuration at C12–C13 causes a significant loss of activity, as can be seen for **12a**,**c** and **17a**,**c**. Both PMB ether (8*S*)-**12a** and methyl ester (8*S*)-**17a** with "natural" (12*R*,13*R*)-epoxide were approximately 1000-fold more potent against the tumor cell lines than their counterparts (8*S*)-**12c** and (8*S*)-**17c** (Table 1, Entries 8–11). The antitumor activities of the diastereomers (8*R*)-**12b** and (8*R*)-**17b** with an inverse configuration at C8 relative to **12a** and **17a** were lower by 1000 orders of magnitude (Table 1, Entries 14 and 15).

Table 1. Cytotoxicity of gephyronic acid (**3**) and its analogues against L-929 (mouse fibroblast) and KB-3-1 (HeLa clone, human cervix carcinoma derived) cell lines.



Entry	Compd.	Configuration		IC_{50} [$\mu g\,mL^{-1}$][a]	
		C8	C12–C13	L-929	KB-3-1
1	**3**	*S*	*R*,*R*	0.051 ± 0.003[b]	0.0074 ± 0.006[b]
2	**9**	–	–	>40	>40
3	**10b**	*R*	–	>40	>40
4	**11b**	*R*	–	3.0 ± 0.3	1.5 ± 0.1
5	**14b**	*R*	–	>40	>40
6	**15b**	*R*	–	4.7 ± 0.5	5.0 ± 0.1
7	**16b**	*R*	–	8.0 ± 0.1	7.0 ± 0.1
8	**12a**	*S*	*R*,*R*	0.0033 ± 0.0006	0.0034 ± 0.0001
9	**17a**	*S*	*R*,*R*	0.0063 ± 0.0006	0.0014 ± 0.0004
10	**12c**	*S*	*S*,*S*	1.7 ± 0.1	2.3 ± 0.5
11	**17c**	*S*	*S*,*S*	4.8 ± 0.2	2.8 ± 0.7
12	*ent*-**17a**	*S*	*R*,*R*	1.9 ± 0.1	2.0 ± 0.1
13	*ent*-**17c**	*S*	*S*,*S*	>40	32 ± 8
14	**12b**	*R*	*R*,*R*	0.8 ± 0.14	1.2 ± 0.2
15	**17b**	*R*	*R*,*R*	4.8 ± 0.2	7.1 ± 0.1
16	**12d**	*R*	*S*,*S*	2.0 ± 0.4	0.49 ± 0.2
17	**17d**	*R*	*S*,*S*	>40	37 ± 0.1
18	*ent*-**17b**	*R*	*R*,*R*	5.8 ± 0.4	11 ± 1
19	*ent*-**17d**	*R*	*S*,*S*	16 ± 3	21 ± 3

[a] Cell proliferation was measured by an MTT assay. The data are mean values ± standard deviation of two assays performed in parallel. [b] Values for natural product **3**.

A further loss of activity by one order of magnitude was observed for product (8*R*)-**17d** with inverse stereochemistry at both C12–C13 and C8 compared with its analogue (8*S*)-**17c** (Table 1, Entries 11 and 17). Our results are consistent with SAR studies of myriaporone **2**, revealing the necessity of the epoxide for biological activity.[15]

Furthermore, the results in Table 1 demonstrate the influence of the C3–C5 stereotriad on cytotoxicity. In general, methyl esters *ent*-**17a** and *ent*-**17b** were less potent than their counterparts **17a**,**b**, reaching IC_{50} values of only 2–11 $\mu g\,mL^{-1}$ (Table 1, Entries 12 and 18). Interestingly, compound *ent*-**17d** with the "unnatural" *R* configuration at C8 revealed slightly increased antitumor activity in comparison with its 8*S*-configured congener *ent*-**17c** (Table 1, Entries 13 and 19). For diastereomers **17c**,**d** the opposite effect was observed.

Furthermore, the antibacterial activities of the compounds in Table 1 were determined by using agar diffusion assays. In this assay the inhibitory effect on the growth of different indicator organisms was investigated. The diameters of the resulting inhibition zones were taken as a measure of antibiotic activity. No growth inhibition with *E. coli* tolC, *Klebsiella pneumoniae*, and *Staphylococcus aureus* was found. But surprisingly, derivative (8*R*)-**17d** with the "unnatural" stereochemistry at C12–C13 and C8 as well as precursor (8*S*)-**16a** showed activities against *Pseudomonas aeruginosa*. In agar diffusion assays with 20 μg/paper disc, inhibition zones of 24 and 27 mm, respectively, were observed. Additional experiments to delineate the unique antibacterial activities of **17d** and **16a** are currently being pursued and will be presented separately.

Conclusions

Complementary aldol strategies for the coupling of fragments **4** and **5** or *ent*-**5** gave access to a variety of dia-

stereomeric gephyronic acid derivatives. The structure–activity relationship (SAR) studies of these compounds have provided evidence for the epoxide in the western part of gephyronic acid (**3**) as well as the C3–C5 stereotriad and the C1 moiety in the eastern part to be the pharmacophoric subunits for the observed cytotoxicity. These results provide the basis for labeling experiments to identify the biological target protein(s) of gephyronic acid (**3**). Studies towards this goal are underway in our laboratories.

Experimental Section

General: ^{1}H and ^{13}C{^{1}H} NMR spectra (125 MHz) were recorded with a Bruker Avance 500 spectrometer. IR spectra were recorded with a Bruker Vektor22 FTIR spectrometer with the MKII Golden Gate Single Reflection Diamant system. Specific rotations were recorded with a Perkin–Elmer 241 polarimeter. Mass spectra were recorded with a Finnigan MAT 95 (CI) or Varian MAT 711 (EI, 70 eV) spectrometer. ESI-MS were measured with a Bruker Daltonics microTOF-Q spectrometer. Flash chromatography was performed on silica gel 60 (Fluka; 40–63 μm). Thin-layer chromatography (TLC) was conducted on Merck silica gel 60 F_{254} plates. Preparative HPLC was performed with a Shimadzu apparatus with a DGU-20A5 Prominence Degasser, LC-20AT Prominence Liquid Chromatograph and SPD-M20A Prominence Diode Array Detector using a Knauer Kromasil 100 Sil 5 μm column (250 × 20 mm). All reactions were performed in dried glassware.

(5*S*,6*S*,7*S*,10*S*,11*R*,12*S*,13*S*)-11-Hydroxy-7-methoxy-5-{2-[(4-methoxybenzyl)oxy]ethyl}-2,2,3,3,6,8,8,10,12,15,15,16,16-tridecamethyl-13-[(1*E*,3*S*)-1,3,5-trimethylhexa-1,4-dienyl]-4,14-dioxa-3,15-disilaheptadecan-9-one (9c, Method B): In analogy to ref.[30], a freshly prepared 1 M solution of LDA in THF (1010 μL, 1.01 mmol, 1.05 equiv.) was added dropwise over 5 min to a solution of **5** (462 mg, 0.96 mmol, 1.00 equiv.) in abs. THF (7.0 mL) at –78 °C under N_2. The reaction mixture was warmed to –50 °C within 15 min and stirred at –50 °C for 30 min. After recooling to –78 °C, HMPA (501 μL, 2.88 mmol, 3.00 equiv.) was added dropwise and the reaction mixture was stirred for 30 min. Then it was cooled to –95 °C, a solution of freshly prepared **4**[18] (344 mg, 1.06 mmol, 1.10 equiv.) in abs. THF (1.0 mL) was added dropwise over 10 min, and the mixture was stirred for a further 10 min. A solution of AcOH (82 μL, 1.44 mmol, 1.5 equiv.) in THF (1.0 mL) was carefully added and the reaction mixture warmed to room temperature. After dilution with Et_2O (10 mL), H_2O (10 mL) was added. The aqueous layer was separated and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. The crude product (*dr* = 89:11 by ^{1}H NMR) was purified by chromatography on SiO_2 (hexanes/EtOAc, 20:1 → 5:1) to give **9c** (93 mg, 0.12 mmol, 12%) and **9d** (16 mg, 0.02 mmol, 2%) as colorless oils (>95% purity each by ^{1}H NMR) together with reisolated **5** (370 mg, 0.77 mmol, 80%).

9c: R_f = 0.61 (*n*-hexane/EtOAc, 4:1); R_t (HPLC) = 18.64 min (*n*-hexane/EtOAc, 96:4, Kromasil, flow 1.0 mL min^{-1}). $[\alpha]_D^{20}$ = +38.2 (*c* = 1.00, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.01 (s, 3 H, SiCH_3), 0.066 (s, 3 H, SiCH_3), 0.074 (s, 3 H, SiCH_3), 0.10 (s, 3 H, SiCH_3), 0.74 (d, *J* = 7.0 Hz, 3 H, 23-H), 0.86 (d, *J* = 7.2 Hz, 3 H, 18-H), 0.88 [s, 9 H, SiC(CH_3)$_3$], 0.89 [s, 9 H, SiC(CH_3)$_3$], 0.97 (d, *J* = 6.7 Hz, 3 H, 25-H), 1.01 (s, 3 H, 21-H), 1.03 (d, *J* = 6.8 Hz, 3 H, 22-H), 1.20 (s, 3 H, 20-H), 1.59 (d, *J* = 1.3 Hz, 3 H, 24-H), 1.60 (d, *J* = 1.3 Hz, 3 H, 26-H), 1.64 (d, *J* = 1.3 Hz, 3 H, 17-H), 1.73 (ddq, *J* = 8.4, 7.2, 7.0 Hz, 1 H, 10-H), 1.77–1.91 (m, 3 H, 2-H$_a$, 2-H$_b$, 4-H), 3.18 (qd, *J* = 6.8, 2.3 Hz, 1 H, 8-H), 3.21 (s, 3 H, 19-H), 3.23 (ddq, *J* = 9.1, 8.8, 6.7 Hz, 1 H, 14-H), 3.44–3.47 (m, 2 H, 1-H$_a$, 1-H$_b$), 3.52 (d, *J* = 3.5 Hz, 1 H, 5-H), 3.69–3.72 (m, 2 H, 3-H, 9-H), 3.74 (d, *J* = 1.7 Hz, 1 H, O*H*), 3.80 (s, 3 H, ArOCH_3), 4.10 (dd, *J* = 7.2, 0.7 Hz, 1 H, 11-H), 4.39 (d, *J* = 11.4 Hz, 1 H, OCH_aH$_b$Ar), 4.42 (d, *J* = 11.4 Hz, 1 H, OCH$_a$$H_b$Ar), 4.94 (dqq, *J* = 8.8, 1.3, 1.3 Hz, 1 H, 15-H), 5.18 (dqd, *J* = 9.2, 1.3, 0.7 Hz, 1 H, 13-H), 6.85–6.88 (m, 2 H, *m*-H), 7.22–7.25 (m, 2 H, *o*-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.9 (Si*C*H$_3$), –4.23 (Si*C*H$_3$), –4.15 (Si*C*H$_3$), –3.4 (Si*C*H$_3$), 9.21 (C-18), 9.21 (C-22), 12.4 (C-24), 13.0 (C-23), 18.1 (C-26), 18.27 [Si*C*(CH$_3$)$_3$], 18.29 [Si*C*(CH$_3$)$_3$], 18.6 (C-20), 21.3 (C-25), 23.5 (C-21), 25.8 (C-17), 26.0 [SiC(*C*H$_3$)$_3$], 26.2 [SiC(*C*H$_3$)$_3$], 31.6 (C-14), 35.1 (C-2), 38.2 (C-4), 41.0 (C-10), 43.8 (C-8), 53.8 (C-6), 55.4 (ArO*C*H$_3$), 60.0 (C-19), 67.1 (C-1), 72.7 (O*C*H$_2$Ar), 73.3 (C-9), 73.4 (C-3), 82.7 (C-11), 86.2 (C-5), 113.9 (C-*m*), 129.3 (C-*o*), 129.5 (C-15), 129.9 (C-12), 130.7 (C-*i*), 132.8 (C-16), 134.1 (C-13), 159.3 (C-*p*), 218.7 (C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 2954 (m), 2929 (m), 2856 (m), 1613 (w), 1514 (m), 1471 (m), 1361 (w), 1248 (s), 1080 (s), 1039 (s), 1003 (s), 833 (vs), 773 (vs) cm^{-1}. MS (ESI): *m*/*z* = 828 [M + Na]$^+$, 695, 531, 503, 447, 403. HRMS (ESI): calcd. for $C_{46}H_{84}NaO_7Si_2^+$ [M + Na]$^+$ 827.5648; found 827.5639.

