Synthesis of the C(1)–C(11) Polyene Fragment of Apoptolidin with a New Sulfur Dioxide-Based Organic Chemistry

Laure C. Bouchez and Pierre Vogel*[a]

In memory of A. Bouchez, father of L.B., who passed away February 2005

Abstract: A new sulfur dioxide-based organic chemistry has been developed as a novel approach for the stereoselective synthesis of polyene fragments based on our one-pot, four-component synthesis of polyfunctional ε-alkanesulfonyl-γ,δ-unsaturated ketones. The flexibility and efficiency of this methodology are illustrated by the preparation of (+)-methyl (2*E*,4*E*,6*E*,8*R*,9*S*)-9-{[(*tert*-butyl)dimethylsilyl]oxy}-2,4,6,8-tetramethyl-11-(triethylsilyl)undeca-2,4,6-trien-10-ynoate, a synthetic intermediate of Nicolaou and co-workers, that corresponds to the C(1)–C(11) fragment of apoptolidin, which was used by the authors in their total synthesis of this promising anticancer agent.

Keywords: Diels–Alder reactions · natural products · polyenes · Ramberg–Bäcklund reactions · total synthesis

Introduction

Apoptosis,[1] or programmed cell death, is an important mechanism in the treatment of cancer. Apoptolidin (Figure 1), isolated from the cultivation broth of an actinomycete identified as *Nocardiopsis sp.*, was found[2] to have considerable potency with regard to selectively induced cell death by apoptosis in rat glia cells transformed with adenovirus E1A and E1A/E1B19 K oncogenes.[3] Apoptolidin was found to be among the top 0.1 % of most selective cytotoxic agents.[4] Owing to its promising biological activity and novel molecular architecture, elegant total synthesis and semisynthetic studies directed toward the preparation of analogues have been already reported by the groups of Koert,[5] Nicolaou,[6] Sulikowski,[7] Fuchs,[8] and Wender,[9] among others.[10]

The methodology previously used to prepare the trienic moiety of apoptolidin (**1**) relied on Wittig olefination, Suzuki coupling, and other methods that are commonly applied in the total syntheses of natural products. We decided to follow the path chosen by Nicolaou and co-workers in our search for a new methodology for the quick construction of its C(1)–C(11) fragment (+)-**2** and analogues (Scheme 1). It applies a new one-pot, four-component synthesis of ε-alkanesulfonyl ketones that condenses 1-silyloxy- or 1-alkoxy-1,3-dienes with enoxysilanes, SO_2, and carbon electrophiles (Scheme 2).[11]

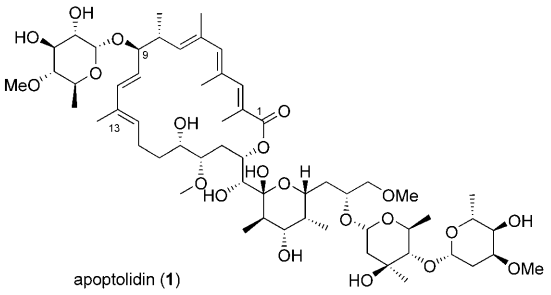
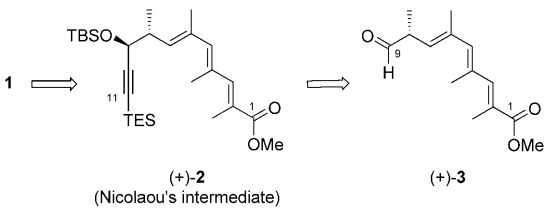


Figure 1. Apoptolidin (**1**).



Scheme 1. Retrosynthetic plan of Nicolaou and co-workers.

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Results and Discussion

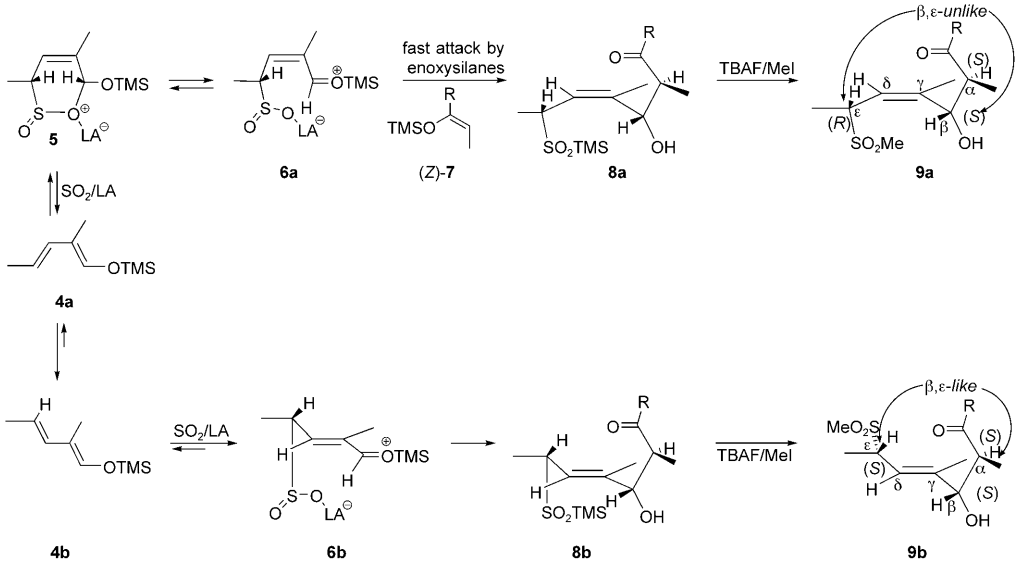
Synthesis and reactivity of 1-trialkylsilyloxy-1,3-dienes: The synthesis of the conjugated (*E*,*E*,*E*)-triene portion of apoptolidin represents a synthetic target that takes advantage of the new C–C bond-forming reaction **4a** + (*Z*)-**7** → **9a** discovered in our group (Scheme 2).[12] This strategy involves a cascade of reactions starting with the face-selective suprafacial hetero-Diels–Alder addition of SO_2 to a 1,3-dienyl ether **4a** promoted by the acid catalyst (LA) to afford the corresponding sultine **5**, which is then ionized in the presence of LA to the zwitterionic intermediate **6a**. The latter then adds to enoxysilanes (oxyallylation) to give the corresponding silyl sulfinate **8a** that can be methylated in situ to provide the corresponding ε-methanesulfonyl ketone **9a** containing a ε-(*Z*)-alkene unit (Scheme 2). Very recently, we demonstrated that our method can also be applied to generate enones of type **8b** that contain exclusively ε-(*E*)-alkene units.[11] We proposed that the (*Z*)-zwitterionic intermediates **6a**, if not quenched quickly by a reactive enoxysilanes, can equilibrate back to the *s-cis*-diene **4a**, which then isomerizes into the *s-trans*-diene **7b** thus allowing the formation of the (*E*)-zwitterionic intermediates **6b**. Its addition to the enoxysilane (*Z*)-**7** affords the corresponding (*E*)-silyl sulfinate **8b**, which is methylated in situ providing enones of type **9b**. Compounds such as **9b** containing ε-(*E*)-alkene units showed a β,ε-*like* relative configuration[11] that was interpreted in terms of preferred addition onto the *anti* face with respect to that occupied by the ε-sulfinate moiety in **6b** (Scheme 2).

Abstract in French: *Une nouvelle approche pour la synthèse stéréosélective des (*E,E,E*)-2,4,6-triénoate d'alkyles est proposée. Elle exploite notre nouvelle méthode de synthèse monotope à quatre composants des ε-alkanesulfonylcétones γ,δ-insaturées. Ainsi la réaction du (*E*)-1-silyloxy-2-méthylpenta-1,3-diène avec le dioxyde de soufre et le 2-triéthylsilyloxybut-2-ène en présence de $(CF_3SO_2)_2NH$ fournit à −78 °C un sulfinate de silyle qui est converti en un mélange 3:3:2:2 des (2′*S*,3*R ou 3S*,4*R ou 4S*,6*R ou 6S*)-4-hydroxy-3,5-diméthyl-7-({[3-(*tert*-*butyl*)diméthylsilyl]oxy}-2-méthyl-prop-1-ylsulfonyl)-4-hydroxy-3,5-diméthyloct-5-én-2-one par réaction avec nBu_4NF et le iodure de (2*S*)-3-méthoxyméthoxy-2-méthylpropyle. Avec 6 réactions et l'isolement de seulement 3 intermédiaires (**27**, **29**, **32**), le (+)-méthyl (2*E*,4*E*,6*E*,8*R*,9*S*)-9-{[(*tert*-*butyl*)diméthylsilyl]oxy}-2,4,6,8-tétraméthyl-11-(triéthylsilyl)undéca-2,4,6-trién-10-ynoate ((+)-**2**) est obtenu avec 22 % de rendement, une pureté stéréochimique (*E,E,E*)- vs (*E,E,Z*)- de 12:1 et un excès énantiomérique de 99 %. Ainsi nous avons pu démontrer l'originalité et l'efficacité de notre méthode (synthèse la plus courte). Le composé (+)-**2** correspond au fragment C(1)–C(11) de l'apoptolidine. Nicolaou et collaborateurs l'ont préparé (11 étapes) et utilisé dans leur synthèse totale de l'apoptolidine, un agent anti-cancéreux très prometteur.*

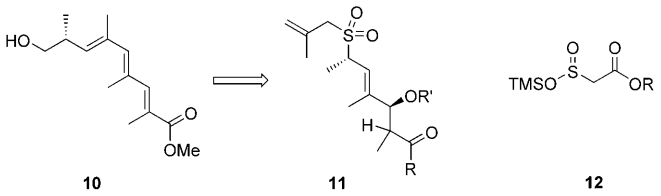
Preparation of a racemic C(1)–C(9) fragment of apoptolidin: In principle, trienol **10** should be obtained from sulfone **11** (Scheme 3) through three transformations: a) enantioselective hydroboration of the methallylsulfonyl group, b) Ramberg–Bäcklund olefination, and c) β-elimination of the R′-OH group. Sulfone **11** should be reached in a one-pot operation applying our chemistry by co-condensing a propionic ester (e.g. R = OMe), 1-silyloxy or 1-alkyloxy-2-methylpenta-1,3-diene, sulfur dioxide, and methallyl bromide.[13] Unfortunately, we discovered that enoxysilanes derived from esters undergo faster ene reaction with SO_2 than oxyallylation with the zwitterionic intermediates of type **6a** or **6b** that result from the reaction of SO_2 with 1-oxypenta-1,3-dienes. This means that the corresponding β-ketosulfinates **12**[14] are formed instead of adducts of type **9a** and **9b**. Therefore, we were forced to use enoxysilanes with R ≠ OR′ and to find a way to solve the problem of transforming the R group into a RO or HO group at a later stage (Scheme 3).

The first step is then based on the addition of SO_2 to trimethylsilyloxy-1,3-pentadiene (**4b**) in the presence of a catalytic amount of bistrifluoromethanesulfonimide (40 %), as an acid promoter, and a 3:2 mixture of (*Z*/*E*)-2-triethylsilyloxy-2-butene (**13**).[15] The resulting sulfinate (±)-**14** is converted in situ into the corresponding ε-(2-methylprop-2-enesulfonyl)-γ,δ-enone (±)-**15** with TBAF as a fluoride source and methallyl bromide as electrophile. A 2:1 mixture of α,β-*syn* and α,β-*anti* diastereomers (±)-**15a** and (±)-**15b** containing (*E*)-alkene units (78 % yield, structure determined by ^{1}H NMR NOESY experiments) was obtained. The least substituted alkene moiety of (±)-**15** was expected to react the fastest with $BH_3{\cdot}Me_2S$ and the carbonyl group of the ketone would react competitively with the other alkene unit.[16] However, owing to a strong chelating effect of methyl ketone with $BH_3{\cdot}Me_2S$, only the reduction of the ketone moiety (±)-**15** was observed. Protection of the alcohol moiety of (±)-**15** as a TBS ether (TBSCl/imidazole, in DMF) resulted in selective hydroboration of the terminal olefin to afford the expected product (±)-**16** (52 %, overall) after oxidative work-up. This produced a 2:2:1:1 mixture of four diastereoisomers. Protection of the hydroxyl group of (±)-**16** was thought to be a necessary step. Thus the TBDPS derivative (±)-**17** was prepared by treating (±)-**16** with TBDPSCl/imidazole in DMF (quantitative yield). Both substrates, (±)-**16** and (±)-**17**, were oxidized with NaOBr in a 2:1 mixture of dioxane/water[17] to generate the corresponding acids that were not isolated, but directly treated with solution of CH_2N_2 in diethyl ether to produce the expected methyl esters (±)-**18** (75 %, overall yield) and (±)-**19** (51 %, overall), respectively, both of which were 2:2:1:1 mixtures of four diastereoisomers (Scheme 4).

Ramberg–Bäcklund reaction: **the key step for the preparation of the conjugated (*E*,*E*,*E*)-triene unit**: Because (±)-**18** containing the nonprotected primary alcohol led to a better yield than its silyl ether (±)-**19**, we then looked for a suitable protection of (±)-**18**. We thus prepared its MOM ether

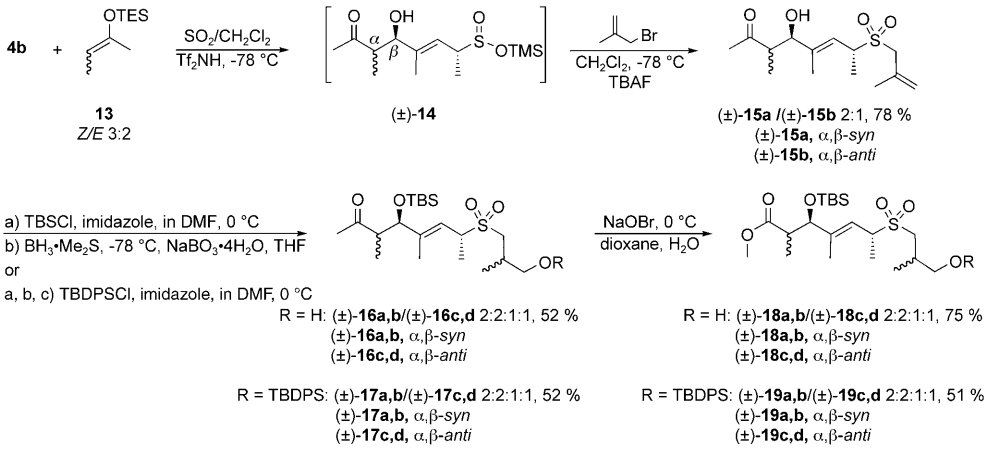


Scheme 2. The one-pot, four-component synthesis of polyfunctional ε-alkanesulfonyl ketones containing either (*Z*)-, or (*E*)-alkene units; proposed mechanisms; for the *like* and *unlike* nomenclature see ref. [11].

