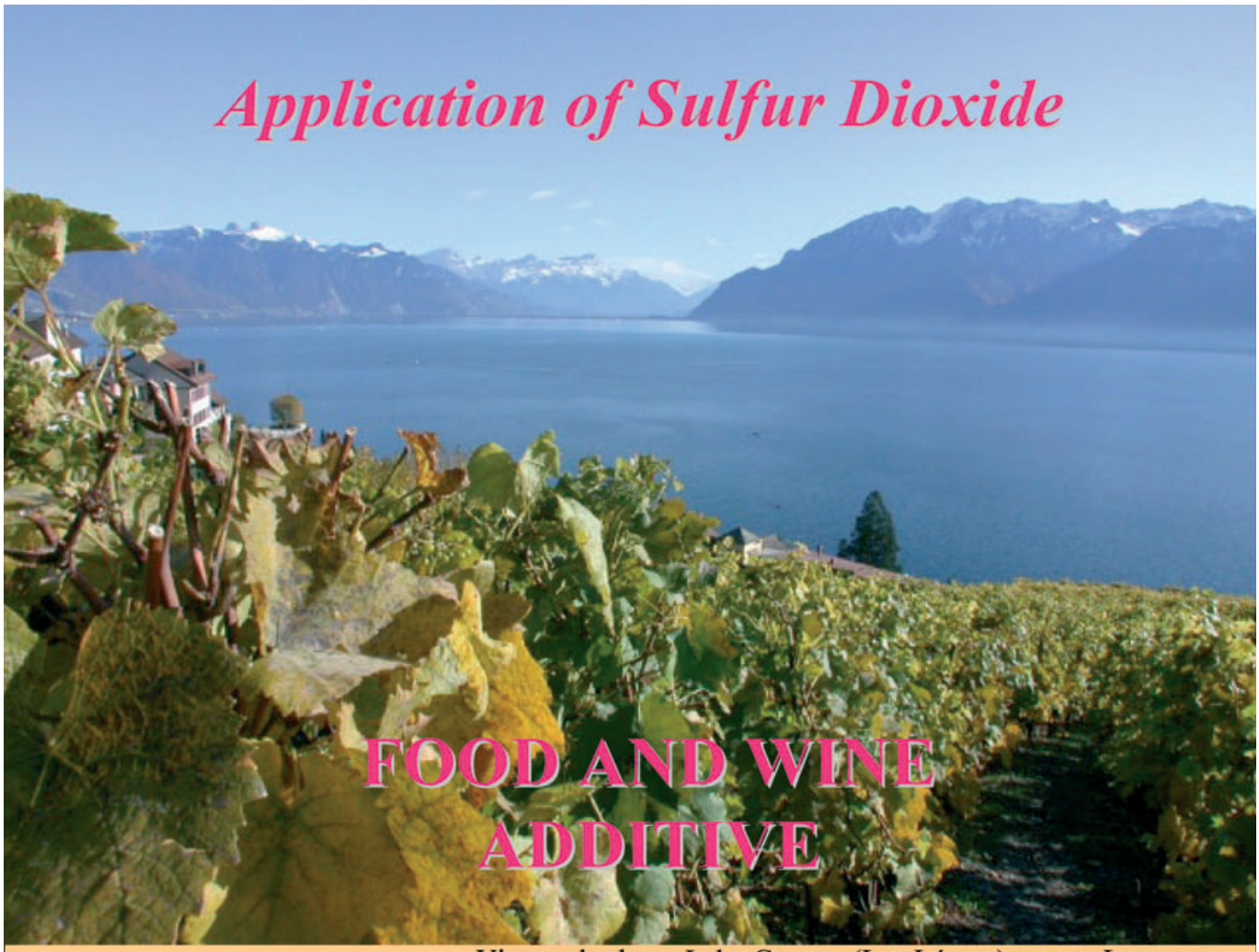
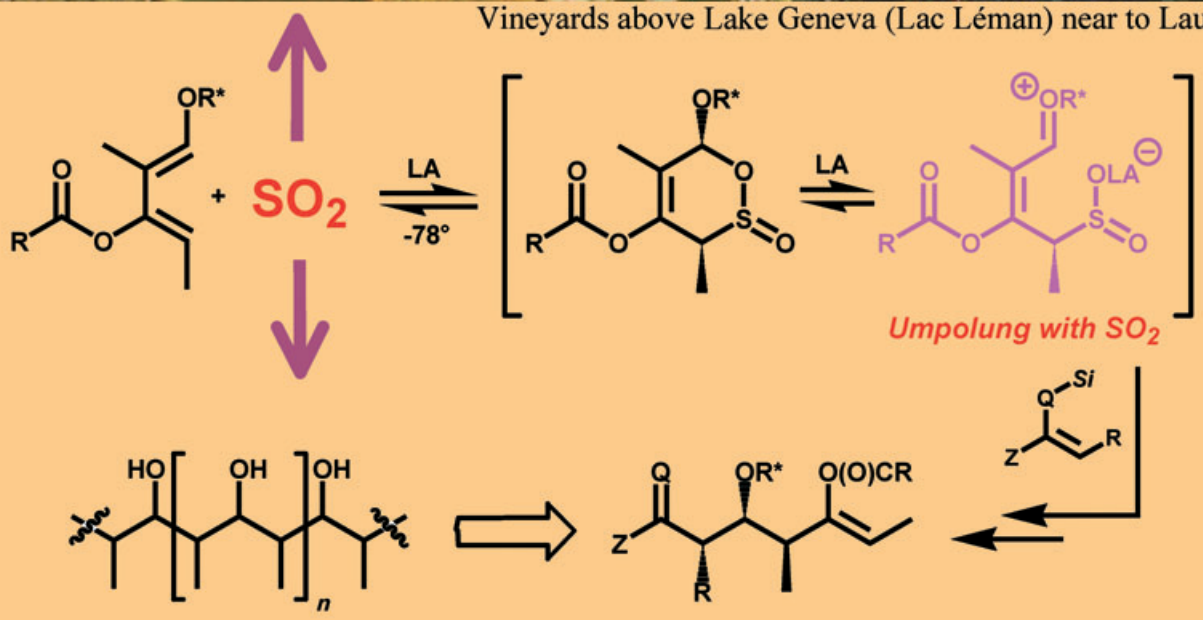
Application of Sulfur Dioxide



Vineyards above Lake Geneva (Lac Léman) near to Lausanne



POLYPROPIONATE SYNTHESIS

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Expeditious Asymmetric Synthesis of a Stereoheptad Corresponding to the C(19)–C(27)-Ansa Chain of Rifamycins: Formal Total Synthesis of Rifamycin S

Māris Turks, Xiaogen Huang, and Pierre Vogel*[a]

Abstract: In the presence of sulfur dioxide and an acid promoter, (−)-(1*E*,3*Z*)-2-methyl-1-((1*S*)-1-phenylethoxy)penta-1,3-dien-3-yl isobutyrate reacts with (*Z*)-3-(trimethylsilyloxy)-pent-2-ene giving a silyl sulfinate intermediate that undergoes, in the presence of palladium catalyst, a desilylation and retro-ene elimination of SO_2 with formation of (−)-(1*Z*,2*S*,3*R*,4*S*)-1-ethylidene-2,4-dimethyl-5-oxo-3-((1*S*)-1-phenylethoxy)-heptyl isobutyrate as major product. This ethyl ketone undergoes cross-aldol reaction with (2*S*)-2-methyl-3-[(*tert*-butyldimethylsilyl)-oxy]propanal giving an aldol that is reduced into a stereoheptad corresponding to the C(19)-C(27)-segment of Rifamycins with high diastereoselectivity and enantiomeric excess.

Keywords: aldol reaction · asymmetric synthesis · Diels–Alder reaction · dienes · polypropionates · sulfur dioxide

Introduction

Rifamycins[1] are antibiotics belonging to the group of naphthalenic ansamycines[2] characterized by an aliphatic bridge (polypropionate chain) linking two non-adjacent centers of an aromatic moiety. They are produced from *Streptomyces mediterranei*[3] and are active against a large variety of organisms, including bacteria, eukaryotes, and viruses.[4] Rifamycins have shown also antitumour[5] and anti-inflammatory activity,[6] but at present are mainly used for the treatment of tuberculosis. Their antimicrobial activity is due to the inhibition of bacterial DNA-dependent RNA polymerase.[7] Several derivatives of Ryfamicin S (**1**) have been prepared and many of them have shown promising activities. For instance, Rifabutin is active against mycobacteria including atypical organisms such as *Mycobacterium avium* and *M. intracellulare* (MAC complex).[8]

The first total synthesis of Rifamycin S was reported by Kishi and co-workers in 1980.[9] The stereoheptad (−)-**2** was a key-intermediate for the construction of the ansa chain. It was obtained in 26 steps and 5.2% overall yield from (2*S*)-3-benzyloxy-2-methylpropanal ((+)-**3a**) (Figure 1). Since then, several total asymmetrical synthesis of **1** have been proposed[10] and the construction of the C(19)–C(27) fragment ((−)-**2** and analogues) of this antibiotic has become a challenging target for the testing of asymmetric synthetic methods and strategies.[11]

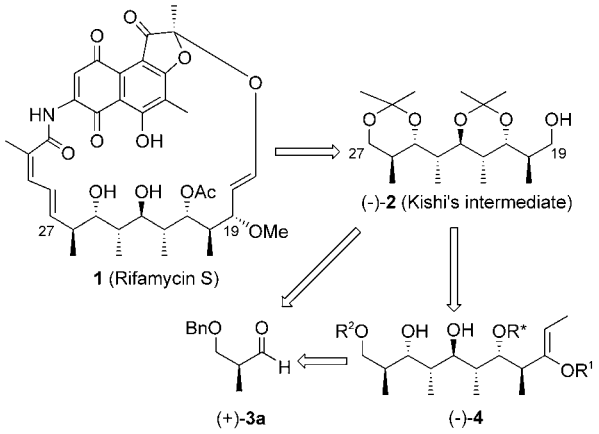

Figure 1. Kishi's retro-synthesis of Rifamycin S.

We have shown recently that enantiomerically enriched 1,3-dioxy-1,3-dienes of type **5** can be condensed with carbon-centered nucleophiles of type **6** in the presence of an excess of SO_2 and a catalytical amount of an acid promoter.[12,13] This generates β,γ-unsaturated silyl sulfinates **7** that, after acidic workup, undergo quick desilylation and desulfation by means of a stereoselective retro-ene elimination of

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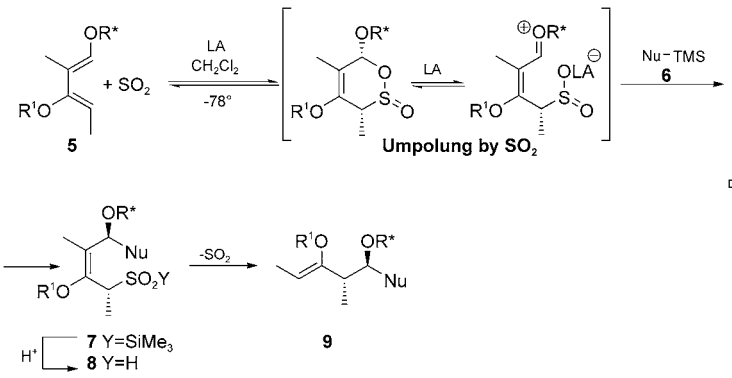


Scheme 1. C–C bond forming reaction between 1,3-dioxy-1,3-dienes and carbon-centered nucleophiles through Umpolung with sulfur dioxide.

SO_2 from **8**, giving products **9** in good yield and diastereoselectivity (Scheme 1).

We thus embarked on the quest to develop this C–C bond-forming reaction[14] and to show its application in natural product synthesis. In this paper, we disclose 1) our findings about reactivity of 1,3-dioxy-1,3-dienes towards SO_2 and 2) a very short synthesis of the C(19)–C(27) segment (−)-**4** which has been converted into (−)-**2**, thus realizing a formal total synthesis of Rifamycin S.

Results and Discussion

Retro-synthetic analysis: Our retro-synthetic plan for the preparation of Kishi's intermediate (−)-**2** is shown in Figure 2. Precursors of (−)-**2** could be ketones of type **10** arising from the cross-aldol reaction (disconnection A) of ethyl ketones **11** and readily available aldehydes (+)-**3a**[15] or (+)-**3b** ((2*S*)-2-methyl-3-[(*tert*-butyldimethylsilyl)oxy]propanal).[16]

Abstract in French: *Une synthèse asymétrique très courte d'un stéréoheptade correspondant au segment C(19)-C(27) de la chaîne ansa des Rifamycines est proposée. La methode utilise une nouvelle réaction de formation de liaison C–C qui exploite la cascade réactionelle suivante: addition hétéro-Diels–Alder du SO_2 sur le 1,3-dioxy-1,3-diène, isobutyrate de (1Z,3Z)-2-méthyl-1-((1S)-1-phényléthoxy)penta-1,3-dièn-3-yle, suivie d'une ionisation promue par un acide fournissant un intermédiaire zwitterionique qui est piégé par le (Z)-3-(triméthylsilyloxy)pent-2-ène (éther d'énol dérivé de la diéthyl cétone). Il se forme un sulfinate de triméthylsilyle β,γ-insaturé qui, en présence d'un catalyseur au palladium, est désilylé et désulfité par élimination rétro-ène en une éthyl cétone, isobutyrate de (1Z,2S,3R,4S)-1-éthylidéne-2,4-diméthyl-5-oxo-3-((1S)-1-phényléthoxy)heptyle), produit majoritaire de la réaction. Cette cétone réagit en aldolisation croisée avec le (2S)-2-méthyl-3-[(tert-butyldiméthylsilyl)oxy]propanal fournissant un aldol qui est réduit en stéréoheptade.*

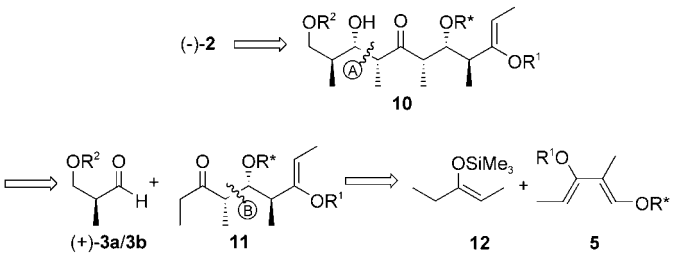
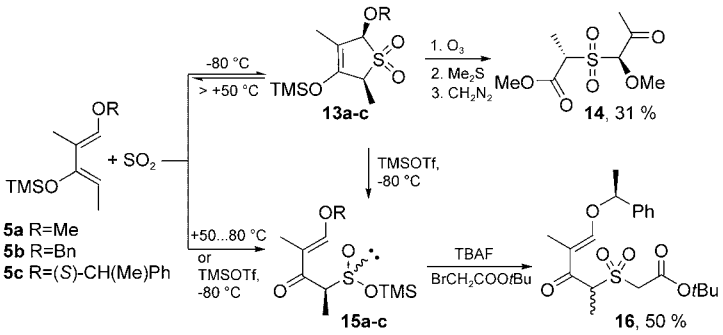


Figure 2. Retro-synthesis of Kishi's intermediate.