9d: R_f = 0.14 (*n*-hexane/EtOAc, 6:1); R_t (HPLC) = 49.55 min (*n*-hexane/EtOAc, 96:4, Kromasil, flow 1.0 mL min^{-1}). $[\alpha]_D^{20}$ = +4.8 (*c* = 0.42, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.03 (s, 3 H, SiCH_3), 0.05 (s, 3 H, SiCH_3), 0.08 (s, 3 H, SiCH_3), 0.11 (s, 3 H, SiCH_3), 0.87 (d, *J* = 7.2 Hz, 3 H, 18-H), 0.887 [s, 9 H, SiC(CH_3)$_3$], 0.889 [s, 9 H, SiC(CH_3)$_3$], 0.96 (d, *J* = 7.1 Hz, 3 H, 23-H), 0.97 (s, 3 H, 21-H), 1.05 (d, *J* = 6.7 Hz, 3 H, 25-H), 1.13 (d, *J* = 6.9 Hz, 3 H, 22-H), 1.18 (s, 3 H, 20-H), 1.57 (dd, *J* = 1.3, 0.7 Hz, 3 H, 24-H), 1.60 (qdd, *J* = 7.1, 3.4, 1.3 Hz, 1 H, 10-H), 1.62 (d, *J* = 1.3 Hz, 3 H, 26-H), 1.66 (d, *J* = 1.3 Hz, 3 H, 17-H), 1.74 (qdd, *J* = 7.2, 3.9, 3.5 Hz, 1 H, 4-H), 1.82 (dddd, *J* = 14.1, 7.0, 7.0, 5.1 Hz, 1 H, 2-H$_a$), 1.86 (dddd, *J* = 14.1, 7.6, 6.5, 6.5 Hz, 1 H, 2-H$_b$), 3.06 (dq, *J* = 9.3, 6.9 Hz, 1 H, 8-H), 3.19 (s, 3 H, 19-H), 3.26 (d, *J* = 1.1 Hz, 1 H, O*H*), 3.31 (ddq, *J* = 9.2, 8.8, 6.7 Hz, 1 H, 14-H), 3.41–3.43 (m, 2 H, 1-H), 3.50 (d, *J* = 3.5 Hz, 1 H, 5-H), 3.70 (ddd, *J* = 7.6, 5.1, 3.9 Hz, 1 H, 3-H), 3.80 (s, 3 H, ArOCH_3), 3.93 (ddd, *J* = 3.4, 1.3, 0.7 Hz, 1 H, 11-H), 4.13 (ddd, *J* = 9.3, 1.3, 0.7 Hz, 1 H, 9-H), 4.38 (d, *J* = 11.5 Hz, 1 H, OCH_aH$_b$Ar), 4.40 (d, *J* = 11.5 Hz, 1 H, OCH$_a$$H_b$Ar), 5.00 (dqq, *J* = 8.8, 1.3, 1.3 Hz, 1 H, 15-H), 5.35 (dqd, *J* = 9.2, 1.3, 1.3 Hz, 1 H, 13-H), 6.84–6.87 (m, 2 H, *m*-H), 7.21–7.24 (m, 2 H, *o*-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –5.1 (Si*C*H$_3$), –4.5 (Si*C*H$_3$), –4.2 (Si*C*H$_3$), –3.4 (Si*C*H$_3$), 8.7 (C-18), 11.6 (C-23), 13.8 (C-24), 16.0 (C-22), 18.1 (C-26), 18.29 [Si*C*(CH$_3$)$_3$], 18.31 [Si*C*(CH$_3$)$_3$], 18.7 (C-20), 21.8 (C-25), 23.7 (C-21), 25.8 (C-17), 26.1 [SiC(*C*H$_3$)$_3$], 26.2 [SiC(*C*H$_3$)$_3$], 31.7 (C-14), 35.3 (C-2), 36.6 (C-10), 38.2 (C-4), 45.4 (C-8), 53.7 (C-6), 55.4 (ArO*C*H$_3$), 59.6 (C-19), 67.1 (C-1), 71.4 (C-9), 72.8 (O*C*H$_2$Ar), 73.6 (C-3), 82.4 (C-11), 85.5 (C-5), 113.9 (C-*m*), 129.3 (C-*o*), 129.7 (C-12), 130.0 (C-15), 130.7 (C-*i*), 131.2 (C-16), 132.1 (C-13), 159.3 (C-*p*), 219.4 (C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 3520 (w), 2955 (m), 2929 (m), 2856 (m), 1694 (w), 1514 (m), 1471 (m), 1462 (m), 1362 (m), 1248 (s), 1081 (s), 1039 (s), 1021 (s), 834 (vs), 773 (vs) cm^{-1}. MS (ESI): *m*/*z* = 828 [M + Na]$^+$, 531, 503, 447, 403, 347. HRMS (ESI): calcd. for $C_{46}H_{84}NaO_7Si_2^+$ [M + Na]$^+$ 827.5648; found 827.5639.

(5*S*,6*S*,7*S*,10*R*,11*R*,12*S*,13*S*)-11-Hydroxy-7-methoxy-5-{2-[(4-methoxybenzyl)oxy]ethyl}-2,2,3,3,6,8,8,10,12,15,15,16,16-tridecamethyl-13-[(1*E*,3*S*)-1,3,5 trimethylhexa-1,4-dienyl]-4,14-dioxa-3,15-disilaheptadecan-9-one (9d, Method C): In analogy to ref.[31], a 1 M solution of $TiCl_4$ in CH_2Cl_2 (374 μL, 374.1 μmol, 2.90 equiv.) and NEt_3 (53 μL, 380.6 μmol, 2.95 equiv.) were successively added dropwise

to a solution of **5** (186.1 mg, 387.0 μmol, 3.00 equiv.) in abs. CH_2Cl_2 (4.0 mL) at –78 °C under N_2 and the reaction mixture was stirred for 1 h. Then a freshly prepared solution of **4** (41.9 mg, 129.0 μmol, 1.00 equiv.) in CH_2Cl_2 (1.0 mL) was added dropwise and the reaction mixture was warmed to 0 °C over 3 h and stirred for a further 30 min. After dilution with CH_2Cl_2 (5 mL), the reaction was quenched by the addition of a sat. $NaHCO_3$ solution (5 mL) and the mixture was warmed to room temperature. The aqueous layer was separated and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. The residue (240 mg, ratio **5/9c/9d** = 8:15:77 by HPLC) was purified by chromatography on SiO_2 (hexanes/EtOAc, 20:1 → 5:1) to give **9d** (63.4 mg, 78.7 μmol, 61%) and **9c** (8.3 mg, 10.3 μmol, 8%) as colorless oils (>95% purity each by ^{1}H NMR).

(5*R*,6*R*,7*R*,10*S*,11*R*,12*S*,13*S*)-11-Hydroxy-7-methoxy-5-{2-[(4-methoxybenzyl)oxy]ethyl}-2,2,3,3,6,8,8,10,12,15,15,16,16-tridecamethyl-13-[(1*E*,3*S*)-1,3,5-trimethylhexa-1,4-dienyl]-4,14-dioxa-3,15-disilaheptadecan-9-one (*ent*-9c): Following method C, from *ent*-**5** (1.05 g, 2.18 mmol) in abs. CH_2Cl_2 (25 mL), a 1 M solution of $TiCl_4$ in CH_2Cl_2 (2.11 mL, 2.11 mmol), NEt_3 (0.30 mL, 2.14 mmol), and **4** (0.24 g, 0.73 mmol) in CH_2Cl_2 (5 mL). Yield: 0.36 g (0.45 mmol, 62%) *ent*-**9c** and 0.09 mg (0.12 mmol, 16%) *ent*-**9d** as colorless oils (>95% purity each by ^{1}H NMR).

***ent*-9c:** R_f = 0.65 (*n*-hexane/EtOAc, 4:1). $[\alpha]_D^{20}$ = +17.3 (*c* = 1.00, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.00 (s, 3 H, SiCH_3), 0.06 (s, 3 H, SiCH_3), 0.08 (s, 3 H, SiCH_3), 0.10 (s, 3 H, SiCH_3), 0.73 (d, *J* = 7.0 Hz, 3 H, 23-H), 0.85 (d, *J* = 7.2 Hz, 3 H, 18-H), 0.88 [s, 9 H, SiC(CH_3)$_3$], 0.89 [s, 9 H, SiC(CH_3)$_3$], 0.97 (d, *J* = 6.8 Hz, 3 H, 25-H), 1.01 (d, *J* = 6.8 Hz, 3 H, 22-H), 1.04 (s, 3 H, 21-H), 1.14 (s, 3 H, 20-H), 1.59 (d, *J* = 1.3 Hz, 3 H, 24-H), 1.60 (d, *J* = 1.3 Hz, 3 H, 26-H), 1.63 (d, *J* = 1.3 Hz, 3 H, 17-H), 1.71–1.78 (m, 1 H, 10-H), 1.78–1.90 (m, 2 H, 2-H_a, 2-H_b), 3.17 (qd, *J* = 6.8, 1.9 Hz, 1 H, 8-H), 3.22 (ddq, *J* = 9.0, 8.9, 6.8 Hz, 1 H, 14-H), 3.25 (s, 3 H, 19-H), 3.42–3.44 (m, 2 H, 1-H_a, 1-H_b), 3.51 (d, *J* = 3.5 Hz, 1 H, 5-H), 3.65–3.71 (m, 2 H, 3-H, 9-H), 3.80 (s, 3 H, ArOCH_3), 4.15 (d, *J* = 6.6 Hz, 1 H, 11-H), 4.39 (d, *J* = 11.8 Hz, 1 H, OCH_aH$_b$Ar), 4.41 (d, *J* = 11.8 Hz, 1 H, OCH$_a$$H_b$Ar), 4.93 (dqq, *J* = 8.9, 1.3, 1.3 Hz, 1 H, 15-H), 5.19 (dq, *J* = 9.0, 1.3 Hz, 1 H, 13-H), 6.85–6.88 (m, 2 H, *m*-H), 7.22–7.25 (m, 2 H, *o*-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.9 (SiCH_3), –4.3 (SiCH_3), –4.2 (SiCH_3), –3.4 (SiCH_3), 9.0 (C-18), 9.4 (C-22), 12.5 (C-24), 12.7 (C-23), 18.1 [SiC(CH$_3$)$_3$], 18.27 (C-26), 18.29 [SiC(CH$_3$)$_3$], 20.0 (C-20), 21.4 (C-25), 22.9 (C-21), 25.8 (C-17), 26.1 [SiC(CH_3)$_3$], 26.2 [SiC(CH_3)$_3$], 31.6 (C-14), 35.0 (C-2), 38.7 (C-10), 41.1 (C-4), 42.9 (C-8), 54.3 (C-6), 55.4 (ArOCH_3), 60.2 (C-19), 67.2 (C-1), 72.8 (OCH_2Ar), 72.9 (C-3), 73.3 (C-9), 81.7 (C-11), 85.3 (C-5), 113.9 (C-*m*), 129.3 (C-*o*), 129.6 (C-15), 129.7 (C-12), 130.7 (C-*i*), 132.8 (C-16), 134.0 (C-13), 159.2 (C-*p*), 219.2 (C-7) ppm. FTIR (ATR): ṽ = 2955 (m), 2929 (m), 2856 (m), 1683 (w), 1514 (m), 1471 (m), 1248 (s), 1079 (s), 1040 (s), 1022 (s), 1003 (s), 834 (vs), 773 (vs) cm^{-1}. MS (ESI): *m*/*z* = 827 [M + Na]$^+$, 531, 503, 447, 403, 347. HRMS (ESI): calcd. for $C_{46}H_{84}NaO_7Si_2^+$ [M + Na]$^+$ 827.5648; found 827.5645.

