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Total Synthesis

Enantioselective Approach to the Right-Hand Substructure of Solanoeclepin A

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Abstract: An enantioselective synthesis of the right-hand substructure of solanoeclepin A has been developed. The key step was an intramolecular [2+2] photocycloaddition between an allene and a butenolide providing a methylenecyclobutane with three quaternary carbon atoms in a complex tetracyclic framework. Other crucial steps included an enantioselective Noyori transfer hydrogenation of a ketone, a diastereoselective silver-mediated silyl dienolate allylation, and a diastereoselective cyclopropanation of an allylic alcohol. The installation of the bridgehead methyl group by reduction of the lactone moiety proved to be troublesome.

Introduction

Solanoeclepin A (**1**) is the hatching agent of potato cyst nematodes, little roundworms posing a serious threat to potato harvests in many countries.[1] The structure of this complex terpenoid was elucidated some 25 years ago by Schenk et al. through X-ray crystallography (Figure 1).[2]

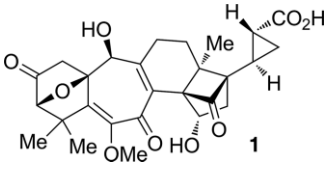
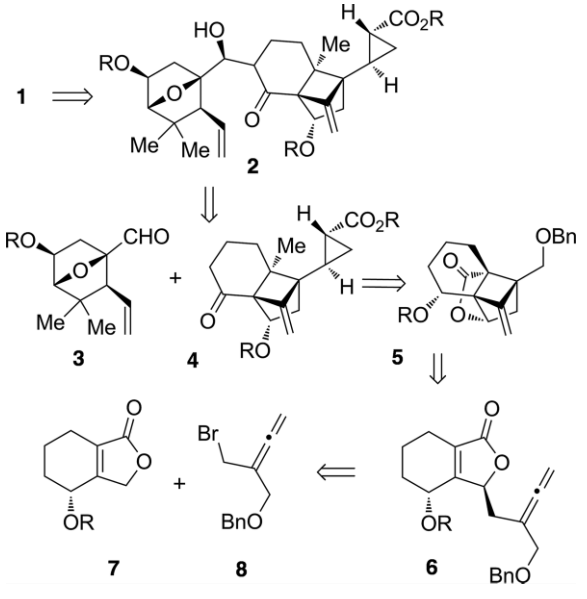


Figure 1. Structure of solanoeclepin A (**1**).

Synthetic studies towards **1** and its synthetic analogues could potentially lead to environmentally benign ways to combat the nematode. Our group[3] and others[4] have reported considerable synthetic progress in this direction. In 2011, the first total synthesis of solanoeclepin A was reported by Tanino et al.[5] Very recently, we completed a formal synthesis of this complex natural product by synthesizing an advanced intermediate in the Tanino synthesis.[6] This work featured an enantioselective approach to the intricate right-hand substructure based on an intramolecular [2+2] photocycloaddition between the double bonds of a vinylboronate and a 3-methyl-2-cyclohexenone.[7]

In this article we report earlier synthetic work from our group toward the right-hand substructure through an intramolecular [2+2] photocycloaddition between an allene and a chiral butenolide.[3h,3i] This work has produced the required carbon skeleton in enantiopure form as will be detailed herein.[8]

Our retrosynthetic analysis of solanoeclepin A (Scheme 1) envisaged the seven-membered ring as the last ring to be formed by ring-closing metathesis (RCM).[3g] The RCM precursor should be available from **2**, which is the aldol product of aldehyde **3** and ketone **4**. The intended coupling of the two fragments through aldol chemistry is a major change from our earlier strategy involving a Nozaki–Hiyama–Kishi coupling reaction. This latter approach appeared problematic in sterically encumbered structures and on a larger scale.[9]



Scheme 1. Retrosynthetic analysis of our approach.

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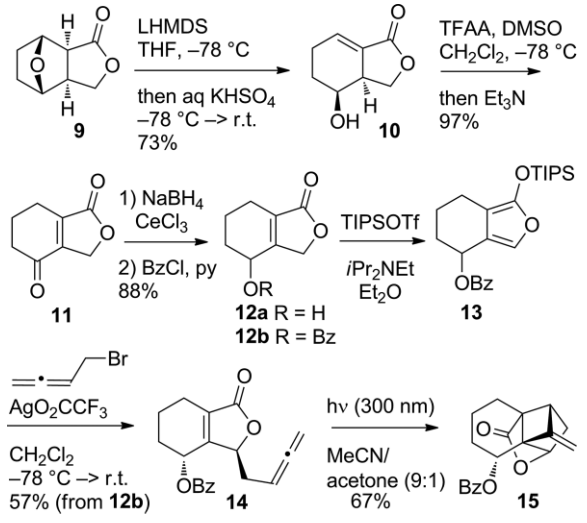
Ketone **4** was expected to arise from **5** by reductive opening of the lactone and introduction of the cyclopropanecarboxylic acid in the correct stereochemical sense. Lactone **5** should be the product of the intramolecular [2+2] photocycloaddition of **6** as the key step. Allene **6** was anticipated to arise from diastereoselective coupling of optically active **7** and allene **8**.

Results and Discussion

Our synthetic endeavor started from the unsaturated lactone **10** (see Scheme 2), which was reported before by Chung et al. to arise from base-induced ring-opening of tricyclic **9**.[10] The latter is available on a large scale starting with the Diels–Alder reaction of furan with maleic anhydride and subsequent reduction. We scaled up the synthesis of **10** from **9** and obtained it as a crystalline solid (m.p. 115 °C, 73 %) directly from the crude reaction mixture without the need of chromatography. The only side-product, obtained in around 10 % yield (based on ^{1}H NMR analysis), was the isomeric β,γ-unsaturated lactone, which could be removed by recrystallization.

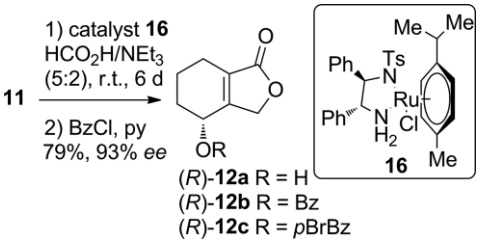


Scheme 2. Synthesis of racemic tetracycle **15**.