Ethyl ketones **11** can be obtained by applying our C–C bond-forming reaction to the condensation reaction of enantiomerically enriched dienes of type **5** with (*Z*)-enoxysilane **12** derived from pentan-3-one.

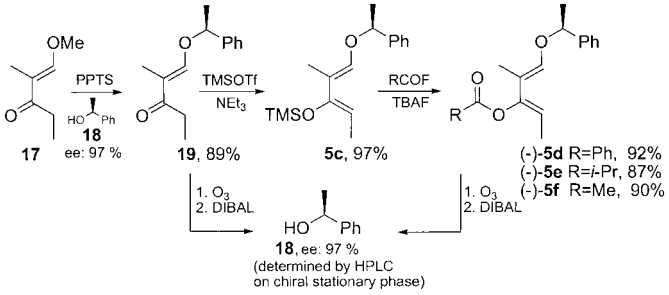
Synthesis and reactivity of 1,3-dioxy-1,3-dienes: In preliminary studies we focused our attention on widely known and readily available 1-alkoxy-3-trialkylsilyloxy-1,3-dienes **5a–c** (Danishefsky's dienes).[17] To our surprise they did not lead to the products expected from our oxyallylation–retro-ene desulfation cascades. Instead, a new type of reactivity of dienes toward SO_2 was discovered. It was observed that such electron-rich dienes undergo an ene reaction pathway[18] and form diastereomeric silylsulfinates **15** (Scheme 2). More careful studies showed that at low tem-



Scheme 2. Formation of diastereomeric silylsulfinates **15**.

perature (−80 °C) and without a Lewis acid, sulfolenes **13** are formed. Their presence was proved spectroscopically and, in the case **13a** by ozonolysis followed by isolation of product **14** as a methyl ester. This cheletropic addition of SO_2 is reversible and at higher temperature (> +50 °C) sulfolenes **13** are in equilibrium with their corresponding dienes **5a–c**, which now undergo ene-type reaction with sulfur dioxide. The same result can be achieved by catalyzing the reaction with a Lewis acid. In such a case, formation of silylsulfinates is observe at low temperatured. It was also possible to show that 3-silyloxysulfolene **13a** gives silylsulfinate **15a** when treated with Lewis acid at low temperature. The presence of ene products **15** was observed by ^1H and ^{13}C NMR spectroscopy and, in the case of **15c** proved by isolation of product **16**. This is the first report of the ene-reactivity of Danishefsky's dienes towards SO_2.

As the 3-silyloxy substituent causes the dienes to undergo fast ene-reactions that compete with other pericyclic reactions, it was decided to change it for other, less electron-releasing and nonmigrating groups. 3-Acyloxy dienes were found to be good candidates.[12,19] As we had observed that the reactivity of the dienes and diastereoselectivity of the oxyallylation reaction fluctuate depending on small changes in the structure of diene, we decided to investigate this matter in more details. The synthesis should be designed so that it allows fast access to differently substituted C(1) and C(3) carbon atoms. Homochiral dienes were synthesized by employing Danishefsky's approach (**17**→(−)-**5c**)[17] and completing the sequence by a silyl–acyl exchange.[20] Moreover, an efficient and practical method was developed to determine the enantiomeric excess of the final dienes and of their precursor **19** (Scheme 3). The necessity to develop



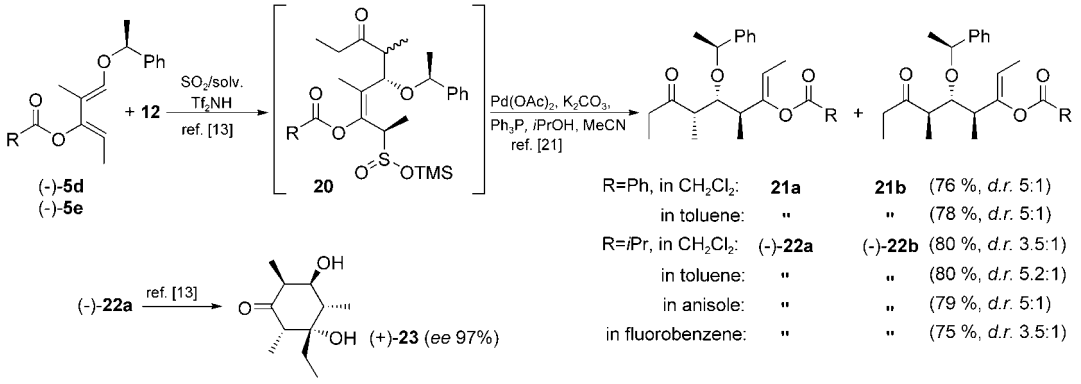
Scheme 3. Preparation of dienes **5d–f** and determination of their *ee*.

such protocol arose from fact that these compounds do not contain easily functionalizable groups and, enantiomers are difficult to resolve by chiral HPLC. Additionally, we sometimes observed partial racemization of phenylethanol under acidic conditions (e.g., pyridinium *para*-tosyl sulfonate); this racemization is not acceptable for the development of asymmetric synthesis using our chemistry. The method involves mild cleavage of the double bond and isolation of a corresponding alcohol, the enantiomeric excess of which can be determined by a plethora of methods, including HPLC or GC on chiral stationary phase. Such an approach can be applied for all chiral vinyl ethers, if necessary. Three different dienes (**5d–f**) bearing a phenylethyl chiral auxiliary were prepared in good yield and without loss of optical purity (no racemization of phenylethanol **18**).

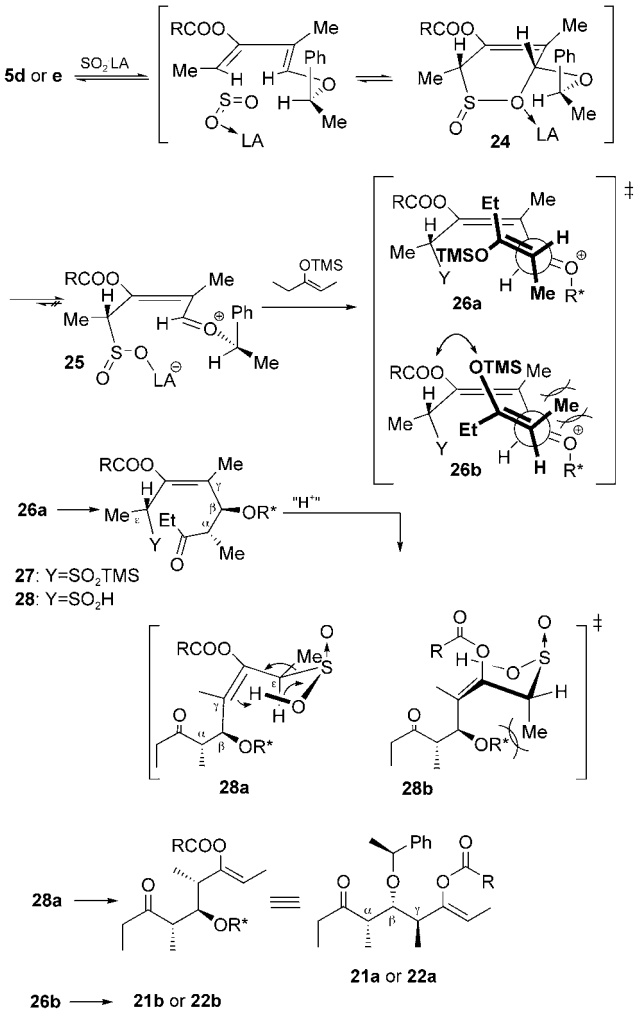
Reactivity of 1-alkoxy-3-acyloxy-1,3-dienes: Recently we reported that 1,3-dioxydiene (−)-**5e** can be condensed with **12** and provided **22a** and **22b** in 67 and 13% yield, respectively. Compound **22a** was converted into the 3,5-dihydroxycyclohexanone unit of Baconipyrone A and B (**23**). By using (1*S*)-phenylethanol with 97% *ee*, compound **23** was obtained without racemization also with 97% *ee* (Scheme 4).[13]

We have tested all three dienes **5d–f** under various conditions, and only **5d** and **5e** gave good yields. Bistrifluoromethane sulfonimide was found to be the best catalyst. For retro-ene desulfation of intermediates **20**, recently developed conditions were applied successfully.[21] The use of previously described $Et_3NH^+TfO^-$ caused degradation, most probably because of β-elimination of the alkoxy group. 3-Acetoxydiene **5f** was slow to react and only 40% of isomeric mixture was isolated together with unreacted starting material. Diene **5d** provided an inseparable mixture of **21a** and **21b**. The ratio of diastereoisomers (**21a/b**) was the same for reactions in CH_2Cl_2 and toluene. In the case of 3-isobutyryloxydiene **5e** we were pleased to find that diastereomeric ratio (*d.r.*) can be enhanced by changing solvent. Thus aromatic solvents with electron-donating groups increased the ratio in favor of isomer **22a**. Moreover, in this case both diastereoisomers were obtained in pure form by flash chromatography on silica gel.

The diastereoselectivity for the reaction of 1-alkoxy-3-acyloxypenta-1,3-dienes **5** with enoxysilanes **12** and SO_2 (Scheme 4) is better than that observed for the reactions of related 1-alkoxy-1,3-dienes with the same enoxysilanes.[14] We can interpret this fact in terms of a highly diastereoselective hetero-Diels–Alder addition of SO_2 to dienes **5d**,**e** in which the C–H bond of the phenylethyl ether resides in the π-plane of the *cis*-butadiene moiety (Scheme 5). Thus, the SO_2 molecule coordinated to the Lewis acid promoter attacks the *syn* face of the diene with respect to the methyl group of the phenylethyl ether moiety, giving a sultine **24**



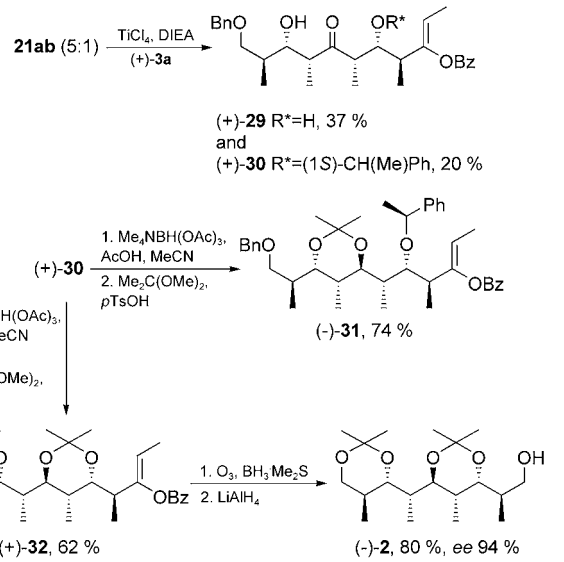
Scheme 4. Preparation of compounds **21a**,**b** and **22a**,**b** under various different reaction conditions.



Scheme 5. Hetero-Diels–Alder addition of SO_2 to dienes **5d**,**e**.

that is ionized irreversibly into zwitterion **25**. There are two possible orientations **26a** and **26b** for the enoxysilane that lead to the α,β-relative configuration in silylsulfinate **27**. Electrostatic interaction between the cationic and anionic part of the zwitterion **25** prohibits rotation about C–C bonds in these species, thus forcing the enoxysilane to attack **25** onto the face *anti* with respect to the sulfinate moiety. As **21a**/**22a** are the major products, orientation **26a** must be favored. The high degree of chirality transfer from the ε-center of **27**/**28** to the γ-center of **21a**/**22a** can be explained by invoking chairlike transitions states **28a** and **28b**. For steric reasons (allylic strain) **28a** is more stable than **28b** and the former controls the stereoselectivity of the reaction.