***ent*-9d:** R_f = 0.42 (*n*-hexane/EtOAc, 4:1). $[\alpha]_D^{20}$ = –13.9 (*c* = 1.00, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.03 (s, 3 H, SiCH_3), 0.04 (s, 3 H, SiCH_3), 0.06 (s, 3 H, SiCH_3), 0.09 (s, 3 H, SiCH_3), 0.86 (d, *J* = 7.2 Hz, 3 H, 18-H), 0.89 [s, 9 H, SiC(CH_3)$_3$], 0.90 (s, 3 H, 21-H), 0.91 [s, 9 H, SiC(CH_3)$_3$], 0.96 (d, *J* = 7.1 Hz, 3 H, 23-H), 1.05 (d, *J* = 6.8 Hz, 3 H, 25-H), 1.12 (d, *J* = 6.8 Hz, 3 H, 22-H), 1.19 (s, 3 H, 20-H), 1.51 (qdd, *J* = 7.1, 3.6, 1.4 Hz, 1 H, 10-H), 1.53 (d, *J* = 1.3 Hz, 3 H, 24-H), 1.62 (d, *J* = 1.4 Hz, 3 H, 26-H), 1.66 (d, *J* = 1.4 Hz, 3 H, 17-H), 1.74–1.91 (m, 3 H, 2-H_a, 2-H_b, 4-H), 3.07 (dq, *J* = 8.8, 6.8 Hz, 1 H, 8-H), 3.20 (s, 3 H, 19-H), 3.21 (br. d, *J* = 1.3 Hz, 1 H, OH), 3.31 (ddq, *J* = 9.2, 8.8, 6.8 Hz, 1 H, 14-H), 3.44–3.48 (m, 2 H, 1-H_a, 1-H_b), 3.53 (d, *J* = 3.6 Hz, 1 H, 5-H), 3.67 (ddd, *J* = 6.7, 5.7, 4.1 Hz, 1 H, 3-H), 3.80 (s, 3 H, ArOCH_3), 3.92 (dd, *J* = 3.7, 1.2 Hz, 1 H, 11-H), 4.09 (ddd, *J* = 8.8, 1.3, 1.3 Hz, 1 H, 9-H), 4.39 (d, *J* = 11.5 Hz, 1 H, OCH_aH$_b$Ar), 4.42 (d, *J* = 11.5 Hz, 1 H, OCH$_a$$H_b$Ar), 4.99 (dqq, *J* = 8.8, 1.4, 1.4 Hz, 1 H, 15-H), 5.34 (dqd, *J* = 9.2, 1.3, 1.2 Hz, 1 H, 13-H), 6.85–6.88 (m, 2 H, *m*-H), 7.22–7.26 (m, 2 H, *o*-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –5.1 (SiCH_3), –4.5 (SiCH_3), –4.2 (SiCH_3), –3.5 (SiCH_3), 9.7 (C-18), 11.7 (C-23), 13.6 (C-24), 14.2 (C-22), 18.1 [SiC(CH$_3$)$_3$], 18.28 (C-26), 18.29 [SiC(CH$_3$)$_3$], 18.9 (C-20), 21.7 (C-25), 23.6 (C-21), 25.8 (C-17), 26.1 [SiC(CH_3)$_3$], 26.2 [SiC(CH_3)$_3$], 31.6 (C-14), 35.0 (C-2), 37.2 (C-10), 38.2 (C-4), 45.0 (C-8), 53.7 (C-6), 55.4 (ArOCH_3), 60.1 (C-19), 67.2 (C-1), 71.6 (C-9), 72.8 (OCH_2Ar), 73.3 (C-3), 82.1 (C-11), 84.7 (C-5), 113.9 (C-*m*), 129.4 (C-*o*), 129.7 (C-12), 129.9 (C-15), 130.7 (C-*i*), 131.4 (C-13), 132.0 (C-16), 159.3 (C-*p*), 218.6 (C-7) ppm. FTIR (ATR): ṽ = 2955 (m), 2930 (m), 2857 (m), 1695 (w), 1514 (m), 1471 (m), 1463 (m), 1362 (m), 1248 (s), 1082 (s), 1039 (s), 1004 (m), 834 (vs), 773 (vs) cm^{-1}. MS (ESI): *m*/*z* = 827 [M + Na]$^+$, 531, 503, 447, 403, 347. HRMS (ESI): calcd. for $C_{46}H_{84}NaO_7Si_2^+$ [M + Na]$^+$ 827.5648; found 827.5644.

(5*S*,6*S*,7*S*,10*R*,12*S*,13*S*)-7-Methoxy-5-{2-[(4-methoxybenzyl)oxy]ethyl}-2,2,3,3,6,8,8,10,12,15,15,16,16-tridecamethyl-13-[(1*E*,3*S*)-1,3,5-trimethylhexa-1,4-dienyl]-4,14-dioxa-3,15-disilaheptadecan-9-one (10b)

Method 1: In analogy to ref.[18,26a], a 2 M solution of NaHMDS in THF (55 μL, 0.11 mmol, 1.4 equiv.) was added dropwise to a solution of **9d** (63.0 mg, 78.2 μmol, 1.0 equiv.) in abs. CS_2 (20 mL) at –78 °C under N_2 and the reaction mixture was stirred for 1 h. After addition of MeI (73 μL, 1.17 mmol, 15.0 equiv.), the reaction mixture was warmed to 0 °C over 3 h and stirred for a further 3 h. The reaction was quenched by the addition of a sat. $NaHCO_3$ solution (15 mL). The aqueous layer was separated and extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The residue was purified by chromatography on SiO_2 (hexanes/EtOAc, 40:1 → 20:1) to give the xanthogenate (51.3 mg, 57.1 μmol, 73%) as a colorless oil (>95% purity by ^{1}H NMR).

Method 2: In analogy to ref.[18,26b], $HSnBu_3$ (101.9 mg, 0.35 mmol, 7.0 equiv.) was quickly added to a solution of the xanthogenate (45.0 mg, 50.3 μmol, 1.0 equiv.) in abs. toluene (10 mL) followed by the dropwise addition of a 1 M solution of Et_3B in hexane (60.4 μL, 60.4 μmol, 1.2 equiv.) at room temperature under N_2. After stirring for 1 h, KF (44 mg, 0.75 mmol, 15.0 equiv.) and H_2O (10 mL) were added. The aqueous layer was separated and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (15 mL), dried ($MgSO_4$), and concentrated. The residue was purified by chromatography on SiO_2 (hexanes/EtOAc, 100:0 → 20:1) to give **10b** (32.5 mg, 41.2 μmol, 82%) as a colorless oil (>95% purity by ^{1}H NMR). R_f = 0.40 (*n*-hexane/EtOAc, 6:1). $[\alpha]_D^{20}$ = +2.5 (*c* = 1.00, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.05 (s, 3 H, SiCH_3), 0.02 (s, 3 H, SiCH_3), 0.08 (s, 3 H, SiCH_3), 0.11 (s, 3 H, SiCH_3), 0.72 (d, *J* = 6.8 Hz, 3 H, 23-H), 0.75 (ddd, *J* = 13.6, 10.1, 4.6 Hz, 1 H, 9-H_a), 0.86 (d, *J* = 7.2 Hz, 3 H, 18-H), 0.89 [s, 9 H, SiC(CH_3)$_3$], 0.90 [s, 9 H, SiC(CH_3)$_3$], 0.98 (d, *J* = 6.7 Hz, 3 H, 25-H), 1.009 (s, 3 H, 21-H), 1.012 (d, *J* = 6.8 Hz, 3 H, 22-H), 1.15 (s, 3 H, 20-H), 1.46 (ddqd, *J* = 10.1, 7.1, 6.8, 3.2 Hz, 1 H, 10-H), 1.52 (d, *J* = 1.4 Hz, 3 H, 24-H), 1.60 (d, *J* = 1.4 Hz, 3 H, 26-H), 1.65 (d, *J* = 1.4 Hz, 3 H, 17-H), 1.74 (qdd, *J* = 7.2, 3.9, 3.5 Hz, 1 H, 4-

H), 1.80 (dddd, J = 14.0, 6.8, 6.8, 5.3 Hz, 1 H, 2-H_a), 1.88 (dddd, J = 14.0, 7.4, 6.8, 6.8 Hz, 1 H, 2-H_b), 2.15 (ddd, J = 13.6, 8.5, 3.2 Hz, 1 H, 9-H_b), 3.01 (dqd, J = 8.5, 6.8, 4.6 Hz, 1 H, 8-H), 3.22 (ddq, J = 9.1, 8.7, 6.8 Hz, 1 H, 14-H), 3.23 (s, 3 H, 19-H), 3.41–3.45 (m, 2 H, 1-H_a, 1-H_b), 3.50 (dd, J = 7.1, 0.7 Hz, 1 H, 11-H), 3.53 (d, J = 3.5 Hz, 1 H, 5-H), 3.72 (ddd, J = 7.4, 5.2, 3.9 Hz, 1 H, 3-H), 3.80 (s, 3 H, ArOCH_3), 4.39 (d, J = 11.7 Hz, 1 H, OCH_aH$_b$Ar), 4.41 (d, J = 11.7 Hz, 1 H, OCH$_a$$H_b$Ar), 4.96 (dqq, J = 8.7, 1.4, 1.4 Hz, 1 H, 15-H), 5.09 (dq, J = 9.1, 1.4, 0.7 Hz, 1 H, 13-H), 6.85–6.87 (m, 2 H, *m*-H), 7.22–7.25 (m, 2 H, *o*-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.9 (SiCH_3), –4.2 (SiCH_3), –4.1 (SiCH_3), –3.4 (SiCH_3), 9.0 (C-18), 12.0 (C-24), 16.9 (C-23), 18.1 [SiC(CH$_3$)$_3$], 18.3 (C-26), 18.4 [SiC(CH$_3$)$_3$], 19.3 (C-20), 20.0 (C-22), 21.5 (C-25), 23.0 (C-21), 25.8 (C-17), 26.1 [SiC(CH$_3$)$_3$], 26.2 [SiC(CH$_3$)$_3$], 31.5 (C-14), 35.2 (C-2), 35.4 (C-10), 37.1 (C-9), 38.6 (C-4), 39.2 (C-8), 53.6 (C-6), 55.4 (ArOCH$_3$), 60.0 (C-19), 67.2 (C-1), 72.8 (OCH$_2$Ar), 73.5 (C-3), 83.5 (C-11), 85.2 (C-5), 113.9 (C-*m*), 129.3 (C-*o*), 129.7 (C-12), 130.0 (C-15), 130.8 (C-*i*), 132.4 (C-13), 133.8 (C-16), 159.3 (C-*p*), 219.4 (C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 2956 (m), 2928 (m), 2856 (m), 1699 (m), 1513 (m), 1462 (m), 1361 (w), 1248 (s), 1078 (s), 1041 (s), 833 (vs), 772 (vs) cm^{-1}. MS (ESI): m/z = 812 [M + Na]$^+$, 680, 431, 403, 271. HRMS (ESI): calcd. for $C_{46}H_{84}NaO_6Si_2^+$ [M + Na]$^+$ 811.5699; found 811.5693.

(3*S*,4*R*,5*S*,8*R*,10*S*,11*S*,12*E*,14*S*)-3,11-Dihydroxy-5-methoxy-1-[(4-methoxybenzyl)oxy]-4,6,6,8,10,12,14,16-octamethylheptadeca-12,15-dien-7-one (11a/11b): In analogy to ref.[32], an anhydrous solution of tetrabutylammonium fluoride, prepared according to ref.[33] from tetrabutylammonium fluoride trihydrate (120 mg, 380 µmol, 10.0 equiv.) and 4 Å molecular sieves (50 mg) in THF (1 mL), was added dropwise to a solution of **10b** (30 mg, 38 µmol, 1.0 equiv.) in abs. THF (2.0 mL) at 0 °C under N_2. Then the reaction mixture was warmed to room temperature, stirred for a further 2 h, and diluted with Et_2O (5 mL). The reaction was quenched by addition of a pH 7 buffer solution (5 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (3× 5 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography on SiO_2 (hexanes/EtOAc/Et_3N, 75:24:1 → 50:49:1) to give the product (18 mg, 32 µmol, 84%) as a colorless oil in a C8 epimeric ratio **11b/11a** = 85:15 (>95% purity by ^{1}H NMR). The epimers could not be separated by chromatography. R_f = 0.23 (*n*-hexane/EtOAc, 2:1). $[\alpha]_D^{20}$ = +14.1 (c = 0.33, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.74 (d, J = 6.8 Hz, 3 H, 23-H), 0.91–0.94 (m, 1 H, 9-H_a), 0.94 (d, J = 7.0 Hz, 3 H, 18-H), 0.99 (d, J = 6.8 Hz, 3 H, 25-H), 1.04 (d, J = 6.8 Hz, 3 H, 22-H), 1.11 (s, 3 H, 20-H), 1.19 (s, 3 H, 21-H), 1.39 (ddqd, J = 8.7, 7.9, 6.8, 3.5 Hz, 1 H, 10-H), 1.53–1.57 (m, 1 H, 4-H), 1.56 (d, J = 1.3 Hz, 3 H, 24-H), 1.61 (d, J = 1.4 Hz, 3 H, 26-H), 1.62–1.66 (m, 1 H, 2-H_a), 1.65 (d, J = 1.4 Hz, 3 H, 17-H), 1.77–1.84 (m, 1 H, 2-H_b), 1.81 (d, J = 3.6 Hz, 1 H, OH), 2.08 (ddd, J = 13.8, 8.8, 3.5 Hz, 1 H, 9-H_b), 2.94 (d, J = 3.0 Hz, 1 H, OH), 3.15 (dqd, J = 8.8, 6.8, 5.2 Hz, 1 H, 8-H), 3.24 (ddq, J = 8.9, 8.8, 6.8 Hz, 1 H, 14-H), 3.37 (s, 3 H, 19-H), 3.55 (ddd, J = 7.9, 3.6, 0.7 Hz, 1 H, 11-H), 3.55–3.68 (m, 2 H, 1-H_a, 1-H_b), 3.59 (d, J = 4.4 Hz, 1 H, 5-H), 3.60–3.65 (m, 1 H, 3-H), 3.80 (s, 3 H, ArOCH_3), 4.42 (s, 2 H, OCH_2Ar), 4.95 (dqq, J = 8.8, 1.4, 1.3 Hz, 1 H, 15-H), 5.18 (dqd, J = 8.9, 1.4, 0.7 Hz, 1 H, 13-H), 6.86–6.89 (m, 2 H, *m*-H), 7.22–7.25 (m, 2 H, *o*-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 9.2 (C-18), 11.6 (C-24), 17.7 (C-23), 18.1 (C-26), 19.4 (C-22), 20.5 (C-20), 21.5 (C-21), 21.8 (C-25), 25.8 (C-17), 31.6 (C-14), 34.5 (C-10), 34.7 (C-2), 37.9 (C-9), 39.8 (C-8), 41.2 (C-4), 53.8 (C-6), 55.4 (ArOCH$_3$), 60.8 (C-19), 69.1 (C-1), 73.0 (C-3), 73.1 (OCH$_2$Ar), 83.5 (C-11), 86.3 (C-5), 114.0 (C-*m*), 129.5 (C-*o*), 129.7 (C-15), 129.8 (C-12), 130.3 (C-*i*), 133.3 (C-13), 133.9 (C-16), 159.4 (C-*p*), 220.9 (C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 3463 (w), 2963 (m), 2926 (m), 2869 (m), 1695 (m), 1513 (s), 1455 (m), 1366 (m), 1248 (vs), 1097 (vs), 1036 (s) cm^{-1}. MS (ESI): m/z = 583 [M + Na]$^+$, 317, 289, 275, 233, 217, 169. HRMS (ESI): calcd. for $C_{34}H_{56}NaO_6^+$ [M + Na]$^+$ 583.3969; found 583.3979.