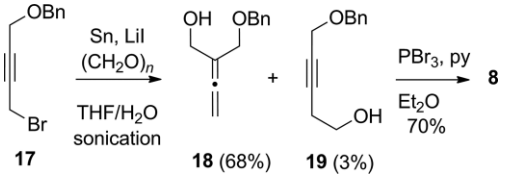
To shift the double bond to obtain the required butenolide, the hydroxy function of **10** was first oxidized to the corresponding ketone. This oxidation proceeded best by using the original Swern protocol with trifluoroacetic anhydride and DMSO.[11] This methodology directly led to conjugated keto lactone **11** (m.p. 57 °C) in excellent yield. Other oxidation protocols (PCC, IBX, Dess–Martin periodinane, TPAP/NMO, Parikh–Doering oxidation) gave intractable mixtures containing aromatization products due to overoxidation.

The ketone now offered the opportunity to introduce chirality by enantioselective reduction. However, we first investigated the following reactions in the racemic series. Luche reduction of **11** gave the racemic alcohol **12a**,[12] which was converted into benzoate **12b**. Conversion of **12b** into the silyloxyfuran **13** was followed by a silver trifluoroacetate mediated coupling reaction[13] with 4-bromobuta-1,2-diene.[14] This method ensured regioselective alkylation at the dienolate γ position[15] but led to a mixture of diastereomers from which the major isomer (for steric reasons presumably **14**) could be isolated by chromatography in 57 % yield from **12b**. The key photochemical [2+2] cycloaddition was carried out in a 9:1 mixture of acetonitrile/acetone at 300 nm in a Rayonet photoreactor. The reaction was complete in 30 min and gave a crystalline product (m.p. 82 °C). X-ray diffraction analysis proved the identity of **15** and therefore also the *trans* stereochemistry of precursor **14**. Thus, in six steps from known **10** we had constructed as a racemate the functionalized skeleton of the right-hand substructure of **1** except for (a handle to connect) the cyclopropane moiety.

Our next objective was to elaborate a pathway that leads to the correct absolute stereochemistry and also includes a functionality to introduce the cyclopropane ring. The first goal required enantioselective reduction of ketone **11**. After several unsatisfactory attempts at Corey–Bakshi–Shibata (CBS) reduction,[16] the best result was obtained by applying the Ru-catalyzed transfer hydrogenation developed by Noyori and co-workers (see Scheme 3).[17] This procedure led to the desired benzoate (+)-**12b** in 93 % *ee*. The absolute configuration of the product was proven by X-ray diffraction analysis of the *p*-bromobenzoate analogue **12c** (see the Supporting Information). The second goal was reached by using allene **8** as a building block. Although **8** had been prepared earlier by our group,[3i] we developed in this work a more convenient route starting from the known propargyl bromide **17** (Scheme 4).[18] Hydroxymethylation of **17** by treatment with tin powder and paraformaldehyde in the presence of lithium iodide gave allene **18** and a small amount of alkyne **19**, which were easily separable.[18,19] From **18**, the desired allenyl bromide **8** was obtained in 70 % through the action of phosphorus tribromide.



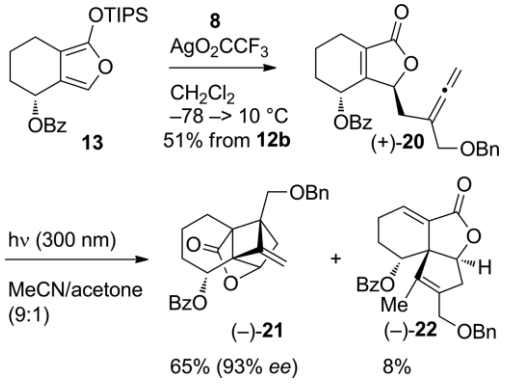
Scheme 3. Enantioselective reduction of ketone **11**.



Scheme 4. Synthesis of allene **8**.

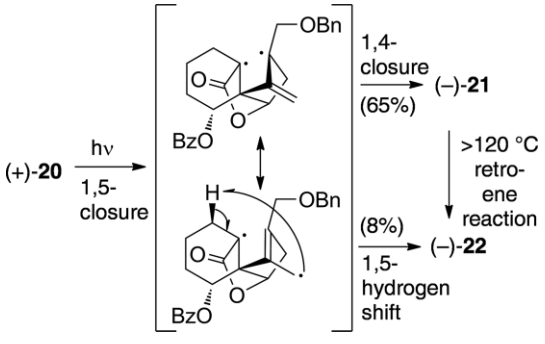
The stage was now set for the preparation of optically active **5**. Thus, butenolide (+)-**12b** (93 % *ee*; see Scheme 5) was converted into the optically active silyloxyfuran **13** as described for the racemate. Silver-mediated coupling of **13** with **8** furnished an approximate 70:30 diastereomeric mixture of products from

which the photolysis precursor (+)-**20** was isolated in 51 % yield from **12b** (Scheme 5) The diastereomeric ratio was somewhat disappointing and could perhaps be improved by choosing a bulkier hydroxy protective group. However, at this point in time the ensuing photochemical reaction was more interesting.



Scheme 5. Synthesis and photocycloaddition of (+)-**20**.