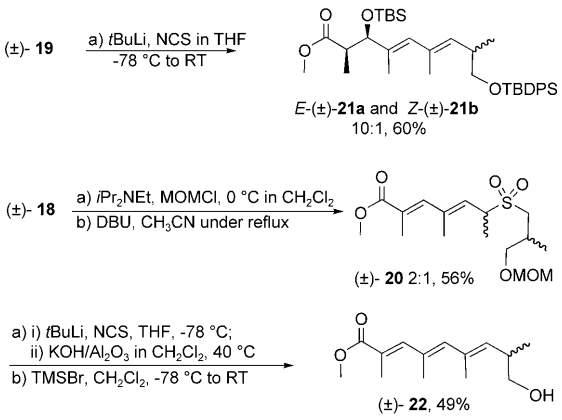


Scheme 3.

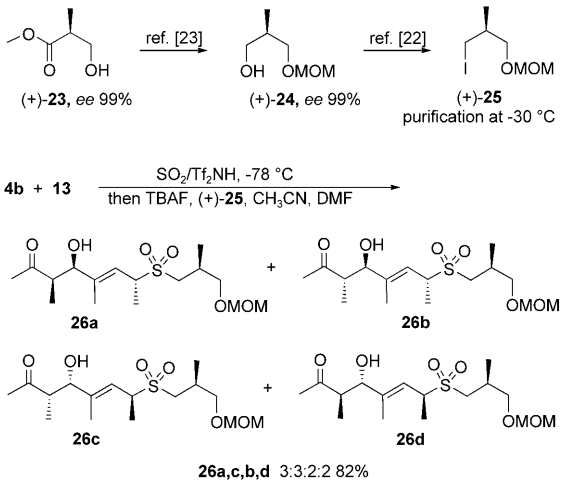
(Scheme 5) under standard conditions. This was followed by the elimination of one equivalent of (*t*Bu)Me_2SiOH on heating in CH_3CN to 105 °C in the presence of DBU (7 equiv)[18] to furnish (*E*,*E*)-dienoate (±)-**20** (56 %, overall) as a 2:1 mixture of two diastereoisomers that were not separated (structures deduced from their ^{1}H, 2D NOESY and ^{13}C NMR spectra). At this point, different substrates bearing either a ketone moiety or an ester moiety were subjected to the Ramberg–Bäcklund reaction[19] to find out which of them can be converted into the desired triene. For all the conditions tested (e.g.: *t*BuLi, *t*BuOK as base followed by NBS, NIS, or NCS as the electrophile, or Chan's conditions[20]: Al_2O_3/KOH/CF_2Br_2), none of the ketone derivatives gave satisfying results, only decomposition was observed. Finally, we found that (±)-**19** can be converted into a 10:1 mixture of (*E*,*E*) and (*E*,*Z*)-diene (±)-**21** in 60 % yield by treatment with *t*BuLi and NCS for the chlorination, and Al_2O_3/KOH for the 1,3-elimination and the cheletropic elimination of SO_2. In the case of (±)-**20**, a racemic triene (±)-**22** was obtained in 49 % yield with *t*BuLi and NIS for the α-iodination of the sulfone, and *t*BuLi again for the 1,3-elimination and the cheletropic elimination of SO_2. The structures of dienes (±)-**20** and trienes (±)-**22** were deduced from their 2D-NOESY 1H NMR spectra after purification



Scheme 4.



Scheme 5.



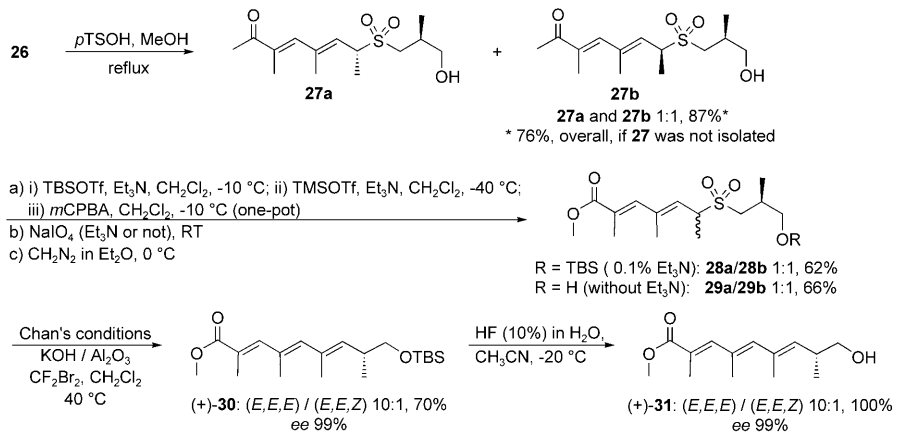
Scheme 6.

by column chromatography on silica gel. Unfortunately, the last deprotecting step was hardly reproducible.[21] Therefore, we searched for a more straightforward strategy to prepare an enantiomerically pure trienic fragment of apoptolidin.

Synthesis of an enantiomerically enriched C(1)–C(11) fragment of apoptolidin [(+)-2]: In an early report,[11] we examined the reactivity of a variety of electrophiles with our silyl sulfinate intermediates. Under standard conditions (1 M solution of TBAF in THF, CH_2Cl_2, −50 to 25 °C in 8 h) only simple electrophiles, such as MeI, allyl-bromide derivatives, and substituted benzyl bromides, reacted to provide the corresponding sulfones. However, we found that the exchange of CH_2Cl_2 for more polar solvent (HMPA, DMF, or CH_3CN) overcame this limitation.[11] Thus, a better route is presented below in which the enantiomerically pure iodide (+)-**25**[22] is used as an electrophile to react with our sulfinate intermediates. This permits the preparation of a C(1)–C(11) fragment of apoptolidin in an enantiomerically pure (99 %) form. Iodide (+)-**25** was derived from the commercially available (*S*)-(+)-methyl-L-β-hydroxyisobutyrate [(+)-**23**] (*ee* 99 %). The primary alcohol was protected as its MOM ether.[23] Reduction of the ester moiety afforded the corresponding alcohol (+)-**24**, which was subsequently substituted by iodide (96 %, overall). The corresponding Mosher's esters, (*R*)-MTPA and (*S*)-MTPA, were prepared from alcohol (+)-**24**. Their ^{19}F NMR spectrum indicated 99 % *ee*. Reaction of the iodo derivative (+)-**25** with the silyl sulfinate intermediate (±)-**14** afforded a 3:3:2:2 mixture of the corresponding (3*RS*,4*RS*,5*E*,7*RS*,2*S*)-aldol **26**, in 82 % yield (Scheme 6).

We then applied same reaction sequence to **26** as that employed in the preparation of ±-**22** (Scheme 5). Unfortunately, none of the conditions tested for the Ramberg–Bäcklund reaction and for the elimination of the hydroxyl moiety were successful. Only decomposition was observed. However, facile acid-induced water elimination was possible with the crude aldols **26**. This led to a 1:1 mixture of (*E*,*E*)-dienones **27a** and **27b** that was isolated in 76 % yield (Scheme 7). All our attempts to carry out the haloform reaction with **27** (NaOBr, NaOCl, KOCl, $NaOH/I_2$, various solvents, 0–10 °C reflux) failed to give the corresponding carboxylic derivatives. This forced us to explore another route for oxidative cleavage of the CH_3−CO bond. To avoid any side reactions, the alcoholic moieties of **27** were protected temporarily as their TBS ethers (Et_3N, TMSOTf). Transformation of the methyl ketone moieties into their trimethylsilyl enol ethers (Et_3N, TMSOTf) and oxidation, either with OsO_4/NMO in *t*BuOH[24] or with *m*-CPBA in CH_2Cl_2,[25] provided the corresponding α-hydroxy-ketones, which were not isolated but reacted directly with $NaIO_4$[26] (7 equiv) in 2:1 MeOH/H_2O. Acidification followed by the addition of diazomethane furnished methyl esters **29a + 29b** with free hydroxyl groups, in 66 % overall yield. Interestingly, depending on the acidity of the medium, it was possible to maintain or to cleave the OTBS group. For instance, when seven equivalents of $NaIO_4$ were used for the oxidative cleavage, alcohol methyl esters **28a + 28b** were obtained, whereas, in the presence of a small amount of Et_3N (0.1 equiv), silyl ethers **28a + 28b** were isolated in 62 % yield. Finally esters **28** were subjected to the Ramberg–Bäcklund reaction conditions and this afforded the desired (*E*,*E*,*E*)-triene (+)-**30** (Scheme 7). The best yield (70 %) was observed on adding **28** to a stirred suspension of KOH/Al_2O_3 in CH_2Cl_2 at −10 °C, followed by heating to +40 °C for 12 h. The (*E*,*E*,*E*)- versus (*E*,*E*,*Z*)-selectivity was better than 10:1 in favor of the all-*trans* triene. The structure of (+)-**30** was confirmed by its spectral data, including its 2D-NOESY ^1H NMR spectrum.

Formal total synthesis of apoptolidin: With the goal of obtaining Nicolaou's synthetic intermediate (+)-**2**, we envisioned converting (+)-**29** into aldehyde (+)-**3** and to couple it with $Et_3SiCH{\equiv}CLi$.[27] Quantitative cleavage of the OTBS group to provide the free alcohol of (+)-**30** was only possible in the presence of HF (10 % in water) in acetonitrile. The corresponding Mosher's esters, (*R*)-MTPA and (*S*)-MTPA, were also prepared from (+)-**31** and showed



Scheme 7.

(^{19}F NMR and ^{13}C NMR) a 99% *ee*. The structure of (+)-**31** proves that of methyl esters **28** and **29**. This work also demonstrates that epimerization at C(8) does not occur during the Ramberg–Bäcklund olefination (Scheme 7).

Unfortunately, all our attempts to oxidize alcohol (+)-**31** into aldehyde (+)-**3** led to decomposition owing to the extreme instability of (+)-**3**. Therefore, the alkyne moiety had to be introduced prior to the Ramberg–Bäcklund reaction. Quantitative oxidation of primary alcohol at C(3′) of **29** by the Dess–Martin reagent[28] furnished the expected mixture of aldehydes that were not isolated but directly reacted stereoselectively with the lithium salt of the triethylsilylacetylene at low temperature to afford a 3:3:1:1 mixture of four diastereoisomers in favor of the "Cram adduct"[29] (2 major *syn* diastereoisomers **32a**: 2*E*,4*E*,6*RS*,2′*R*,3′*S* (59% isolated) and 2 minor *anti* diastereoisomers **32b**: 2*E*,4*E*,6*RS*,2′*R*,3′*R* (12% isolated); 71%, overall). Protection of the free alcohol of **32a** provided the corresponding TBS ethers (TBSCl/imidazole in DMF, quantitative) which were directly added to a suspension of KOH/Al_2O_3 in CH_2Cl_2, at −10 °C. Subsequent heating to 40 °C for 12 h induced the Ramberg–Bäcklund reaction (Scheme 8). After purification by flash chromatography on silica gel, a 12:1 mixture of the desired (*E*,*E*,*E*)-triene (+)-**2** and its (*E*,*E*,*Z*)-isomer was isolated in 72% yield (99% *ee*). The spectral data of (+)-**2** were identical to those reported for this compound.[6]

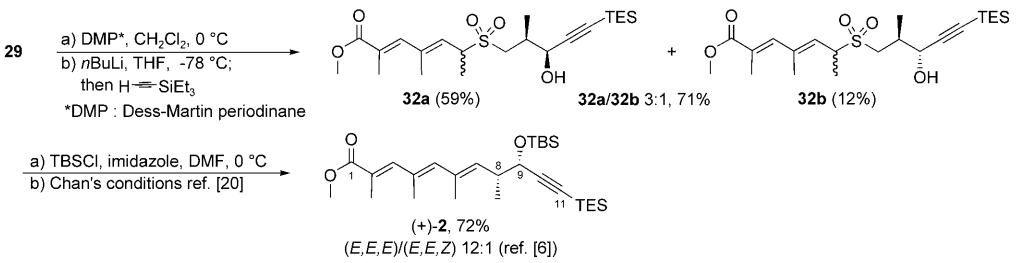
Conclusion

Two main synthetic routes towards the synthesis of the trienic fragment of apoptolidin have been developed on the basis of our one-pot, four-component synthesis of polyfunctional sulfones. The C(1)–C(11) fragment (+)-**2** of apoptolidin, prepared by Nicolaou in 11 steps, has been obtained in only seven steps and with a overall yield of 22%. Our method requires the isolation of only three synthetic intermediates (**27**, **29**, **32**), thus making this approach the shortest and most efficient one reported so far for the synthesis of (+)-**2**. Because this compound is an intermediate in the total asymmetric synthesis of apoptolidin, we have therefore realized a formal total synthesis of this natural product that is an important anticancer agent.

Experimental Section

General: Commercial reagents (Fluka, Aldrich) were used without purification. Solvents were distilled prior to use: THF from Na and benzophenone, MeOH from Mg and I_2, CH_2Cl_2 from CaH_2. Liquid/solid flash chromatography (FC): columns of silica gel (0.040–0.63 mm, Merck No. 9385 silica gel 60, 240–400 mesh). Eluent: mixture of light petroleum ether (PE) and ethyl acetate (EtOAc), if not stated otherwise. TLC for reaction monitoring: Merck silica gel 60 F_{254} plates; detection with a UV lamp, Pancaldi reagent, or $KMnO_4$. IR spectra: Perkin–Elmer 1420 spectrometer. ^{1}H NMR spectra: Bruker ARX-400 spectrometer (400 MHz); δ(H) relative to the solvent's residual ^{1}H signal [$CHCl_3$, δ(H) = 7.27; CD_2Cl_2, δ(H) = 5.30] as the internal reference; all ^{1}H assignments were confirmed by 2D-COSY spectra. ^{13}C NMRspectra: same instrument as above (100.6 MHz); δ(C) relative to the solvent's C signal [$CDCl_3$, δ(C) = 77.1; CD_2Cl_2, δ(H) = 53.5] as the internal reference; ^{19}F NMR spectra: same instrument as above (396 MHz); δ(F) relative to F signal of $CFCl_3$ [$CFCl_3$, δ(F) = 0] as the internal reference; coupling constants *J* in Hz. MS: Nermag R-10-10C, chemical ionization (NH_3) mode *m*/*z*: (amu) [% relative base peak (100%)], HRMS: Jeol AX-505. Elemental analyses: Ilse Beetz, 96301 Kronach (Germany).