Preparation of advanced intermediate type 10 and completion of the synthesis: In a first attempt to generate a ketone of type **10** (Scheme 6) through a cross-aldol reaction, a 5:1 mixture of **21a** and **21b** was treated with 3-benzyloxy aldehyde (+)-**3a**. Treatment of **21a**,**b** in CH_2Cl_2 with $TiCl_4$ and Hünig's base ($(iPr)_2NEt$) at −78 °C[22] followed by addition

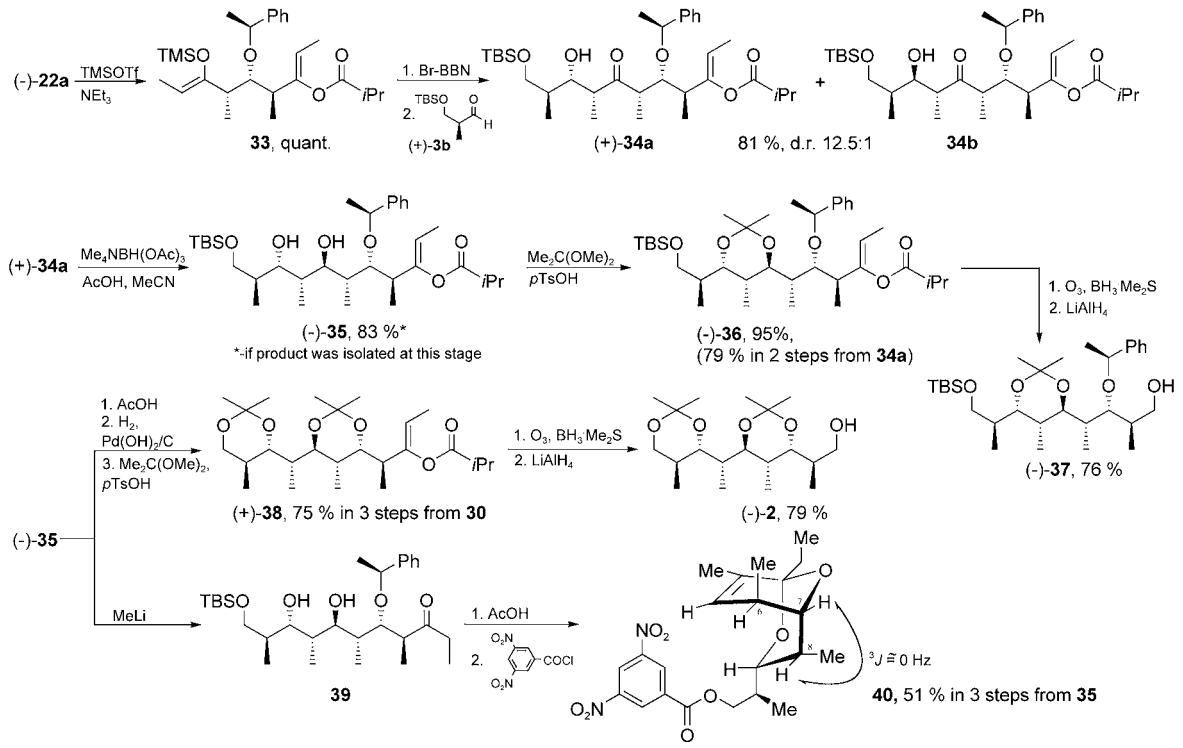


Scheme 6. Cross-aldol reaction of a 5:1 mixture of **21a** and **21b**.

of (+)-**3a** gave a mixture of aldols from which (+)-**29** and (+)-**30** were isolated in 37 and 20% yield, respectively, by column chromatography on silica gel.

Stereoselective *anti* reduction of ketone (+)-**30** under Evans' conditions[23] furnished a diol that was not isolated, but converted directly into acetonide (−)-**31** (74%, overall yield). The *anti* relationship of the 1,3-dioxacyclohexane moiety of (−)-**31** was confirmed by the ^{13}C NMR spectrum ($\delta_C(Me) = 23.5$, 25.4 ppm, $\delta_C(C_{quat}) = 100.1$ ppm).[24] Alternatively, Evans' reduction of aldol (+)-**30** followed by treatment with anhydrous $FeCl_3$ (CH_2Cl_2, 0 °C)[25] and $Me_2C(OMe)_2$/*p*TsOH provided the bis-acetonide (+)-**32** (62%, overall), the NMR data of which confirmed its structure and has the same configuration as stereoheptad (−)-**2**. Ozonolysis of (+)-**32**; subsequent reductive workup gave (−)-**2** in 80% yield (Scheme 6). Its spectral data were identical to those reported[9] for this compound. Mosher's ester[26] of (−)-**2** showed (^{19}F NMR spectroscopy) a 94% *ee*, thus indicating partial loss of optical purity (the starting diene (−)-**5d** had an *ee* of 97%), most probably because of high racemization tendency of aldehyde (+)-**3a**.

Because the route shown in Scheme 6 led to partial cleavage of the phenylethyl ether and to partial racemized (−)-**2**, we examined another route for the cross-aldol condensation that employs ethyl ketone (−)-**22a**, which can be obtained readily as a single diastereomer (Scheme 7). Compound (−)-**22a** was converted into *Z*-enoxysilane **33** quantitively. An exchange reaction with 9-bromo-9-borabicyclo[3.3.1]nonane (Br-BBN) in CH_2Cl_2 generated the corresponding *Z*-enoxyborane,[27] which was treated with aldehyde (+)-**3b**[16], a compound more stable that benzyl ether (+)-**3a**. This produced a 12.5:1 mixture of diastereomeric aldols (+)-**34a** and **34b** (81%), which were separated by flash column chromatography. The major aldol (+)-**34a** underwent reduction under Evans' conditions to give diol (−)-**35**, which was pro-



Scheme 7. Cross-aldol condensation of ethyl ketone (−)-**22a**.

tected as its acetonide (−)-**36** under standard conditions (δ_C(Me) = 23.6, 25.6 ppm, $\delta_C(C_{quat})$ = 100.1 ppm). Its ozonolysis and subsequent reduction gave (−)-**37** in 76% yield (60% based on (+)-**34a**). Diol (−)-**35** is a stereoheptad equivalent to Kishi's intermediate (−)-**2**. Its structure was confirmed by converting it into the spiroketal **40** (Scheme 7). The isobutyryl group of (−)-**35** was cleaved on treatment with MeLi. Then, β-elimination and desilylation with AcOH and esterification of the primary alcohol with 3,5-dinitrobenzoyl chloride gave **40**. Spectral data of **40**, especially NOE's in its 2D ^{1}H NMR spectrum and vicinal coupling constants, confirmed the structure (6,7-*anti* and 7,8-*anti* relationship). The Mosher's ester of (−)-**37** indicated a 99% *ee*. Therefore the optical purity has increased from 97% *ee* for the starting diene (−)-**5e** thanks to the aldol reaction with (+)-**3b** (with >99% *ee*). Finally the diol (−)-**35** was converted into Kishi's fragment (−)-**2**, which unambiguously proved its absolute configuration. Thus, desilylation with AcOH and selective hydrogenation under mild conditions (H_2, $Pd(OH)_2$/C, 1 bar, 1 h) followed by bis-acetonide formation provided product (+)-**38**. In the last step, ozonolysis of (+)-**38** with subsequent reductive workup gave (−)-**2** in 79% yield. In summary, Kishi's advanced intermediate (−)-**2** has been synthesized with 25% yield in eight steps (four isolated intermediates) starting from inexpensive and readily available chiral diene (−)-**5e**. Similarly, our own advanced stereoheptad (−)-**37**, which bears orthogonal protecting groups and corresponds to the *ansa* chain of Rifamycin S, was prepared with 30% yield in six steps (four isolated intermediates) from diene (−)-**5e**.

Conclusion

A very short synthesis of stereoheptads corresponding to the C(19)–C(27) segment of Rifamycins has been developed by applying our C–C bond-forming methodology based on the reaction cascade that condenses enantiomerically enriched (1*E*,3*Z*)-2-methyl-1-(1-phenylethoxy)penta-1,3-dien-3-yl isobutyrate to the (*Z*)-trimethylsilyl enol ether of pentan-3-one in the presence of an excess of SO_2 and an acid promoter, followed by a retro-ene desulfation . The ethyl ketones so-obtained undergo highly diastereoselective aldol condensations with (*S*)-2-methyl-3-[(*tert*-butyldimethylsilyl)oxy]propanal giving aldols that are transformed into stereoheptads.

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 by UV light, Pancaldi reagent, or $KMnO_4$. IR spectra: Perkin–Elmer-1420 spectrometer. ^{1}H NMR spectra: Bruker-ARX-400 spectrometer (400 MHz); δ(H) in ppm relative to the solvent's residual ^{1}H signal ($CHCl_3$, δ(H) = 7.27 ppm; CD_2Cl_2, δ(H) = 5.30 ppm) as internal reference; all ^{1}H assignments were confirmed by 2D-COSY spectra. ^{13}C NMR spectra: same instrument as above (100.6 MHz); δ(C) in ppm relative to solvent's C signal ($CDCl_3$, δ(C) = 77.1 ppm; CD_2Cl_2, δ(H) = 53.5 ppm) as internal reference; ^{19}F NMR spectra: same instrument as above (396 MHz); δ(F) in

ppm relative to F signal of $CFCl_3$ ($CFCl_3$, $\delta(F)=0$ ppm) as 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, D-96301 Kronach (Germany).

Methyl 2-((1-methoxy-2-oxopropyl)sulfonyl)propanoate (14): SO_2 (2 mL) was condensed at −196 °C into a degassed solution of **5a**[17] (0.506 g, 2.53 mmol) in CD_2Cl_2 (3 mL). The mixture was stirred at −78 °C for 2 h. An aliquot (~0.1 mL) was cannulated into an NMR tube at −78 °C and diluted by an additional amount of CD_2Cl_2 (0.5 mL). ^1H and ^{13}C NMR spectra of 2-(methoxy)-3,5-dimethyl-4-(trimethylsilyloxy)dihydrothiophene-1,1-dioxyde (**13a**) were registered at −78 °C. ^1H NMR (CD_2Cl_2, 400 MHz, −78 °C): $\delta=4.67$ (s, 1H; H-C(2)), 3.49 (s, 3H; H-C(1′)), 3.34 (q, $J=6.8$ Hz, 1H; H-C(5)), 1.59 (s, 3H; CH_3-C(3)), 1.28 (d, $J=7.4$ Hz, 3H; CH_3-C(5)), 0.17 ppm (s, 9H; TMSO-C(4)); ^{13}C NMR (CD_2Cl_2, 100.6 MHz, −78 °C): $\delta=146.6$, 111.6, 97.2, 58.7, 58.5, 13.3, 9.9, −0.6 ppm. Ozone was bubbled through the reaction mixture until a greenish-blue color was observed. The ozone generator was switched off and oxygen flow was continued until decoloration of the solution occurred. The mixture was degassed at −20 °C (0.01 mbar) with partial evaporation of CH_2Cl_2. Diethyl ether (6 mL) was added, followed by a saturated aqueous solution of NH_4Cl (1 mL). The mixture was stirred for 30 min at 0 °C, and extracted with Et_2O (4×15 mL). The combined organic layers were treated with a solution of CH_2N_2 (~10 equiv) in Et_2O at 0 °C; the mixture was stirred for 1 h at the same temperature, after which it was evaporated and the residue was purified by FC (PE/EtOAC 1:1). Yield 0.19 g (31%); oily solid, $R_f=0.38$ (PE/EtOAc 1:1); ^1H NMR ($CDCl_3$, 400 MHz): $\delta=$ 5.24 (s, 1H; H-C(3)), 4.38 (q, $J=7.5$ Hz, 1H; H-C(4)), 3.82, 3.81 (2 s, 6H; H-C(1′), H-C(1″)), 2.35 (s, 3H; H-C(1)), 1.60 ppm (d, $J=7.5$ Hz, 3H; H-C(4′)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=202.0$, 166.6, 98.1, 62.3, 61.1, 53.3, 27.5, 8.8 ppm; IR (film): $\tilde{\nu}=2955$, 2850, 1745, 1450, 1320, 1206, 1140, 1105 cm^{-1}; CI-MS (NH_3): m/z (%): 256 (100) [M+18], 234 (3), 203 (1), 174 (2), 129 (5), 103 (1), 86 (3); elemental analysis calcd (%) for $C_8H_{14}O_6S$ (238.26): C 40.33, H 5.92; found: C 40.36, H 5.89.

Trimethylsilyl ester of 5-methoxy-4-methyl-3-oxopent-4-ene-2-sulfinic acid (15a)

Method A: Compound **5a** (20 mg, 0.1 mmol) was placed in a NMR tube, CD_2Cl_2 (0.4 mL) was added. The tube was degassed three times at −196 °C and 0.01 mbar. Sulfur dioxide (0.2 mL), previously degassed three times at −196 °C and 0.01 mbar, was condensed into the tube at −196 °C, and the tube was sealed. When ^1H and ^{13}C NMR spectra were run at −78 °C, compound **13a** was observed. When temperature was slowly increased to +50 °C formation of **15a** was observed. It was complete at +80 °C.