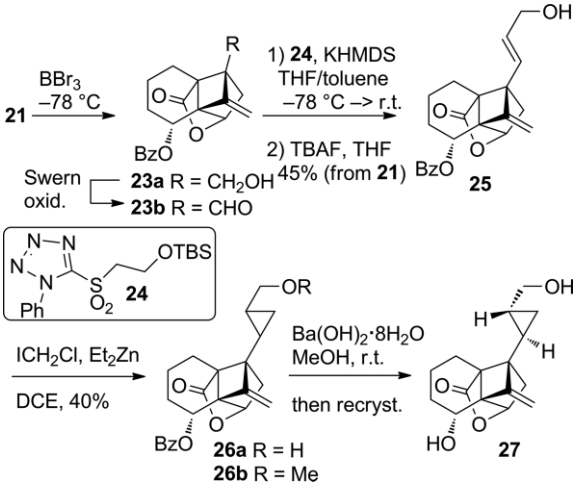
Irradiation of **20** at 300 nm for 45 min led to complete conversion of the starting material. Facile chromatographic purification led to the desired [2+2] adduct **21** as a colorless oil in 65 % yield ($[\alpha]_D^{20}$ = –19, *c* = 2.0, $CHCl_3$). This yield was remarkable in view of the compactness of the molecule with three quaternary carbon atoms in the cyclobutane ring. The major side-product (8 % yield, $[\alpha]_D^{20}$ = –117, *c* = 2.0, $CHCl_3$) was assigned structure **22** on the basis of extensive 2D NMR and NOE difference experiments. These types of products are known from separate work by our group as thermal decomposition products of [2+2] cycloadducts derived through a retro-ene mechanism.[20] However, adduct **21** appeared to be thermally stable up to 120 °C, so that **22** probably arose from a 1,5-hydrogen shift in the 1,4-biradical intermediate of the [2+2] photocycloaddition. Scheme 6 summarizes the most probable mechanisms for the formation of **21** and **22**.



Scheme 6. Mechanism for the formation of **21** and **22**.

To proceed from **21** to the key intermediate **4**, introduction of the cyclopropane moiety and reductive opening of the lactone to install the bridgehead methyl group were required. Both transformations were independently investigated to determine the best procedures and their eventual order.

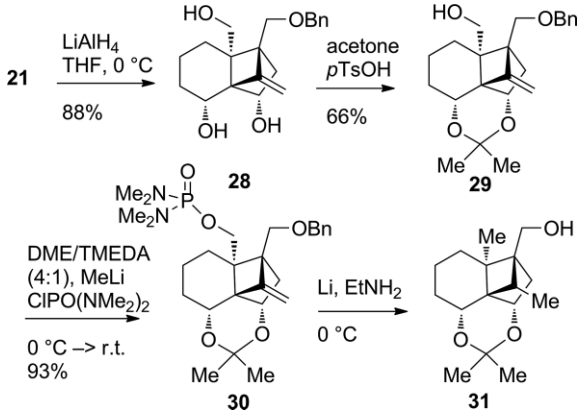
The attachment of the cyclopropane moiety started with the treatment of **21** with boron tribromide to deprotect the required hydroxy function (Scheme 7) to provide **23a**. Subsequent Swern oxidation furnished aldehyde **23b**. This aldehyde was subjected to reaction with the α-sulfonyl carbanion of **24** according to the procedure of Pospisil and Marko.[21] This Julia–Kocienski-type olefination led to pure (*E*)-allylic alcohol **25** after desilylation. The sequence of four steps from **21** to **25** furnished an overall yield of 45 %, and the lactone and benzoate were left untouched. Hydroxy-assisted cyclopropanation of **25** proceeded well with the reagent formed from diethylzinc and chloro(iodo)methane as described by Denmark and Edwards.[22] Cyclopropane **26a** was isolated as a 90:10 mixture of stereoisomers in 40 % yield. The major product (46 %) obtained was the *O*-methyl ether **26b** (60:40 ratio of diastereomers).[23] Saponification of **26a** with barium hydroxide followed by recrystallization led to crystals of the major isomer, which were suitable for X-ray diffraction analysis. The crystal structure showed that this isomer was **27** and featured all the carbon atoms and the desired stereochemistry of the right-hand substructure of the natural product.



Scheme 7. Introduction of the cyclopropane moiety.

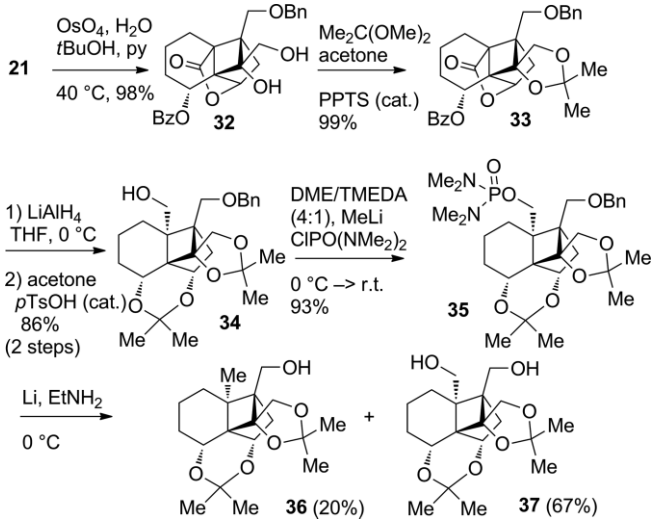
To investigate the reductive opening of the lactone and installation of the bridgehead methyl group, lactone **21** was first reduced by using $LiAlH_4$, and the resulting triol **28** was treated with acetone in the presence of a catalytic amount of acid (Scheme 8). The expected dioxolane **29** was the only product obtained in an overall yield of 58 % from **21**. The stage was now set to replace the remaining hydroxy group by hydrogen without touching the alkene or benzyl group. This appeared to be a difficult task. Oxidation of **29** to the aldehyde using Dess–Martin periodinane was facile but the following Wolff–Kishner reduction failed. Likewise, attempted removal of tosylate using lithium triethylborohydride and removal of pentafluorophenyl thionocarbonate using Bu_3SnH/AIBN were equally unsuccessful. Finally, the Ireland procedure involving reductive cleavage of an *N*,*N*,*N*′,*N*′-tetramethylphosphoramidate was more successful.[25] Thus, conversion of **29** into phosphoramidate **30** proceeded well, and the ensuing reduction using excess lithium in ethylamine furnished **31** containing the bridgehead methyl group

(yield was not determined). The concomitant removal of the benzyl group was of no concern, but the unexpected reduction of the alkene under these conditions was a serious problem. More detailed experiments indicated that the generation of the bridgehead methyl group occurred after the other two reductions. The conclusion was that the alkene had to be protected prior to generation of the bridgehead methyl group. As the final goal was the cyclobutanone, a logical option was oxidation of the exocyclic methylene group to a diol, which then should be transformed into the ketone by periodate cleavage.