2:1 Mixture of methyl ketones (±)-15a,b: $HN(SO_2CF_3)_2$ (0.5 M in CH_2Cl_2, 44.4 mL, 22.2 mmol, 0.5 equiv) in anhydrous CH_2Cl_2 (2 mL) was



Scheme 8.

degassed by freeze–thaw cycles on the vacuum line. SO_2 (5 mL, 114.0 mmol, 34 equiv), dried through a column packed with basic alumina and phosphorus pentoxide, was transferred on the vacuum line to the CH_2Cl_2 solution frozen at −196 °C. The mixture was allowed to melt at −78 °C. After 1 h at this temperature, a solution of (*E*,*E*)-2-methyl-1-trimethylsilyloxy-1,3-pentadiene (10 g, 44.3 mmol, 1 equiv) and 1:1 mixture of (*E*/*Z*)-2-trimethylsilyloxybut-2-ene (24.2 g, 0.13 mol, 3 equiv) in CH_2Cl_2 (20 mL) was added slowly. The mixture was stirred at −78 °C for 12 h. Excess SO_2 and solvent were evaporated under reduced pressure (10^{-1} Torr) to dryness while the temperature rose to 25 °C (≈1 h). A 1 M solution of nBu$_4$NF in THF (1 equiv) and 3-bromo-2-methylpropene (14.95 g, 11.2 mL, 0.11 mol, 2 equiv) were added under an Ar atmosphere at −78 °C. The mixture was stirred for 1 h at this temperature, followed by 1 h at −40 °C, and then gradually allowed to reach 20 °C in ≈10 h. After the addition of H_2O (40 mL), and neutralization with an aqueous saturated solution of $NaHCO_3$ (10 mL), the mixture was extracted with CH_2Cl_2 (30 mL, 3 times). The combined organic extracts were washed with brine (30 mL, 2×), dried (Na_2SO_4), and the solvent eliminated under reduced pressure. The residue was purified by FC (light petroleum ether/EtOAc 3:2, R_f = 0.22) to give a 2:1 mixture of (±)-**15a** and (±)-**15b** as yellow oil with strawberry-like smell (9.96 g, 78%). A pure fraction of the major α,β-*syn* diastereoisomer (±)-**15a** was isolated (6 g, 69.47%).

(±)-15a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.62 (d, 1H, ^3J(H6,H7) = 9.9, H-C(6)), 5.24 (brs, 1H, Ha-C(3′)), 5.09 (brs, 1H, Hb-C(3′)), 4.45 (d, 1H, ^3J(H4,H3) = 4.9, H-C(4)), 3.99 (dq, 1H, ^3J(H7,H6) = 9.9, ^3J(H7,H8) = 6.7, H-C(7)), 3.63 (d, AB, 1H, ^2J = 13.6, Ha-C(1′)), 3.59 (d, AB, 1H, ^2J = 13.6, Hb-C(1′)), 2.67 (dq, 1H, ^3J(H3,H4) = (H3,Me3) = 6.7, H-C(3)), 2.17 (s, 3H, H-C(1)), 2.00 (s, 3H, *Me*-C(5)), 1.71 (s, 3H, *Me*-C(2′)), 1.46 (d, 3H, ^3J(H8,H7) = 6.7, H-C(8)), 1.14 (d, 3H, ^3J(Me3,H3) = 6.7, *Me*-C(3)); ^{13}C NMR(100.6 MHz, $CDCl_3$): δ = 213.5 (s, CO), 143.2 (s, C(2′)), 133.6 (s, C(5)), 120.7 (t, ^1J(C,H) = 157, C(3′)), 120.6 (d, ^1J(C,H) = 161, C(6)), 74.6 (t, ^1J(C,H) = 145, C(1′)), 58.4 (d, ^1J(C,H) = 132, C(4)), 57.3 (d, ^1J(C,H) = 142, C(7)), 49.6 (d, ^1J(C,H) = 148, C(3)), 29.3 (q, ^1J(C,H) = 132, C(1)), 23.4 (q, ^1J(C,H) = 138, *Me*-C(2′)), 20.7 (q, ^1J(C,H) = 139, *Me*-C(5)), 14.3 (q, ^1J(C,H) = 137, C(8)), 10.6 (q, ^1J(C,H) = 129, *Me*-C(3)); IR (film): $\tilde{\nu}$ = 3460, 2970, 2935, 2910, 1705, 1630, 1455, 1360, 1295, 1120, 1010 cm^{-1}; UV (CH_3CN): λ_{max} = 211 nm (ε = 5786); CI-MS (NH_3): *m*/*z* (%): 306 (100) $[M+H_2O]^+$, 289 (34) $[M+H]^+$; elemental analysis calcd (%) for for $C_{14}H_{24}O_4S$ (288.14): C 58.30, H 8.39; found: C 58.36, H 8.52.

2:2:1:1 Mixture of compounds (±)-17a–d: Imidazole (1.71 g, 25.1 mmol, 1.2 equiv) followed by TBSCl (3.47 g, 22.9 mmol, 1.1 equiv) were added at 0 °C to a 2:1 solution of (±)-**15a**,**b** (6 g, 20.9 mmol, 1 equiv) in anhydrous DMF (40 mL). After stirring at 20 °C for 12 h under an Ar atmosphere, the crude mixture was treated with an aqueous saturated solution of $NaHCO_3$ (60 mL) and extracted with Et_2O (3×100 mL). The combined organic extracts were washed with brine (2×60 mL), dried (Na_2SO_4), and the solvent evaporated under reduced pressure. To a cooled (−78 °C) solution of the resulting crude mixture (1 equiv), the complex BH_3·Me_2S (95% in Me_2S) in anhydrous THF (2 mL) was added dropwise (1.7 g, 20.9 mmol, 1 equiv). The cooling bath was then removed, and the mixture was stirred at 20 °C under an Ar atmosphere for 30 min. $NaBO_3$·4H_2O (6.4 g, 41.7 mmol, 2 equiv) in water (3 mL) was added and the mixture stirred overnight at 20 °C. The reaction mixture was diluted with ice/water (1 mL) and extracted with Et_2O (3×10 mL). The combined organic extracts were washed with brine (2×15 mL), dried (Na_2SO_4), and the solvent evaporated under reduced pressure. FC (petroleum ether/ethyl acetate 45:55, R_f = 0.29) gave a 2:2:1:1 mixture of (±)-**17a**,**b**,**c**,**d** as a yellow oil (4.56 g, 52%). R_f = 0.29 (petroleum ether/ethyl acetate 45:55); IR (film): $\tilde{\nu}$ = 3456, 3050, 2970, 2934, 2847, 1782, 1610, 1478, 1456, 1271, 1250, 1143, 1066, 848, 729 cm^{-1}; UV (CH_3CN): λ_{max} = 220 nm (ε = 5938); CI-MS (NH_3): *m*/*z* (%): calcd for $C_{20}H_{40}O_5SSi$: 420.680; found: 438 (20) $[M+H_2O]^+$, 421 (4) $[M+H]^+$, 109 (100).

(±)-17a,**b**: The NMR spectra of (±)-**17a** and (±)-**17b** (α,β-*syn* with either 2′*R* or 2′*S* configuration) overlap for all ^{1}H and ^{13}C signals. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.15 (d, 1H, ^3J(H6,H7) = 10.8, H-C(6)), 4.58 (d, 1H, ^3J(H4,H3) = 8.3, H-C(4)), 4.06 (dq, 1H, ^3J(H7,H6) = 10.8, ^3J(H7,H8) = 6.9, H-C(7)), 3.82 (m, 1H, Ha-C(3′)), 3.55 (m, 1H, Hb-C(3′)), 3.13 (dd, 1H, ^2J = 14.2, ^3J(H1′,H2′) = 5.6, H-C(1′)), 2.86 (m, 2H, H-C(1′), H-C(3)), 2.47 (qdddd, 1H, ^3J(H2′,H3′a,b) = ^3J(H2′,H1′a,b) = ^3J(H2′,Me2′) = 5.6, H-C(2′)), 2.13 (s, 3H, H-C(1)), 1.85 (s, 3H, *Me*-C(5)), 1.70 (brs,1H, H-OH), 1.38 (d, 3H, ^3J(H8,H7) = 6.9, H-C(8)), 1.19 (d, 3H, ^3J(Me2′,H2′) = 6.7, *Me*-C(2′)), 1.17 (d, 3H, ^3J(Me3,H3) = 6.72, *Me*-C(3)), 0.92 (s, 9H, *t*Bu-Si), 0.12 (s, 3H, Me_2-Si), 0.09 (s, 3H, Me_2-Si); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 210.6 (s, CO), 136.2 (s, C(5)), 125.8 (d, ^1J(C,H) = 143, C(6)), 72.1 (d, ^1J(C,H) = 139, C(4)), 68.2 (t, ^1J(C,H) = 145, C(3′)), 66.5 (t, ^1J(C,H) = 148, C(1′)), 57.8 (d, ^1J(C,H) = 137, C(7)), 52.6 (d, ^1J(C,H) = 140, C(3)), 52.2 (d, ^1J(C,H) = 128, C(2′)), 31.2 (q, ^1J(C,H) = 130, C(1)), 25.8 (q, ^1J(C,H) = 128, *t*Bu-Si), 20.6 (q, ^1J(C,H) = 135, *Me*-C(5)), 18.6 (s, C_{quat}-*t*Bu-Si), 17.8 (q, ^1J(C,H) = 122, C(8)), 15.3 (q, ^1J(C,H) = 130, *Me*-C(2′)), 14.2 (q, ^1J(C,H) = 132, *Me*-C(3)), 4.76 (q, ^1J(C,H) = 122, Me_2-Si), −0.09 (q, ^1J(C,H) = 126, Me_2-Si).

(±)-17c,**d**: The NMR spectra of (±)-**17c** and (±)-**17d** (α,β-*syn* with either 2′*R* or 2′*S* configuration) overlap for all ^{1}H and ^{13}C signals. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.15 (d, 1H, ^3J(H6,H7) = 10.8, H-C(6)), 4.58 (d, 1H, ^3J(H4,H3) = 8.3, H-C(4)), 4.06 (dq, 1H, ^3J(H7,H6) = 10.8, ^3J(H7,H8) = 6.9, H-C(7)), 3.82 (m, 1H, Ha-C(3′)), 3.55 (m, 1H, Hb-C(3′)), 3.26 (dd, 1H, ^2J = 14.2, ^3J(H1′,H2′) = 5.6, H-C(1′)), 2.77 (m, 2H, H-C(1′), H-C(3)), 2.47 (qdddd, 1H, ^3J(H2′,3′a,b) = ^3J(H2′,H1′a,b) = ^3J(H2′-Me2′) = 5.6, H-C(2′)), 2.16 (s, 3H, H-C(1)), 1.85 (s, 3H, *Me*-C(5)), 1.70 (brs,1H, H-OH), 1.45 (d, 3H, ^3J(H8,H7) = 6.9, H-C(8)), 1.19 (d, 3H, ^3J(Me2′,H2′) = 6.7, *Me*-C(2′)), 1.17 (d, 3H, ^3J(Me3,H3) = 6.72, *Me*-C(3)), 0.92 (s, 9H, *t*Bu-Si), 0.12 (s, 3H, Me_2-Si), 0.09 (s, 3H, Me_2-Si); ^{13}C NMR(100.6 MHz, $CDCl_3$): δ = 210.6 (s, CO), 136.2 (s, C(5)), 125.8 (d, ^1J(C,H) = 143, C(6)), 72.4 (d, ^1J(C,H) = 139, C(4)), 68.2 (t, ^1J(C,H) = 145, C(3′)), 66.5 (t, ^1J(C,H) = 148, C(1′)), 57.8 (d, ^1J(C,H) = 137, C(7)), 52.8 (d, ^1J(C,H) = 140, C(3)), 52.4 (d, ^1J(C,H) = 128, C(2′)), 31.5 (q, ^1J(C,H) = 130, C(1)), 25.9 (q, ^1J(C,H) = 128, *t*Bu-Si), 20.9 (q, ^1J(C,H) = 135, *Me*-C(5)), 18.6 (s, C_{quat}-*t*Bu-Si), 17.8 (q, ^1J(C,H) = 122, C(8)), 15.7 (q, ^1J(C,H) = 130, *Me*-C(2′)), 14.6 (q, ^1J(C,H) = 132, *Me*-C(3)), 4.79 (q, ^1J(C,H) = 122, Me_2-Si), −0.09 (q, ^1J(C,H) = 126, Me_2-Si).

2:2:1:1 Mixture of (±)-methyl esters (±)-18a–d: The solution of hypobromite was first prepared by slow addition of Br_2 (6.69 g, 2.15 mL, 41.8 mmol, 3.2 equiv) to a yellow solution of NaOH (5.23 g, 130.8 mmol, 10 equiv) in dioxane/water 4:1 (250 mL) at a temperature between −10 °C and 0 °C. After a 20 min period, the resulting hypobromite was transferred into the above solution of (±)-**17a–d** (5.5 g, 13.08 mmol, 1 equiv) in dioxane/water 4:1 (125 mL) at −10 °C. After 3 h below 10 °C, an additional portion of hypobromite (Br_2; 2.23 g, 0.72 mL, 13.9 mmol, 1.1 equiv; in a solution of NaOH (1.74 g, 43.6 mmol, 3.3 equiv) in dioxane/water 4:1 (50 mL)) was added to complete the reaction. The crude mixture was then treated with an aqueous saturated solution of $Na_2S_2O_3$ (50 mL, until disappearance of the color of the bromine) and acidified with 1 N HCl to pH 3. The resulting mixture was extracted with Et_2O (3× 100 mL). The combined organic extracts were washed with brine (2× 150 mL), dried (Na_2SO_4), and the solvent evaporated under reduced pressure. The residue was used in the next step without further purification. To this crude mixture (5.6 g, 13.01 mmol, 1 equiv) in Et_2O (50 mL) was added a solution of diazomethane (0.1 M in Et_2O) until a yellow color persisted. After 30 min at 0 °C, the reaction mixture was quenched with AcOH (0.5 mL) and concentrated under reduced pressure. FC (petroleum ether/ethyl acetate 3:2) gave a 2:2:1:1 mixture of (±)-**18a**,**b**,**c**,**d** (4.29 g, 75%). R_f = 0.31 (petroleum ether/ethyl acetate 3:2); IR (film): $\tilde{\nu}$ = 3456, 2957, 2934, 2859, 1737, 1461, 1377, 1298, 1258, 1134, 1077, 839, 788 cm^1; UV (CH_3CN): λ_{max} = 224 nm (ε = 7562), 196 (8260); CI-MS (NH_3): *m*/*z* (%): calcd for $C_{20}H_{40}O_6SSi$: 436.680; found: 454 (72) $[M+H_2O]^+$, 437 (11) $[M+H]^+$; elemental analysis calcd (%) for $C_{20}H_{40}O_6SSi$ (436.68): C 55.01, H 9.23; found: C 55.21, H 9.40.