Method B: Compound **5a** (20 mg, 0.1 mmol, 1 equiv) was placed in a NMR tube, and CD_2Cl_2 (0.4 mL) was added. The tube was degassed three times at −196 °C and 0.01 mbar. Sulfur dioxide (0.2 mL), previously degassed three times at −196 °C and 0.01 mbar was condensed into the tube at −196 °C. The contents of the tube was allowed to warm to −80 °C, after which it was removed from vacuum line under argon flow and sealed by septum. TMSOTf (3.6 μL, 0.02 mmol, 0.2 equiv) was added and the ^1H NMR spectrum was registered after 5 h at −78 °C. ^1H NMR (CD_2Cl_2, 400 MHz, −78 °C): $\delta=7.33$ (s, 1H; H-C(5)), 4.23 (q, $J=7.4$ Hz, 1H; H-C(2)), 3.79 (s, 3H; H-C(1′)), 1.42 (s, 3H; CH_3-C(4)), 1.26 (d, $J=$ 7.4 Hz, 3H; CH_3-C(1)), 0.21 ppm (s, 9H; TMSO-SO-C(2)); ^{13}C NMR (CD_2Cl_2, 100.6 MHz, +25 °C): $\delta=194.1$, 167.9, 114.9, 70.1, 62.3, 10.9, 7.0, 1.0 ppm. (In the presence of a Lewis acid, exchange of trimethylsilyl group within the silyl sulfinate moiety is fast on the NMR-timescale.[18])

Trimethylsilyl ester of 5-benzyloxy-4-methyl-3-oxopent-4-ene-2-sulfinic acid (15b): Compound 15b was prepared by method described for obtaining **15a**, but with **5b**[14d] instead of **5a**. Compound **13b** was observed in the temperature range −78 °C to +60 °C. ^1H NMR spectra of 2-(benzyloxy)-3,5-dimethyl-4-(trimethylsilyloxy)-dihydrothiophene-1,1-dioxyde (**13b**) was registered at +10 °C: ^1H NMR (CD_2Cl_2, 400 MHz, +10 °C): $\delta=7.35$–7.25 (m, 5H; arom), 4.96 (d, $J=11.6$ Hz, 1H; Ha-C(1′)), 4.79 (br s, 1H; H-C(2)), 4.62 (d, $J=11.6$ Hz, 1H; Hb-C(1′)), 3.32 (dq, $J=7.2$, 1.9 Hz, 1H; H-C(5)), 1.61 (s, 3H; CH_3-C(3)), 1.38 (d, $J=7.0$ Hz, 3H; CH_3-C(5)), 0.21 ppm (s, 9H; TMSO-C(4)). When temperature was slowly increased to +80 °C the formation of **15b** as two diastereoisomers in 1.8:1 ratio was observed. The reaction was over at +80 °C. ^1H NMR (CD_2Cl_2, 400 MHz, +10 °C; signals of major isomer noted with *): $\delta=$ 7.46, 7.44* (2 br s, 1H; H-C(5)), 7.33–7.30 (m, 5H; arom), 5.06, 5.05* (2 s, 2H; H-C(1′)), 3.93, 3.86* (q, $J=6.7$ Hz, 1H; H-C(2)), 1.63*, 1.56 (2 br s, 3H; CH_3-C(4)), 1.32, 1.28* (2 d, $J=6.7$ Hz, 3H; CH_3-C(1)), 0.15, 0.09* ppm (2 s, 9H; TMSO-SO-C(2)); ^{13}C NMR (CD_2Cl_2, 100.6 MHz, +10 °C): $\delta=196.2$*, 195.4, 163.7*, 163.5, 137.9, 137.4*, 130.4*, 130.3, 130.2*, 130.1, 129, 112.9, 112.8*, 97.1, 96.8*, 60.7, 58.8*, 13.3*, 10.8, 9.9, 9.8*, 1.5*, 1.2 ppm.

***tert*-Butyl ester of (4-methyl-3-oxo-5-(1-phenylethoxy)-pent-4-ene-2-sulfonyl)acetic acid (16)**: Sulfur dioxide (8 mL, ~40 equiv) was condensed in a two-necked flask at −196 °C. It was allowed to melt at −78 °C and CH_2Cl_2 (5 mL) was added followed by TMSOTf (0.16 mL, 0.90 mmol, 0.2 equiv). The mixture was stirred at −78 °C for 20 min. The solution of diene **5c**[17] (1.3 g, 4.48 mmol, 1 equiv) in CH_2Cl_2 (3 mL) was added slowly and dropwise at 80 °C under vigorous stirring and Ar atmosphere. The reaction mixture was stirred for 36 h at −70 °C. Sulfur dioxide was evaporated at −78 °C (0.1 mbar) for 6 h, then at room temperature for 1 h. The crude mixture was diluted with CH_2Cl_2 (5 mL) and cooled to −78 °C. A solution of TBAF (1 M in THF, 8.96 mL, 8.96 mmol, 2 equiv) was added at −78 °C followed by bromo *tert*-butyl acetate (1.32 mL, 8.96 mmol, 2 equiv). The mixture was allowed to reach room temperature and stirred for 16 h. The reaction mixture was poured into saturated aqueous solution of $NaHCO_3$ (60 mL) and extracted with EtOAc (3× 30 mL). The combined organic layers were washed with brine (60 mL), dried (Na_2SO_4), and evaporated in vacuo. The residue was purified by FC (PE/EtOAc 8:2). Yield 0.89 g (50%) of inseparable mixture (1.3:1) of diastereoisomers. Both isomers can be characterized by their ^1H and ^{13}C NMR spectra. Colorless oil, $R_f=0.5$ (PE/EtOAc 7:3); major isomer: ^1H NMR ($CDCl_3$, 400 MHz,): $\delta=7.45$ (q, $J=1.3$ Hz, 1H; H-C(5)), 7.45–7.29 (m, 10H; arom), 5.14 (q, $J=6.4$ Hz, 1H; H-C(1′)), 4.56 (q, $J=$ 7.0 Hz, 1H; H-C(2)), 4.04 (d, $J=14.5$ Hz, 1H; Ha-C(1″)), 3.95 (d, $J=$ 14.5 Hz, 1H; Hb-C(1″)), 1.83 (d, $J=1.3$ Hz, 3H; CH_3-C(4)), 1.66 (d, $J=$ 6.4 Hz, 3H; H-C(2′)), 1.53 (d, $J=7.0$ Hz, 3H; H-C(1)), 1.51 ppm (s, 9H; $(CH_3)_3$COOC-(1″)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=190.9$, 161.8, 161.4, 141.2, 128.9, 128.5, 125.9, 117.8, 117.5, 84.0, 83.0, 63.1, 55.8, 27.8, 23.5, 13.1, 8.7 ppm; minor isomer: ^1H NMR ($CDCl_3$, 400 MHz): $\delta=7.58$ (q, $J=1.3$ Hz, 1H; H-C(5)), 7.45–7.29 (m, 5H; arom), 5.17 (q, $J=6.4$ Hz, 1H; H-C(1′)), 4.65 (q, $J=7.0$ Hz, 1H; H-C(2)), 3.97 (d, $J=14.5$ Hz, 1H; Ha-C(1″)), 3.89 (d, $J=14.5$ Hz, 1H; Hb-C(1″)), 1.85 (br s, 3H; CH_3-C(4)), 1.68 (d, $J=6.4$ Hz, 3H; H-C(2′)), 1.61 (d, $J=7.0$ Hz, 3H; H-C(1)), 1.46 ppm (s, 9H; $(CH_3)_3$COOC-(1″)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=$ 191.4, 161.9, 160.7, 140.9, 128.8, 128.4, 125.8, 117.5, 83.9, 83.2, 63.0, 56.1, 27.9, 23.3, 13.3, 8.9 ppm; IR (film) (mixture of isomers): $\tilde{\nu}=2980$, 1730, 1625, 1455, 1375, 1325, 1210, 1145, 1030 cm^{-1}; HRMS (MALDI-TOF) (mixture of isomers): m/z calcd for $C_{20}H_{28}O_6SNa^+$: 419.1504; found: 419.1531; elemental analysis (mixture of isomers) calcd (%) for $C_{20}H_{28}O_6S$ (396.50): C 60.58, H 7.12; found: C 60.50, H 7.18.

(−)-(1*E*,3*Z*)-2-Methyl-1-((1*S*)-1-phenylethoxy)penta-1,3-dien-3-ol benzoate (5d):

General procedure: Triethylamine (64 mL, 0.46 mol, 2.3 equiv) followed by trimethylsilyl triflate (39.8 mL, 0.22 mol, 1.1 equiv) was added to a solution of keto derivative **19**[17] (97% *ee*; 43.7 g, 0.2 mol, 1 equiv) in Et_2O (1.2 L) cooled to −20 °C,. The reaction mixture was stirred for 3 h at −20 °C and then 1 h at 0 °C. Cold pentane (−30 °C; 2 L) was added, and the suspension was quickly filtered through a small pad of silica gel (suspended in pentane containing 2% NEt_3). The organic layer was washed with an ice-cold aqueous solution of $NaHCO_3$ (0.5 L), an ice-cold aqueous solution of citric acid solution (2×0.5 L), again an ice-cold aqueous solution of $NaHCO_3$ (2×0.5 L), and brine (2×0.5 L), dried (Na_2SO_4), and evaporated. Crude product **5c** (56.3 g, 97%) was sufficiently pure for the next step. Benzoyl fluoride (15.5 mL, 0.14 mol, 1.01 equiv) followed by a 1 M THF solution of TBAF (2.8 mL, 2.8 mmol, 0.02 equiv) was added to a solution of the silyl derivative **5c** (41 g, 0.14 mol) in THF (160 mL) at −15 °C. The mixture was stirred at this temperature for 30 min. (^1H NMR control). The solvent was evaporated and residue purified by FC (CH_2Cl_2), yielding 41.9 g (92%) of (−)-**5d**. Colorless oil, $R_f=0.8$

(CH_2Cl_2); $[\alpha]_D^{25}=-22$ ($c=1.0$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=8.09$ (d, $J=7.4$, 2H; Bz), 7.63 (t, $J=7.3$, 1H; Bz), 7.49 (t, $J=7.7$, 2H; Bz), 7.32–7.21 (m, 5H; Ph), 6.30 (s, 1H; H-C(1)), 5.31 (q, $J=7.0$, 1H; H-C(1′)), 4.74 (q, $J=6.4$, 1H; H-C(4)), 1.88 (s, 3H; CH_3-C(2)), 1.59 (d, $J=7.0$, 3H; H-C(2′)), 1.51 ppm (d, $J=6.4$, 3H; H-C(5)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=164.0$, 147.4, 142.7, 142.6, 133.3, 130.1, 129.5, 128.6, 128.5, 127.7, 125.9, 110.0, 108.6, 80.2, 23.5, 11.3, 10.5 ppm; IR (film): $\tilde{\nu}=3355$, 3060, 2975, 1730, 1660, 1635, 1490, 1450, 1245, 1175, 1090 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{21}H_{22}O_3Na^+$: 345.1467; found: 345.1434.

(−)-(1*E*,3*Z*)-2-Methyl-1-((1*S*)-1-phenylethoxy)penta-1,3-dien-3-ol isobutyrate (5e): Compound **5e** was prepared by the same procedure as for **5d**, but with isobutyryl fluoride instead of benzoyl fluoride. Yield 87%; colorless oil; $R_f=0.8$ (CH_2Cl_2); $[\alpha]_D^{25}=-40$ ($c=2.0$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz,): $\delta=7.37$–7.26 (m, 5H; arom), 6.20 (s, 1H; H-C(1)), 5.18 (q, $J=7.4$ Hz, 1H; H-C(4)), 4.78 (q, $J=6.8$ Hz, 1H; H-C(1′)), 2.60 (sept, $J=7.4$ Hz, 1H; $(CH_3)_2CHCOO$-C(3)), 1.80 (s, 3H; CH_3-C(2)), 1.54 (d, $J=6.2$ Hz, 3H; H-C(5)), 1.51 (d, $J=6.8$ Hz, 3H; H-C(2′)), 1.16, 1.13 ppm (2d, 6H; $J=6.8$ Hz, $(CH_3)_2$CHCOO-C(3)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=173.5$, 146.9, 142.7, 142.1, 128.5, 127.7, 126.0, 110.0, 108.1, 80.0, 34.0, 23.6, 19.0, 11.0, 10.3 ppm; IR (film): $\tilde{\nu}=3060$, 2930, 1760, 1665, 1640, 1450, 1375, 1215, 1190 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{18}H_{24}O_3Na^+$: 311.1623; found: 311.1684.

(−)-(1*E*,3*Z*)-2-Methyl-1-((1*S*)-1-phenylethoxy)penta-1,3-dien-3-ol acetate (5f): Compound **5f** was prepared by the same procedure as for **5d**, but with acetyl fluoride instead of benzoyl fluoride. Yield 90%; colorless oil; $R_f=0.75$ (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.39$–7.28 (m, 5H; arom), 6.23 (s, 1H; H-C(1)), 5.21 (q, $J=7.0$ Hz, 1H; H-C(4)), 4.84 (q, $J=6.4$ Hz, 1H; H-C(1′)), 2.12 (s, 3H; CH_3-COO-C(3)), 1.84 (d, 3H; $J=1.3$ Hz,CH_3-C(2)), 1.56 (d, $J=6.4$ Hz, 3H; H-C(2′)), 1.55 ppm (d, $J=7.0$ Hz, 3H; H-C(5)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=168.2$, 147.2, 142.7, 142.3, 128.5, 127.7, 125.9, 110.0, 108.3, 80.1, 23.6, 20.3, 11.2, 10.3 ppm; IR (film): $\tilde{\nu}=3055$, 2930, 1755, 1660, 1635, 1450, 1380, 1220 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{16}H_{20}O_3Na^+$: 283.1310; found: 283.1320.

General procedure for determination of enantiomeric excess of compounds 19 and 5d–f: Ozone was bubbled through the solution of **19** (0.05 g, 0.23 mmol, 1 equiv) in diethyl ether (1 mL) at −78°C until it turned blue. The ozone generator was turned off and oxygen was pass through the solution until the decoloration of the reaction mixture. A solution of diisobutylaluminium hydride (1M in hexane; 1.38 mL, 1.38 mmol, 6 equiv) was added slowly at −78°C. The reaction mixture was allowed to reach room temperature and stirred for 4 h. It was diluted with a 10% aqueous solution of K/Na tartrate (5 mL), and stirring was continued for 1 h. The resulting biphasic mixture was extracted with Et_2O (3×5 mL). The combined organic layers were washed with brine (5 mL), dried (Na_2SO_4), and evaporated. The crude mixture containing pure **18** was analyzed by chiral-phase HPLC (Daicel OD-H column, $\lambda=267$ nm, $v=1.5$ mL min^{-1}, hexane/*i*PrOH 99:1): (−)-(S)-**18**: $t_R=20.66$ min; (+)-(*R*)-**18**: $t_R=16.30$ min.

In the case of dienes **5d–f** of DIBAL (8 equiv) was used and the crude product was filtered through florisil and then analyzed by HPLC.