(2*S*,3*R*,4*S*,6*R*,8*S*,9*S*,11*R*)-4-Methoxy-2-{2-[(4-methoxybenzyl)-oxy]ethyl}-3,5,5,9,11-pentamethyl-8-[(1*E*,3*S*)-1,3,5-trimethylhexa-1,4-dienyl]-1,7-dioxaspiro[5.5]undecane (13a): A solution of PPTS (1.2 mg, 4.8 µmol, 0.3 equiv.) in abs. MeOH (0.2 mL) was added dropwise to a solution of **11a/11b** (*dr* = 15:85, 9.0 mg, 16.0 µmol, 1.0 equiv.) in abs. MeOH (2.0 mL) under N_2 at room temperature and the reaction mixture was stirred for 24 h. Then it was diluted with Et_2O (5 mL) and the reaction was quenched by the addition of a sat. $NaHCO_3$ solution (5 mL). The aqueous layer was separated and extracted with Et_2O (3× 5 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. The remaining colorless oil (10 mg) was purified by flash chromatography on SiO_2 (hexanes/EtOAc/Et_3N, 95:4:1) to give **13a** (7.1 mg, 12.6 µmol, 79%) as a colorless solid (*dr* > 99:1, 99% purity by GC). R_f = 0.57 (*n*-hexane/EtOAc, 2:1). $[\alpha]_D^{20}$ = +20.8 (c = 0.27, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.58 (d, J = 6.4 Hz, 3 H, 23-H), 0.92 (d, J = 7.0 Hz, 3 H, 18-H), 0.94 (d, J = 6.7 Hz, 3 H, 25-H), 0.95 (d, J = 6.5 Hz, 3 H, 22-H), 0.98 (s, 3 H, 20-H), 1.08 (s, 3 H, 21-H), 1.13 (ddd, J = 13.5, 12.5, 11.9 Hz, 1 H, 9-H_a), 1.41–1.48 (m, 2 H, 9-H_b, 10-H), 1.55 (d, J = 1.3 Hz, 3 H, 24-H), 1.61 (d, J = 1.3 Hz, 3 H, 26-H), 1.66 (d, J = 1.3 Hz, 3 H, 17-H), 1.71 (dddd, J = 14.1, 7.9, 7.9, 2.5 Hz, 1 H, 2-H_a), 1.89 (dqd, J = 12.5, 6.3, 4.6 Hz, 1 H, 8-H), 1.94 (dddd, J = 14.2, 11.1, 5.7, 5.0 Hz, 1 H, 2-H_b), 2.10 (ddq, J = 10.2, 7.2, 7.0 Hz, 1 H, 4-H), 3.20 (d, J = 10.2 Hz, 1 H, 5-H), 3.23 (ddq, J = 9.1, 8.7, 6.7 Hz, 1 H, 14-H), 3.30 (d, J = 9.8 Hz, 1 H, 11-H), 3.43 (s, 3 H, 19-H), 3.64–3.70 (m, 2 H, 1-H_a, 1-H_b), 3.80 (s, 3 H, ArOCH_3), 4.02 (ddd, J = 11.1, 7.2, 2.5 Hz, 1 H, 3-H), 4.46 (d, J = 11.5 Hz, 1 H, OCH_aH$_b$Ar), 4.49 (d, J = 11.5 Hz, 1 H, OCH$_a$$H_b$Ar), 4.91 (dqq, J = 8.7, 1.3, 1.3 Hz, 1 H, 15-H), 5.09 (dq, J = 9.0, 1.3 Hz, 1 H, 13-H), 6.86–6.90 (m, 2 H, *m*-H), 7.27–7.31 (m, 2 H, *o*-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.5 (C-24), 15.0 (C-18), 17.8 (C-23), 18.1 (C-26), 19.5 (C-20), 19.7 (C-22), 21.7 (C-25), 23.3 (C-21), 25.8 (C-17), 30.1 (C-2), 31.4 (C-14), 32.2 (C-10), 34.1 (C-8), 35.9 (C-4), 40.5 (C-9), 45.8 (C-6), 55.4 (ArOCH$_3$), 61.4 (C-19), 69.1 (C-1), 72.9 (OCH$_2$Ar), 73.7 (C-3), 83.3 (C-11), 84.6 (C-5), 104.0 (C-7), 113.9 (C-*m*), 129.5 (C-*o*), 129.6 (C-12), 129.9 (C-15), 131.0 (C-*i*), 131.7 (C-16), 134.0 (C-13), 159.2 (C-*p*) ppm. FTIR (ATR): $\tilde{\nu}$ = 2953 (s), 2922 (vs), 2852 (s), 1613 (w), 1513 (m), 1455 (m), 1377 (m), 1247 (s), 1082 (vs), 1038 (s), 1023 (s) 974 (m), 820 (w) cm^{-1}. MS (ESI): m/z = 543 [M + H]$^+$, 511, 493, 335, 235, 121 [$CH_2C_6H_4OMe$]$^+$. HRMS (ESI): calcd. for $C_{34}H_{54}O_5^+$ [M + H]$^+$ 543.4044; found 543.4039.

General Procedure for the Removal of the PMB Group: In analogy to ref.[27], a solution of DDQ (1.3 equiv.) in CH_2Cl_2 (0.6 mL) was added dropwise to a solution of **10** or **13a** (1.0 equiv.) in CH_2Cl_2/pH 7 buffer (8:1, 5.4 mL) at 0 °C under N_2. The reaction mixture was warmed to room temperature and stirred for a further 1 h. After dilution with CH_2Cl_2, the reaction was quenched by the addition of a sat. $NaHCO_3$ solution (10 mL). The aqueous layer was separated and extracted with EtOAc (3× 10 mL). The combined extracts were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The residue was purified by chromatography on SiO_2 with hexanes/EtOAc (15:1 or 10:1 for **13b**) to give the alcohol as a colorless oil.

(5*S*,6*S*,7*S*,10*R*,12*S*,13*S*)-7-Methoxy-5-(2-hydroxyethyl)-2,2,3,3,6,8,8,10,12,15,15,16,16-tridecamethyl-13-[(1*E*,3*S*)-1,3,5-tri-

methylhexa-1,4-dienyl]-4,14-dioxa-3,15-disilaheptadecan-9-one (10b′): From **10b** (47.1 mg, 59.7 μmol): yield: 30.4 mg (45.3 μmol, 76%). R_f = 0.15 (*n*-hexane/EtOAc, 6:1). $[\alpha]_D^{20}$ = –0.8 (*c* = 0.39, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.06 (s, 3 H, SiCH_3), 0.01 (s, 3 H, SiCH_3), 0.11 (s, 3 H, SiCH_3), 0.13 (s, 3 H, SiCH_3), 0.71 (d, *J* = 6.8 Hz, 3 H, 23-H), 0.75 (ddd, *J* = 13.6, 10.1, 4.3 Hz, 1 H, 9-H_a), 0.87 (d, *J* = 7.2 Hz, 3 H, 18-H), 0.89 [s, 9 H, SiC-(CH_3)$_3$], 0.91 [s, 9 H, SiC(CH_3)$_3$], 0.98 (d, *J* = 6.7 Hz, 3 H, 25-H), 1.02 (d, *J* = 6.8 Hz, 3 H, 22-H), 1.10 (s, 3 H, 21-H), 1.16 (s, 3 H, 20-H), 1.39 (ddqd, *J* = 10.1, 7.2, 6.8, 3.0 Hz, 1 H, 10-H), 1.51 (d, *J* = 1.3 Hz, 3 H, 24-H), 1.59 (d, *J* = 1.3 Hz, 3 H, 26-H), 1.64 (d, *J* = 1.3 Hz, 3 H, 17-H), 1.72 (qdd, *J* = 7.2, 4.7, 2.7 Hz, 1 H, 4-H), 1.81–1.85 (m, 2 H, 2-H_a, 2-H_b), 1.98 (m, 1 H, O*H*), 2.18 (ddd, *J* = 13.6, 9.0, 3.0 Hz, 1 H, 9-H_b), 3.03 (dqd, *J* = 9.0, 6.7, 4.4 Hz, 1 H, 8-H), 3.22 (ddq, *J* = 9.1, 8.7, 6.7 Hz, 1 H, 14-H), 3.29 (s, 3 H, 19-H), 3.47 (d, *J* = 7.2 Hz, 1 H, 11-H), 3.50 (d, *J* = 2.7 Hz, 1 H, 5-H), 3.56–3.62 (m, 1 H, 1-H_a), 3.66–3.72 (m, 1 H, 1-H_b), 3.89 (ddd, *J* = 5.9, 5.9, 4.7 Hz, 1 H, 3-H), 4.95 (dqq, *J* = 8.7, 1.3, 1.3 Hz, 1 H, 15-H), 5.08 (dq, *J* = 9.1, 1.3 Hz, 1 H, 13-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.9 (Si*C*H$_3$), –4.2 (Si*C*H$_3$), –4.0 (Si*C*H$_3$), –3.6 (Si*C*H$_3$), 9.6 (C-18), 11.9 (C-24), 16.9 (C-23), 18.1 (C-26), 18.3 [Si*C*(CH$_3$)$_3$], 18.4 [Si*C*(CH$_3$)$_3$], 19.8 (C-22), 20.8 (C-20), 21.47 (C-25), 21.53 (C-21), 25.8 (C-17), 26.1 [SiC(*C*H$_3$)$_3$], 26.2 [SiC(*C*H$_3$)$_3$], 31.5 (C-14), 35.4 (C-10), 37.17 (C-9), 37.19 (C-2), 38.8 (C-4), 39.1 (C-8), 54.2 (C-6), 60.0 (C-1), 60.4 (C-19), 74.0 (C-3), 83.5 (C-11), 85.2 (C-5), 129.7 (C-12), 129.9 (C-15), 132.5 (C-13), 133.7 (C-16), 220.1 (C-7) ppm. FTIR (ATR): ṽ = 2956 (m), 2929 (m), 2857 (m), 1698 (m), 1472 (m), 1386 (m), 1252 (m), 1105 (m), 1066 (s), 1004 (s), 863 (m), 833 (vs), 772 (vs) cm^{-1}. MS (ESI): *m*/*z* = 692 [M + Na]$^+$, 559, 431. HRMS (ESI): calcd. for $C_{38}H_{76}NaO_5Si_2^+$ [M + Na]$^+$ 691.5123; found 691.5133.

2-{(2*S*,3*R*,4*S*,6*R*,8*S*,9*S*,11*R*)-4-Methoxy-3,5,5,9,11-pentamethyl-8-[(1*E*,3*S*)-1,3,5-trimethylhexa-1,4-dienyl]-1,7-dioxaspiro[5.5]undecan-2-yl}ethanol (13b): From **13a** (7.0 mg, 12.9 μmol); yield: 4.5 mg (10.6 μmol, 82%), colorless oil (>95% purity by ^{1}H NMR). R_f = 0.43 (*n*-hexane/EtOAc, 2:1). $[\alpha]_D^{20}$ = +50.0 (*c* = 0.23, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.62 (d, *J* = 6.5 Hz, 3 H, 23-H), 0.96 (d, *J* = 7.0 Hz, 3 H, 18-H), 0.97 (d, *J* = 6.5 Hz, 3 H, 22-H), 0.98 (d, *J* = 6.7 Hz, 3 H, 25-H), 1.03 (s, 3 H, 20-H), 1.10 (s, 3 H, 21-H), 1.15 (ddd, *J* = 13.0, 12.6, 11.3 Hz, 1 H, 9-H_a), 1.48–1.52 (m, 1 H, 9-H_b), 1.50–1.53 (m, 1 H, 10-H), 1.52–1.57 (m, 1 H, 2-H_a), 1.58 (d, *J* = 1.4 Hz, 3 H, 24-H), 1.62 (d, *J* = 1.3 Hz, 3 H, 26-H), 1.65 (d, *J* = 1.3 Hz, 3 H, 17-H), 1.95 (dqd, *J* = 12.6, 6.5, 4.7 Hz, 1 H, 8-H), 1.98–2.04 (m, 1 H, 2-H_b), 2.05 (dqd, *J* = 8.6, 7.0, 6.6 Hz, 1 H, 4-H), 2.11 (br. s, 1 H, O*H*), 3.17 (d, *J* = 8.6 Hz, 1 H, 5-H), 3.25 (ddq, *J* = 9.0, 8.7, 6.7 Hz, 1 H, 14-H), 3.42 (s, 3 H, 19-H), 3.50 (d, *J* = 10.0 Hz, 1 H, 11-H), 3.85–3.89 (m, 2 H, 1-H_a, 1-H_b), 4.16 (ddd, *J* = 11.2, 6.6, 2.0 Hz, 1 H, 3-H), 4.94 (dqq, *J* = 8.7, 1.3, 1.3 Hz, 1 H, 15-H), 5.12 (dq, *J* = 9.0, 1.4 Hz, 1 H, 13-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.5 (C-24), 15.5 (C-18), 17.6 (C-23), 18.1 (C-26), 19.58 (C-22), 19.62 (C-20), 21.8 (C-25), 23.7 (C-21), 25.8 (C-17), 31.4 (C-14), 32.2 (C-10), 32.8 (C-2), 34.1 (C-8), 36.6 (C-4), 40.5 (C-9), 45.4 (C-6), 60.7 (C-19), 62.7 (C-1), 75.3 (C-3), 83.1 (C-11), 85.1 (C-5), 104.1 (C-7), 129.7 (C-15), 129.8 (C-12), 131.7 (C-16), 134.1 (C-13) ppm. FTIR (ATR): ṽ = 3390 (w), 2964 (s), 2923 (vs), 1454 (m), 1378 (m), 1082 (vs), 1068 (vs), 975 (m) cm^{-1}. MS (CI): *m*/*z* (%) = 423 (20) [M + H]$^+$, 391 (13), 251 (15), 228 (100), 164 (29), 121 (38) [$CH_2C_6H_4OMe$]$^+$, 86 (24). HRMS (ESI): calcd. for $C_{26}H_{46}NaO_4^+$ [M + Na]$^+$ 445.3288; found 445.3292.