(±)-18a,**b**: The NMR spectra of (±)-**18a** and (±)-**18b** (α,β-*syn* with either 2′*R* or 2′*S* configuration) overlap for all ^{1}H and ^{13}C signals. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.34 (d, 1H, ^3J(H5,H6) = 10.9, H-C(5)), 4.19 (d, 1H, ^3J(H3,H2) = 8.6, H-C(3)), 3.8 (dq, 1H, ^3J(H6,H5) = 10.9, ^3J(H6,H7) = 7.4, H-C(6)), 3.7 (s, 4H, Ha-C(3′) and *Me*O), 3.50 (m, 1H, Hb-C(3′)), 3.23 (dd, 1H, ^2J = 13.4, ^3J(H1′,H2′) = 6.1, Ha-C(1′)), 2.75 (dd, 1H, ^2J = 13.4, ^3J(H1′,H2′) = 6.1, Hb-C(1′)), 2.62 (m, 1H, H-

C(2)), 2.48 (m, 1H, H-C(2′)), 1.75 (s, 3H, *Me*-C(4)), 1.46 (d, 3H, ^3J(H7,H6) = 7.4, H-C(7)), 1.18 (d, 3H, ^3J(Me2′,H2′) = 6.7, *Me*-C(2′)), 1.19 (d, 3H, ^3J(Me3,H3) = 7.04, *Me*-C(3)), 0.90 (s, 9H, *t*Bu-Si), 0.08 (s, 3H, Me_2-Si), 0.01 (s, 3H, Me_2-Si); ^{13}C NMR(100.6 MHz, $CDCl_3$): δ = 172.9 (s, CO), 141.2 (s, C(4)), 120.7 (d, ^1J(C,H) = 153, C(5)), 78.0 (d, ^1J(C,H) = 146, C(3)), 64.5 (t, ^1J(C,H) = 140, C(3′)), 55.2 (t, ^1J(C,H) = 145, C(1′)), 49.6 (q, ^1J(C,H) = 126, *Me*O), 49.2 (d, ^1J(C,H) = 128, C(6)), 43.2 (d, ^1J(C,H) = 148, H-C(2)), 29.2 (d, ^1J(C,H) = 133, C(2′)), 24.2 (q, ^1J(C,H) = 137, *t*BuSi-C(4)), 22.0 (s, C_{quat}-*t*Bu), 21 (q, ^1J(C,H) = 125, *Me*-C(5)), 16.0 (q, ^1J(C,H) = 132, H-C(8)), 15 (s, C-*t*Bu), 14.3 (q, ^1J(C,H) = 129, *Me*-C(2′)), 12.2 (q, ^1J(C,H) = 128, *Me*-C(3)), −1.60 (q, ^1J(C,H) = 120, Me_2Si), −7.11 (q, ^1J(C,H) = 122, Me_2-Si).

(±)-18c,d: The NMR spectra of (±)-**18c** and (±)-**18d** (α,β-*syn* with either 2′*R* or 2′*S* configuration) overlap for all ^{1}H and ^{13}C signals. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.37 (d, 1H, ^3J(H6,H7) = 10.9, H-C(6)), 4.19 (d, 1H, ^3J(H4,H3) = 8.6, H-C(4)), 3.8 (dq, 1H, ^3J(H7,H6) = 10.9, ^3J(H7,H8) = 7.4, H-C(7)), 3.6 (s, 4H, Ha-C(3′) and *Me*O), 3.50 (m, 1H, H-C(3′)), 3.07 (dd, 1H, ^2J = 13.4, ^3J(H1′,H2′) = 6.1, Ha-C(1′)), 2.65 (dd, 1H, ^2J = 13.4, ^3J(H1′,H2′) = 6.1, Hb-C(1′)), 2.62 (m, 1H, H-C(3)), 2.45 (m, 1H, H-C(2′)), 1.65 (s, 3H, *Me*-C(5)), 1.46 (d, 3H, ^3J(H8,H7) = 7.4, H-C(8)), 1.19 (d, 3H, ^3J(Me2′,H2′) = 6.7, *Me*-C(2′)), 1.18 (d, 3H, ^3J(Me3,H3) = 7.04, *Me*-C(3)), 0.90 (s, 9H, *t*Bu-Si), 0.08 (s, 3H, Me_2Si), 0.01 (s, 3H, Me_2-Si); ^{13}C NMR(100.6 MHz, $CDCl_3$): δ = 173.0 (s, CO), 141.0 (s, C(4)), 120.6 (d, ^1J(C,H) = 153, C(5)), 78.0 (d, ^1J(C,H) = 146, C(3)), 64.5 (t, ^1J(C,H) = 140, C(3′)), 54.9 (t, ^1J(C,H) = 145, C(1′)), 49.4 (q, ^1J(C,H) = 126, *Me*O), 49.0 (d, ^1J(C,H) = 128, C(6)), 43.1 (d, ^1J(C,H) = 148, H-C(2)), 27.9 (d, ^1J(C,H) = 133, C(2′)), 24.2 (q, ^1J(C,H) = 137, *t*Bu-Si), 22.0 (s, C_{quat}-*t*Bu), 20.9 (q, ^1J(C,H) = 127, *Me*-C(4)), 16.0 (q, ^1J(C,H) = 132, H-C(7)), 14.9 (s, C-*t*Bu), 13.3 (q, ^1J(C,H) = 129, *Me*-C(2′)), 11.2 (q, ^1J(C,H) = 128, *Me*-C(2)), −1.60 (q, ^1J(C,H) = 120, Me_2Si), −6.52 (q, ^1J(C,H) = 122, Me_2-Si).

2:2:1:1 Mixture of methyl esters (±)-19a–d: Imidazole (611 mg, 8.9 mmol, 1.2 equiv) followed by TBDPSCl (2.12 g, 1.97 mL, 7.6 mmol, 1.2 equiv) were added at 0 °C to the above solution of (±)-**17a–d** (3.26 g, 6.9 mmol, 1 equiv) in anhydrous DMF (20 mL). After stirring at 20 °C for 12 h under an Ar atmosphere, the crude mixture was treated with a saturated aqueous solution of $NaHCO_3$ (60 mL) and extracted with Et_2O (3× 100 mL). The combined organic extracts were washed with brine (2× 60 mL), dried (Na_2SO_4), and the solvent evaporated under reduced pressure. The same procedure as for the preparation of compound (±)-**18a–d** was then applied to the crude mixture of TBDPS-protected methyl ketone. FC (petroleum ether/ethyl acetate 3:2) gave a 2:2:1:1 mixture of (±)-**19a,b,c,d** as a colorless oil (2.37 g, 51%, overall). R_f = 0.31 (petroleum ether/ethyl acetate 3:2); IR (film): $\tilde{\nu}$ = 2957, 2932, 2858, 1735, 1714, 1473, 1429, 1300, 1258, 1131, 1082, 939, 839, 778 cm^{-1}; CI-MS (NH_3): *m*/*z* (%): calcd for $C_{36}H_{58}O_6SSi_2$: 675.079; found: 693 (18) $[M+H_2O]^+$, 675 (100) $[M+H]^+$; elemental analysis calcd (%) for $C_{36}H_{58}O_6SSi_2$ (675.08): C 64.05, H 8.66; found: C 64.09, H 8.71.

(±)-19a,b: The NMR spectra of (±)-**19a** and (±)-**19b** (α,β-*syn* with either 2′*R* or 2′*S* configuration) overlap for all ^{1}H and ^{13}C signals. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, 4H, ^3J = 8.0, H-C(ar)), 7.48–7.41 (m, 6H, H-C(ar)), 5.41 (d, 1H, ^3J(H5,H6) = 9.9, H-C(5)), 4.32 (d, 1H, ^3J(H3,H2) = 6.1, H-C(3)), 3.81 (dq, 1H, ^3J(H6,H5) = 9.9, ^3J(H6,H7) = 6.7, H-C(6)), 3.65 (m, 4H, *Me*O and Ha-C(3′)), 3.53 (m, 1H, Hb-C(3′)), 3.22 (dd, 1H, ^2J = 13.1, ^3J(H1′,H2′) = 6.7, Ha-C(1′)), 2.65 (m, 2H, H-C(3) and Hb-C(1′)), 2.50 (m, 1H, H-C(2′)), 1.74 (s, 3H, *Me*-C(4)), 1.43 (d, 3H, ^3J(H8,H7) = 6.7, H-C(8)), 1.17 (d, 3H, ^3J(Me2′,H2′) = 6.7, *Me*-C(2′)), 1.15 (d, 3H, ^3J(Me2,H2) = 7.1, *Me*-C(2)), 1.09 (s, 9H, *t*Bu-Si), 0.90 (s, 9H, *t*Bu-Si), 0.04 (s, 3H, Me_2-Si), −0.01 (s, 3H, Me_2-Si); ^{13}C NMR(100.6 MHz, $CDCl_3$): δ = 174.8 (s, CO), 144.2 (s, C(4)), 136.0 (s, 2C(ar)), 133.7 (d, 5C, ^1J(C,H) = 132, C(ar)), 130.1 (d, 5C, ^1J(C,H) = 134, C(ar)), 120.9 (d, ^1J(C,H) = 150, C(5)), 78.5 (d, ^1J(C,H) = 141, C(3)), 68.1 (t, ^1J(C,H) = 140, C(3′)), 58.6 (t, ^1J(C,H) = 142, C(1′)), 52.6 (q, ^1J(C,H) = 129, *Me*O), 45.5 (d, ^1J(C,H) = 132, C(6)), 40.9 (d, ^1J(C,H) = 148, C(2)), 29.2 (d, ^1J(C,H) = 133, C(2′)), 25.9 (q, ^1J(C,H) = 137, *t*Bu-Si), 24.2 (q, ^1J(C,H) = 135, *t*Bu-Si), 22.0 (q, ^1J(C,H) = 124, C(4)), 19.7 and 18.4 (2s, C_{quat}-*t*Bu), 17.5 (q, ^1J(C,H) = 122, C(7)), 14.6 (q, ^1J(C,H) = 132, *Me*-C(2′)), 12.7 (q, ^1J(C,H) = 130, *Me*-C(2)), −3.90 (q, ^1J(C,H) = 126, Me_2-Si), −4.08 (q, ^1J(C,H) = 124, Me_2-Si).

(±)-19c,d: The NMR spectra of (±)-**19c** and (±)-**19d** (α,β-*syn* with either 2′*R* or 2′*S* configuration) overlap for all ^{1}H and ^{13}C signals. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (d, 4H, ^3J = 8.0, H-C(ar)), 7.48–7.41 (m, 6H, H-C(ar)), 5.44 (d, 1H, ^3J(H6,H7) = 9.9, H-C(5)), 4.29 (d, 1H, ^3J(H3,H2) = 6.4, H-C(3)), 3.81 (dq, 1H, ^3J(H6,H5) = 9.9, ^3J(H6,H7) = 6.7, H-C(6)), 3.69 (m, 4H, *MeO*, Ha-C(3′)), 3.53 (m, 1H, H-C(3′)), 3.14 (dd, 1H, ^2J = 13.4, ^3J(H1′,H2′) = 6.9, Ha-C(1′)), 2.65 (m, 2H, H-C(3) and Hb-C(1′)), 2.52 (m, 1H, H-C(2′)), 1.71 (s, 3H, *Me*-C(4)), 1.43 (d, 3H, ^3J(H7,H6) = 6.7, H-C(7)), 1.17 (d, 3H, ^3J(Me2′,H2′) = 6.7, *Me*-C(2′)), 1.15 (d, 3H, ^3J(Me2,H2) = 7.1, *Me*-C(2)), 1.09 (s, 9H, *t*Bu-Si), 0.90 (s, 9H, *t*Bu-Si), 0.05 (s, 3H, Me_2-Si), −0.02 (s, 3H, Me_2-Si); ^{13}C NMR(100.6 MHz, $CDCl_3$): δ = 174.8 (s, CO), 143.8 (s, C(4)), 135.9 (s, 2C(ar)), 133.5 (d, 5C, ^1J(C,H) = 132, C(ar)), 130.0 (d, 5C, ^1J(C,H) = 134, C(ar)), 120.3 (d, ^1J(C,H) = 152, C(5)), 78.4 (d, ^1J(C,H) = 139, C(3)), 68.0 (t, ^1J(C,H) = 140, C(3′)), 58.4 (t, ^1J(C,H) = 142, C(1′)), 51.9 (q, ^1J(C,H) = 129, *Me*O), 45.6 (d, ^1J(C,H) = 132, C(6)), 40.8 (d, ^1J(C,H) = 146, C(2)), 29.2 (d, ^1J(C,H) = 133, C(2′)), 26.1 (q, ^1J(C,H) = 137, *t*BuSi), 24.2 (q, ^1J(C,H) = 135, *t*BuSi), 21.3 (q, ^1J(C,H) = 141, C(4)), 19.7 and 18.4 (2s, C_{quat}-*t*Bu), 17.6 (q, ^1J(C,H) = 122, C(8)), 14.4 (q, ^1J(C,H) = 132, *Me*-C(2′)), 12.3 (q, ^1J(C,H) = 130, *Me*-C(2)), −3.90 (q, ^1J(C,H) = 126, Me_2Si), −4.09 (q, ^1J(C,H) = 124, Me_2Si).

2:1 Mixture of dienoates (±)-(*E*,*E*)-21a, and (±)-(*E*,*Z*)-21b: A solution of *t*BuLi (1.5 M in THF, 0.74 mL, 1.11 mmol, 3 equiv) was added dropwise to the above solution of (±)-**19a–d** (250 mg, 0.37 mmol, 1 equiv) in anhydrous THF (1 mL) cooled to −100 °C,. The mixture was stirred at −100 °C for 30 min, and a solution of NIS (99 mg, 0.44 mmol, 1.2 equiv) in anhydrous THF (1 mL) at −100 °C was added with a cannula. The resultant mixture was allowed to warm to room temperature overnight and then transferred with a cannula to a suspension of alumina-supported potassium hydroxide in dry CH_2Cl_2 (2 mL). The crude mixture was stirred at 20 °C for 48 h under an Ar atmosphere. After dilution with CH_2Cl_2 (10 mL), the supported base was removed by suction filtration through a pad of Celite. The reaction vessel and filter cake were rinsed thoroughly with CH_2Cl_2 (10 mL). The organic layer was washed with brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. FC (petroleum ether/ethyl acetate 97:3, R_f = 0.37) gave a 2:1 mixture of (±)-(*E*,*E*)-**21a** and (±)-(*E*,*Z*)-**21b** as a colorless oil (134 mg, 60%). The structure was confirmed with a NOESY spectrum: NOE's between H-C(5)↔H-C(7), H-C(4)↔H-C(7) and Me-C(4)↔Me-C(6) were observed. IR (film): $\tilde{\nu}$ = 3420, 3070, 2960, 2930, 2855, 2360, 1700, 1660, 1470, 1430, 1360, 1260, 1110 cm^{-1}; CI-MS (NH_3): *m*/*z* (%): calcd for $C_{35}H_{54}O_4Si_2$: 594.911; found: 612 (100) $[M+H_2O]^+$, 595 (12) $[M+H]^+$; elemental analysis calcd (%) for $C_{35}H_{54}O_4SSi_2$ (594.91): C 70.65, H 8.66; found: C 70.69, H 9.15.