Scheme 8. Attempted installation of the bridgehead methyl group.

Execution of this plan began with the osmium tetroxide oxidation of **21** to furnish diol **32** in excellent yield as a single diastereomer (see Scheme 9). Protection of the diol as an acetonide gave **33**, which was easily transformed into the desired alcohol **34** by lactone reduction and diol protection as carried out earlier (see Scheme 7). Derivatization to form the phosphordiamidate **35** proceeded well, but the reduction with lithium in ethylamine presented another difficult problem; in addition to the desired product **36**, the major product was diol **37**, which indicates an undesired cleavage of the phosphordiamidate. This type of cleavage has been described before, but it has been reported that such a side-product was formed in only a small amount by using sodium naphthalenide for the reduction.[26] However, attempts to reduce **35** with sodium naphthalenide gave mainly decomposition products and no trace of **36**.



Scheme 9. Installation of the bridgehead methyl group.

Conclusions

The entire carbon skeleton of the right-hand substructure of solanoeclepin A (**1**) has been synthesized in an efficient manner by the intramolecular [2+2] photocycloaddition of optically active allene butenolide (+)-**20** (93 % *ee*) as the key step to produce the desired tetracyclic (–)-**21** in good yield. The required cyclopropane moiety was readily installed to provide **26**. On the other hand, the transformation of the lactone into the bridgehead methyl group proved problematic. In further work we will therefore abandon the lactone approach and direct our efforts toward the application of the intramolecular [2+2] photocycloaddition with the key methyl group in place right from the beginning.[6]

Experimental Section

General: All reactions involving oxygen- or moisture-sensitive compounds were carried out under dry nitrogen. THF was distilled from sodium/benzophenone, and dichloromethane and acetonitrile were distilled from calcium hydride. The acetone used for the irradiation experiments was of spectrophotometric grade. All commercially available chemicals were used as received. NMR spectra were recorded with a Bruker ARX 400 spectrometer operating at 400 or 100 MHz for ^{1}H and ^{13}C NMR analysis. Unless otherwise stated, $CDCl_3$ was used as solvent. Chemical shifts (δ) are given in ppm and are referenced to internal solvent signals. IR spectra were recorded with a Bruker IFS 28 FT spectrometer. Mass spectra and accurate mass determinations were performed with a JEOL JMX SX/SX102A spectrometer coupled to a JEOL MS-MP7000 data system. The photoreactions were carried out in a quartz reaction vessel with a Rayonet RPR 300 nm. Elemental analyses were performed by Dornis & Kolbe Microanalytisches Laboratorium (Mülheim an der Ruhr, Germany). CCDC 1502312 (for **27**), 1502313 (for racemic **15**), and 1502314 [for (*R*)-**12c**] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

4-Hydroxy-3a,4,5,6-tetrahydroisobenzofuran-1(3*H*)-one (10):[10] A solution of lactone **9** (10 g, 64.8 mmol) in THF (400 mL) was cooled to –78 °C and a freshly prepared solution of LiHMDS [prepared by slow addition of HMDS (21.9 mL, 105.3 mmol, 1.5 equiv.) to *n*BuLi (59.8 mL, 1.6 M in hexanes, 95.7 mmol, 1.4 equiv.) at 0 °C] was added slowly. After the addition was complete, the viscous yellow mixture was stirred for an additional 30 min and subsequently quenched by the addition of 10 % aqueous $KHSO_4$ (200 mL) at –78 °C. The ice bath was removed, and the mixture was warmed to room temperature. The layers ware separated, and the aqueous layer was extracted with EtOAc (5 × 100 mL) saturating the aqueous layer with NaCl before the final extraction. The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to give a crystalline residue. Recrystallization from a mixture of petroleum ether 40–60 and EtOAc afforded alcohol **10** (7.3 g, 73 %) as a crystalline solid. M.p. 115–116 °C. IR (neat): $\tilde{\nu}$ = 3442, 2917, 1739, 1681 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.91 (d, J = 3.2 Hz, 1 H), 4.51 (t, J = 8.7 Hz, 1 H), 4.33–4.28 (m, 2 H), 3.16–3.08 (m, 1 H), 2.5–2.35 (m, 2 H), 2.08–2.02 (m, 2 H), 1.78–1.69 (m, 1 H) ppm. ^{13}C NMR (100 MHz,

$CDCl_3$): δ = 170.7, 136.6, 125.3, 67.9, 61.6, 40.8, 27.7, 20.9 ppm. $C_8H_{10}O_3$ (154.06): calcd. C 62.33, H 6.54; found C 62.53, H 6.60.

6,7-Dihydroisobenzofuran-1,4(3*H*,5*H*)-dione (11): A solution of trifluoroacetic anhydride (18.3 mL, 129.7 mmol, 2.0 equiv.) in CH_2Cl_2 (180 mL) was cooled to –78 °C. Then a solution of DMSO (9.7 mL, 136.2 mmol, 2.1 equiv.) in CH_2Cl_2 (180 mL) was added dropwise, and the mixture was stirred for 1 h. Then a solution of **10** (10 g, 64.9 mmol) in CH_2Cl_2 (310 mL) was added dropwise, and the mixture was stirred for 1 h. Then Et_3N (25 mL) was added, and the mixture was stirred for 30 min. The cooling bath was removed, and the mixture was warmed to room temperature. Then a saturated aqueous solution of $NaHCO_3$ (300 mL) was added, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (300 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (petroleum ether 40–60/EtOAc, 2:1) to give **11** (9.6 g, 97 %) as a colorless solid. M.p. 57–58 °C; R_f = 0.28 (petroleum ether 40–60/EtOAc, 2:1). IR (neat): $\tilde{\nu}$ = 2949, 1763, 1687 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.98 (t, *J* = 3.0 Hz, 2 H), 2.63–2.57 (m, 4 H), 2.26–2.19 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.1, 172.4, 150.9, 144.6, 68.6, 38.1, 22.9, 20.6 ppm. HRMS (EI): calcd. for $C_8H_8O_3$ 152.0473; found 152.0468. $C_8H_8O_3$ (152.05): calcd. C 63.15, H 5.30; found C 63.12, H 5.33.