(1*Z*,2*S*,3*R*,4*S*)-1-Ethylidene-2,4-dimethyl-5-oxo-3-((1*S*)-1-phenylethoxy)heptyl benzoate (21a): A two-necked 100 mL flask was flame dried and filled with Argon. Then CH_2Cl_2 (18 mL) and $(CF_3SO_2)_2NH$ (7 mL, 0.5M in CH_2Cl_2, 3.50 mmol, 0.2 equiv) were added. The system was frozen by liquid nitrogen and connected to the vacuum line. SO_2 (20 mL) was condensed into the flask, which was allowed to warm to −80°C by using an acetone/dry-ice cooling bath. After 30 min, the mixture of diene (−)-**5d** (5.68 g, 17.6 mmol, 1 equiv) and enoxysilane **12** (7 mL, 35.2 mmol, 2 equiv) in CH_2Cl_2 (16 mL) was introduced dropwise to the reaction flask. After the addition, the stirring was continued overnight at −80°C. Then all the SO_2 and CH_2Cl_2 were evaporated in vacuo. The resulting viscous mixture was dissolved in anhydrous acetonitrile (40 mL). In another flask, $[Pd(OAc)_2]$ (0.40 g, 1.76 mmol, 0.1 equiv), PPh_3 (0.46 g, 1.76 mmol, 0.1 equiv) and anhydrous K_2CO_3 (0.48 g, 3.50 mmol, 0.2 equiv) were prepared. This pre-prepared solution in acetonitrile was added, followed by the introduction of isopropanol (10 mL). The mixture was heated to 80°C for 30 min. A saturated aqueous solution of $NaHCO_3$ (50 mL) was added, and the mixture was extracted with EtOAc (3×70 mL). The combined organic layers were washed with brine (80 mL), dried (Na_2SO_4), and evaporated. The residue was purified by FC (PE/EtOAc 6:1). Yield: 5.46 g (76%) of a 5:1 mixture of **21a** and **21b**. The two diastereomers could not be separated. Only **21a** could be characterized by NMR spectra of the mixture: Yellow oil; $R_f=0.22$ (PE/EtOAc 10:1); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=8.2$–7.0 (m, 10H arom.), 5.31 (dq, $J=7.1$, 1.2 Hz, 1H; H-C(1′)), 4.42 (q, $J=6.5$ Hz, 1H; H-C(1″)), 3.84 (dd, $J=6.2$, 4.3 Hz, 1H; H-C(3)), 2.85 (m, 1H; H-C(4)), 2.72 (dq, $J=6.8$, 6.8 Hz, 1H; H-C(2)), 2.29 (dq, $J=18.2$, 7.1 Hz, 1H; Ha-C(6)), 2.20 (dq, $J=18.2$, 7.1 Hz, 1H; Hb-C(6)), 1.52 (dd, $J=6.8$, 1.2 Hz, 1H; H-C(2′)), 1.37 (d, $J=6.5$ Hz, 3H; H-C(2″)), 1.21 (d, $J=7.1$ Hz, 3H; CH_3-C(4)), 0.98 (d, $J=7.1$ Hz, 3H; CH_3-C(2)), 0.86 ppm (d, $J=7.4$ Hz, 3H; H-C(7)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=212.9$, 164.1, 149.8, 142.5, 134.0–125.0 (m, C arom.), 112.9, 76.8, 76.7, 47.7, 40.4, 34.2, 23.4, 13.4, 12.9, 10.9, 7.6 ppm; IR (film): $\tilde{\nu}=2975$, 1735, 1600, 1490, 1450, 1375, 1260, 1175, 1090, 1070, 1025 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{26}H_{32}O_4Na^+$: 431.2198; found: 431.2143.

(−)-(1*Z*,2*S*,3*R*,4*S*)-1-Ethylidene-2,4-dimethyl-5-oxo-3-((1*S*)-1-phenylethoxy)heptyl isobutyrate (22a) and (−)-(1*Z*,2*S*,3*R*,4*R*)-1-ethylidene-2,4-dimethyl-5-oxo-3-((1*S*)-1-phenylethoxy)heptyl isobutyrate (22b): A solution of Tf_2NH in CH_2Cl_2 (0.5M, 9.3 mL, 4.65 mmol, 0.25 equiv) was diluted with toluene (40 mL). Sulfur dioxide (40 mL) was condensed at −196°C. The mixture was stirred at −78°C for 20 min. The solution of diene (−)-**5e** (5.36 g, 1.6 mmol, 1 equiv) and (z)-3-trimethylsilyloxy pent-3-ene (**12**) (10.8 mL, 55.8 mmol, 3 equiv) in toluene (6 mL) were added slowly and dropwise at −80°C. The reaction mixture was stirred at −80°C for 36 h. Sulfur dioxide was evaporated at −78°C (0.1 mbar) for 5 h, then at room temperature for 1 h. The residual solution (~30 mL) was diluted with MeCN (50 mL) and transferred into a suspension of $[Pd(OAc)_2]$ (0.45 g, 1.86 mmol, 0.1 equiv), Ph_3P (0.49 g, 1.86 mmol, 0.1 equiv), K_2CO_3 (1.60 g, 11.5 mmol, 0.62 equiv) in MeCN (70 mL). Isopropanol (50 mL) was added, and the mixture was heated under reflux for 20 min, cooled to room temperature and partitioned between aqeous $NaHCO_3$ and EtOAc. The water phase was extracted with EtOAc (3× 50 mL). The combined organic extracts were washed successively with a saturated aqueous $NaHCO_3$, brine, and water, dried over $MgSO_4$, and evaporated. The residue was purified by FC (PE/EA 98:2). Yield of **22a**: 4.66 g, 67%; **22b**: 0.9 g, 13%.

Data for ***22a***: Colorless oil; $R_f=0.4$ (PE/EtOAc 9:1); $[\alpha]_D^{25}=-18$, ($c=0.5$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.32$–7.24 (m, 5H; arom), 5.21 (q, $J=6.8$ Hz, 1H; H-C(1′)), 4.44 (q, $J=6.8$ Hz, 1H; H-C(1″)), 3.77 (t, $J=5.5$ Hz, 1H; H-C(3)), 2.69 (dq, $J=5.5$, 6.8 Hz, 1H; H-C(2)), 2.64 (m, 2H; H-C(4), H-C($CH(CH_3)_2$)), 2.19 (dq, AB-syst, $J=17.9$, 7.4 Hz, 1H; Ha-C(6)), 2.09 (dq, AB-syst, $J=17.9$, 7.4 Hz, 1H; Hb-C(6)), 1.45 (dd, $J=6.8$, 1.2 Hz, 3H; H-C(2′)), 1.37 (d, $J=7.4$ Hz, 3H; H-C(2″)), 1.22 (d, $J=6.8$ Hz, 6H; H-C($CH(CH_3)_2$)), 1.10 (d, $J=7.4$ Hz, 3H; CH_3-C(2)), 0.99 (d, $J=6.8$ Hz, 3H; CH_3-C(4)) 0.82 ppm (t, $J=7.4$ Hz, 3H; H-C(7)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=213.0$, 149.6, 143.6, 128.3, 127.5, 126.8, 112.5, 76.9, 76.7, 47.8, 40.9, 34.2, 33.9, 23.6, 19.2, 19.1, 13.3, 12.5, 10.9, 7.7 ppm; IR (film): $\tilde{\nu}=2965$, 2880, 1755, 1710, 1610, 1460, 1385, 1135 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{23}H_{34}O_4Na^+$: 397.2355; found: 397.2345; elemental analysis calcd (%) for $C_{23}H_{34}O_4$ (374.51): C 73.76, H 9.15; found: C 73.77, H 9.09.

Data for ***22b***: Colorless oil; $R_f=0.45$ (PE/EtOAc 9:1); $[\alpha]_D^{25}=-46$ ($c=1.7$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.33$–7.18 (m, 5H; arom), 5.21 (dq, $J=6.8$, 1.2 Hz, 1H; H-C(1′)), 4.40 (q, $J=6.8$ Hz, 1H; H-C(1″)), 3.60 (dd, $J=8.0$, 4.3 Hz, 1H; H-C(3)), 2.84–2.79 (m, 1H; H-C(2)), 2.77 (quint, $J=7.4$ Hz, 1H; H-C(4)), 2.56 (sept., $J=6.8$ Hz, 1H; $(CH_3)_2CHCOO$-C(1)), 2.41 (dq, AB-syst, $J=17.8$, 7.4 Hz, 1H; Ha-C(6)), 2.28 (dq, AB-syst, $J=17.8$, 7.4 Hz, 1H; Hb-C(6)), 1.46 (dd, $J=6.8$, 1.2 Hz, 3H; H-(C2′)), 1.34 (d, $J=6.2$ Hz, 3H; H-C(2″)), 1.17 (d, $J=6.8$ Hz, 6H; $(CH_3)_2$CHCOO-C(1)), 1.13 (d, $J=6.8$ Hz, 3H; CH_3-C(2)), 0.90 (t, $J=7.4$ Hz, 3H; H-C(7)), 0.88 ppm (d, $J=6.8$ Hz, 3H; CH_3-C(4)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=213.9$, 174.5, 149.9, 143.3, 128.3, 127.5, 126.6, 111.5, 79.2, 76.4, 47.8, 38.7, 36.4, 40.9, 34.2, 24.1, 19.0, 13.6, 12.3, 7.5 ppm; IR (film): $\tilde{\nu}=2975$, 2935, 2875, 1745, 1715, 1455, 1370, 1240, 1140, 1080 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{23}H_{34}O_4Na^+$:

397.2355; found: 397.2359; elemental analysis calcd (%) for $C_{23}H_{34}O_4$ (374.51): C 73.76, H 9.15; found: C 73.80, H 9.05.

Aldols (+)-29 and (+)-30: $TiCl_4$ (0.18 mL, 1.71 mmol, 1.1 equiv) was added dropwise to a stirred solution of the 5:1 mixture of ketones **21a,b** (0.2 M, 0.635 g, 1.56 mmol, 1 equiv) in CH_2Cl_2 at −78 °C under argon, giving a yellow slurry. After 2 min, *N*,*N*-diisopropylethylamine (DIPEA; 0.32 mL, 1.87 mmol, 1.2 equiv) was added dropwise. The resulting deep red solution was stirred at −78 °C for 1.5 h. After the dropwise addition of aldehyde (+)-**3a** (0.33 g, 1.56 mmol, 1.2 equiv), stirring was continued at −78 °C for 1.5 h. The reaction was terminated by adding a saturated aqueous solution of NH_4Cl at −78 °C. The resulting mixture was slowly warmed to room temperature. The mixture was extracted with diethyl ether (3×30 mL). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), and evaporated under vacuo. The residue was purified by FC (PE/EtOAc 5:1). Yield: 0.183 g (20 %) of (+)-**30** and 0.277 g (37 %) of (+)-**29**.

*Data for (+)-**30***: Colorless oil; R_f=0.22 (PE/EtOAc 5:1); $[\alpha]_D^{25}$=+1.3 (c=1.65 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.00–7.00 (m, 15H; arom), 5.32 (q, J=6.5 Hz, 1H; H-C(1′)), 4.47, 4.44 (2d, J=10.0 Hz, 2H; PhCH_2O-C(9)), 4.45 (q, J=6.5 Hz, 1H; H-C(1″)), 3.79 (dd, J=4.2, 5.4 Hz, 1H; H-C(3)), 3.61 (dd, J=9.0, 4.5 Hz, 1H; Ha-C(9)), 3.54 (dt, J=9.3, 1.9 Hz, 1H; H-C(7)), 3.46 (d, J=2.0 Hz, 1H; OH), 3.43 (dd, J=9.0, 6.2 Hz, 1H; Hb-C(9)), 3.03 (dq, J=5.4, 7.0 Hz, 1H; H-C(4)), 2.86 (ddq, J=4.2, 1.3, 6.8 Hz, 1H; H-C(2)), 2.67 (dq, J=1.9, 7.0 Hz, 1H; H-C(6)), 1.79 (m, 1H; H-C(8)), 1.52 (dd, J=6.7, 1.3 Hz, 3H; H-C(2′)), 1.37 (d, J=6.4 Hz, 3H; H-C(2″)), 1.24 (d, J=7.1 Hz, 3H; CH_3-C(2)), 1.04 (d, J=6.8 Hz, 3H; CH_3-C(6)), 1.00 (d, J=6.8 Hz, 3H; CH_3-C(4)), 0.78 ppm (d, J=6.8 Hz, 3H; CH_3-C(8)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ=217.4, 164.1, 149.9, 143.0, 138.4, 133.3–125.0 (m, Carom), 112.9, 76.7, 76.6, 73.6, 73.3, 72.3, 46.1, 45.8, 40.8, 35.8, 23.5, 13.6, 13.4, 11.1, 8.7 ppm; IR (film): $\tilde{\nu}$=3505, 2975, 2360, 1730, 1700, 1600, 1495, 1450, 1370, 1260, 1090, 1070, 1025, cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{37}H_{46}O_6Na^+$: 609.3192; found: 609.3132.

*Data for (+)-**29***: Colorless oil; R_f=0.38 (PE/EtOAc 1:1); $[\alpha]_D^{25}$=+17 (c=1.46 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.20–7.20 (m, 10H; arom), 5.42 (q, J=6.8 Hz, 1H; H-C(1′)), 4.48, 4.45 (2d, J=10.1 Hz, 2H; PhCH_2O-C(9), 3.83 (dt, J=8.9, 2.5 Hz, 1H; H-C(3)), 3.78 (dt, J=8.3, 3.1 Hz, 1H; H-C(7)), 3.65–3.43 (m, 2H; H-C(9)), 2.93 (dq, J=7.1, 3.4 Hz, H-C(6)), 2.82 (dq, J=6.5, 3.1 Hz, H-C(4)), 2.52 (dq, J=8.9, 7.1 Hz, H-C(2)), 1.86 (m, 1H; H-C(7)), 1.52 (d, J=6.8 Hz, C-H(1′)), 1.12 (d, J=6.8 Hz, CH_3-C(2)), 1.10 (d, J=6.8 Hz, CH_3-C(4)), 1.08 (d, J=7.1 Hz, CH_3-C(6)), 0.87 ppm (d, J=7.4 Hz, CH_3-C(8)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ=217.3, 165.4, 148.6, 138.2, 135.0–125.0 (9C, arom), 114.9, 73.8, 73.6, 73.2, 71.3, 46.0, 44.7, 43.5, 35.7, 14.5, 14.0, 11.0, 10.1, 8.2 ppm; IR (film): $\tilde{\nu}$=3500, 2970, 2360, 1715, 1455, 1375, 1260, 1175, 1095, 1070, 1025 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{29}H_{38}O_6Na^+$: 505.2566; found: 505.2503.