(±)-(*E*,*E*)-21a: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, 4H, ^3J = 8.3, H-C(ar)), 7.41 (t, 6H, ^3J = 8.3, H-C(ar)), 5.87 (brs, 1H, H-C(5)), 5.04 (d, 1H, ^3J(H7,H8) = 9.9, H-C(7)), 4.28 (d, 1H, ^3J(H3,H2) = 6.9, H-C(3)), 3.49 (dd, 1H, ^2J = 13.1, ^3J(H9,H8) = 6.7, Ha-C(9)), 3.41 (dd, 1H, ^2J = 13.1, ^3J(H9,H8) = 6.7, Hb-C(9)), 3.28 (dq, 1H, ^3J(H_2,H_3) = 6.9, ^3J(H_2-Me_2) = 6.7, H-C(2)), 2.55 (m, 1H, H-C(8)), 1.73 (s, 3H, *Me*-C(4)), 1.64 (s, 3H, *Me*-C(6)), 1.15 (d, 3H, ^3J(Me2,H2) = 6.7, *Me*-C(2)), 1.12 (d, 3H, ^3J(Me8,H8) = 6.7, *Me*-C(8)), 1.06 (s, 9H, *t*BuSi), 0.90 (s, 9H, *t*Bu-Si), 0.1 (s, 3H, Me_2-Si), 0.02 (s, 3H, Me_2-Si); ^{13}C NMR(100.6 MHz, $CDCl_3$): δ = 179.0 (s, CO), 136.0 (s, C(6)), 134.3 (s, 2 C(ar)), 134.0 (s, C(4)), 132.5 and 130.1 (2d, ^1J(C,H) = 132, 10 C(ar)), 127.9 (d, ^1J(C,H) = 150, C(5)), 125.9 (d, ^1J(C,H) = 150, C(7)), 78.8 (d, ^1J(C,H) = 154, C(3)), 66.9 (t, ^1J(C,H) = 156, C(9)), 43.9 (d, ^1J(C,H) = 148, C(2)), 34.4 (d, ^1J(C,H) = 139, C(8)), 25.2 (q, ^1J(C,H) = 142, *t*Bu-Si), 24.7 (q, ^1J(C,H) = 150, *t*Bu-Si), 19.7 and 18.4 (2 s, C_{quat}-*t*Bu), 17.8 (q, ^1J(C,H) = 142, *Me*-C(6)), 16.7 (q, ^1J(C,H) = 142, *Me*-C(4)), 15.9 (q, ^1J(C,H) = 138, *Me*-C(2)), 11.7 (q, ^1J(C,H) = 131, *Me*-C(8)), −3.90 (q, ^1J(C,H) = 127, Me_2-Si), −6.06 (q, ^1J(C,H) = 126, Me_2-Si).

(±)-(*E*,*Z*)-21b: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, 4H, ^3J = 8.3, H-C(ar)), 7.41 (t, 6H, ^3J = 8.3, H-C(ar)), 5.79 (brs, 1H, H-C(5)), 5.04 (d, 1H, ^3J(H7,H8) = 9.9, H-C(7)), 4.28 (d, 1H, ^3J(H3,H2) = 6.9, H-C(3)), 3.49 (dd, 1H, ^2J = 13.1, ^3J(H9,H8) = 6.7, Ha-C(9)), 3.41 (dd, 1H, ^2J =

13.1, ^3J(H9,H8) = 6.7, Hb-C(9)), 3.28 (dq, 1H, ^3J(H_2,H_3) = 6.9, ^3J(H_2-Me_2) = 6.7, H-C(2)), 2.55 (m, 1H, H-C(8)), 1.72 (s, 3H, *Me*-C(4)), 1.63 (s, 3H, *Me*-C(6)), 1.13 (d, 3H, ^3J(Me2,H2) = 6.7, *Me*-C(2)), 1.11 (d, 3H, ^3J(Me8,H8) = 6.7, *Me*-C(8)), 1.05 (s, 9H, *t*BuSi), 0.88 (s, 9H, *t*Bu-Si), 0.08 (s, 3H, Me_2-Si), −0.02 (s, 3H, Me_2-Si); ^{13}C NMR(100.6 MHz, $CDCl_3$): δ = 179.0 (s, CO), 135.0 (s, C(6)), 134.3 (s, 2 C(ar)), 134.0 (s, C(4)), 132.5 and 130.1 (2d, ^1J(C,H) = 132, 10 C(ar)), 127.9 (d, ^1J(C,H) = 150, C(5)), 125.9 (d, ^1J(C,H) = 150, C(7)), 78.8 (d, ^1J(C,H) = 154, C(3)), 66.9 (t, ^1J(C,H) = 156, C(9)), 43.9 (d, ^1J(C,H) = 148, C(2)), 34.4 (d, ^1J(C,H) = 139, C(8)), 25.2 (q, ^1J(C,H) = 142, *t*Bu-Si), 24.7 (q, ^1J(C,H) = 150, *t*Bu-Si), 19.7 and 18.4 (2s, C-*t*Bu), 17.2 (q, ^1J(C,H) = 142, *Me*-C(6)), 16.4 (q, ^1J(C,H) = 144, *Me*-C(4)), 15.9 (q, ^1J(C,H) = 133, *Me*-C(2)), 10.9 (q, ^1J(C,H) = 131, Me-C(8)), −3.98 (q, ^1J(C,H) = 128, Me_2-Si), −5.1 (q, ^1J(C,H) = 128, Me_2-Si).

2:1 Mixture of dienoates (±)-20a,b: $MeOCH_2Cl$ (560.3 mg, 6.96 mmol, 0.53 mL, 1.5 equiv) was added to a cooled solution (0 °C) of (±)-**18a–d** (2 g, 4.64 mmol, 1 equiv) and *N*,*N*-diisopropylethylamine (1.16 g, 9.29 mmol, 1.54 mL, 2 equiv) in anhydrous CH_2Cl_2 (20 mL). The mixture was stirred under an Ar atmosphere for 1 h at 0 °C and then overnight at 20 °C. After dilution with CH_2Cl_2 (10 mL), the mixture was washed successively with water, 10% HCl (10 mL), aqueous saturated solution of $NaHCO_3$ (2×10 mL), and brine (2×10 mL). The combined organic extracts were dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. The resulting crude solution (brownish oil) was mixed with anhydrous CH_3CN (25 mL), and the mixture was heated under reflux overnight in the presence of DBU (4.95 g, 4.85 mL, 26.2 mmol, 7 equiv). It was then diluted with CH_2Cl_2 (20 mL) and washed with brine (2×20 mL). The combined aqueous layers were extracted with CH_2Cl_2 (3×20 mL) and the combined organic extracts were dried (Na_2SO_4). The solvent was evaporated under reduced pressure under reflux. FC (petroleum ether/ethyl acetate 7:3) gave a 2:1 mixture of (±)-**20a** and (±)-**20b** as a colorless oil (830 mg, 70%). R_f = 0.34 (petroleum ether/ethyl acetate 7:3); IR (film): $\tilde{\nu}$ = 2965, 2934, 2879, 1737, 1667, 1631, 1456, 1379, 1294, 1214, 1126, 1043, 919 cm^{-1}; CI-MS (NH_3): *m*/*z* (%): calcd for $C_{16}H_{28}O_6S$: 348.456; found: 366 (100) $[M+H_2O]^+$, 349 (17) $[M+H]^+$; elemental analysis calcd (%) for $C_{16}H_{28}O_6S$ (348.46): C 55.15, H 8.10; found: C 55.54, H 8.32.

(±)-20a: ^{1}H NMR (400 MHz, $CDCl_3$)δ = 7.07 (s, 1H, H-C(3)), 5.60 (d, 1H, ^3J(H5,H6) = 9.9, H-C(5)), 4.63 (s, 2H, CH_2-MOM), 3.57 (m, 2H, Ha-C(3′) and H-C(6)), 3.39 (s, 3H, CH_3-MOM), 3.37 (s, 3H, *Me*O), 3.27 (dd, 1H, ^2J = 13.8, ^3J(H3′,H2′) = 6.7, Hb-C(3′)), 2.78 (dd, 1H, ^2J = 14.4, ^3J(H1′,H2′) = 6.7, Ha-C(1′)), 2.63 (m, 1H, Hb-C(1′)), 2.32 (qdddd, 1H, ^3J(H2′,H1′) = ^3J(H2′,H3′) = ^3J(H2′-Me2′) = 6.7, H-C(2′)), 2.20 (s, 3H, *Me*-C(2)), 1.91 (s, 3H, *Me*-C(4)), 1.17 (d, 3H, ^3J(H7,H6) = 6.7, H-C(7)), 1.06 (d, 3H, ^3J(Me2′,H2′) = 6.7, *Me*-C(2′)); ^{13}C NMR(100.6 MHz, $CDCl_3$): δ = 169.3 (s, CO), 143.1 (s, C(2)), 139.9 (d, ^1J(C,H) = 160, C(3)), 133.8 (s, C(4)), 127.4 (d, ^1J(C,H) = 158, C(5)), 96.9 (t, ^1J(C,H) = 165, CH_2-MOM), 71.6 (t, ^1J(C,H) = 143, C(3′)), 55.9 (q, ^1J(C,H) = 148, *Me*O), 55.7 (q, ^1J(C,H) = 148, *Me*-MOM), 55.1 (t, ^1J(C,H) = 146, C(1′)), 53.3 (d, ^1J(C,H) = 146, C(6)), 29.4 (d, ^1J(C,H) = 137, C(2′)), 18.1 (q, ^1J(C,H) = 137, *Me*-C(5)), 17.9 (q, ^1J(C,H) = 131, *Me*-C(2)), 16.8 (q, ^1J(C,H) = 131, C(7)), 13.7 (q, ^1J(C,H) = 145, *Me*-C(2′)).

(±)-20b: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.11 (s, 1H, H-C(3)), 5.60 (d, 1H, ^3J(H5,H6) = 9.9, H-C(5)), 4.71 (s, 2H, CH_2-MOM), 3.57 (m, 2H, H-C(6) and Ha-C(3′)), 3.39 (s, 3H, CH_3-MOM), 3.37 (s, 3H, *Me*O), 3.27 (dd, 1H, ^2J = 13.8, ^3J(H3′,H2′) = 6.1, Hb-C(3′)), 2.78 (dd, 1H, ^2J = 14.4, ^3J(H1′,H2′) = 6.1, Ha-C(1′)), 2.63 (m, 1H, Hb-C(1′)), 2.32 (o, 1H, ^3J(H2′,H1′) = ^3J(H2′,H3′) = ^3J(H2′,Me2′) = 6.1, H-C(2′)), 2.17 (s, 3H, *Me*-C(2)), 1.90 (s, 3H, *Me*-C(4)), 1.16 (d, 3H, ^3J(H7,H6) = 7.1, H-C(7)), 1.06 (d, 3H, ^3J(C,Me2′,H2′) = 7.4, *Me*-C(2′)); ^{13}C NMR(100.6 MHz, $CDCl_3$): δ = 169.3 (s, CO), 141.9 (s, C(2)), 139.9 (d, ^1J(C,H) = 160, C(3)), 133.4 (s, C(4)), 127.1 (d, ^1J(C,H) = 158, C(5)), 95.7 (t, ^1J(C,H) = 162, CH_2-MOM), 71.6 (t, ^1J(C,H) = 143, C(3′)), 55.9 (q, ^1J(C,H) = 148, *Me*O), 55.7 (q, ^1J(C,H) = 148, CH_3-MOM), 55.1 (t, ^1J(C,H) = 146, C(1′)), 52.5 (d, ^1J(C,H) = 146, C(6)), 29.0 (d, ^1J(C,H) = 137, C(2′)), 17.8 (q, ^1J(C,H) = 137, *Me*-C(4)), 17.6 (q, ^1J(C,H) = 131, *Me*-C(2)), 16.5 (q, ^1J(C,H) = 131, C(7)), 13.6 (q, ^1J(C,H) = 130, *Me*-C(2′)).

Racemic triene (±)-(*E*,*E*,*E*)-22: A solution of 2:1 mixture of (±)-**20** (38 mg, 0.1 mmol) in anhydrous THF (2 mL) was cooled to −100 °C, and a solution of *t*BuLi (1.5 M in THF, 0.2 mL, 0.3 mmol, 3 equiv) was added dropwise. After stirring at −100 °C for 40 min, a solution of NIS (0.43 mg, 0.2 mmol, 2 equiv) in anhydrous THF (1 mL) at −100 °C was added to the reaction with a cannula. The resultant mixture was allowed to warm to 20 °C overnight. The mixture was cooled once again to −100 °C before addition of *t*BuLi (0.6 mL, 0.9 mmol, 9 equiv) and then stirred at 20 °C for 4 h under an Ar atmosphere. After dilution with Et_2O (5 mL), the mixture was washed with aqueous saturated solution of NH_4Cl (3×10 mL) and then with brine (3×10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The crude residue was then added to anhydrous CH_2Cl_2 (2 mL) and cooled to −78 °C before the addition of TMSBr (16.5 mg, 0.11 mmol, 1.1 equiv). After 2 h at this temperature, the reaction mixture was allowed to warm to RT within 5 h. It was then diluted with CH_2Cl_2 (5 mL), neutralized with aqueous saturated solution of $NaHCO_3$, and washed with brine (2× 10 mL). The combined aqueous layers were extracted with CH_2Cl_2 (3× 10 mL) and the combined organic extracts were dried (Na_2SO_4), and the solvent evaporated under reduced pressure under with FC (petroleum ether/ethyl acetate 3:2) to give a colorless oil (7.5 mg, 32%). R_f = 0.25 (petroleum ether/ethyl acetate 3:2).

(±)-(*E*,*E*,*E*)-22a: ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 7.11 (s, 1H, H-C(3)), 6.12 (s, 1H, H-C(5)), 5.01 (d, 1H, ^3J(H7,H8) = 9.2, H-C(7)), 3.52 (m, 2H, H-C(9)), 2.67 (m, 1H, H-C(8)), 2.09 (s, 3H, ^3J(Me2,H3) = 1.2, *Me*-C(2)), 1.98 (s, 6H, *Me*-C(4), *Me*-C(6)), 1.01 (d, 3H, ^3J(Me8,H8) = 7.1, *Me*-C(8)); ^{13}C NMR(100 MHz, CD_3Cl, 283 K): δ = 169.1 (s, C(1)), 144.1 (d, ^1J(H,C) = 160, C(3)), 139.5 (s, C(2)), 133.4 (s, C(4)), 132.7 (d, ^1J(H,C) = 161, C(5)), 130.8 (s, C(6)), 124.7 (d, ^1J(H,C) = 159, C(7)), 61.7 (d, ^1J(H,C) = 156, C(8)), 52.5 (q, ^1J(H,C) = 141, OCH_3), 51.8 (t, ^1J(H,C) = 145, C(9)), 17.9 (q, ^1J(H,C)) = 129, *Me*-C(2)), 17.7 (q, ^1J(H,C)) = 129, *Me*-C(4)), 17.2 (q, ^1J(H,C)) = 128, *Me*-C(6)), 13.8 (q, ^1J(H,C)) = 129, *Me*-C(8)); IR (film): $\tilde{\nu}$ = 3500, 3090, 2970, 2955, 1710, 1620, 1480, 1410, 1380, 1265, 1120 cm^{-1}; MALDI-HRMS: *m*/*z*: calcd for $C_{14}H_{22}O_3Na$: 238.1569, found 238.1574 $[M+Na]^+$.