4-Hydroxy-4,5,6,7-tetrahydroisobenzofuran-1(3*H*)-one (12a): $CeCl_3 \cdot 7H_2O$ (2.4 g, 6.5 mmol, 1.0 equiv.) was added to a solution of ketone **11** (1.0 g, 6.5 mmol) in MeOH (30 mL). The mixture was cooled to –78 °C, and $NaBH_4$ (249 mg, 6.7 mmol, 1.0 equiv.) was added in small portions. After the addition was complete, the mixture was stirred for 30 min followed by the addition of water (30 mL). The resulting mixture was warmed to room temperature and extracted with CH_2Cl_2 (5 × 40 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to give pure racemic alcohol **12a** (989 mg, 99 %) as a colorless oil.

(*R*)-4-Hydroxy-4,5,6,7-tetrahydroisobenzofuran-1(3*H*)-one (12a): Ketone **11** (12 g, 78.9 mmol) was added to a solution of [RuCl(*p*-cymene){(*R*,*R*)-Ts-dpen}] (505 mg, 0.789 mmol, 1 mol-%) in HCO_2H/Et_3N (5:2, 78 mL) and stirred at room temperature for 6 d. When the reaction was complete, the mixture was diluted with EtOAc (200 mL), transferred to a separation funnel, and a saturated aqueous solution of $NaHCO_3$ was carefully added. The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 100 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (petroleum ether 40–60/EtOAc, 1:2) to give alcohol **12a** (10.8 g, 89 %) as a brown oil. R_f = 0.32 (petroleum ether 40–60/EtOAc, 1:2). IR (neat): $\tilde{\nu}$ = 3427, 2942, 1738, 1676 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.94 (dt, *J* = 17.5, 2.5 Hz, 1 H), 4.79–4.73 (m, 1 H), 4.50 (br. s, 1 H), 3.73 (d, *J* = 6.5 Hz, 1 H), 2.13–2.10 (m, 2 H), 2.06–1.98 (m, 1 H), 1.93–1.85 (m, 1 H), 1.71–1.60 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.6, 162.4, 127.5, 70.9, 64.2, 31.5, 19.7, 19.4 ppm. HRMS (FAB): calcd. for $C_8H_{11}O_3$ $[MH]^+$ 155.0708; found 155.0708 [*ee* and optical rotation of the benzoate derivative (+)-**12b** were determined].

(*R*)-1-Oxo-1,3,4,5,6,7-hexahydroisobenzofuran-4-yl benzoate [(+)-12b]: Pyridine (17.1 mL, 210 mmol, 3 equiv.) was added to a solution of alcohol (*R*)-**12a** (10.8 g, 70.0 mmol; obtained from the enantioselective reduction of **11**) in CH_2Cl_2 (450 mL). The mixture was cooled to 0 °C, and benzoyl chloride (23.4 mL, 210 mL, 3 equiv.) was added dropwise. The ice bath was removed, and the mixture was stirred at room temperature for 18 h. The reaction was quenched by the addition of water (200 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc, 4:1 to 3:1) to afford **12b** (16.3 g, 90 %) as a colorless oil. $[\alpha]_D^{20}$ = +139 (*c* = 1.0, $CHCl_3$); R_f = 0.23 (petroleum ether 40–60/EtOAc, 4:1). IR (neat): $\tilde{\nu}$ = 2937, 1759, 1716 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.4 Hz, 2 H), 7.62 (t, *J* = 7.4 Hz, 1 H), 7.46 (t, *J* = 8.0 Hz, 2 H), 5.80 (t, *J* = 5.4 Hz, 1 H), 4.85 (dt, *J* = 17.6, 2.6 Hz, 2 H), 2.43–2.35 (m, 1 H), 2.34–2.26 (m, 1 H), 2.21–2.13 (m, 1 H), 2.09–1.97 (m, 2 H), 1.95–1.87 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.0, 166.1, 156.6, 133.5, 131.1, 129.6, 129.2, 128.5, 70.9, 66.0, 28.1, 20.0, 19.0 ppm. HRMS (FAB): calcd. for $C_{15}H_{15}O_4$ $[MH]^+$ 259.0970; found 259.0966. HPLC: Daicel Chiralcel OD-H, *i*PrOH/*n*-heptane, 10:90 (0.8 mL/min, λ = 254 nm): t_R = 25.43 min (minor) and t_R = 29.63 min (major), 93 % *ee*. (Racemic **12b** was prepared according to the same procedure from racemic **12a** and was isolated as a white solid. M.p. 84–85 °C.)

(*R*)-1-Oxo-1,3,4,5,6,7-hexahydroisobenzofuran-4-yl 4-Bromobenzoate (12c): Pyridine (202 µL, 1.98 mmol, 3 equiv.) was added to a solution of alcohol **12a** (100 mg, 0.66 mmol, 93 % *ee*) in CH_2Cl_2 (6 mL). The mixture was cooled to 0 °C, and *p*-bromobenzoyl chloride (289 mg, 3 equiv.) was added. The ice bath was removed, and the mixture was stirred at room temperature for 18 h. The reaction was quenched by the addition of water (5 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (petroleum ether 40–60/EtOAc, 4:1) to give **12c** (193 mg, 87 %) as a white crystalline solid. R_f = 0.26 (petroleum ether 40–60/EtOAc, 4:1). IR (neat): $\tilde{\nu}$ = 1756, 1715, 1682, 1589 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.6 Hz, 2 H), 7.59 (d, *J* = 8.5 Hz, 2 H), 5.76 (t, *J* = 5.2 Hz, 1 H), 4.85 (d, *J* = 17.5 Hz, 1 H), 4.77 (dt, *J* = 17.5, 2.7 Hz, 1 H), 2.39–2.34 (m, 1 H), 2.29–2.23 (m, 1 H), 2.18–2.11 (m, 1 H), 2.07–1.79 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.9, 165.4, 156.2, 131.8, 131.3, 131.1, 128.7, 128.1, 70.8, 66.3, 28.1, 20.0, 19.0 ppm. HRMS (FAB): calcd. for $C_{15}H_{14}BrO_4$ $[MH]^+$ 337.0075; found 337.0073. Recrystallization from a mixture of petroleum ether/EtOAc furnished enantiopure crystals suitable for X-ray diffraction analysis (for crystal data see Supporting Information). M.p. 117–118 °C. $[\alpha]_D^{20}$ = +125 (*c* = 1.0, $CHCl_3$). HPLC: Daicel Chiralcel OD-H, *i*PrOH/*n*-heptane, 10:90 (0.8 mL/min, λ = 254 nm): t_R = 25.07 min, >99 % *ee*. (Racemic **12c** was prepared according to the same procedure from racemic **12a** and was isolated as a white solid. M.p. 97–98 °C.)