General Procedure for the Synthesis of Methyl 3,11-Bis{[*tert*-butyl-(dimethyl)silyl]oxy}-5-methoxy-4,6,6,8,10,12,14,16-octamethyl-7-oxoheptadeca-12,15-dienoates (14): Analogous to ref.[18], DMSO (3.0 equiv.) was added dropwise to a solution of oxalyl chloride (2.0 equiv.) in CH_2Cl_2 (6 mL) under N_2 at –78 °C and the reaction mixture stirred for 30 min. Then a solution of the respective alcohol (41 or 236 μmol, 1.0 equiv.) in CH_2Cl_2 (1 mL) was added dropwise over 2 min and the reaction mixture was stirred for a further 30 min. After dropwise addition of NEt_3 (6.0 equiv.), the reaction mixture was warmed to room temperature. The reaction was quenched by the addition of H_2O and the aqueous layer was separated and extracted with Et_2O (3 × 5 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated to give the intermediate aldehyde as a colorless oil, which was treated without further purification.

Analogous to ref.[18,34], 2-methyl-2-butene (4.5 equiv.) and KH_2PO_4 (7.0 equiv.) were added to a solution of the freshly prepared aldehyde (1.0 equiv.) in *t*BuOH/H_2O (4:1, 6 mL) at room temperature followed by the dropwise addition of a solution of $NaClO_2$ (2.5 equiv.) in H_2O (0.4 mL) and the reaction mixture was stirred for 1 h. The reaction was quenched by the addition of a sat. NH_4Cl solution (5 mL) and the aqueous layer was separated and extracted with CH_2Cl_2 (5 × 5 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated to give the intermediate carboxylic acid, which was treated without further purification.

Analogous to ref.[18,35], a 2 M solution of $TMSCHN_2$ in hexane (2.0 equiv.) was added dropwise to a solution of the carboxylic acid (1.0 equiv.) in CH_2Cl_2/MeOH (4:1, 5 mL) under N_2 at room temperature and the reaction mixture was stirred for 1 h. The solvent was removed and the crude product purified by chromatography on SiO_2 (hexanes/EtOAc, 50:1).

Methyl (3*S*,4*S*,5*S*,8*R*,10*S*,11*S*,12*E*,14*S*)-3,11-Bis{[*tert*-butyl(dimethyl)silyl]oxy}-5-methoxy-4,6,6,8,10,12,14,16-octamethyl-7-oxoheptadeca-12,15-dienoate [(8*R*)-14b]: From the respective alcohol (27.5 mg, 41.1 μmol); yield: 26.3 mg (37.8 μmol, 92%), colorless oil. R_f = 0.43 (*n*-hexane/EtOAc, 6:1). $[\alpha]_D^{20}$ = –6.2 (*c* = 1.00, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = –0.06 (s, 3 H, SiCH_3), 0.01 (s, 3 H, SiCH_3), 0.08 (s, 3 H, SiCH_3), 0.13 (s, 3 H, SiCH_3), 0.71 (d, *J* = 6.8 Hz, 3 H, 23-H), 0.75 (ddd, *J* = 13.6, 10.2, 4.6 Hz, 1 H, 9-H_a), 0.887 [s, 9 H, SiC(CH_3)$_3$], 0.890 (d, *J* = 7.2 Hz, 3 H, 18-H), 0.892 [s, 9 H, SiC(CH_3)$_3$], 0.98 (d, *J* = 6.8 Hz, 3 H, 25-H), 1.02 (d, *J* = 6.8 Hz, 3 H, 22-H), 1.05 (s, 3 H, 21-H), 1.17 (s, 3 H, 20-H), 1.45 (ddqd, *J* = 10.2, 7.1, 6.6, 3.2 Hz, 1 H, 10-H), 1.52 (d, *J* = 1.4 Hz, 3 H, 24-H), 1.60 (d, *J* = 1.4 Hz, 3 H, 26-H), 1.65 (d, *J* = 1.4 Hz, 3 H, 17-H), 1.80 (qdd, *J* = 7.2, 4.3, 3.3 Hz, 1 H, 4-H), 2.16 (ddd, *J* = 13.6, 8.6, 3.2 Hz, 1 H, 9-H_b), 2.48 (dd, *J* = 15.2, 5.6 Hz, 1 H, 2-H_a), 2.63 (dd, *J* = 15.2, 7.2 Hz, 1 H, 2-H_b), 3.02 (dqd, *J* = 8.6, 6.7, 4.6 Hz, 1 H, 8-H), 3.22 (ddq, *J* = 9.3, 8.7, 6.7 Hz, 1 H, 14-H), 3.24 (s, 3 H, 19-H), 3.49 (d, *J* = 7.1 Hz, 1 H, 11-H), 3.54 (d, *J* = 3.3 Hz, 1 H, 5-H), 3.66 (s, 3 H, CO_2CH_3), 4.05 (ddd, *J* = 7.2, 5.6, 4.3 Hz, 1 H, 3-H), 4.95 (dqq, *J* = 8.7, 1.4, 1.4 Hz, 1 H, 15-H), 5.08 (dq, *J* = 9.3, 1.4 Hz, 1 H, 13-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.9 (Si*C*H$_3$), –4.5 (Si*C*H$_3$), –4.2 (Si*C*H$_3$), –3.7 (Si*C*H$_3$), 9.2 (C-18), 11.9 (C-24), 16.9 (C-23), 18.1 [Si*C*(CH$_3$)$_3$], 18.2 (C-18), 18.4 [Si*C*(CH$_3$)$_3$], 19.3 (C-20), 20.0 (C-22), 21.5 (C-25), 23.0 (C-21), 25.8 (C-17), 26.09 [SiC(*C*H$_3$)$_3$], 26.11 [SiC(*C*H$_3$)$_3$], 31.5 (C-14), 35.4 (C-10), 37.1 (C-9), 39.1 (C-8), 39.4 (C-4), 40.7 (C-2), 51.7 (CO_2CH_3), 53.5 (C-6), 60.1 (C-19), 72.8 (C-3), 83.6 (C-11), 84.7 (C-5), 129.7 (C-12), 129.9 (C-15), 132.4 (C-13), 133.7 (C-16), 172.3 (C-1), 219.3 (C-7) ppm. FTIR (ATR): ṽ = 2956 (m), 2929 (m), 2857 (m), 1741 (m), 1699 (m), 1472 (m), 1462 (m), 1387 (w), 1253 (m), 1098 (m), 1067 (s), 1020 (m), 835 (vs), 773 (vs) cm^{-1}. MS (ESI): *m*/*z* = 720 [M + Na]$^+$, 565, 433, 289, 157, 115. HRMS (ESI): calcd. for $C_{39}H_{76}NaO_6Si_2^+$ [M + Na]$^+$ 719.5073; found 719.5055.

General Procedure for the Synthesis of Methyl 3,11-Dihydroxy-5-methoxy-4,6,6,8,10,12,14,16-octamethyl-7-oxoheptadeca-12,15-dien-

oates (15): NEt_3 (3.60 mL) and $3HF{\cdot}NEt_3$ (3.30 mL) were added to a solution of **14** (1.0 equiv.) in abs. MeCN (7.5 mL) at room temperature under N_2 in a Teflon vessel and the reaction mixture was stirred for 7 d. Then it was poured into a sat. solution of $NaHCO_3$ (40 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (4 × 25 mL). The combined organic extracts were dried ($MgSO_4$), concentrated, and the residue purified by flash chromatography on SiO_2 (hexanes/EtOAc/Et_3N, 80:19:1) to give **15** and mono-deprotected product **16**, which was treated under the same conditions to give **15**.

Methyl (3*S*,4*R*,5*S*,8*R*,10*S*,11*S*,12*E*,14*S*)-3,11-Dihydroxy-5-methoxy-4,6,6,8,10,12,14,16-octamethyl-7-oxoheptadeca-12,15-dienoate [(8*R*)-15b]: From (8*R*)-**14b** (22.8 mg, 32.7 μmol); yield: 10.4 mg (22.2 μmol, 68%), colorless oil. R_f = 0.30 (*n*-hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = +4.6 (*c* = 0.35, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.75 (d, *J* = 6.8 Hz, 3 H, 23-H), 0.95 (d, *J* = 7.1 Hz, 3 H, 18-H), 0.96 (ddd, *J* = 13.6, 8.6, 5.1 Hz, 1 H, 9-H_a), 0.99 (d, *J* = 6.7 Hz, 3 H, 25-H), 1.09 (d, *J* = 6.8 Hz, 3 H, 22-H), 1.15 (s, 3 H, 20-H), 1.19 (s, 3 H, 21-H), 1.38 (ddqd, *J* = 8.6, 8.2, 6.8, 3.4 Hz, 1 H, 10-H), 1.559 (qdd, *J* = 7.2, 4.3, 3.3 Hz, 1 H, 4-H), 1.563 (d, *J* = 1.4 Hz, 3 H, 24-H), 1.61 (d, *J* = 1.4 Hz, 3 H, 26-H), 1.65 (d, *J* = 1.4 Hz, 3 H, 17-H), 1.74 (d, *J* = 3.2 Hz, 1 H, O*H*), 2.10 (ddd, *J* = 13.6, 9.0, 3.4 Hz, 1 H, 9-H_b), 2.44 (dd, *J* = 16.0, 3.7 Hz, 1 H, 2-H_a), 2.53 (dd, *J* = 16.0, 9.2 Hz, 1 H, 2-H_b), 3.02 (d, *J* = 3.6 Hz, 1 H, O*H*), 3.18 (dqd, *J* = 9.0, 6.9, 5.1 Hz, 1 H, 8-H), 3.24 (ddq, *J* = 9.0, 8.9, 6.7 Hz, 1 H, 14-H), 3.39 (s, 3 H, 19-H), 3.56 (dd, *J* = 8.2, 3.2 Hz, 1 H, 11-H), 3.58 (d, *J* = 4.3 Hz, 1 H, 5-H), 3.69 (s, 3 H, CO_2CH_3), 3.91 (dddd, *J* = 9.2, 3.7, 3.6, 3.3 Hz, 1 H, 3-H), 4.95 (dqq, *J* = 8.9, 1.4, 1.4 Hz, 1 H, 15-H), 5.19 (dq, *J* = 9.0, 1.4 Hz, 1 H, 13-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 9.1 (C-18), 11.6 (C-24), 17.7 (C-23), 18.1 (C-26), 19.5 (C-22), 20.0 (C-20), 21.76 (C-21), 21.79 (C-25), 25.8 (C-17), 31.6 (C-14), 34.5 (C-10), 37.8 (C-9), 39.4 (C-2), 39.7 (C-8), 40.6 (C-4), 51.9 (CO_2CH_3), 53.9 (C-6), 60.9 (C-19), 70.2 (C-3), 83.5 (C-11), 86.0 (C-5), 129.6 (C-15), 129.9 (C-12), 133.3 (C-13), 133.8 (C-16), 173.4 (C-1), 220.9 (C-7) ppm. FTIR (ATR): ṽ = 3467 (w), 2966 (s), 2927 (s), 2875 (m), 1737 (s), 1696 (s), 1439 (s), 1376 (m), 1170 (s), 1098 (s), 990 (vs) cm^{-1}. MS (ESI): *m*/*z* = 491 [M + Na]$^+$, 451, 433, 157, 102. HRMS (ESI): calcd. for $C_{27}H_{48}NaO_6^+$ [M + Na]$^+$ 491.3343; found 491.3349.