3:3:2:2 Mixture of aldols 26a–d: The mixture was prepared as described above for the preparation of (±)-**16**, staring from (*E*,*E*)-2-methyl-1-trimethylsilyloxy-1,3-pentadiene (6.3 g, 36.9 mmol, 1 equiv) and a 1:1 mixture of (*E*/*Z*)-2-triethylsilyloxy-2-butene (16 g, 92.3 mmol, 2.5 equiv). The reaction mixture was quenched with a 1 M solution of Bu_4NF in THF (36.9 mL, 36.9 mmol, 1 equiv) and (+)-**25** (27 g, 110.7 mmol, 3 equiv) in DMF/CH_3CN 4:1 (125 mL). FC (petroleum ether/ethyl acetate 9:1) gave residual back (+)-**25** and then (petroleum ether/ethyl acetate 2:3) a 1:1:1:1 mixture of **26a–d** as yellow oil (10.6 g, 82%). R_f = 0.45 (petroleum ether/ethyl acetate 2:3); IR (film): $\tilde{\nu}$ = 3350, 2980, 2950, 1720, 1655, 1440, 1375, 1310, 1225, 1210, 1120, 1040, 795 cm^{-1}; MALDI-HRMS: *m*/*z*: calcd for $C_{16}H_{30}O_6SNa$: 373.1661, found 373.1698 $[M+Na]^+$.

Compounds 26a,c: The NMR spectra of (±)-**26a** and (±)-**26c** overlap for all ^{1}H and ^{13}C signals. ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 5.41 (d, 1H, ^3J(H6,H7) = 10.2, H-C(6)), 4.67–4.64 (m, 2H, CH_2-MOM), 4.52 (d, 1H, ^3J(H4,H3) = 7.1, H-C(4)), 4.07 (m, 1H, H-C(7)), 3.61 (m, 1H, H-C(3′)), 3.48 (m, 1H, H-C(3′)), 3.39 (s, 3H, OCH_3-MOM), 3.25 (dd, 1H, ^2J = 13.2, ^3J(H1′,H2′) = 7.1, H-C(1′)), 3.02–2.90 (m, 1H, H-C(1′)), 2.54 (m, 1H, H-C(2′)), 2.15 (s, 3H, H-C(1)), 1.83 (s, 3H, *Me*-C(5)), 1.46 (d, 3H, ^3J(H8,H7) = 6.4, H-C(8)), 1.23 (d, 3H, ^3J(Me3,H3) = 6.4, *Me*-C(3)), 0.97 (d, 3H, ^3J(Me2′,H2′) = 7.1, *Me*-C(2′)); ^{13}C NMR(100 MHz, $CDCl_3$, 283 K): δ = 210.9 (s, C(2)), 144.0 (s, C(5)), 119.8 (d, ^1J(H,C) = 168, C(6)), 96.4 (t, ^1J(H,C) = 151, CH_2-MOM), 71.7 (d, ^1J(H,C) = 136, C(7)), 58.3 (q, ^1J(H,C) = 144, OCH_3-MOM), 52.4 (d, ^1J(H,C) = 139, C(2′)), 50.5 (d, ^1J(H,C) = 142, C(4)), 44.1 (d, ^1J(H,C) = 139, C(3)), 40.1 (t, ^1J(H,C) = 129, C(1′)), 39.5 (t, ^1J(H,C) = 131, C(3′)), 29.8 (q, ^1J(H,C) = 132, C(1)), 17.8 (q, ^1J(H,C)) = 131, *Me*-C(3)), 15.2 (q, ^1J(H,C)) = 136, *Me*-C(5)), 14.9 (q, ^1J(H,C)) = 133, C(8)), 7.8 (q, ^1J(H,C)) = 135, *Me*-C(2′)).

Compounds 26b,d: The NMR spectra of (±)-**26b** and (±)-**26d** overlap for all ^{1}H and ^{13}C signals. ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 5.41 (d, 1H, ^3J(H6,H7) = 10.2, H-C(6)), 4.67–4.64 (m, 2H, CH_2-MOM), 4.51 (d, 1H, ^3J(H4,H3) = 7.1, H-C(4)), 4.07 (m, 1H, H-C(7)), 3.61 (m, 1H,

H-C(3′)), 3.48 (m, 1H, H-C(3′)), 3.38 (s, 3H, OC*H*$_3$-MOM), 3.20 (dd, 1H, ^2J = 13.2, ^3J(H1′,H2′) = 7.1, H-C(1′)), 3.02–2.90 (m, 1H, H-C(1′)), 2.54 (m, 1H, H-C(2′)), 2.15 (s, 3H, H-C(1)), 1.83 (s, 3H, *Me*-C(5)), 1.37 (d, 3H, ^3J(H8,H7) = 6.4, H-C(8)), 1.17 (d, 3H, ^3J(Me3,H3) = 6.4, *Me*-C(3)), 0.94 (d, 3H, ^3J(Me2′,H2′) = 7.1, *Me*-C(2′)); ^{13}C NMR(100 MHz, $CDCl_3$, 283 K): δ = 210.9 (s, C(2)), 143.8 (s, C(5)), 119.6 (d, ^1J(H,C) = 170, C(6)), 96.1 (t, ^1J(H,C) = 158, *C*H$_2$-MOM), 71.7 (d, ^1J(H,C) = 154, C(7)), 57.6 (q, ^1J(H,C) = 145, OCH$_3$-MOM), 52.0 (d, ^1J(H,C) = 136, C(2′)), 50.5 (d, ^1J(H,C) = 142, C(4)), 44.1 (d, ^1J(H,C) = 139, C(3)), 39.8 (t, ^1J(H,C) = 132, C(1′)), 38.1 (t, ^1J(H,C) = 137, C(3′)), 28.6 (q, ^1J(H,C) = 136, C(1)), 17.7 (q, ^1J(H,C)) = 129, *Me*-C(3)), 15.2 (q, ^1J(H,C)) = 128, *Me*-C(5)), 14.8 (q, ^1J(H,C)) = 129, C(8)), 7.8 (q, ^1J(H,C)) = 130, *Me*-C(2′)).

1:1 Mixture of dienes 27a,b: *p*-TsOH (1.3 g, 6.8 mmol, 0.8 equiv) in one portion was added to a solution of the above mixture **26a–d** (4 g, 11.3 mmol, 1 equiv) in MeOH (40 mL). The reaction mixture was heated under reflux under Ar for 2 h and stirred at 20 °C for 7 h. After the addition of Et_2O (40 mL), and neutralization with an aqueous saturated solution of $NaHCO_3$ (40 mL), the organic extract was washed with brine (3× 50 mL), dried (Na_2SO_4), and the solvent evaporated under reduced pressure. FC (cyclohexane/ethyl acetate 3:7) gave a 1:1 mixture of **27a** and **27b** as a colorless oil (2.5 g, 76 %). Structure was confirmed with a NOESY experiment. NOEs between H-C(4)↔H-C(6), and Me-C(3)↔Me-C(5) were observed. R_f = 0.30 (cyclohexane/ethyl acetate 3:7); IR (film): $\tilde{\nu}$ = 3350, 2960, 2885, 2935, 1705, 1655, 1625, 1460, 1375, 1310, 1245, 1130, 1030, 850 cm^{-1}; UV (CH_3CN): λ_{max} = 234 nm, (ε = 10000); MALDI-HRMS: *m*/*z*: calcd for $C_{14}H_{24}O_4SNa$: 311.1293, found: 311.1144 [*M*+Na]$^+$; elemental analysis calcd (%) for $C_{14}H_{24}O_4S$ (288.14): C 58.30, H 8.39; found: C 58.30, H 8.38.

Compound 27a: ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 6.96 (s, 1H, H-C(4)), 5.55 (dq, 1H, ^3J(H6,H7) = 10.2, ^4J(H6,Me5) = 1.2, H-C(6)), 4.02 (dq, 1H, ^3J(H7,H6) = 10.2, ^3J(H7,H8) = 6.4, H-C(7)), 3.81 (m, 1H, Ha-C(3′)), 3.54 (m, 1H, Hb-C(3′)), 3.26 (dd, 1H, ^2J = 14.1, ^3J(H1′,H2′) = 6.4, Ha-C(1′)), 2.88 (dd, 1H, ^2J = 14.1, ^3J(H1′,H2′) = 6.4, Hb-C(1′)), 2.48 (m, 1H, H-C(2′)), 2.38 (s, 3H, H-C(1)), 2.00 (s, 3H, *Me*-C(3)), 1.97 (d, 3H, ^4J(Me5,H6) = 1.2, *Me*-C(5)), 1.5 (d, 3H, ^3J(H8,H7) = 6.4, H-C(8)), 1.17 (d, 3H, ^3J(Me2′,H2′) = 7.4, *Me*-C(2′)); ^{13}C NMR(100 MHz, $CDCl_3$, 283 K): δ = 194.2 (s, C(2)), 144.3 (s, C(3)), 141.7 (d, ^1J(H,C) = 160, C(4)), 138.1 (s, C(5)), 127.3 (d, ^1J(H,C) = 159, C(6)), 66.7 (t, ^1J(H,C) = 141, C(1′)), 59.8 (t, ^1J(H,C) = 139, C(3′)), 53.3 (d, ^1J(H,C) = 128, C(7)), 31.3 (d, ^1J(H,C) = 136, C(2′)), 26.3 (q, ^1J(H,C) = 131, C(1)), 17.9 (q, ^1J(H,C)) = 130, *Me*-C(3)), 17.7 (q, ^1J(H,C)) = 135, *Me*-C(5)), 13.5 (q, ^1J(H,C)) = 128, C(8)), 13.1 (q, ^1J(H,C)) = 131, *Me*-C(2′)).

Compound 27b: ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 6.96 (s, 1H, H-C(4)), 5.55 (dq, 1H, ^3J(H6,H7) = 10.2, ^4J(H6,Me5) = 1.2, H-C(6)), 4.0 (dq, 1H, ^3J(H7,H6) = 10.2, ^3J(H7,H8) = 6.4, H-C(6)), 3.81 (m, 1H, Ha-C(3′)), 3.54 (m, 1H, Hb-C(3′)), 3.17 (dd, 1H, ^2J = 13.5, ^3J(H1′a,H2′) = 6.4, Ha-C(1′)), 2.78 (dd, 1H, ^2J = 13.5, ^3J(H1′b,H2′) = 6.4, Hb-C(1′)), 2.48 (m, 1H, H-C(2′)), 2.38 (s, 3H, H-C(1)), 2.00 (s, 3H, *Me*-C(3)), 1.97 (d, 3H, ^4J(Me5,H6) = 1.2, *Me*-C(5)), 1.5 (d, 3H, ^3J(H8,H7) = 6.4, H-C(8)), 1.17 (d, 3H, ^3J(Me2′,H2′) = 7.4, *Me*-C(2′)); ^{13}C NMR(100 MHz, $CDCl_3$, 283 K): δ = 194.2 (s, C(2)), 144.1 (s, C(3)), 141.6 (d, ^1J(H,C) = 162, C(4)), 137.9 (s, C(5)), 127.2 (d, ^1J(H,C) = 156, C(6)), 66.6 (t, ^1J(H,C) = 148, C(1′)), 58.9 (t, ^1J(H,C) = 139, C(3′)), 53.0 (d, ^1J(H,C) = 133, C(7)), 31.2 (d, ^1J(H,C) = 135, C(2′)), 26.3 (q, ^1J(H,C) = 130, C(1)), 17.8 (q, ^1J(H,C)) = 132, *Me*-C(3)), 17.5 (q, ^1J(H,C)) = 131, *Me*-C(5)), 13.3 (q, ^1J(H,C)) = 129, C(8)), 13.1 (q, ^1J(H,C)) = 128, *Me*-C(2′)).

1:1 Mixture of dienoates 28a,b: Et_3N (1.14 mL, 8.2 mmol, 1.1 equiv), followed by TBSOTf (1.5 mL, 7.5 mmol, 1 equiv) was added to a solution of the above mixture of **27a,b** (2.1 g, 7.47 mmol, 1 equiv) in anhydrous CH_2Cl_2 (15 mL) at −10 °C. After 20 min at this temperature, the formation of protected intermediate was complete. Et_3N (3.2 mL, 22.4 mmol, 3 equiv) followed by TMSOTf (1.69 mL, 9.3 mmol, 1.2 equiv) were added to the mixture at −40 °C. After 15 min at this temperature, the formation of silyl enol Et_2O was complete. *m*-CPBA (70 %, 7.4 g, 30 mmol, 4 equiv) was added, and the mixture was stirred at −10 °C for 8 h. After the reaction was complete (TLC), the mixture was extracted with CH_2Cl_2 (3× 40 mL). The combined organic phases were washed with i) aqueous saturated solution of citric acid (2×15 mL), ii) brine (2×50 mL), dried (Na_2SO_4), and the solvents were removed under vacuum. The residue was dissolved in a solution of MeOH/H_2O 2:1 (150 mL), then $NaIO_4$ (4.8 g, 22.41 mmol, 3 equiv) was added in one portion followed by a catalytic amount of Et_3N (0.1 mL, 0.75 mmol, 0.1 equiv). After 8 h at 20 °C, the mixture was diluted with EtOAc (150 mL) and washed with an aqueous saturated solution of citric acid (2×100 mL) and then with an aqueous saturated solution of NH_4Cl (5×100 mL). The aqueous layer was extracted with CH_2Cl_2 (2×100 mL), the combined organic phases were dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. A solution of CH_2N_2 (0.1 M in Et_2O) was added to the crude mixture dissolved in Et_2O (40 mL) and MeOH (1 mL) at 0 °C, until a yellow coloration persisted. After 30 min, the reaction mixture was treated with a dilute solution of acetic acid (10 %, 3 mL) to quench the excess diazomethane. The solvent was evaporated under reduced pressure. FC (petroleum ether/ethyl acetate 85:15) gave a 1:1 mixture of **28a** and **28b** as a colorless oil (1.95 g, 62 %). R_f = 0.31 (petroleum ether/ethyl acetate 85:15); IR (film): $\tilde{\nu}$ = 2955, 2860, 1755, 1715, 1630, 1460, 1370, 1300, 1255, 1115, 1080, 1025, 845, 775 cm^{-1}; MALDI-HRMS: *m*/*z*: calcd for $C_{20}H_{38}O_5SSiNa$: 441.2107, found: 441.2124 [*M*+Na]$^+$.