Silyloxyfuran 13: Ethyldiisopropylamine (1.2 equiv.) was added to a stirred solution of butenolide **12b** in dry diethyl ether (0.1 M). The mixture was cooled to 0 °C, and TIPSOTf (1.15 equiv.) was added dropwise. The mixture was allowed to gradually warm to room temperature overnight. The reaction was quenched by the addition of petroleum ether 40–60 and water. The organic layer was separated, washed with water, a saturated aqueous solution of $NaHCO_3$, and brine, and dried with $MgSO_4$. The solvent was removed in vacuo to afford crude **13** as a yellow oil, which was directly used without further purification. ^1H NMR (C_6D_6): δ = 8.26–8.23 (m, 2 H), 7.27 (s, 1 H), 7.24–7.12 (m, 3 H), 6.19 (t, *J* = 4.4 Hz, 1 H), 2.57 (dt, *J* = 15.2, 5.2 Hz, 1 H), 2.37–2.29 (m, 1 H), 1.97–1.90 (m, 2 H), 1.77–1.70 (m, 1 H), 1.60–1.54 (m, 1 H), 1.33–1.24 (m, 3 H), 1.19 (d, *J* = 6.5 Hz, 18 H) ppm.

Photosubstrate 14: A suspension of silver trifluoroacetate (225 mg, 1.15 mmol, 1.15 equiv.) in dry CH_2Cl_2 (5 mL) was cooled to –78 °C. A solution of **13** (prepared from 1 mmol of racemic **12b**) in CH_2Cl_2 (5 mL) was added to this suspension followed by the slow dropwise addition of a solution of 4-bromobuta-1,2-diene (140 mg,

1.05 mmol, 1.05 equiv.) in CH_2Cl_2 (2 mL) at –78 °C, and the stirred mixture was gradually warmed to 10 °C. The mixture was filtered through Celite and the filter cake washed with CH_2Cl_2 (2 × 25 mL). The solvent was removed in vacuo, and the residue was purified by column chromatography (petroleum ether 40–60/EtOAc, 5:1) to give **14** (178 mg, 57 %) as a colorless oil. R_f = 0.20 (petroleum ether 40–60/EtOAc, 5:1). IR (neat): $\tilde{\nu}$ = 2936, 1956, 1760, 1717 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, J = 7.1 Hz, 2 H), 7.61 (t, J = 7.4 Hz, 1 H), 7.48 (t, J = 8.0 Hz, 2 H), 5.78 (t, J = 5.0 Hz, 1 H), 5.16–5.12 (m, 1 H), 5.08–4.94 (m, 1 H), 4.77–4.64 (m, 2 H), 2.77–2.69 (m, 1 H), 2.58–2.49 (m, 1 H), 2.49–2.38 (m, 1 H), 2.32–2.24 (m, 1 H), 2.15–1.85 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.6, 172.2, 165.8, 158.3, 133.5, 132.4, 129.6, 129.3, 128.5, 82.9, 80.7, 75.4, 65.0, 30.9, 28.4, 20.1, 18.7 ppm. HRMS (FAB): calcd. for $C_{19}H_{19}O_4$ $[MH]^+$ 311.1283; found 311.1283.

Irradiation of 14: A solution of allene **14** (60 mg, 0.19 mmol) in MeCN/acetone (9:1, v/v, 30 mL) was degassed by bubbling argon through the solution for 30 min. The mixture was irradiated for 30 min keeping the mixture under argon during the irradiation. The mixture was concentrated in vacuo, and the residue was purified by column chromatography (petroleum ether 40–60/EtOAc, 5:1) to give **15** (40 mg, 67 %) as a colorless oil, which solidified on standing. M.p. 81–82 °C; R_f = 0.24 (petroleum ether 40–60/EtOAc, 5:1). IR (neat): $\tilde{\nu}$ = 2947, 2867, 1773, 1716 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, J = 7.0 Hz, 2 H), 7.58 (t, J = 7.5 Hz, 1 H), 7.46 (t, J = 7.5 Hz, 2 H), 5.66 (t, J = 2.8 Hz, 1 H), 4.95–4.94 (m, 1 H), 4.88 (s, 1 H), 4.70 (s, 1 H), 3.05 (s, 1 H), 2.33 (d, J = 13.7 Hz, 1 H), 2.21 (dd, J = 11.9, 4.0 Hz, 1 H), 1.97–1.92 (m, 1 H), 1.85–1.70 (m, 3 H), 1.63–1.50 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3, 165.9, 150.6, 133.2, 129.8, 129.8, 128.5, 97.4, 78.6, 66.8, 65.9, 52.2, 48.8, 37.4, 26.5, 20.7, 16.6 ppm. HRMS (FAB): calcd. for $C_{19}H_{19}O_4$ $[MH]^+$ 311.1283; found 311.1283. Crystals suitable for X-ray diffraction analysis were obtained by slow concentration of a solution of **15** in a mixture of diethyl ether/petroleum ether 40–60 (for crystal data see the Supporting Information).