Acetonide (−)-31: Anhydrous AcOH (0.46 mL) was added to a solution of $Me_4NBH(OAc)_3$ (0.23 g, 0.87 mmol, 8 equiv) in CH_3CN (1 mL). After 30 min, the mixture was cooled to −40 °C and a solution of (+)-**30** (64 mg, 0.109 mmol, 1 equiv) in CH_3CN (0.35 mL) was added dropwise. The resulting mixture was stirred at −20 °C for 16 h. The reaction was quenched by an aqueous solution K/Na tartrate (0.5 N 1.3 mL) and extracted with diethyl ether (3×20 mL). The isolated diol (50 mg, 0.085 mmol, 1 equiv) was dissolved in CH_2Cl_2 (1.5 mL), after which dimethoxypropane (0.08 mL) and *p*TsOH·H_2O (1 mg) were added at 0 °C. After 1 h, the reaction was quenched by saturated aqueous solution of $NaHCO_3$ (10 mL), and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated under vacuo. The residue was purified by FC (PE/EtOAc 10:1) giving the corresponding product (−)-**31** (51 mg, 74 % in two steps). Colorless oil; R_f=0.22 (PE/EA 10:1); $[\alpha]_D^{25}$=−16 (c=0.52 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.1–7.1 (m, 15H; arom), 5.34 (q, J=6.8 Hz, 1H; H-C(2)), 4.52 (q, J=6.2 Hz, 1H; H-C(1′)), 4.49, 4.45 (2d, J=9.3 Hz, 2H; PhCH_2O-C(9)), 3.81 (dd, J=5.9, 1.3 Hz, 1H; H-C(5)), 3.55 (m, 2H; H-C(9), Ha-C(11)), 3.41 (dd, J=8.6, 6.2 Hz, 1H; Hb-C(11)), 2.86 (dd, J=6.8, 8.0 Hz, 1H; H-C(7)), 2.78 (dq, J=5.9, 6.8 Hz, 1H; H-C(4)), 1.78 (m, 1H; H-C(10)), 1.74 (dq, J=8.0, 7.4 Hz, 1H; H-C(6)), 1.66 (m, 1H; H-C(8)), 1.55(d, J=6.8 Hz, 3H; H-C(1)), 1.36 (d, J=6.5 Hz, 3H; H-C(2′)), 1.16 (s, 3H; CH_3-($C_{acetonide}$), 1.14 (d, J=6.8 Hz, 3H; CH_3-C(4)), 0.97 (d, J=7.4 Hz, 3H; CH_3-C(6)), 0.93 (s, 3H; CH_3-($C_{acetonide}$), 0.91 (d, J=6.8 Hz, 3H; CH_3-C(10)), 0.75 ppm (d, J=6.8 Hz, 3H; CH_3-C(8)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ=164.3, 150.6, 145.1, 138.9, 133.2–126.0 (m, C arom), 111.98, 100.1, 76.9, 76.6, 76.5, 73.2, 72.6, 69.8, 42.1, 38.9, 35.5, 33.7, 25.4, 24.4, 23.5, 13.3, 13.0, 12.5, 10.9, 10.7 ppm; IR (film): $\tilde{\nu}$=2975, 2360, 1730, 1600, 1490, 1450, 1375, 1315, 1260, 1225, 1175, 1090, 1025, 1000 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{40}H_{52}O_6Na^+$: 651.3662; found: 651.3661; elemental analysis calcd (%) for $C_{40}H_{52}O_6$ (628.48): C 76.40, H 8.33; found: C 76.47, H 8.36.

Diacetonide (+)-(32): Anhydrous AcOH (4.2 mL) was added to a solution of $Me_4NBH(OAc)_3$ (1.64 g, 5.31 mmol, 12 equiv) in CH_3CN (6.5 mL). After 30 min, the mixture was cooled to −40 °C and a solution of (+)-**30** (0.39 g, 0.67 mmol, 1 equiv) in CH_3CN (2.5 mL) was added dropwise. The resulting mixture was stirred at −20 °C for 48 h. The reaction was quenched by an aqueous solution of potassium sodium tartrate (0.5 N, 10 mL) and extracted with diethyl ether (3×30 mL). The isolated diol (0.31 g, 0.52 mmol, 1 equiv) and anhydrous $FeCl_3$ (0.34 g, 2.1 mmol, 4 equiv) were mixed in CH_2Cl_2 (6 mL) at 0 °C. After 30 min the reaction was quenched by a saturated aqueous solution of NH_4Cl (15 mL), and extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), and concentrated in vacuo. The resulting mixture was dissolved in anhydrous CH_2Cl_2 (10 mL), after which dimethoxypropane (1.5 mL, 11.85 mmol, 22.8 equiv) and *p*TsOH·H_2O (8 mg, 0.01 equiv) were added at 0 °C. After 1 h, the reaction mixture was quenched by a saturated aqueous solution of $NaHCO_3$ (15 mL) and extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), and evaporated in vacuo. The residue was purified by FC (PE/EtOAc 10:1). Yield: 0.20 g, 62 %, over three steps; yellow-greenish oil; R_f=0.19 (PE/EA 10:1); $[\alpha]_D^{25}$=+18 (c=0.74 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.2–7.4 (m, 5H; arom), 5.29 (q, J=7.1 Hz, 1H; H-C(1′)), 3.86 (dd, J=10.9, 1.9 Hz, 1H; H-C(7)), 3.77 (dd, J=10.9, 3.8 Hz, 1H; H-C(3)), 3.69 (dd, J=11.5, 5.1 Hz, 1H; Ha-C(9)), 3.51 (dd, J=11.5, 1.5 Hz, 1H; Hb-C(9)), 3.28 (dd, J=6.4, 8.9 Hz, 1H; H-C(5)), 2.49 (dq, J=7.0, 10.9 Hz, 1H; H-C(2)), 1.84 (ddt, J=11.5, 6.5, 4.5 Hz, 1H; H-C(8)), 1.73 (m, 2H; H-C(6), H-C(4)), 1.51 (d, J=6.8 Hz, 3H; H-C(2′)), 1.39, 1.37, 1.35, 1.31 (4 s, 12H; CH_3-($C_{acetonide}$)), 1.01 (d, J=6.8 Hz, 3H; CH_3-C(2)), 0.92 (d, J=6.8 Hz, 3H; CH_3-C(4)), 0.87 (d, J=6.8 Hz, 3H; CH_3-C(6)), 0.69 ppm (d, J=6.8 Hz, 3H; CH_3-C(8)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ=164.2, 150.0, 133.0, 130.4, 128.4, 111.6, 100.5, 98.0, 74.2, 72.8, 66.6, 39.7, 39.2, 36.4, 30.4, 29.8, 25.9, 23.5, 19.0, 14.3, 12.6, 12.1, 11.1, 7.7 ppm; IR (film): $\tilde{\nu}$=2985, 1735, 1455, 1390, 1260, 1240, 1200, 1175, 1145, 1095, 1065, 1025, 1010 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{28}H_{42}O_6Na^+$: 497.2879; found: 497.2877; elemental analysis calcd (%) for $C_{28}H_{42}O_6$ (474.63): C 70.86, H 8.92; found: C 70.88, H 8.99.

C(19)–C(27) fragment of Rifamycin S (−)-2: Compound (+)-**32** (36 mg, 0.075 mmol, 1 equiv) was dissolved in anhydrous Et_2O (4 mL). Ozone was bubbled through the solution at −78 °C until it turned blue. Then O_2 was passed through the solution until the color disappeared. The resulting mixture was quenched by BH_3·Me_2S (0.04 mL, 0.42 mmol, 5.6 equiv) at −78 °C. The solution was stirred for additional 20 h at −78 °C. Then it was quenched by methanol at −78 °C, and warmed up slowly to room temperature. The mixture was evaporated in vacuo, and the residue was taken up by anhydrous diethyl ether (10 mL). $LiAlH_4$ (9 mg, 0.23 mmol, 3 equiv) was added, and the resulting mixture was heated under reflux at 50 °C for 2 h. It was quenched by a saturated aqueous solution of NH_4Cl (5 mL) and extracted with diethyl ether (3×10 mL). The combined organic layers were washed with brine (2×10 mL), dried (Na_2SO_4), and evaporated. The residue was purified by FC (PE/EtOAc 3:1) providing pure (−)-**2** (21 mg, 80 %). The enantiomeric excess was 94.0 %, as determined by means of the Mosher's esters (see below). The same method was applied to prepare (−)-**2** (0.13 g, 79 %) from (+)-**38** (0.21 g). The data for (−)-**2** were identical to those reported previously for this compound.[9] White solid; R_f=0.21 (PE/EA 3:1); m.p. 79 °C (Lit. 80 °C); $[\alpha]_D^{25}$=−3.7 (c=0.75 in $CHCl_3$), (Lit. $[\alpha]_D^{25}$=−6.25 (c=0.75 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ=3.72 (dd, J=1.9, 10.4 Hz, 1H), 3.53–3.20 (m, 4H), 3.23 (dd, J=6.4, 10.3 Hz, 1H), 1.81–1.67 (m, 4H), 1.31, 1.30,

1.28, 1.24 (4 s, 12H), 0.87, 0.80, 0.71, 0.63 ppm (4d, $J=7.0$ Hz, 12H), ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=100.3$, 97.8, 75.8, 74.3, 72.5, 69.0, 66.4, 39.1, 36.5, 34.7, 30.2, 29.7, 25.9, 23.3, 18.9, 12.8, 12.4, 11.9, 7.6 ppm; IR (film): $\tilde{\nu}=3477$, 2969, 1462, 1384, 1268, 1234, 1199, 1177, 1150, 1051, 1008, 881 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{19}H_{36}O_5Na^+$: 367.2460; found: 367.2472.

(*R*)-MTPA (MTPA = α-methoxy-α-(trifluoromethyl)phenylacetic acid) ester of (−)-2, general procedure: A catalytic amount of DMAP and (+)-(*S*)-MTPA chloride (18 mg, 0.069 mmol, 1.6 equiv) was added to a solution of (−)-**2** (15 mg, 0.044 mmol, 1 equiv) in anhydrous pyridine (1 mL). 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 successively with a saturated aqueous solution of $CuSO_4$ (4×7 mL), water (10 mL), 10% aqueous solution of citric acid (4×7 mL), and aqueous saturated solution of $NaHCO_3$ (3×5 mL), dried (Na_2SO_4), and evaporated in vacuo. Yield 24 mg, 94%. All the NMR measurements were done on the crude sample. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.7$–7.3 (m, 5H; arom), 4.44 (dd, $J=3.7$, 11.1 Hz, 1H), 4.26 (dd, $J=6.2$, 10.5 Hz, 1H), 3.82 (dd, $J=2.5$, 10.5 Hz, 1H), 3.69 (dd, $J=4.9$, 11.1 Hz, 1H), 3.57 (s, 3H), 3.51 (m, 2H), 3.27 (dd, $J=6.8$, 9.9 Hz, 1H), 1.97 (m, 1H), 1.84 (m, 1H), 1.73 (m, 2H), 1.38 (s, 3H), 1.34 (s, 3H), 1.26 (s, 3H), 2.13 (s, 3H), 0.89 (m, 9H), 0.69 ppm (d, $J=6.8$ Hz, 3H); ^{19}F NMR ($CDCl_3$, 376.7 MHz): $\delta=-71.83$ (s, F_3C, major, 97% by integration), −71.91 ppm (s, F_3C, minor, 3% by integration).

(*S*)-MTPA ester of (−)-2: The same procedure described above above was used, 95%. The ^{19}F NMR data proved that the two trifluoromethyl signals in both diastereomeric esters correspond to the two enantiomers of the starting alcohols, since they had the same chemical shifts. ^{19}F NMR ($CDCl_3$, 376.7 MHz): $\delta=-71.83$ (s, F_3C, minor); −71.91 ppm (s, F_3C, major).

Aldol product (+)-34a: NEt_3 (2.5 mL, 20.02 mmol, 2.5 equiv) followed by TMSOTf (1.74 mL, 9.61 mmol, 1.2 equiv) was added to a solution of (−)-**22a** (3.0 g, 8.01 mmol, 1 equiv) in CH_2Cl_2 (45 mL) at −20 °C. The reaction mixture was allowed to reach +20 °C in 2 h. Cold pentane (300 mL; −50 °C) was added, and the resulting suspension was filtered through a small pad of silica gel (suspended in pentane containing 2% of NEt_3). The organic phase was sequentially washed with a 15% aqueous solution of citric acid (3×70 mL), saturated aqueous solution of $NaHCO_3$ (3×50 mL), and brine (2×50 mL), dried (anhydrous Na_2SO_4), and evaporated in vacuo. The resulting oil (**33**) was dried under reduced pressure (0.06 Torr, 24 h). Yield 3.77 g (quant. with ca. 95% purity).