Compound 28a: ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 7.12 (s, 1H, H-C(3)), 5.54 (dq, 1H, ^3J(H5,H6) = 10.0, ^4J(H5,Me4) = 0.9, H-C(5)), 3.95 (dq, 1H, ^3J(H6,H5) = 10.0, ^3J(H6,H7) = 7.1, H-C(6)), 3.79 (s, 3H, OC*H*$_3$), 3.65 (m, 1H, Ha-C(3′)), 3.44 (m, 1H, Hb-C(3′)), 3.33 (dd, 1H, ^2J = 13.4, ^3J(H1′,H2′) = 4.6, Ha-C(1′)), 2.74 (dd, 1H, ^2J = 13.4, ^3J(H1′,H2′) = 5.2, Hb-C(1′)), 2.42 (m, 1H, H-C(2′)), 2.03 (s, 3H, *Me*-C(2)), 1.95 (d, 3H, ^4J(Me4,H5) = 0.9, *Me*-C(4)), 1.52 (d, 3H, ^3J(H7,H6) = 7.1, H-C(7)), 1.16 (d, 3H, ^3J(Me2′,H2′) = 6.5, *Me*-C(2′)), 0.89 (s, 9H, *t*BuSi), 0.06 (s, 6H, *Me*$_2$-Si); ^{13}C NMR(100 MHz, $CDCl_3$, 283 K): δ = 168.9 (s, C(1)), 141.1 (d, ^1J(H,C) = 165, C(3)), 139.1 (s, C(2)), 129.8 (s, C(4)), 127.0 (d, ^1J(H,C) = 159, C(5)), 66.7 (t, ^1J(H,C) = 148, C(1′)), 58.9 (d, ^1J(H,C) = 138, C(6)), 53.2 (t, ^1J(H,C) = 136, C(3′)), 52.5 (q, ^1J(H,C) = 131, OC*H*$_3$), 31.1 (d, ^1J(H,C) = 135, C(2′)), 25.6 (q, ^1J(H,C) = 129, C-*C*(*CH*$_3$)$_3$Si), 18.6 (s, C-*C*(CH$_3$)$_3$Si), 17.7 (q, ^1J(H,C)) = 131, *Me*-C(2)), 17.7 (q, ^1J(H,C)) = 131, *Me*-C(4)), 14.5 (q, ^1J(H,C)) = 130, C(7)), 13.8 (q, ^1J(H,C)) = 133, *Me*-C(2′)), −5.2 (q, ^1J(H,C)) = 122, C-*Me*$_2$Si).

Compound 28b: ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 7.12 (s, 1H, H-C(3)), 5.54 (dq, 1H, ^3J(H5,H6) = 10.3, ^4J(H5,Me4) = 0.9, H-C(5)), 3.95 (dq, 1H, ^3J(H6,H5) = 10.3, ^3J(H6,H7) = 7.1, H-C(6)), 3.79 (s, 3H, OC*H*$_3$), 3.65 (m, 1H, Ha-C(3′)), 3.44 (m, 1H, Hb-C(3′)), 3.18 (dd, 1H, ^2J = 13.5, ^3J(H1′,H2′) = 8.3, Ha-C(1′)), 2.58 (dd, 1H, ^2J = 13.5, ^3J(H1′b,H2′) = 6.5, Hb-C(1′)), 2.42 (m, 1H, H-C(2′)), 2.03 (s, 3H, *Me*-C(2)), 1.95 (d, 3H, ^4J(Me4,H5) = 0.9, *Me*-C(4)), 1.52 (d, 3H, ^3J(H8,H7) = 7.1, H-C(6)), 1.16 (d, 3H, ^3J(Me2′,H2′) = 6.4, *Me*-C(2′)), 0.89 (s, 9H, *t*BuSi), 0.06 (s, 6H, *Me*$_2$-Si); ^{13}C NMR(100 MHz, $CDCl_3$, 283 K): δ = 168.9 (s, C(1)), 141.1 (d, ^1J(H,C) = 165, C(3)), 139.1 (s, C(2)), 129.8 (s, C(4)), 127.0 (d, ^1J(H,C) = 159, C(5)), 66.7 (t, ^1J(H,C) = 148, C(1′)), 58.9 (d, ^1J(H,C) = 138, C(6)), 53.2 (t, ^1J(H,C) = 136, C(3′)), 52.5 (q, ^1J(H,C) = 131, OC*H*$_3$), 31.1 (d, ^1J(H,C) = 135, C(2′)), 25.6 (q, ^1J(H,C) = 129, C-*C*(*CH*$_3$)$_3$Si), 18.6 (s, C-*C*(CH$_3$)$_3$Si), 17.7 (q, ^1J(H,C)) = 131, *Me*-C(2)), 17.7 (q, ^1J(H,C)) = 131, *Me*-C(4)), 14.5 (q, ^1J(H,C)) = 130, C(7)), 13.8 (q, ^1J(H,C)) = 133, *Me*-C(2′)), −5.2 (q, ^1J(H,C)) = 122, C-*Me*$_2$Si).

1:1 Mixture of dienoates 29a,b: Same procedure as for the preparation of ester **28a,b**. Only $NaIO_4$ was added for the cleavage of the α-hydroxy ketone. No catalytic amount of Et_3N was added. Purification by FC (petroleum ether/ethyl acetate 35:65, R_f = 0.35) gave a 1:1 mixture of **29a** and **29b** as a colorless oil (1.55 g, 66 %). IR (film): $\tilde{\nu}$ = 3300, 2985, 2950, 2860, 1755, 1715, 1630, 1460, 1350, 1255, 1130, 1080, 1020, 935, 880 cm^{-1}; UV (CH_3CN): λ_{max} = 270 nm (ε = 9300), 249 nm (15100); MALDI-HRMS: *m*/*z*: calcd for $C_{14}H_{24}O_5SNa$: 327.1242, found 327.1304 [*M*+Na]$^+$; elemental analysis calcd (%) for $C_{14}H_{24}O_5S$ (304.13): C 55.24, H 7.95; found: C 55.19, H 7.78.

Compound 29a: ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 7.13 (s, 1H, H-C(3)), 5.52 (dq, 1H, ^3J(H5,H6) = 11.6, ^4J(H5,Me4) = 1.2, H-C(5)), 3.99 (dq, 1H, ^3J(H6,H5) = 11.6, ^3J(H6,H7) = 7.1, H-C(6)), 3.80 (s, 3H, OC*H*$_3$), 3.72 (m, 1H, Ha-C(3′)), 3.53 (m, 1H, Hb-C(3′)), 3.14 (dd, 1H, ^2J = 13.4, ^3J(H1′,H2′) = 6.4, Ha-C(1′)), 2.77 (dd, 1H, ^2J = 13.4, ^3J(H1′,H2′) = 6.4, Hb-C(1′)), 2.48 (m, 1H, H-C(2′)), 2.03 (s, 3H, *Me*-

C(2)), 1.96 (d, 3H, ^4J(Me4,H5) = 1.2, *Me*-C(4)), 1.53 (d, 3H, ^3J(H7,H6) = 7.1, H-C(7)), 1.18 (d, 3H, ^3J(Me2′,H2′) = 7.1, *Me*-C(2′)); ^{13}C NMR(100 MHz, $CDCl_3$, 283 K): δ = 168.9 (s, C(1)), 141.1 (d, ^1J(H,C) = 162, C(3)), 139.1 (s, C(2)), 129.8 (s, C(4)), 127.0 (d, ^1J(H,C) = 149, C(5)), 66.7 (t, ^1J(H,C) = 152, C(1′)), 58.9 (d, ^1J(H,C) = 139, C(6)), 53.2 (t, ^1J(H,C) = 138, C(3′)), 52.5 (q, ^1J(H,C) = 140, O*C*H$_3$), 31.1 (d, ^1J(H,C) = 137, C(2′)), 17.5 (q, ^1J(H,C)) = 134, *Me*-C(2)), 17.4 (q, ^1J(H,C)) = 134, *Me*-C(4)), 14.5 (q, ^1J(H,C)) = 125, C(7)), 13.8 (q, ^1J(H,C)) = 132, *Me*-C(2′)).

Compound 29b: ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 7.13 (s, 1H, H-C(3)), 5.52 (dq, 1H, ^3J(H5,H6) = 11.6, ^4J(H5,Me4) = 1.2, H-C(5)), 3.99 (dq, 1H, ^3J(H6,H5) = 11.6, ^3J(H6,H7) = 7.1, H-C(6)), 3.80 (s, 3H, OCH_3), 3.72 (m, 1H, H-C(3′)), 3.53 (m, 1H, H-C(3′)), 3.25 (dd, 1H, ^2J = 13.5, ^3J(H1′,H2′) = 6.4, Ha-C(1′)), 2.88 (dd, 1H, ^2J = 13.5, ^3J(H1′,H2′) = 6.4, Hb-C(1′)), 2.48 (m, 1H, H-C(2′)), 2.04 (s, 3H, *Me*-C(2)), 1.96 (d, 3H, ^4J(Me4,H5) = 1.2, *Me*-C(4)), 1.53 (d, 3H, ^3J(H7,H6) = 7.1, H-C(7)), 1.18 (d, 3H, ^3J(Me2′,H2′) = 7.1, *Me*-C(2′)); ^{13}C NMR(100 MHz, $CDCl_3$, 283 K): δ = 168.9 (s, C(1)), 141.1 (d, ^1J(H,C) = 162, C(3)), 139.1 (s, C(2)), 129.8 (s, C(4)), 127.0 (d, ^1J(H,C) = 149, C(5)), 66.7 (t, ^1J(H,C) = 152, C(1′)), 58.9 (d, ^1J(H,C) = 139, C(6)), 53.2 (t, ^1J(H,C) = 138, C(3′)), 52.5 (q, ^1J(H,C) = 140, O*C*H$_3$), 31.1 (d, ^1J(H,C) = 137, C(2′)), 17.5 (q, ^1J(H,C)) = 134, *Me*-C(2)), 17.4 (q, ^1J(H,C)) = 134, *Me*-C(4)), 14.5 (q, ^1J(H,C)) = 125, C(7)), 13.8 (q, ^1J(H,C)) = 132, *Me*-C(2′)).

Triene (+)-30: A solution of 1:1 mixture of **28a** and **28b** (40 mg, 0.047 mmol, 1 equiv) in CF_2Br_2 (5 mL) was added dropwise to a suspension of alumina-supported potassium hydroxide (800 mg) in anhydrous CH_2Cl_2 (2 mL) at 0 °C. The crude mixture was then stirred 14 h under an Ar atmosphere at 40 °C. After dilution with CH_2Cl_2 (15 mL), the supported base was removed by suction filtration through a pad of Celite. The reaction vessel and filter cake were rinsed thoroughly with CH_2Cl_2 (10 mL). The organic layer was washed with brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. FC (cyclohexane/ethyl acetate 90:2) gave (+)-**30** as a colorless oil (12 mg, 70%, *E*/*Z* 10:1). The structure was confirmed with by NOESY experiments. NOEs between H-C(3)↔H-C(5), H-C(5)↔H-C(7), Me-C(2)↔Me-C(4) and Me-C(4)↔Me-C(6) were observed. R_f = 0.4 (cyclohexane/ethyl acetate 90:2); $[\alpha]_{589}^{25}$ = +18.1, (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 7.15 (brs, 1H, H-C(3)), 6.09 (brs, 1H, H-C(5)), 5.18 (d, 1H, ^3J(H7,H8) = 9.6, H-C(7)), 3.75 (s, 3H, *C*H$_3$CO$_2$), 3.43 (m, 2H, H-C(9)), 2.67 (dddq, 1H, ^3J(H8,H7) = 9.6, ^3J(H8,H9a) = 7.0, ^3J(H8,Me8) = 6.6, ^3J(H8,H9b) = 6.4, H-C(8)), 2.06 (brs, 3H, *Me*-C(2)), 2.01 (brs, 3H, *Me*-C(4)), 1.80 (brs, 3H, *Me*-C(6)), 1.01 (d, 3H, ^3J(Me8,H8) = 6.6, *Me*-C(8)), 0.89 (s, 9H, *t*BuSi), 0.06 (s, 6H, *Me*$_2$-Si); ^{13}C NMR(100 MHz, $CDCl_3$, 283 K): δ = 168.9 (s, C(1)), 144.1 (d, ^1J(H,C) = 160, C(3)), 139.1 (s, C(2)), 133.8 (s, C(4)), 132.5 (d, ^1J(H,C) = 158, C(5)), 131.6 (s, C(6)), 125.4 (d, ^1J(H,C) = 154, C(7)), 61.4 (d, ^1J(H,C) = 142, C(8)), 52.8 (t, ^1J(H,C) = 138, C(9)), 52.5 (q, ^1J(H,C) = 133, O*C*H$_3$), 24.4 (q, ^1J(H,C) = 129, C-C*(CH$_3$)$_3$*Si), 20.0 (s, C-C(CH$_3$)$_3$Si), 18.1 (q, ^1J(H,C)) = 129, *Me*-C(2)), 17.8 (q, ^1J(H,C)) = 131, *Me*-C(4)), 17.4 (q, ^1J(H,C)) = 129, *Me*-C(6)), 14.2 (q, ^1J(H,C)) = 130, *Me*-C(8)), 13.8 (q, ^1J(H,C)) = 130, *Me*-C(2′)), −5.4 (q, ^1J(H-C)) = 123, C-*Me*$_2$Si); IR (film): $\tilde{\nu}$ = 2960, 2880, 1755, 1720, 1630, 1255, 1030, 845, 805 cm^{-1}; UV (CH_3CN): λ_{max} = 232 nm (ε = 17540); MALDI-HRMS: *m*/*z*: calcd for $C_{20}H_{36}O_3SiNa$: 375.2331, found 375.2257 [*M*+Na]$^+$; elemental analysis calcd (%) for $C_{20}H_{36}O_3Si$ (352.24): C 68.13, H 10.29; found: C 68.23, H 10.49.