General Procedure for the Preparation of Epoxides 12 and 17: In analogy to ref.[36], a 5.5 M solution of *t*BuOOH in nonane (1.5 equiv.) was added dropwise under N_2 to a solution of Ti(O*i*Pr)$_4$ (0.2 equiv.) in abs. CH_2Cl_2 (4.0 mL) and 4 Å mol. sieves (10 pellets) at –20 °C and the reaction mixture was stirred for 30 min. Then a solution of **11a/11b** or the respective **15** (1.0 equiv.) in CH_2Cl_2 (1.0 mL) was added dropwise and the reaction mixture stirred for a further 14 h. After the addition of a sat. $FeSO_4$ solution (5 mL), the reaction mixture was warmed to room temperature. The aqueous layer was separated and extracted with CH_2Cl_2 (4 × 5 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. The diastereomeric mixture of **12a/12c/12b/12d** (7:8:38:47, by ^{1}H NMR) was separated by preparative HPLC (Kromasil, 100 Sil 5 μm, *n*-hexane/EtOAc/Et_3N, 95:4:1, flow 10 mL min^{-1}). The crude diastereomeric epoxides **17** were purified by chromatography on SiO_2 (hexanes/EtOAc/Et_3N, 75:24:1 → 50:49:1).

(1*S*,2*S*,7*S*,8*R*,9*S*)-1,9-Dihydroxy-7-methoxy-11-[(4-methoxybenzyl)oxy]-2,4,6,6,8-pentamethyl-1-{2-methyl-3-[(*S*)-4-methylpent-3-en-2-yl]oxiran-2-yl}undecan-5-one (12): From **11a/11b** (*dr* = 15:85, 62.5 mg, 111.4 μmol), *t*BuOOH in nonane (30.0 μL, 167.2 μmol), and Ti(O*i*Pr)$_4$ (9.9 μL, 33.4 μmol) was obtained **12a** (3.2 mg, 5.6 μmol, 5%), **12c** (3.8 mg, 6.7 μmol, 6%), **12b** (21.8 mg, 37.9 μmol, 34%), and **12d** (26.9 mg, 46.8 μmol, 42%) as colorless oils (ca. 95% purity by ^{1}H NMR).

(8*S*)-12a: R_f = 0.33 (*n*-hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = +36.1 (*c* = 0.18, CH_2Cl_2). ^{1}H NMR (500 MHz, CD_3OD): δ = 0.81 (d, *J* = 6.8 Hz, 3 H, 23-H), 0.88 (d, *J* = 7.2 Hz, 3 H, 18-H), 0.98 (d, *J* = 6.6 Hz, 3 H, 22-H), 1.06 (d, *J* = 6.6 Hz, 3 H, 25-H), 1.07 (s, 3 H, 21-H), 1.13 (ddd, *J* = 13.7, 10.0, 3.5 Hz, 1 H, 9-H_a), 1.17 (s, 3 H, 20-H), 1.23 (s, 3 H, 24-H), 1.53 (ddqd, *J* = 10.0, 9.4, 6.6, 3.1 Hz, 1 H, 10-H), 1.65–1.72 (m, 2 H, 2-H_a, 4-H), 1.65 (d, *J* = 1.4 Hz, 3 H, 26-H), 1.69 (d, *J* = 1.4 Hz, 3 H, 17-H), 1.74 (ddd, *J* = 13.7, 10.7, 3.0 Hz, 1 H, 9-H_b), 1.76–1.82 (m, 1 H, 2-H_b), 2.34 (ddq, *J* = 10.0, 9.2, 6.6 Hz, 1 H, 14-H), 2.58 (d, *J* = 9.2 Hz, 1 H, 13-H), 2.63 (d, *J* = 9.4 Hz, 1 H, 11-H), 3.18 (dqd, *J* = 10.3, 6.7, 3.6 Hz, 1 H, 8-H), 3.29 (s, 3 H, 19-H), 3.48 (d, *J* = 3.0 Hz, 1 H, 5-H), 3.57–3.62 (m, 2 H, 1-H_a, 1-H_b), 3.64 (ddd, *J* = 8.9, 4.0, 3.9 Hz, 1 H, 3-H), 3.78 (s, 3 H, ArOC*H*$_3$), 4.43 (s, 2 H, OC*H*$_2$Ar), 4.99 (dqq, *J* = 10.0, 1.4, 1.4 Hz, 1 H, 15-H), 6.87–6.90 (m, 2 H, *m*-H), 7.25–7.28 (m, 2 H, *o*-H) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 9.0 (C-18), 11.9 (C-24), 16.1 (C-23), 16.7 (C-22), 18.5 (C-26), 19.1 (C-25), 20.3 (C-20), 22.0 (C-21), 26.0 (C-17), 33.7 (C-14), 35.2 (C-10), 36.2 (C-2), 38.4 (C-9), 39.3 (C-8), 41.2 (C-4), 55.4 (C-6), 55.8 (ArO*C*H$_3$), 60.5 (C-19), 65.4 (C-12), 68.8 (C-1), 68.9 (C-13), 73.4 (C-3), 73.8 (O*C*H$_2$Ar), 83.4 (C-11), 88.2 (C-5), 114.8 (C-*m*), 126.6 (C-15), 130.5 (C-*o*), 131.8 (C-*i*), 133.2 (C-16), 160.8 (C-*p*), 222.2 (C-7) ppm. FTIR (ATR): ṽ = 3465 (w), 2965 (m), 2926 (s), 2856 (m), 1695 (m), 1613 (m), 1513 (s), 1456 (s), 1384 (m), 1247 (vs), 1096 (vs), 1033 (vs), 995 (m), 821 (m) cm^{-1}. MS (APCI): *m*/*z* (%) = 559 (100) [M – OH]$^+$, 541 (21), 527 (11), 447 (13), 413 (9), 389 (41). HRMS (APCI): calcd. for $C_{34}H_{54}O_6^+$ [M – OH]$^+$ 559.3993; found 559.3986.

(8*S*)-12c: R_f = 0.46 (*n*-hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = +14.4 (*c* = 0.17, CH_2Cl_2). ^{1}H NMR (500 MHz, CD_3OD): δ = 0.89 (d, *J* = 7.2 Hz, 3 H, 18-H), 0.99 (d, *J* = 6.7 Hz, 3 H, 22-H), 1.00 (d, *J* = 6.8 Hz, 3 H, 23-H), 1.01 (d, *J* = 7.1 Hz, 3 H, 25-H), 1.07 (s, 3 H, 21-H), 1.17 (s, 3 H, 20-H), 1.25 (ddd, *J* = 13.6, 11.0, 2.9 Hz, 1 H, 9-H_a), 1.31 (s, 3 H, 24-H), 1.53 (ddd, *J* = 13.6, 11.1, 3.0 Hz, 1 H, 9-H_b), 1.63 (d, *J* = 1.4 Hz, 3 H, 26-H), 1.64–1.73 (m, 2 H, 2-H_a, 4-H), 1.71 (d, *J* = 1.4 Hz, 3 H, 17-H), 1.75–1.80 (m, 1 H, 2-H_b), 1.83 (dqdd, *J* = 11.0, 6.6, 6.0, 3.0 Hz, 1 H, 10-H), 2.36 (ddq, *J* = 9.1, 9.1, 6.8 Hz, 1 H, 14-H), 2.69 (d, *J* = 9.1 Hz, 1 H, 13-H), 3.06 (d, *J* = 6.0 Hz, 1 H, 11-H), 3.15 (dqd, *J* = 11.1, 6.6, 3.1 Hz, 1 H, 8-H), 3.31 (s, 3 H, 19-H), 3.47 (d, *J* = 3.0 Hz, 1 H, 5-H), 3.58–3.62 (m, 2 H, 1-H_a, 1-H_b), 3.64 (ddd, *J* = 9.1, 3.9, 3.9 Hz, 1 H, 3-H), 3.78 (s, 3 H, ArO*C*H$_3$), 4.44 (s, 2 H, OC*H*$_2$Ar), 5.08 (dqq, *J* = 9.1, 1.4, 1.4 Hz, 1 H, 15-H), 6.87–6.90 (m, 2 H, *m*-H), 7.25–7.28 (m, 2 H, *o*-H) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 9.0 (C-18), 13.8 (C-24), 16.3 (C-23), 16.5 (C-22), 17.8 (C-25), 18.3 (C-26), 20.2 (C-20), 22.0 (C-21), 26.0 (C-17), 33.4 (C-14), 33.7 (C-10), 36.1 (C-9), 36.2 (C-2), 39.0 (C-8), 41.2 (C-4), 55.3 (C-6), 55.7 (ArO*C*H$_3$), 60.5 (C-19), 63.7 (C-12), 66.4 (C-13), 68.8 (C-1), 73.3 (C-3), 73.8 (O*C*H$_2$Ar), 80.1 (C-11), 88.2 (C-5), 114.8 (C-*m*), 128.6 (C-15), 130.5 (C-*o*), 131.7 (C-*i*), 133.4 (C-16), 160.8 (C-*p*), 222.0 (C-7) ppm. FTIR (ATR): ṽ = 3486 (w), 2964 (m), 2930 (m), 2873 (m), 1696 (m), 1613 (m), 1513 (m), 1456 (m), 1384 (m), 1247 (vs), 1095 (vs), 1035 (s), 987 (m), 821 (m) cm^{-1}. MS (APCI): *m*/*z* (%) = 559 (100) [M – OH]$^+$, 541 (26), 527 (9), 389 (16), 361 (9). HRMS (APCI): calcd. for $C_{34}H_{54}O_6^+$ [M – OH]$^+$ 559.3993; found 559.3984.

(8*R*)-12b: R_f = 0.34 (*n*-hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = +19.4 (*c* = 0.57, CH_2Cl_2). ^{1}H NMR (500 MHz, CD_3OD): δ = 0.81 (d, *J* = 6.8 Hz, 3 H, 23-H), 0.89 (d, *J* = 7.2 Hz, 3 H, 18-H), 0.92 (ddd, *J* = 13.7, 8.4, 5.8 Hz, 1 H, 9-H_a), 1.03 (d, *J* = 6.8 Hz, 3 H, 22-H), 1.062 (s, 3 H, 21-H), 1.063 (d, *J* = 6.6 Hz, 3 H, 25-H), 1.18 (s, 3 H, 20-H),

1.22 (s, 3 H, 24-H), 1.43 (ddqd, J = 9.2, 8.4, 6.7, 4.1 Hz, 1 H, 10-H), 1.63 (d, J = 1.4 Hz, 3 H, 26-H), 1.67 (qdd, J = 7.2, 3.9, 3.0 Hz, 1 H, 4-H), 1.69 (d, J = 1.4 Hz, 3 H, 17-H), 1.69 (dddd, J = 14.1, 9.0, 5.6, 5.6 Hz, 1 H, 2-H_a), 1.79 (dddd, J = 14.1, 7.6, 6.3, 4.0 Hz, 1 H, 2-H_b), 2.11 (ddd, J = 13.7, 8.0, 4.1 Hz, 1 H, 9-H_b), 2.34 (ddq, J = 10.0, 9.3, 6.6 Hz, 1 H, 14-H), 2.60 (d, J = 9.3 Hz, 1 H, 13-H), 2.67 (d, J = 9.2 Hz, 1 H, 11-H), 3.26 (dqd, J = 8.0, 6.8, 5.8 Hz, 1 H, 8-H), 3.29 (s, 3 H, 19-H), 3.55 (d, J = 3.0 Hz, 1 H, 5-H), 3.57–3.62 (m, 2 H, 1-H_a, 1-H_b), 3.64 (ddd, J = 9.0, 4.0, 3.9 Hz, 1 H, 3-H), 3.78 (s, 3 H, ArOCH_3), 4.43 (s, 2 H, OCH_2Ar), 5.00 (dqq, J = 10.0, 1.4, 1.4 Hz, 1 H, 15-H), 6.88–6.91 (m, 2 H, m-H), 7.25–7.28 (m, 2 H, o-H) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 8.9 (C-18), 12.1 (C-24), 17.2 (C-23), 18.5 (C-26), 19.1 (C-25), 19.5 (C-22), 19.9 (C-20), 22.3 (C-21), 26.0 (C-17), 33.7 (C-14), 35.5 (C-10), 36.2 (C-2), 39.7 (C-9), 40.2 (C-8), 41.2 (C-4), 55.0 (C-6), 55.8 (ArOCH_3), 60.3 (C-19), 65.4 (C-12), 68.8 (C-13), 68.9 (C-1), 73.3 (C-3), 73.8 (OCH_2Ar), 83.9 (C-11), 87.9 (C-5), 114.8 (C-m), 126.5 (C-15), 130.6 (C-o), 131.7 (C-i), 133.1 (C-16), 160.8 (C-p), 222.4 (C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 3471 (w), 2969 (m), 2931 (s), 2871 (m), 1695 (m), 1613 (m), 1513 (s), 1456 (s), 1385 (m), 1246 (vs), 1096 (vs), 1034 (vs), 994 (m), 821 (m), 736 (m) cm^{-1}. MS (APCI): m/z (%) = 594 (11) $[M + NH_4]^+$, 559 (100) $[M - OH]^+$, 541 (22), 527 (36), 447 (13), 423 (11), 389 (100), 371 (22). HRMS (APCI): calcd. for $C_{34}H_{54}O_6^+$ $[M - OH]^+$ 559.3993; found 559.3987.