*Data for **33***: Colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.31$–7.24 (m, 5H; arom), 5.22 (q, $J=7.0$ Hz, 1H; H-C(1′)), 4.50 (q, $J=6.4$ Hz, 1H; H-C(1″)), 4.39 (q, $J=6.4$ Hz, 1H; H-C(6)), 3.67 (dd, $J=7.0$, 3.8 Hz, 1H; H-C(3)), 2.72 (sept., $J=7.0$ Hz, 1H; $(CH_3)_2CHCOO$-C(1)), 2.56 (quint, $J=7.0$ Hz, 1H; H-C(2)), 2.17 (dq, $J=7.0$, 5.8 Hz, 1H; H-C(4)), 1.48 (d, $J=6.4$ Hz, 3H; H-C(2″)), 1.35 (dd, $J=7.0$, 1.3 Hz, 3H; H-C(2′)), 1.34 (d, $J=6.4$ Hz, 3H; H-C(7)), 1.30, 1.29 (2d, $J=6.8$ Hz, 6H; $(CH_3)_2$CHCOO-C(1)), 1.07 (d, $J=7.0$ Hz, 3H; CH_3-C(2)), 0.90 (d, $J=6.4$ Hz, 3H; CH_3-C(4)), 0.12 ppm (s, 9H; TMSO-C(5)); HRMS (MALDI-TOF): m/z calcd for $C_{26}H_{42}O_5SiNa^+$: 469.2750; found: 469.2761.

2,6-Di-*tert*-butylpyridine (0.253 mL, 1.13 mmol, 0.2 equiv), followed by solution of 9-BBN-Br in CH_2Cl_2 (1 M, 5.63 mL, 5.63 mmol, 1.0 equiv) were added to a solution of enoxysilane **33** (2.65 g, (95% purity), 5.63 mmol, 1.0 equiv) in CH_2Cl_2 (60 mL) under an argon atmosphere at room temperature. The resulting mixture was stirred for 2 h at room temperature, before being cooled to −78 °C. A solution of the aldehyde (+)-**3b** (2.15 g, (90% purity), 9.58 mmol, 1.7 equiv) in CH_2Cl_2 (7 mL) was added at −78 °C. After 8 h at −78 °C, the reaction mixture was quenched by the addition of 1:1 mixture of MeOH/saturated aqueous solution $NaHCO_3$ (100 mL). The resulting mixture was extracted with CH_2Cl_2 (4×30 mL), EtOAc (2×30 mL). Each organic layer was washed seperately with brine, then combined and evaporated. The residue was dissolved in MeOH (50 mL), and aqueous 30% H_2O_2 (25 mL) was added at 0 °C. The mixture was allowed to reach room temperature and was stirred for 5 h. A saturated aqueous solution of $Na_2S_2O_3$ (200 mL) was added at 0 °C. The mixture was extracted with EtOAc (4×30 mL). The combined organic layers were washed with saturated aqueous solution of NaCl, dried (Na_2SO_4), filtered, and evaporated. The resulting oil was purified by FC (CH_2Cl_2/EtOAc 99.5:1.5): 2.24 g (75%) of (+)-**34a** and 0.19 g (6%) of **34b**.

*Data for (+)-**34a***: Colorless oil; $R_f=0.25$ (CH_2Cl_2/EtOAc 98:2); $[\alpha]_D^{25}=+7$, ($c=0.55$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.33$–7.23 (m, 5H; arom), 5.24 (q, $J=7.0$ Hz, 1H; H-C(1′)), 4.49 (q, $J=6.4$ Hz, 1H; H-C(1″)), 3.75 (t, $J=4.6$ Hz, 1H; H-C(3)), 3.72 (dd, $J=9.6$, 4.8 Hz, 1H; Ha-C(9)), 3.61 (br s, 1H; HO-C(7)), 3.60 (dd, $J=9.6$, 5.8 Hz, 1H; Hb-C(9)), 3.47 (dt, $J=9.6$, 1.9 Hz, 1H; H-C(7)), 2.94 (dq, $J=7.0$, 4.5 Hz, 1H; H-C(4)), 2.72 (dq, $J=7.0$, 5.0 Hz, 1H; H-C(2)), 2.65–2.58 (m, 2H; H-C(6), $(CH_3)_2CHCOO$-C(1)), 1.62 (dquint, $J=9.6$, 5.6 Hz, 1H; H-C(8)), 1.47 (d, $J=7.0$ Hz, 3H; H-C(2′)), 1.39 (d, $J=6.4$ Hz, 3H; H-C(2″)), 1.23, 1.22 (2d, $J=7.0$ Hz, 6H; $(CH_3)_2$CHCOO-C(1)), 1.14 (d, $J=7.0$ Hz, 3H; CH_3-C(2)), 1.02 (d, $J=7.0$ Hz, 3H; CH_3-C(4)), 1.00 (d, $J=7.0$ Hz, 3H; CH_3-C(6)), 0.90 (s, 9H; TBSO-C(9)), 0.74 (d, $J=7.0$ Hz, 3H; CH_3-C(8)), 0.07, 0.06 ppm (2 s, 6H; TBSO-C(9)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=217.4$, 174.6, 149.8, 143.7, 128.4, 127.6, 126.7, 112.5, 76.7, 76.2, 72.8, 66.5, 45.8, 45.7, 41.4, 37.6, 34.2, 26.0, 23.7, 19.3, 19.1, 18.4, 13.5, 13.2, 12.8, 11.0, 8.9, −5.3, −5.4 ppm; IR (film): $\tilde{\nu}=3520$, 2970, 2930, 2890, 2860, 1750, 1700, 1490, 1470, 1390, 1250, 1135, 1085 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{33}H_{56}O_6SiNa^+$: 599.3744; found: 599.3754; elemental analysis calcd (%) for $C_{33}H_{56}O_6Si$ (576.88): C 68.71, H 9.78; found: C 68.60, H 9.79.

*Data for **34b***: ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.31$–7.21 (m, 5H; arom), 5.28 (q, $J=7.0$ Hz, 1H; H-C(1′)), 4.53 (q, $J=6.4$ Hz, 1H; H-C(1″)), 3.96–3.94 (m, 2H; H-C(9)), 3.67 (t, $J=5.0$ Hz, 1H; H-C(3)), 2.89 (dq, $J=7.0$, 3.8 Hz, 1H; H-C(4)), 2.84 (d, $J=3.2$ Hz, 1H; H-C(7)), 2.79 (dq, $J=9.6$, 7.0 Hz, 1H; H-C(2)), 2.71–2.61 (m, 2H; H-C(6)), $(CH_3)_2CHCOO$-C(1)), 1.70–1.65 (m, 1H; H-C(8)), 1.47 (d, $J=6.4$ Hz, 3H; H-C(2′)), 1.37 (d, $J=6.4$ Hz, 3H; H-C(2″)), 1.24, 1.23 (2d, $J=7.0$ Hz, 6H; $(CH_3)_2$CHCOO-C(1)), 1.14 (d, $J=7.0$ Hz, 3H; CH_3-C(2)), 1.03 (d, $J=7.0$ Hz, 3H; CH_3-C(4)), 0.89 (s, 9H; TBSO-C(9)), 0.88 (d, $J=6.8$ Hz, 3H; CH_3-C(6)), 0.84 (d, $J=7.0$ Hz, 3H; CH_3-C(8)), 0.06 ppm (s, 6H; TBSO-C(9)); HRMS (MALDI-TOF): m/z calcd for $C_{33}H_{56}O_6SiNa^+$: 599.3744; found: 599.3761.

Acetonide (−)-36: Anhydrous AcOH (10 mL) was added to a solution of $Me_4NBH(OAc)_3$ (8.80 g, 33.3 mmol, 15 equiv) in CH_3CN (5.0 mL) at 0 °C. After 10 min, a solution of (+)-**34a** (1.28 g, 2.22 mmol, 1 equiv) in CH_3CN (2.5 mL) was added dropwise. The resulting mixture was stirred at −0 °C for 36 h. The reaction was quenched by an aqueous solution of potassium sodium tartrate (0.5 N, 100 mL) and extracted with EtOAc (4×30 mL). The combined organic layers were washed with aqueous saturated solutions of $NaHCO_3$ and brine, dried (Na_2SO_4), filtered, and evaporated in vacuo. The resulting diol (−)-**35** (1.25 g) was employed directly in next the step. An analytical sample was obtained by FC of an aliquot. (In another trial the yield of isolated (−)-**35** was 83%) Colorless oil; $R_f=0.32$ (DCM/EtOAc 96:4); $[\alpha]_D^{25}=-15$, ($c=0.25$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.37$–7.28 (m, 5H; arom), 5.30 (q, $J=6.9$ Hz, 1H; H-C(1′)), 4.54 (q, $J=6.5$ Hz, 1H; H-C(1″)), 4.00 (br s, 1H; HO-C(5)), 3.87 (dd, $J=8.3$, 1.0 Hz, 1H; H-C(3)), 3.69 (d, $J=9.4$ Hz, 1H; H-C(5)), 3.64 (d, $J=5.9$ Hz, 2H; H-C(9)), 2.94 (ddd, $J=6.5$, 3.3, 2.6 Hz, 1H; H-C(7)), 2.73 (sept, $J=6.9$ Hz, 1H; $(CH_3)_2CHCOO$-C(1)), 2.62 (quint, $J=7.5$ Hz, 1H; H-C(2)), 2.55 (d, $J=7.1$ Hz, 1H; HO-C(7)), 1.74 (dq, $J=7.9$, 6.3 Hz, 1H; H-C(4)), 1.73–1.67 (m, 1H; H-C(8)), 1,55 (dm, $J=6.9$ Hz, 1H; H-C(6)), 1.50 (d, $J=6.9$ Hz, 3H; H-C(2′)), 1.40 (d, $J=6.5$ Hz, 3H; H-C(2″)), 1.29 (d, $J=6.9$ Hz, 6H; $(CH_3)_2$CHCOO-C(1)), 1.01 (d, $J=7.1$ Hz, 3H; CH_3-C(2)), 0.88 (s, 9H; TBSO-C(9)), 0.81 (d, $J=6.9$ Hz, 3H; CH_3-C(6)), 0.75 (d, $J=6.9$ Hz, 3H; CH_3-C(4)), 0.69 (d, $J=6.9$ Hz, 3H; CH_3-C(8)), 0.06 ppm (s, 6H; TBSO-C(9)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): $\delta=174.6$, 150.4, 144.7, 128.3, 127.6, 126.9, 111.9, 78.0 (2 signals), 77.8, 74.6, 68.1, 42.2, 37.9, 37.5, 34.4, 33.8, 25.9, 23.5, 19.3, 18.2, 14.6, 12.9, 11.0, 10.7, 10.5, −5.4, −5.5 ppm; IR (film): $\tilde{\nu}=3455$, 2930, 2860, 1755, 1695, 1455, 1385, 1255, 1075 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{33}H_{58}O_6SiNa^+$: 601.3900; found: 601.3918; elemental analysis calcd (%) for $C_{33}H_{58}O_6Si$ (578.90): C 68.47, H 10.10; found: C 68.84, H 10.33.

*p*TsOH·H_2O (21 mg, 0.11 mmol, 0.05 equiv) was added to a solution of the crude diol (−)-**35** (1.25 g) in dimethoxypropane (20 mL) at room temperature. The reaction mixture was stirred for 2 h at room temperature, neutralized with solid $NaHCO_3$, filtered, and evaporated. The residue was purified by FC (PE/EtOAc 20:1). Yield 1.09 g 79% of (−)-**36** (over 2 steps). Colorless oil; R_f=0.8(PE/EtOAc 9:1); $[\alpha]_D^{25}=-11$, (c= 0.34 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.33–7.29, 7.24–7.19 (2 m, 5H; arom), 5.22 (q, J=7.0 Hz, 1H; H-C(2)), 4.54 (d, J=6.4 Hz, 1H; H-C(2′)), 3.72 (dd, J=5.8, 1.3 Hz, 1H; H-C(5)), 3.56 (d, J=3.8 Hz, 2H; H-C(11)), 3.51 (dd, J=10.9, 3.8 Hz, 1H; H-C(9)), 2.82 (t, J=7.0 Hz, 1H; H-C(7)), 2.65 (sept, J=7.0 Hz, 1H; $(CH_3)_2CHCOO$-C(1)), 2.62 (dq, J=7.0, 6.4 Hz, 1H; H-C(4)), 1.68 (dq, J=7.0, 6.4 Hz, 1H; H-C(6)), 1.63–1.56 (m, 2H; H-C(8), H-C(10)), 1.17 (d, J=6.4 Hz, 3H; H-C(1)), 1.34 (d, J=6.4 Hz, 3H; H-C(2′)), 1.27, 1.26 (2d, J=7.0 Hz, 6H; $(CH_3)_2$CHCOO-C(1)), 1.18 (s, 3H; CH_3-($C_{acetonide}$)), 1.04 (d, J=7.0 Hz, 3H; CH_3-C(4)), 0.93 (s+d, J=7.0, 6H; CH_3-($C_{acetonide}$), CH_3-(C6)), 0.89 (s, 9H; TBSO-C(11)), 0.83 (d, J=7.0 Hz, 3H; CH_3-C(10)), 0.70 (d, J=7.0 Hz, 3H; CH_3-C(8)), 0.02, 0.01 ppm (2s, 6H; TBSO-C(11)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ=174.7, 150.5, 145.5, 128.2, 127.1, 126.4, 111.6, 100.1, 76.7 (3 signals), 69.4, 64.4, 42.5, 38.7, 35.5, 35.3, 34.4, 26.0, 25.6, 24.5, 23.6, 19.3, 19.2, 18.4, 13.1, 12.9, 12.5, 10.9, 10.8, −5.4, −5.5 ppm; IR (film): $\tilde{\nu}$= 2970, 2930, 2855, 1750, 1695, 1470, 1375, 1250, 1220, 1135, 1085 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{36}H_{62}O_6SiNa^+$: 641.4213; found: 641.4239; elemental analysis calcd (%) for $C_{36}H_{62}O_6Si$ (618.96): C 69.86, H 10.10; found: C 69.86, H 10.04.