General procedure for the preparation of (*S*)-MTPA esters 31a: A 10% solution of HF in water (0.4 mL) was slowly added to a solution of (+)-**30** (8 mg, 22.7 mmol) in CH_3CN (4 mL) at −20 °C. After 3 h, the crude mixture was neutralized with an aqueous saturated solution of $NaHCO_3$ (≈10 mL), washed with brine (3×10 mL) and extracted with Et_2O (3×20 mL). The combined organic extracts were dried (Na_2SO_4), and the solvent was evaporated under reduced pressure under reflux. The crude alcohol (1 mg) in absolute pyridine (0.5 mL) was added to the corresponding α-methoxy-α-trifluoromethylphenylacetyl chloride (2 equiv) at −20 °C. The mixture was allowed to reach 20 °C and stirred for 2 h. It was then chilled to −20 °C, and *N*,*N*-dimethylamino ethanol (5 equiv) was added. The mixture was allowed to warm to 20 °C and stirred for 1 h. It was diluted with Et_2O (30 mL), washed with aqueous saturated solution of $CuSO_4$ (4×7 mL), water (10 mL), aqueous solution of 2 M HCl (4×7 mL), aqueous saturated solution of $NaHCO_3$ (3×5 mL), dried over Na_2SO_4, and concentrated under vacuum under reflux. All the NMR measurements were carried out on the crude sample (colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 7.52, 7.41 (m, 5H, H-C(ar)), 7.14 (brs, 1H, H-C(3)), 6.01 (brs, 1H, H-C(5)), 5.19 (d, 1H, ^3J(H7,H8) = 8.7 H-C(7)), 4.13 (m, 2H, H-C(9)), 3.79 (s, 3H, *C*H$_3$CO$_2$), 3.55 (s, 3H, H-OCH_3), 2.80 (m, 1H, H-C(8)), 2.01 (brs, 3H, *Me*-C(2)), 1.97 (brs, 3H, *Me*-C(4)), 1.83 (brs, 3H, *Me*-C(6)), 1.01 (d, 3H, ^3J(Me8,H8) = 6.8, *Me*-C(8)); ^{19}F NMR ($CDCl_3$ + CCl_3F, 376.7 MHz): δ = −77.62 (s, CF_3-C(2′)); MALDI-HRMS: *m*/*z*: calcd for $C_{24}H_{29}F_3O_5Na$: 477.1865, found 477.1874 [M+Na]$^+$.

(*R*)-MTPA ester 31b: This ester was also obtained as a colorless oil following the procedure described for the preparation of **31a**. ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 7.56, 7.43 (m, 5H, H-C(ar)), 7.14 (brs, 1H, H-C(3)), 6.01 (brs, 1H, H-C(5)), 5.20 (dq, 1H, ^3J(H7,H8) = 8.7, ^4J(H7,Me6) = 1.2, H-C(7)), 4.08 (m, 2H, H-C(9)), 3.77 (s, 3H, *C*H$_3$CO$_2$), 3.54 (s, 3H, H-OCH_3), 2.76 (m, 1H, H-C(8)), 2.03 (brs, 3H, *Me*-C(2)), 1.98 (brs, 3H, *Me*-C(4)), 1.82 (brs, 3H, *Me*-C(6)), 1.03 (d, 3H, ^3J(Me8,H8) = 6.8, *Me*-C(8)); ^{19}F NMR ($CDCl_3$ + CCl_3F, 376.7 MHz): δ = −77.43 (s, CF_3-C(2′)); MALDI-HRMS: *m*/*z*: calcd for $C_{24}H_{29}F_3O_5Na$: 477.1865, found 477.1882 [*M*+Na]$^+$.

3:3:1:1 Mixture of compounds 32a and 32b: To a solution of 1:1 mixture of **29a**,**b** (200 mg, 0.66 mmol) in CH_2Cl_2 (6 mL) at −10 °C, was added the Dess–Martin periodinane (697 mg, 1.64 mmol, 2.5 equiv) in one portion. The crude mixture was then vigorously stirred at 20 °C for 2 h under an Ar atmosphere. After completion of the reaction (TLC), the crude mixture was cooled to 0 °C, diluted with CH_2Cl_2 (15 mL), and $Na_2S_2O_5$ was added (1 g, 6.4 mmol, 10 equiv). The organic layer was quickly washed with a saturated aqueous solution of NH_4Cl (3×15 mL), dried over Na_2SO_4 and concentrated under reduced pressure (temperature of the bath: 10 °C, to avoid decomposition) of the aldehyde intermediate. A solution of *n*-BuLi, 1.6 M in hexane (0.41 mL, 0.65 mmol, 0.98 equiv) was added dropwise to a solution of (triethylsilyl)acetylene (0.11 mL, 0.59 mmol, 0.9 equiv) in anhydrous THF (2 mL) under an Ar atmosphere at −100 °C. After 30 min at −100 °C, the solution was transferred with a cannula to the solution of the crude mixture of aldehyde in anhydrous THF at −100 °C. The crude reaction mixture was stirred at −100 °C for 1 h and then allowed to warm to 0 °C within 2 h. The mixture was diluted with EtOAc (10 mL) and washed with i) an aqueous saturated solution of NH_4Cl (2×10 mL) and ii) brine (2×10 mL). The aqueous layer was extracted with Et_2O (3×100 mL). The combined organic extracts were dried (Na_2SO_4), and the solvent evaporated under reduced pressure. The crude reaction mixture contains a 3:1 mixture of 2′*R*,3′*S* (Cram adduct) and 2′*R*,3′*R* (anti-Cram adduct) diastereoisomers. FC (cyclohexane/ethyl acetate 8:2) gave a pure fraction of **32a** (173 mg, 59%) and a pure fraction of **32b** (35 mg, 12%); colorless oil; R_f = 0.4 (cyclohexane/ethyl acetate 4:1); IR (film): $\tilde{\nu}$ = 3400, 2985, 2950, 2210, 1740, 1710, 1615, 1455, 1480, 1365, 1275, 1125, 1085, 1045, 795 cm^{-1}; UV (CH_3CN): λ_{max} = 265 nm (ε = 10000), 240 (11000); MALDI-HRMS: *m*/*z*: calcd for $C_{25}H_{42}NaO_5SSiNa$: 505.2420, found 505.2411 [*M*+Na]$^+$; elemental analysis calcd (%) for $C_{25}H_{42}O_5SSi$ (482.25): C 62.20, H 8.77; found: C 62.23, H 8.81.

Compound 32a: ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 7.13 (s, 1H, H-C(3)), 5.52 (brs, 1H, H-C(5)), 4.41 (dd, 1H, ^3J(H3′,H2′) = 10.2, ^3J(H3′,OH) = 5.2, H-C(3′)), 3.99 (m, 1H, H-C(6)), 3.79 (s, 3H, OCH_3), 3.37 (m, 1H, Ha-C(1′)), 2.87 (dd, 1H, ^2J = 14.3, ^3J(H1b′,H2′) = 8.3, Hb-C(1′)), 2.54 (m, 1H, H-C(2′)), 2.34 (d, 1H, ^3J(H(OH),H3′ = 5.2, H-(OH)), 2.03 (d, 3H, ^4J(Me2,H3) = 1.2, *Me*-C(2)), 1.95 (d, 3H, ^4J(Me4,H5) = 1.2, *Me*-C(4)), 1.32–1.24 (m, 6H, H-C(7) and *Me*-C(2′)), 1.00 (t, 9H, ^3J(CH$_3$-CH$_2$) = 8.2, C*H*$_3$-CH$_2$Si), 0.57 (q, 6H, ^3J(CH$_2$-CH$_3$) = 8.2, C*H*$_2$Si); ^{13}C NMR(100 MHz, $CDCl_3$, 283 K): δ = 168.9 (s, C(1)), 141.0 (d, ^1J(H,C) = 169, C(3)), 139.1 (s, C(2)), 129.8 (s, C(4)), 127.7 (d, ^1J(H,C) = 147, C(5)), 108.0 (s, C(4′)), 86.7 (s, C(5′)), 67.7 (t, ^1J(H,C) = 150, C(1′)), 59.4 (d, ^1J(H,C) = 136, C(6)), 52.6 (q, ^1J(H,C) = 140, OCH_3), 40.5 (d, ^1J(H,C) = 132, C(3′)), 31.5 (d, ^1J(H,C) = 137, C(2′)), 21.9 (q, ^1J(H,C)) = 134, *Me*-C(2)), 17.4 (q, ^1J(H,C)) = 134, *Me*-C(4)),

14.5 (q, ^1J(H,C)) = 125, C(7)), 13.8 (q, ^1J(H,C)) = 132, *Me*-C(2′)), 8.0 (t, ^1J(H,C)) = 130, *Me*-CH_2Si), −2.9 (q, ^1J(H,C)) = 127, CH_2Si).

Compound 32b: ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 7.13 (s, 1H, H-C(3)), 5.51 (s, 1H, H-C(5)), 4.41 (t, 1H, ^3J(H3′,H2′) = 10.2, ^3J(H3′,OH) = 5.2, H-C(3′)), 3.99 (m, 1H, H-C(6)), 3.80 (s, 3H, OCH_3), 3.37 (m, 1H, Ha-C(1′)), 2.78 (dd, 1H, ^2J = 13.4, ^3J(H1b′,H2′) = 6.2, Hb-C(1′)), 2.60 (m, 1H, H-C(2′)), 2.39 (d, 1H, ^3J(H(OH),H3′ = 5.2, H-OH), 2.03 (d, 3H, ^4J(Me2,H3) = 1.2, *Me*-C(2)), 1.95 (d, 3H, ^4J(Me4,H5) = 1.2, *Me*-C(4)), 1.32–1.24 (m, 6H, *Me*-C(6) and H-C(7)), 1.00 (t, 9H, ^3J(CH_3-CH_2) = 8.2, CH_3-CH_2Si), 0.57 (q, 6H, ^3J(CH_2-CH_3) = 8.2, CH_2Si); ^{13}C NMR(100 MHz, $CDCl_3$, 283 K): δ = 168.9 (s, C(1)), 140.9 (d, ^1J(H,C) = 162, C(3)), 139.1 (s, C(2)), 127.5 (s, C(4)), 127.0 (d, ^1J(H,C) = 158, C(5)), 108.0 (s, C(4′)), 86.9 (s, C(5′)), 66.6 (t, ^1J(H,C) = 151, C(1′)), 59.4 (d, ^1J(H,C) = 149, C(6)), 52.8 (q, ^1J(H,C) = 143, OCH_3), 40.5 (d, ^1J(H,C) = 134, C(3′)), 31.4 (d, ^1J(H,C) = 130, C(2′)), 22.3 (q, ^1J(H,C)) = 129, *Me*-C(2)), 17.4 (q, ^1J(H,C)) = 128, *Me*-C(4)), 14.5 (q, ^1J(H,C)) = 128, C(7)), 13.8 (q, ^1J(H,C)) = 129, *Me*-C(2′)), 8.0 (t, ^1J(H,C)) = 130, *Me*-CH_2Si), −2.9 (q, ^1J(H,C)) = 127, CH_2Si).

Triene (+)-2: Imidazole (16.5 mg, 0.24 mmol, 2.2 equiv) followed by TBSCl (40.9 mg, 0.27 mmol, 2.4 equiv) was added to a solution of the pure isolated product **32a** (50 mg, 0.11 mmol, 1 equiv) in anhydrous DMF (8 mL). The mixture was stirred under an Ar atmosphere overnight at 20 °C. The crude mixture was then treated with aqueous saturated solution of $NaHCO_3$ (30 mL) and extracted with Et_2O (3 × 50 mL). The combined organic extracts were washed with brine (2 × 50 mL), dried (Na_2SO_4), and the solvent evaporated under reduced pressure. To a suspension of alumina-supported potassium hydroxide (1 g) in anhydrous CH_2Cl_2 (3 mL) at 0 °C, was added dropwise a solution of protected alcohol (60 mg, 0.11 mmol, 1 equiv) in CF_2Br_2 (8 mL). The crude mixture was stirred under an Ar atmosphere at 40 °C for 14 h. After dilution with CH_2Cl_2 (15 mL), the supported base was removed by suction filtration through a pad of Celite. The reaction vessel and filter cake were rinsed thoroughly with CH_2Cl_2 (10 mL). The organic layer was directly concentrated under reduced pressure. FC (hexane/ethyl acetate 9:1) gave a 12:1 mixture of (+)-**2** as a colorless oil (38 mg, 72 %). Spectral data were the same as those published by Nicolaou.[6] R_f = 0.4 (hexane/ethyl acetate 9:1); $[\alpha]_{589}^{25}$ = +51.7, (*c* = 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 283 K): δ = 7.15 (brs, 1H, H-C(3)), 6.02 (brs, 1H, H-C(5)), 5.27 (d, 1H, ^3J(H7,H8) = 10.2, H-C(7)), 4.19 (d, 2H, ^3J(H9,H8) = 5.9, H-C(9)), 5.75 (s, 1H, OCH_3), 2.72 (ddq, 1H, ^3J(H8,H7) = 10.2, ^3J(H8,Me8) = 6.6, ^3J(H8,H9) = 5.9, H-C(8)), 2.06 (d, 3H, ^4J(Me2,H3) = 1.2, *Me*-C(2)), 2.03 (d, 3H, ^4J(Me4,H5) = 1.2, *Me*-C(4)), 1.80 (brs, 3H, *Me*-C(6)), 1.02–0.97 (m, 12H, CH_3-CH_2Si and *Me*-C(8)), 0.91 (s, 9H, *t*Bu), 0.57 (q, 6H, ^3J(CH_2-CH_3) = 7.4, CH_2Si), 0.14 and 0.11 (s, 6H, ^3J(CH_2-CH_3) = 7.4, (CH_3)$_2$Si); ^{13}C NMR(100 MHz, $CDCl_3$, 283 K): δ = 168.9 (s, C(1)), 144.1 (d, ^1J(H,C) = 164, C(3)), 139.1 (s, C(2)), 133.8 (s, C(4)), 132.5 (d, ^1J(H,C) = 162, C(5)), 131.6 (s, C(6)), 125.4 (d, ^1J(H,C) = 160, C(7)), 108.0 (s, C(10)), 86.9 (s, C(11)), 67.6 (d, ^1J(H,C) = 142, C(9)), 52.0 (q, ^1J(H,C) = 138, OCH_3), 40.5 (d, ^1J(H,C) = 132, C(8)), 25.4 (q, ^1J(H,C) = 126, C-C(CH_3)$_3$Si), 18.4 (s, C_{quat}-C(CH_3)$_3$Si), 17.5 (q, ^1J(H,C)) = 135, *Me*-C(2)), 16.5 (q, ^1J(H,C)) = 126, *Me*-C(4)), 14.1 (q, ^1J(H,C)) = 130, *Me*-C(6)), 7.4 (t, ^1J(H,C)) = 122, *Me*-CH_2Si), 4.3 (q, ^1J(H,C)) = 129, *Me*-C(8)), −4.5 (q, ^1J(H,C)) = 123, CH_2Si), −5.1 (q, ^1J(H,C)) = 120, C-Me_2Si); IR (film): $\tilde{\nu}$ = 2960, 2880, 2150, 1755, 1605, 1270, 1030, 845, 805, 795 cm^{-1}; UV (CH_3CN): λ_{max} = 230 nm (ε = 19310); MALDI-HRMS: *m*/*z*: calcd for $C_{28}H_{50}NaO_3Si_2Na$: 513.3196, found 513.3207 $[M+Na]^+$; elemental analysis calcd (%) for $C_{28}H_{50}O_3Si_2$ (490.33): C 68.51, H 10.27; found: C 68.33, H 10.29.

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