(8*R*)-12d: R_f = 0.58 (*n*-hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = +11.3 (c = 0.34, CH_2Cl_2). ^{1}H NMR (500 MHz, CD_3OD): δ = 0.90 (d, J = 7.2 Hz, 3 H, 18-H), 0.95–1.03 (m, 1 H, 9-H_a), 0.99 (d, J = 6.8 Hz, 3 H, 23-H), 1.01 (d, J = 6.8 Hz, 3 H, 22-H), 1.07 (s, 3 H, 21-H), 1.08 (d, J = 6.9 Hz, 3 H, 25-H), 1.20 (s, 3 H, 20-H), 1.31 (s, 3 H, 24-H), 1.56 (dqdd, J = 10.5, 6.8, 4.8, 3.0 Hz, 1 H, 10-H), 1.64 (d, J = 1.3 Hz, 3 H, 26-H), 1.62–1.67 (m, 1 H, 4-H), 1.71 (d, J = 1.3 Hz, 3 H, 17-H), 1.67–1.72 (m, 1 H, 2-H_a), 1.79 (dddd, J = 14.0, 6.9, 6.9, 4.0 Hz, 1 H, 2-H_b), 2.01 (ddd, J = 13.5, 10.2, 3.0 Hz, 1 H, 9-H_b), 2.40 (ddq, J = 9.2, 9.1, 6.9 Hz, 1 H, 14-H), 2.82 (d, J = 9.2 Hz, 1 H, 13-H), 3.170 (dqd, J = 9.5, 6.8, 4.3 Hz, 1 H, 8-H), 3.171 (d, J = 4.8 Hz, 1 H, 11-H), 3.30 (s, 3 H, 19-H), 3.56 (d, J = 2.9 Hz, 1 H, 5-H), 3.54–3.61 (m, 2 H, 1-H_a, 1-H_b), 3.65 (ddd, J = 8.9, 3.9, 3.9 Hz, 1 H, 3-H), 3.78 (s, 3 H, ArOCH_3), 4.43 (s, 2 H, OCH_2Ar), 5.11 (dqq, J = 9.1, 1.3, 1.3 Hz, 1 H, 15-H), 6.87–6.90 (m, 2 H, m-H), 7.24–7.27 (m, 2 H, o-H) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 8.9 (C-18), 14.5 (C-24), 17.5 (C-23), 17.7 (C-25), 18.4 (C-26), 20.0 (C-20), 20.2 (C-22), 22.2 (C-21), 26.0 (C-17), 33.6 (C-14), 34.0 (C-10), 36.2 (C-2), 36.6 (C-9), 40.0 (C-8), 41.3 (C-4), 54.8 (C-6), 55.7 (ArOCH_3), 60.3 (C-19), 64.1 (C-12), 65.9 (C-13), 68.7 (C-1), 73.3 (C-3), 73.7 (OCH_2Ar), 79.7 (C-11), 88.0 (C-5), 114.8 (C-m), 128.8 (C-15), 130.5 (C-o), 131.7 (C-i), 133.3 (C-6), 160.8 (C-p), 222.1 (C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 3479 (w), 2966 (s), 2928 (s), 2873 (m), 1694 (m), 1613 (w), 1513 (s), 1457 (s), 1384 (m), 1247 (vs), 1096 (vs), 1035 (s), 997 (s), 820 (m) cm^{-1}. MS (ESI): m/z = 599 $[M + Na]^+$, 487, 459, 333, 245, 121 $[CH_2C_6H_4OMe]^+$. HRMS (ESI): calcd. for $C_{34}H_{56}NaO_7^+$ $[M + Na]^+$ 599.3918; found 599.3922.

Methyl (3*S*,4*R*,5*S*,8*R*,10*S*,11*S*)-3,11-Dihydroxy-5-methoxy-4,6,6,8,10-pentamethyl-11-{(2*R*,3*R*)-2-methyl-3-[(*S*)-4-methylpent-3-en-2-yl]oxiran-2-yl}-7-oxoundecanoate [(8*R*)-17b]: From **15b** (7.1 mg, 15.1 μmol); yield: 3.7 mg (7.6 μmol, 50%), colorless oil. R_f = 0.26 (*n*-hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = +18.4 (c = 0.14, MeOH). ^{1}H NMR (500 MHz, CD_3OD): δ = 0.82 (d, J = 6.8 Hz, 3 H, 23-H), 0.90 (d, J = 7.2 Hz, 3 H, 18-H), 0.93 (ddd, J = 13.6, 8.4, 5.9 Hz, 1 H, 9-H_a), 1.05 (d, J = 6.8 Hz, 3 H, 22-H), 1.07 (d, J = 6.6 Hz, 3 H, 25-H), 1.09 (s, 3 H, 21-H), 1.19 (s, 3 H, 20-H), 1.23 (s, 3 H, 24-H), 1.43 (ddqd, J = 9.2, 8.4, 6.8, 4.0 Hz, 1 H, 10-H), 1.64 (d, J = 1.3 Hz, 3 H, 26-H), 1.66–1.73 (m, 1 H, 4-H), 1.70 (d, J = 1.4 Hz, 3 H, 17-H), 2.12 (ddd, J = 13.6, 8.0, 4.0 Hz, 1 H, 9-H_b), 2.34 (ddq, J = 10.0, 9.2, 6.6 Hz, 1 H, 14-H), 2.48 (dd, J = 15.1, 8.8 Hz, 1 H, 2-H_a), 2.55 (dd, J = 15.1, 4.8 Hz, 1 H, 2-H_b), 2.61 (d, J = 9.2 Hz, 1 H, 13-H), 2.68 (d, J = 9.2 Hz, 1 H, 11-H), 3.28 (dqd, J = 8.0, 6.8, 5.9 Hz, 1 H, 8-H), 3.30 (s, 3 H, 19-H), 3.54 (d, J = 2.8 Hz, 1 H, 5-H), 3.68 (s, 3 H, CO_2CH_3), 3.98 (ddd, J = 8.8, 4.8, 3.9 Hz, 1 H, 3-H), 5.01 (dqq, J = 10.0, 1.4, 1.3 Hz, 1 H, 15-H) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 8.8 (C-18), 12.0 (C-24), 17.2 (C-23), 18.4 (C-26), 19.0 (C-25), 19.5 (C-22), 19.9 (C-20), 22.0 (C-21), 25.9 (C-17), 33.7 (C-14), 35.5 (C-10), 39.7 (C-9), 40.2 (C-8), 40.9 (C-4), 41.3 (C-2), 52.1 (CO_2CH_3), 55.0 (C-6), 60.3 (C-19), 65.3 (C-12), 68.8 (C-13), 72.7 (C-3), 83.9 (C-11), 87.7 (C-5), 126.6 (C-15), 133.1 (C-16), 174.1 (C-1), 222.0 (C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 3490 (w), 2969 (m), 2930 (m), 1734 (m), 1696 (m), 1456 (s), 1385 (m), 1251 (m), 1170 (m), 1096 (s), 1047 (s), 989 (vs) cm^{-1}. MS (ESI): m/z = 507 $[M + Na]^+$, 467, 102. HRMS (ESI): calcd. for $C_{27}H_{48}NaO_7^+$ $[M + Na]^+$ 507.3292; found 507.3296.

(8*R*)-17d: Yield: 3.0 mg (6.2 μmol, 41%), colorless oil. R_f = 0.42 (*n*-hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = +4.2 (c = 0.12, MeOH). ^{1}H NMR (500 MHz, CD_3OD): δ = 0.91 (d, J = 7.2 Hz, 3 H, 18-H), 0.97–1.01 (m, 1 H, 9-H_a), 1.00 (d, J = 6.8 Hz, 3 H, 23-H), 1.03 (d, J = 6.8 Hz, 3 H, 22-H), 1.101 (s, 3 H, 20-H), 1.103 (d, J = 6.8 Hz, 3 H, 25-H), 1.21 (s, 3 H, 21-H), 1.32 (s, 3 H, 24-H), 1.52–1.61 (m, 1 H, 10-H), 1.65 (d, J = 1.3 Hz, 3 H, 26-H), 1.69 (qdd, J = 7.2, 3.9, 2.9 Hz, 1 H, 4-H), 1.72 (d, J = 1.3 Hz, 3 H, 17-H), 2.02 (ddd, J = 13.3, 10.3, 2.9 Hz, 1 H, 9-H_b), 2.42 (ddq, J = 9.2, 9.1, 6.9 Hz, 1 H, 14-H), 2.48 (dd, J = 15.1, 8.6 Hz, 1 H, 2-H_a), 2.56 (dd, J = 15.1, 4.8 Hz, 1 H, 2-H_b), 2.83 (d, J = 9.1 Hz, 1 H, 13-H), 3.15–3.22 (m, 1 H, 8-H), 3.18 (d, J = 4.8 Hz, 1 H, 11-H), 3.31 (s, 3 H, 19-H), 3.55 (d, J = 2.9 Hz, 1 H, 5-H), 3.68 (s, 3 H, CO_2CH_3), 3.98 (ddd, J = 8.6, 4.8, 3.9 Hz, 1 H, 3-H), 5.12 (dqq, J = 9.2, 1.3, 1.3 Hz, 1 H, 15-H) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 8.8 (C-18), 14.5 (C-24), 17.5 (C-23), 17.7 (C-25), 18.4 (C-26), 20.0 (C-20), 20.2 (C-22), 22.1 (C-21), 26.0 (C-17), 33.6 (C-14), 34.0 (C-10), 36.6 (C-9), 40.0 (C-8), 41.0 (C-4), 41.3 (C-2), 52.1 (CO_2CH_3), 54.8 (C-6), 60.3 (C-19), 64.1 (C-12), 65.9 (C-13), 72.7 (C-3), 79.7 (C-11), 87.9 (C-5), 128.8 (C-15), 133.3 (C-16), 174.1 (C-1), 222.0 (C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 3461 (w), 2921 (s), 2851 (s), 1737 (s), 1694 (s), 1459 (m), 1385 (m), 1163 (m), 1099 (s), 988 (s) cm^{-1}. MS (ESI): m/z = 507 $[M + Na]^+$, 467, 242, 193, 157, 118, 102. HRMS (ESI): calcd. for $C_{27}H_{48}NaO_7^+$ $[M + Na]^+$ 507.3292; found 507.3287.

Methyl (3*R*,4*S*,5*R*,8*R*,10*S*,11*S*)-3,11-Dihydroxy-5-methoxy-4,6,6,8,10-pentamethyl-11-{(2*R*,3*R*)-2-methyl-3-[(*S*)-4-methylpent-3-en-2-yl]oxiran-2-yl}-7-oxoundecanoate (*ent*-17b): From *ent*-**15b** (4.5 mg, 9.6 μmol); yield: 2.2 mg (4.5 μmol, 47%), colorless oil. R_f = 0.30 (*n*-hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = –27.3 (c = 0.15, MeOH). ^{1}H NMR (500 MHz, CD_3OD): δ = 0.83 (d, J = 6.8 Hz, 3 H, 23-H), 0.89 (d, J = 7.2 Hz, 3 H, 18-H), 0.95 (ddd, J = 13.5, 7.8, 6.6 Hz, 1 H, 9-H_a), 1.04 (d, J = 6.7 Hz, 3 H, 22-H), 1.06 (s, 3 H, 21-H), 1.07 (d, J = 6.6 Hz, 3 H, 25-H), 1.20 (s, 3 H, 20-H), 1.22 (s, 3 H, 24-H), 1.35–1.42 (m, 1 H, 10-H), 1.64 (d, J = 1.3, Hz, 3 H, 26-H), 1.69 (d, J = 1.3 Hz, 3 H, 17-H), 1.73 (qdd, J = 7.2, 3.6, 2.8 Hz, 1 H, 4-H), 2.05 (ddd, J = 13.5, 7.4, 4.3 Hz, 1 H, 9-H_b), 2.34 (ddq, J = 10.1, 9.2, 6.6 Hz, 1 H, 14-H), 2.48 (dd, J = 15.2, 8.7 Hz, 1 H, 2-H_a), 2.55 (dd, J = 15.2, 4.6 Hz, 1 H, 2-H_b), 2.61 (d, J = 9.2 Hz, 1 H, 13-H), 2.68 (d, J = 9.2 Hz, 1 H, 11-H), 3.28 (dqd, J = 7.4, 6.7, 6.6 Hz, 1 H, 8-H), 3.31 (s, 3 H, 19-H), 3.52 (d, J = 2.8 Hz, 1 H, 5-H), 3.69 (s, 3 H, CO_2CH_3), 3.98 (ddd, J = 8.7, 4.6, 3.6 Hz, 1 H, 3-H), 5.01 (dqq, J = 10.1, 1.3, 1.3 Hz, 1 H, 15-H) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 8.9 (C-18), 11.9 (C-24), 17.5 (C-23), 18.4 (C-26), 18.9 (C-22), 19.0 (C-25), 20.2 (C-20), 21.8 (C-21), 25.9 (C-17), 33.7 (C-14), 35.8 (C-10), 39.7 (C-9), 40.2 (C-8), 40.9 (C-4), 41.2 (C-2), 52.1 (CO_2CH_3), 55.1 (C-6), 60.4 (C-19), 65.3 (C-12), 68.8 (C-13), 72.8 (C-3), 83.7 (C-11), 87.5 (C-5), 126.5 (C-15), 133.1 (C-16),

174.2 (C-1), 222.2 (C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 3323 (w), 2978 (m), 2938 (m), 1713 (s), 1377 (m), 1258 (m), 1121 (s), 1083 (s), 1044 (vs), 880 (m), 845 (m) cm^{-1}. MS (ESI): *m*/*z* = 507 [M + Na]$^+$, 118, 102. HRMS (ESI): calcd. for $C_{27}H_{48}NaO_7^+$ [M + Na]$^+$ 507.3292; found 507.3297.