2-[(Benzyloxy)methyl]buta-2,3-dien-1-ol (18): Tin powder (Aldrich, particle size <45 μm, 99.8 % trace metals basis; 1.49 g, 12.5 mmol, 1.0 equiv.) and lithium iodide (1.68 g, 12.5 mmol, 1.0 equiv.) were added to a solution of **17** (3.0 g, 12.5 mmol) in THF/H_2O (2:1, 75 mL). The mixture was sonicated for 20 min, after which paraformaldehyde (1.51 g, 50 mmol, 4.0 equiv.) was added. Sonication was continued until all the starting material was consumed. A saturated aqueous solution of $NaHCO_3$ was added, and the mixture was extracted three times with EtOAc. The combined organic layers were dried with magnesium sulfate and concentrated in vacuo. Column chromatography (PE/EtOAc, 1:3) gave **18** (1.63 g, 8.51 mmol, 68 %) together with a minor amount of **19** (71 mg, 0.38 mmol, 3 %). The spectroscopic and analytical data for **18** are in accordance with previously reported data.[17]

{[2-(Bromomethyl)buta-2,3-dien-1-yl]oxymethyl}benzene (8): Pyridine (10 μL) was added to a solution of **18** (200 mg, 1.05 mmol) in Et_2O (200 μL). The mixture was cooled to 0 °C, PBr_3 (50 μL, 0.53 mmol, 0.5 equiv.) was added dropwise, and the reaction mixture was stirred at 0 °C for 30 min. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (20 mL), and the mixture was extracted three times with Et_2O (15 mL). The combined organic layers were dried with magnesium sulfate and concentrated in vacuo. Column chromatography (PE/EtOAc, 95:5) gave **8** as a colorless oil (186 mg, 0.73 mmol, 70 %). The spectroscopic and analytical data for **8** are in accordance with previously reported data.[3i]

Photosubstrate (+)-20: Silyloxyfuran **13** [prepared from (+)-**12** (2.5 g, 9.68 mmol)] was dissolved in CH_2Cl_2 (210 mL) and cooled to –78 °C. Then CF_3CO_2Ag (2.35 g, 10.65 mmol, 1.1 equiv.) was added in small portions. After the addition was complete, a solution of allenic bromide **8** (2.69 g, 10.65 mmol, 1.1 equiv.) in CH_2Cl_2 (20 mL) was added dropwise. The mixture was allowed to slowly warm to 10 °C and filtered through Celite. The filtrate was concentrated in vacuo and the residue purified by column chromatography (petroleum ether 40–60/EtOAc, 4:1) to provide (+)-**20** (2.1 g, 51 %) as a light-yellow oil. $[\alpha]_D^{20}$ = +42 (c = 0.77, $CHCl_3$); R_f = 0.22 (petroleum ether 40–60/EtOAc, 4:1). IR (neat): $\tilde{\nu}$ = 2947, 2861, 1957, 1760, 1717, 1602 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, J = 7.0 Hz, 2 H), 7.56 (t, J = 7.5 Hz, 1 H), 7.42 (t, J = 7.5 Hz, 2 H), 7.30–7.21 (m, 5 H), 5.79 (t, J = 5.0 Hz, 1 H), 5.21–5.16 (m, 1 H), 4.83–4.79 (m, 1 H), 4.78–4.68 (m, 1 H), 4.43 (d, J = 11.8 Hz, 1 H), 4.39 (d, J = 11.8 Hz, 1 H), 4.05–3.93 (m, 2 H), 2.77–2.72 (m, 1 H), 2.46–2.33 (m, 2 H), 2.22–2.16 (m, 1 H), 2.08–1.78 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.4, 172.3, 165.7, 158.6, 137.8, 133.4, 132.0, 129.6, 129.3, 128.5, 128.3, 127.8, 127.5, 94.9, 80.3, 76.7, 71.6, 71.0, 65.0, 31.7, 28.3, 20.0, 18.6 ppm. HRMS (FAB): calcd. for $C_{27}H_{27}O_5$ $[MH]^+$ 431.1858; found 431.1852.

Irradiation of (+)-20: A solution of photosubstrate (+)-**20** (8.0 g, 18.58 mmol) in a mixture of MeCN/acetone (9:1, 930 mL) was degassed by bubbling argon through the solution for 30 min. The mixture was irradiated for 45 min keeping the mixture under argon during the irradiation. The mixture was then concentrated in vacuo, and the residue was purified by chromatography (petroleum ether 40–60/EtOAc, 3:1) to give two chromatographic fractions. The first fraction provided (–)-**21** (5.2 g, 65 %) as a viscous colorless oil and the second fraction provided (–)-**22** (600 mg, 8 %) as a light-yellow oil.

Data for (–)-21: $[\alpha]_D^{20}$ = –19 (c = 1.0, $CHCl_3$); R_f = 0.41 (petroleum ether 40–60/EtOAc, 3:1). IR (neat): $\tilde{\nu}$ = 3030, 2944, 2865, 1774, 1717, 1601 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, J = 8.0 Hz, 2 H), 7.52 (t, J = 7.4 Hz, 1 H), 7.41 (t, J = 7.8 Hz, 2 H), 7.34–7.24 (m, 5 H), 5.61 (t, J = 2.5 Hz, 1 H), 4.88 (d, J = 4.0 Hz, 1 H), 4.76 (d, J = 1.3 Hz, 1 H), 4.64 (d, J = 1.3 Hz, 1 H), 4.48 (s, 2 H), 3.66 (d, J = 10.6 Hz, 1 H), 3.63 (d, J = 10.6 Hz, 1 H), 2.22–2.15 (m, 2 H), 1.90–1.83 (m, 2 H), 1.73–1.61 (m, 2 H), 1.54–1.48 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.7, 165.8, 151.0, 137.8, 133.1 (3 C), 129.7 (2 C), 129.6 (2 C), 128.4, 127.6 (2 C), 127.3, 96.3, 78.6, 73.1, 65.7, 65.5, 65.0, 58.5, 53.4, 39.4, 26.5, 19.1, 16.3 ppm. HRMS (FAB): calcd. for $C_{27}H_{27}O_5$ $[MH]^+$ 431.1858; found 431.1840.