Stereoheptad (−)-37: Ozone was bubbled through a solution of (−)-**36** (0.19 g, 0.31 mmol, 1 equiv) in anhydrous Et_2O (50 mL) at 78°C until it turned blue. Then O_2 was passed through it until the disappearance of the color. The resulting mixture was quenched by BH_3·Me_2S (0.23 mL, 2.45 mmol, 8 equiv) at −78°C. The solution was stirred for 12 h at −78°C. The mixture diluted by additional Et_2O (100 mL), washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated. The residue was redissolved in anhydrous Et_2O (50 mL), after which $LiAlH_4$ (35 mg, 0.92 mmol, 3 equiv) was added at −15°C. The resulting reaction mixture was left to reach room temperature and then heated under reflux for 30 min. It was carefully quenched by a saturated aqueous solution of NH_4Cl (20 mL), the layers were separated, and the aqueous phase was additionally extracted with diethyl ether (3×20 mL). The combined organic layers were washed with brine (2×10 mL), dried (Na_2SO_4), and evaporated. FC gave **37** (0.122 g, 76%). Colorless oil; R_f=0.28 (CH_2Cl_2/EtOAc 97:3); $[\alpha]_D^{25}=-25$, (c=0.55 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.34–7.29, 7.26–7.21 (2 m, 5H; arom), 4.53 (q, J=6.8 Hz, 1H; H-C(1′)), 3.64 (d, J=5.5 Hz, 1H; H-C(3)), 3.62–3.50 (m, 5H; H-C(9), H-C(7), H-C(1)), 3.28 (br d, J=6.2 Hz, 1H; HO-C(1)), 2.74 (dd, J= 9.7, 6.8 Hz, 1H; H-C(5)), 2.12 (ddt, J=9.1, 7.0, 5.2 Hz, 1H; H-C(2)), 1.69 (dq, J=8.6, 7.4 Hz, 1H; H-C(4)), 1.67–1.55 (m, 2H; H-C(8), H-C(6)), 1.43 (d, J=6.2 Hz, 3H; H-C(2′)), 1.17 (s, 3H; CH_3-($C_{acetonide}$)), 0.96 (d, J=6.8 Hz, 3H; CH_3-C(4)), 0.89 (d, J=6.8 Hz, 3H; CH_3-C(2)), 0.88 (s, 9H; TBSO-C(9)), 0.84 (s, 3H; CH_3-($C_{acetonide}$)), 0.83, 0.77 (2d, J=6.8 Hz, 6H; CH_3-C(8), CH_3-C(6)), 0.01, 0.00 ppm (2s, 6H; TBSO-C(9)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ=145.0, 128.4, 127.5, 126.5, 100.6, 78.5, 77.9, 76.6, 69.5, 66.2, 64.3, 39.1, 38.4, 36.4, 35.2, 26.0, 25.4, 24.1, 23.4, 18.4, 12.8, 12.7, 12.3, 10.8, −5.4, −5.5 ppm; IR (film): $\tilde{\nu}$=3490, 2960, 2930, 2855, 1600, 1470, 1380, 1250, 1220, 1085, 1030 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{30}H_{54}O_5SiNa^+$: 545.3638; found: 545.3631; elemental analysis calcd (%) for $C_{30}H_{54}O_5Si$ (522.83): C 68.92, H 10.41; found: C 68.92, H 10.50.

(*R*)-MTPA ester of (−)-37: See the general procedure for preparing MTPA esters of (−)-**2**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.58–7.56 (m, 2H; arom), 7.43–7.41 (m, 3H; arom), 7.31–7.21 (m, 5H; arom), 4.47 (dd, J=10.5, 4.1 Hz, Ha-C(1)), 4.43 (q, J=6.8 Hz, H-C(1′)), 4.40 (dd, J=10.5, 6.2 Hz, Hb-C(1)), 3.70–3.68, 3.62–3.50 (2 m, 4H; H-C(3), H-C(7), H-C(9)), 2.77 (dd, J=9.9, 6.2 Hz, 1H; H-C(5)), 2.06 (m, 1H; H-C(2)), 1.64 (quint, J=7.4 Hz, 1H; H-C(4)), 1.61–1.52 (m, 2H; H-C(8), H-C(6)), 1.31 (d, J=6.8 Hz, 3H; H-C(2′)), 1.18 (s, 3H; CH_3-($C_{acetonide}$)), 0.99 (s, 3H; CH_3-($C_{acetonide}$)), 0.97 (d, J=7.4 Hz, 3H; CH_3-C(4)), 0.88 (s, 9H; TBSO-C(9)), 0.86 (d, J=6.8 Hz, 3H; CH_3-C(2)), 0.82, 0.77 (2d, J=6.8 Hz, 6H; CH_3-C(8), CH_3-C(6)), 0.02, 0.01 ppm (2s, 6H; TBSO-C(9)); ^{19}F NMR ($CDCl_3$, 396 MHz): δ=−71.87 ppm; HRMS (MALDI-TOF): m/z calcd for $C_{40}H_{61}F_3O_7SiNa^+$: 761.4036; found: 761.4046.

(*S*)-MTPA ester of (−)-37: ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.58–7.56 (m, 2H; arom), 7.43–7.41 (m, 3H; arom), 7.30–7.28 (m, 4H; arom), 7.25–7.21 (m, 51H; arom), 4.60 (dd, J=10.1, 4.3 Hz, Ha-C(1)), 4.51 (q, J= 6.8 Hz, H-C(1′)), 4.30 (dd, J=11.1, 6.5 Hz, Hb-C(1)), 3.70–3.68, 3.61–3.49 (2 m, 4H; H-C(3), H-C(7), H-C(9)), 2.80 (dd, J=9.2, 6.2 Hz, 1H; H-C(5)), 2.07 (dq, J=7.7, 6.8 Hz, 1H; H-C(2)), 1.66 (quint, J=7.4 Hz, 1H; H-C(4)), 1.63–1.53 (m, 2H; H-C(8), H-C(6)), 1.36 (d, J=6.2 Hz, 3H; H-C(2′)), 1.18 (s, 3H; CH_3-($C_{acetonide}$)), 1.00 (s, 3H; CH_3-($C_{acetonide}$)), 0.98 (d, J=6.8 Hz, 3H; CH_3-C(4)), 0.89 (s, 9H; TBSO-C(9)), 0.87 (d, J=6.8 Hz, 3H; CH_3-C(2)), 0.82, 0.70 (2d, J=6.8 Hz, 6H; CH_3-C(8), CH_3-C(6)), 0.03, 0.02 ppm (2s, 6H; TBSO-C(9)); ^{19}F NMR ($CDCl_3$, 396 MHz): δ= −71.87 ppm; HRMS (MALDI-TOF): m/z calcd for $C_{40}H_{61}F_3O_7SiNa^+$: 761.4036; found: 761.4033. The *ee* was determined by comparing integral of the dd signal of the (*S*)-ester at 4.60 ppm (1H) with the total integral from signals 4.47, 4.43, 4.40 ppm (3H) in the (*R*)-ester. A signal at 4.60 ppm was not observed at all in the spectrum of the (*R*)-ester. Conclusion: *ee*≧99%.

Diacetonide (+)-38: A solution of diol (−)-**35** (0.41 g, 0.71 mmol) in AcOH (15 mL) was diluted with water (8 mL) and heated at +65°C for 3 h. The solvent was evaporated in vacuo, and the residue redissolved in MeOH (30 mL). $Pd(OH)_2$ (10% on activated charcol, 0.20 g) was added and the resulting suspension was stirred at room temperature under H_2 atmosphere (1 bar) for 1 h. The solution was saturated with N_2, filtered through Celite, and evaporated in vacuo. The resulting tetrol was dissolved in CH_2Cl_2 (10 mL) and cooled to 5°C. Dimethoxypropane (5 mL) was added, followed by *p*TsOH·H_2O (7 mg, 0.037 mmol, ~5 mol% of (+)-**35**)). After 2 h at 0°C the reaction mixture was quenched by a saturated aqueous solution of $NaHCO_3$ (15 mL) and extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), and evaporated in vacuo. The residue was purified by FC (hexane/EtOAc 9:1). Yield: 0.234 g, 75%, over three steps. Colorless oil; R_f=0.58 (hexane/EtOAc 8:2); $[\alpha]_D^{25}=+10.5$ (c=0.2 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ=5.16 (q, J=7.0 Hz, 1H; H-C(1′)), 3.86 (dd, J=10.5, 2.2 Hz, 1H; H-C(7)), 3.70 (dd, J=11.4, 4.9 Hz, 1H; Ha-C(9)), 3.66 (dd, J=10.5, 3.7 Hz, 1H; H-C(3)), 3.52 (t, J= 11.4 Hz, 1H; Hb-C(9)), 3.27 (dd, J=9.6, 6.5 Hz, 1H; H-C(5)), 2.71 (sept, J=7.0 Hz, 1H; $(CH_3)_2CHCOO$-C(1)), 2.34 (dq, J=10.8, 7.0 Hz, 1H; H-C(2)), 1.85 (ddt, J=11.1, 7.1, 4.9 Hz, 1H; H-C(8)), 1.79–1.68 (m, 2H; H-C(6), H-C(4)), 1.43 (d, J=6.8 Hz, 3H; H-C(2′)), 1.39, 1.35, (2s, 6H; CH_3-($C_{acetonide\ 7,9}$)), 1.28 (s, 6H; CH_3-($C_{acetonide\ 3,5}$)), 1.27, 1.26 (2d, J= 7.1 Hz, 6H; $(CH_3)_2$CHCOO-C(1)), 0.92 (d, J=7.1 Hz, 3H; CH_3-C(2)), 0.89, 0.87 (2d, J=6.8, 7.1 Hz, 6H; CH_3-C(4), CH_3-C(6)), 0.71 ppm (d, J= 6.8 Hz, 3H; CH_3-C(8)); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ=174.5, 149.7, 111.1, 100.6, 98.1, 74.3, 72.9, 70.5, 66.7, 39.6, 39.3, 36.4, 34.3, 30.5, 29.9, 25.7, 23.6, 19.4, 19.3, 19.1, 14.2, 12.7, 12.2, 11.0, 7.9 ppm; IR (film): $\tilde{\nu}$= 2970, 2925, 2855, 1755, 1695, 1465, 1455, 1385, 1230, 1180, 1145 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{25}H_{44}O_6Na^+$: 463.3036; found: 463.3031; elemetal analysis calcd (%) for $C_{25}H_{44}O_6$ (440.61): C 68.15, H 10.07; found: C 68.22 , H 9.98.

(2*S*)-2-((1′*S*,3′*S*,4′*S*,5′*S*,6′*S*)-1-Ethyl-4′,6′,8′-trimethyl-2′,9′dioxabicyclo-[3.3.1]non-7′-en-3′-yl)propyl 3,5-dinitrobenzoate (40): A solution of diol (−)-**35** (0.14 g, 0.24 mmol, 1 equiv) in Et_2O (5 mL) was added dropwise at −78°C to a solution of MeLi·LiBr (2M, 0.80 mL, 1.6 mmol, 6.6 equiv) in Et_2O (5 mL). After 4 h at −78°C the reaction mixture was carefully poured at room temperature into a saturated aqueous solution of NH_4Cl (20 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (5×20 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), and evaporated. The residue was dissolved in 90% aqueous acetic acid (10 mL) and heated at 65°C overnight. The solvent was evaporated, and traces of acetic acid were eliminated by azeotropic evaporation with toluene (2×10 mL) and pyridine (10 mL). The resulting oil was dissolved in pyridine (10 mL), and 3,5-dinitrobenzoyl chloride (0.28 g, 1.21 mmol, 5 equiv) was added at 15°C. The reaction mixture was stirred for 3 h at room temperature. It was diluted by Et_2O (100 mL), washed successively with a saturated aqueous solution of $CuSO_4$ (4×20 mL), water (1×20 mL), and saturated aqueous

$NaHCO_3$ (2×20 mL), dried over anhydrous Na_2SO_4, filtered, and evaporated. The residue was purified by FC. Yield 55 mg, 51%; colorless oil; R_f=0.71(PE/EtOAc 8:2); ^{1}H NMR (C_6H_6, 400 MHz): δ=8.70 (d, J= 2.0 Hz, 2H; H-C(2_{Ar})), 8.44 (t, J=2.0 Hz, 1H; H-C(4_{Ar})), 5.79 (dm, J= 4.7 Hz, 1H; H-C(7′)), 4.53 (dd, J=10.8, 2.7 Hz, 1H; Ha-C(1)), 4.35 (dd, J=10.8, 5.4 Hz, 1H; Hb-C(1)), 3.91 (dd, J=10.7, 2.7 Hz, 1H; H-C(3′)), 3.52 (s, 1H; H-C(5′)), 1.94 (m, 1H; H-C(2)), 1.89 (dd, J=13.5, 7.0 Hz, 1H; Ha-(CH_3CH_2-C(1′))), 1.74 (dd, J=13.5, 7.0 Hz, 1H; Hb-(CH_3CH_2-C(1′))),1.65 (dq, J=7.0, 4.7 Hz, 1H; H-C(6′)), 1.54 (d, J=1.4 Hz, 3H; CH_3-C(8′)), 1.12 (t, J=7.0 Hz, 3H; H-(CH_3CH_2-C(1′))), 1.09 (d, J= 7.0 Hz, 3H; CH_3-C(4′)), 1.04 (d, J=7.0 Hz, 3H; CH_3-C(6′)), 1.03 (m, 1H; H-C(4′)), 0.69 ppm (d, J=6.7 Hz, 3H; CH_3-C(3)); ^{13}C NMR (C_6H_6, 100.6 MHz): δ=162.4, 148.3, 133.5, 130.9, 130.5, 128.5, 121.9, 97.7, 79.7, 69.8, 68.2, 35.0, 34.8, 34.4, 30.1, 20.7, 18.2, 12.6, 12.2, 7.2 ppm; IR (film): $\tilde{\nu}$=3100, 2965, 2880, 1730, 1630, 1550, 1455, 1345, 1280, 1175, 1175, 1095 cm^{-1}; HRMS (MALDI-TOF): m/z calcd for $C_{22}H_{28}N_2O_8Na^+$: 471.1743; found: 471.1761; elemetal analysis calcd (%) for $C_{22}H_{28}N_2O_8$ (448.47): C 58.92, H 6.29; found: C 58.68, H 6.36.

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