***ent*-17d:** Yield: 2.0 mg (4.0 μmol, 42%), colorless oil. R_f = 0.46 (*n*-hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = –11.8 (*c* = 0.17, MeOH). ^{1}H NMR (500 MHz, CD_3OD): δ = 0.90 (d, *J* = 7.2 Hz, 3 H, 18-H), 1.00 (d, *J* = 6.7 Hz, 3 H, 23-H), 1.02 (ddd, *J* = 13.5, 10.0, 3.9 Hz, 1 H, 9-H_a), 1.03 (d, *J* = 6.8 Hz, 3 H, 22-H), 1.05 (s, 3 H, 21-H), 1.10 (d, *J* = 6.9 Hz, 3 H, 25-H), 1.23 (s, 3 H, 20-H), 1.30 (s, 3 H, 24-H), 1.50 (dqdd, *J* = 10.0, 6.7, 4.9, 3.0 Hz, 1 H, 10-H), 1.65 (d, *J* = 1.3 Hz, 3 H, 26-H), 1.72 (d, *J* = 1.4 Hz, 3 H, 17-H), 1.73 (qdd, *J* = 7.2, 3.8, 2.9 Hz, 1 H, 4-H), 1.98 (ddd, *J* = 13.5, 10.1, 3.0 Hz, 1 H, 9-H_b), 2.41 (ddq, *J* = 9.2, 9.1, 6.9 Hz, 1 H, 14-H), 2.49 (dd, *J* = 15.2, 8.7 Hz, 1 H, 2-H_a), 2.54 (dd, *J* = 15.2, 4.7 Hz, 1 H, 2-H_b), 2.81 (d, *J* = 9.2 Hz, 1 H, 13-H), 3.16 (d, *J* = 4.9 Hz, 1 H, 11-H), 3.19 (dqd, *J* = 10.1, 6.9, 3.9 Hz, 1 H, 8-H), 3.30 (s, 3 H, 19-H), 3.55 (d, *J* = 2.9 Hz, 1 H, 5-H), 3.69 (s, 3 H, CO_2CH_3), 3.98 (ddd, *J* = 8.7, 4.7, 3.8 Hz, 1 H, 3-H), 5.11 (dqq, *J* = 9.1, 1.4, 1.3 Hz, 1 H, 15-H) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 9.0 (C-18), 14.3 (C-24), 17.67 (C-23), 17.67 (C-25), 18.4 (C-26), 19.5 (C-22), 20.2 (C-20), 21.9 (C-21), 26.0 (C-17), 33.5 (C-14), 34.4 (C-10), 36.8 (C-9), 39.9 (C-8), 40.9 (C-4), 41.2 (C-2), 52.1 (CO_2CH_3), 54.9 (C-6), 60.4 (C-19), 64.0 (C-12), 66.0 (C-13), 72.8 (C-3), 79.6 (C-11), 87.4 (C-5), 128.8 (C-15), 133.3 (C-16), 174.2 (C-1), 221.7 (C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 3330 (m), 2978 (m), 2937 (m), 1713 (s), 1446 (w), 1337 (s), 1259 (m), 1122 (s), 1082 (vs), 1044 (vs), 880 (m), 845 (m) cm^{-1}. MS (ESI): *m*/*z* = 507 [M + Na]$^+$, 102. HRMS (ESI): calcd. for $C_{27}H_{48}NaO_7^+$ [M + Na]$^+$ 507.3292; found 507.3295.

Methyl (3*R*,4*S*,5*R*,8*S*,10*S*,11*S*)-3,11-Dihydroxy-5-methoxy-4,6,6,8,10-pentamethyl-11-{(2*R*,3*R*)-2-methyl-3-[(*S*)-4-methylpent-3-en-2-yl]oxiran-2-yl}-7-oxoundecanoate (*ent*-17a): From *ent*-**15a** (16.3 mg, 34.8 μmol); yield: 6.1 mg (12.5 μmol, 36%), colorless oil. R_f = 0.29 (*n*-hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = +15.3 (*c* = 0.40, MeOH). ^{1}H NMR (500 MHz, CD_3OD): δ = 0.84 (d, *J* = 6.7 Hz, 3 H, 23-H), 0.89 (d, *J* = 7.2 Hz, 3 H, 18-H), 0.99 (d, *J* = 6.6 Hz, 3 H, 22-H), 1.07 (d, *J* = 6.6 Hz, 3 H, 25-H), 1.11 (s, 3 H, 21-H), 1.158 (s, 3 H, 20-H), 1.160 (ddd, *J* = 13.5, 10.3, 3.5 Hz, 1 H, 9-H_a), 1.25 (s, 3 H, 24-H), 1.55 (ddqd, *J* = 10.3, 9.4, 6.7, 3.0 Hz, 1 H, 10-H), 1.65 (d, *J* = 1.3, Hz, 3 H, 26-H), 1.70 (d, *J* = 1.3 Hz, 3 H, 17-H), 1.71 (qdd, *J* = 7.2, 3.7, 2.9 Hz, 1 H, 4-H), 1.77 (ddd, *J* = 13.5, 10.5, 3.0 Hz, 1 H, 9-H_b), 2.36 (ddq, *J* = 10.0, 9.3, 6.6 Hz, 1 H, 14-H), 2.49 (dd, *J* = 15.2, 8.6 Hz, 1 H, 2-H_a), 2.54 (dd, *J* = 15.2, 5.0 Hz, 1 H, 2-H_b), 2.62 (d, *J* = 9.3 Hz, 1 H, 13-H), 2.66 (d, *J* = 9.4 Hz, 1 H, 11-H), 3.18 (dqd, *J* = 10.3, 6.6, 3.6 Hz, 1 H, 8-H), 3.33 (s, 3 H, 19-H), 3.50 (d, *J* = 2.9 Hz, 1 H, 5-H), 3.69 (s, 3 H, CO_2CH_3), 3.97 (ddd, *J* = 8.6, 5.0, 3.7 Hz, 1 H, 3-H), 5.02 (dqq, *J* = 10.0, 1.3, 1.3 Hz, 1 H, 15-H) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 8.8 (C-18), 11.9 (C-24), 16.0 (C-23), 16.8 (C-22), 18.4 (C-26), 19.0 (C-25), 20.3 (C-20), 21.8 (C-21), 25.9 (C-17), 33.7 (C-14), 35.2 (C-10), 38.4 (C-9), 39.1 (C-8), 40.9 (C-4), 41.2 (C-2), 52.1 (CO_2CH_3), 55.4 (C-6), 60.5 (C-19), 65.4 (C-12), 68.9 (C-13), 72.7 (C-3), 83.4 (C-11), 87.6 (C-5), 126.5 (C-15), 133.2 (C-16), 174.1 (C-1), 221.7 (C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 3495 (w), 2969 (m), 2928 (m), 1736 (m), 1696 (m), 1455 (m), 1385 (m), 1171 (m), 1098 (s), 1047 (m), 991 (m), 780 (s) cm^{-1}. MS (ESI): *m*/*z* = 507 [M + Na]$^+$, 395, 367, 333, 197. HRMS (ESI): calcd. for $C_{27}H_{48}NaO_7^+$ [M + Na]$^+$ 507.3292; found 507.3287.

***ent*-17c:** Yield: 8.8 mg (18.1 μmol, 52%), colorless oil. R_f = 0.40 (*n*-hexane/EtOAc, 1:1). $[\alpha]_D^{20}$ = –10.9 (*c* = 0.50, MeOH). ^{1}H NMR (500 MHz, CD_3OD): δ = 0.89 (d, *J* = 7.2 Hz, 3 H, 18-H), 1.007 (d, *J* = 6.7 Hz, 3 H, 23-H), 1.007 (d, *J* = 6.7 Hz, 3 H, 22-H), 1.02 (d, *J* = 6.9 Hz, 3 H, 25-H), 1.11 (s, 3 H, 20-H), 1.15 (s, 3 H, 21-H), 1.27 (ddd, *J* = 13.6, 11.2, 3.0 Hz, 1 H, 9-H_a), 1.32 (s, 3 H, 24-H), 1.57 (ddd, *J* = 13.6, 11.0, 2.8 Hz, 1 H, 9-H_b), 1.64 (d, *J* = 1.3 Hz, 3 H, 26-H), 1.71 (d, *J* = 1.3 Hz, 3 H, 17-H), 1.73 (qdd, *J* = 7.2, 3.7, 2.9 Hz, 1 H, 4-H), 1.83 (dqdd, *J* = 11.2, 6.7, 6.1, 2.8 Hz, 1 H, 10-H), 2.37 (ddq, *J* = 9.1, 9.1, 6.9 Hz, 1 H, 14-H), 2.49 (dd, *J* = 15.2, 8.7 Hz, 1 H, 2-H_a), 2.55 (dd, *J* = 15.2, 4.9 Hz, 1 H, 2-H_b), 2.70 (d, *J* = 9.1 Hz, 1 H, 13-H), 3.05 (d, *J* = 6.1 Hz, 1 H, 11-H), 3.16 (dqd, *J* = 10.8, 6.7, 3.0 Hz, 1 H, 8-H), 3.34 (s, 3 H, 19-H), 3.50 (d, *J* = 2.9 Hz, 1 H, 5-H), 3.68 (s, 3 H, CO_2CH_3), 3.96 (ddd, *J* = 8.7, 4.9, 3.7 Hz, 1 H, 3-H), 5.09 (dqq, *J* = 9.1, 1.3, 1.3 Hz, 1 H, 15-H) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 8.8 (C-18), 13.7 (C-24), 16.47 (C-22), 16.49 (C-23), 17.8 (C-25), 18.3 (C-26), 20.2 (C-20), 21.9 (C-21), 26.0 (C-17), 33.5 (C-14), 33.8 (C-10), 36.3 (C-9), 38.7 (C-8), 40.9 (C-4), 41.2 (C-2), 52.1 (CO_2CH_3), 55.3 (C-6), 60.5 (C-19), 63.8 (C-12), 66.4 (C-13), 72.7 (C-3), 80.2 (C-11), 87.6 (C-5), 128.6 (C-15), 133.4 (C-16), 174.1 (C-1), 221.6 (C-7) ppm. FTIR (ATR): $\tilde{\nu}$ = 3493 (w), 2967 (s), 2933 (s), 2877 (m), 1735 (s), 1697 (s), 1455 (m), 1384 (m), 1168 (m), 1098 (s), 989 (s), 781 (s) cm^{-1}. MS (ESI): *m*/*z* = 507 [M + Na]$^+$, 395, 367, 333, 197. HRMS (ESI): calcd. for $C_{27}H_{48}NaO_7^+$ [M + Na]$^+$ 507.3292; found 507.3288.

Cell Proliferation Assay: L-929 mouse fibroblast and KB-3-1 cervix carcinoma cell lines were obtained from the German Collection of Microorganisms and Cell Cultures (DSMZ) and cultivated at 37 °C and 10% CO_2 in DME medium (high glucose) supplemented with 10% fetal calf serum. Cell culture reagents came from Life Technologies Inc. (GIBCO BRL). Growth inhibition was measured in 96-well plates. Serial dilutions (60 μL) of the test compounds were added to aliquots (120 μL) of the suspended cells (50000 mL^{-1}). After 5 d, the metabolic activity in each well was determined through an MTT assay.[29] The values were related to control cells and IC_{50} values were determined from the resulting concentration-dependent activity curves. The data are means ± standard deviation of two assays performed in parallel.

Antibacterial Assay: Antibacterial activities were determined by agar diffusion assays using paper discs of 6 mm diameter soaked with 20 μL of a methanolic solution of the test compound (1 mg mL^{-1}). The organisms were grown on standard medium and seeded into a liquid agar medium to a final optical density of 0.01. Plates were incubated at 30 °C and bacterial growth was observed after 1 d. The diameter of resulting inhibition zones were taken as a measure of the antibiotic activity.

Supporting Information (see footnote on the first page of this article): Stereochemistry at C8 by comparison of proton shifts; synthesis and characterization of xanthogenates, compounds **10** and alcohols thereof, and derivatives *ent*-**14**–*ent*-**16**; byproduct formation under deoxygenation and acetalization reactions; example curves of MTT assays and some IC_{50} values.

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