Data for (–)-22: $[\alpha]_D^{20}$ = –117 (c = 2.0, $CHCl_3$); R_f = 0.22 (petroleum ether 40–60/EtOAc, 3:1). IR (neat): $\tilde{\nu}$ = 1758, 1714 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, J = 7.2 Hz, 2 H), 7.51 (t, J = 7.4 Hz, 1 H), 7.38 (t, J = 7.8 Hz, 2 H), 7.29–7.20 (m, 5 H), 7.06 (t, J = 3.6 Hz, 1 H), 5.29 (t, J = 2.8 Hz, 1 H), 4.71 (d, J = 4.6 Hz, 1 H), 4.44 (d, J = 11.8 Hz, 1 H), 4.38 (d, J = 11.8 Hz, 1 H), 4.07 (s, 2 H), 2.87 (d, J = 17.7 Hz, 1 H), 2.69 (d, J = 18.0 Hz, 1 H), 2.45–2.39 (m, 2 H), 2.17–2.11 (m, 1 H), 2.05–1.97 (m, 1 H), 1.56 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 165.1, 137.7, 136.3, 136.2, 133.2, 133.0, 129.3, 128.3, 128.1, 127.7, 127.5, 127.4, 83.1, 71.8, 68.7, 65.6, 61.9, 37.9, 23.7, 21.1, 11.8 ppm. HRMS (FAB): calcd. for $C_{27}H_{27}O_5$ $[MH]^+$ 431.1858; found 431.1864.

Alcohol 23a: A solution of **21** (500 mg, 1.16 mmol) in CH_2Cl_2 (15 mL) was cooled to –78 °C, and a solution of BBr_3 (2.3 mL, 1 M in CH_2Cl_2, 2.3 mmol, 2.3 equiv.) was added dropwise. The reaction mixture was stirred for 2.5 h and quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (15 mL). The mixture was warmed to room temperature, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 15 mL) and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by chromatography (petroleum

ether 40–60/EtOAc, 1:1) to give alcohol **23a** (348 mg, 86 %) as a crystalline solid. M.p. 155–157 °C. $[\alpha]_D^{20}$ = –37.1 (*c* = 1.0, $CHCl_3$); R_f = 0.23 (petroleum ether 40–60/EtOAc, 1:1). IR (neat): $\tilde{\nu}$ = 3483, 2945, 2867, 1770, 1716, 1601 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 7.0 Hz, 2 H), 7.53 (t, *J* = 7.5 Hz, 1 H), 7.42 (t, *J* = 7.4 Hz, 2 H), 5.62, (t, *J* = 2.6 Hz, 1 H), 4.94 (d, *J* = 4.0 Hz, 1 H), 4.79 (d, *J* = 1.5 Hz, 1 H), 4.69 (d, *J* = 1.5 Hz, 1 H), 3.92 (d, *J* = 12.0 Hz, 1 H), 3.85 (d, *J* = 12.0 Hz, 1 H), 2.25 (d, *J* = 13.7 Hz, 1 H), 2.16 (dd, *J* = 11.8, 4.0 Hz, 1 H), 1.92–1.83 (m, 2 H), 1.76–1.64 (m, 3 H), 1.58–1.48 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3, 165.9, 151.0, 133.2, 129.8, 129.7, 128.5, 96.5, 78.8, 65.7, 65.4, 59.9, 58.2, 53.3, 38.8, 26.5, 19.0, 16.4 ppm. HRMS (FAB): calcd. for $C_{20}H_{21}O_5$ $[MH]^+$ 341.3837; found 341.1390. $C_{20}H_{20}O_5$ (340.13): calcd. C 70.57, H 5.92; found C 70.52, H 6.03.

Aldehyde 23b: A solution of oxalyl chloride (0.88 mL, 2 M in CH_2Cl_2, 1.76 mmol, 1.2 equiv.) was diluted with CH_2Cl_2 (1.3 mL) and cooled to 78 °C. Then a solution of DMSO (272 µL, 3.82 mmol, 2.6 equiv.) in CH_2Cl_2 (0.44 mL) was added dropwise, and the mixture was stirred for 30 min. Then a solution of alcohol **23a** (500 mg, 1.47 mmol) in CH_2Cl_2 was added dropwise, and the mixture was again stirred for 45 min. Then Et_3N (1.02 mL, 7.35 mmol, 5 equiv.) was added, and the mixture was stirred for 30 min followed by the addition of water (5 mL). The mixture was warmed to room temperature, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to give the crude aldehyde **23b**, which was used without further purification. IR (neat): $\tilde{\nu}$ = 2950, 1777, 1716, 1601 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.77 (s, 1 H), 7.98 (d, *J* = 7.0 Hz, 2 H), 7.54 (t, *J* = 7.4 Hz, 1 H), 7.42 (t, *J* = 7.8 Hz, 2 H), 5.64 (t, *J* = 2.7 Hz, 1 H), 5.13 (d, *J* = 1.9 Hz, 1 H), 4.99 (d, *J* = 4.0 Hz, 1 H), 4.85 (d, *J* = 1.8 Hz, 1 H), 2.47–2.40 (m, 2 H), 2.01–1.71 (m, 4 H), 1.61–1.51 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.7, 173.3, 165.8, 148.4, 133.4, 129.8, 129.5, 128.6, 99.2, 78.1, 65.8, 65.2, 64.3, 55.4, 39.2, 26.4, 19.6, 16.2 ppm. HRMS (FAB): calcd. for $C_{20}H_{19}O_5$ $[MH]^+$ 339.1232; found 339.1233.

Allylic Alcohol 25: Crude aldehyde **23b** was dissolved in THF (15 mL), and sulfone **24** (593 mg, 1.62 mmol, 1.1 equiv.)[21] was added. The mixture was cooled to –78 °C, and a solution of potassium bis(trimethylsilyl)amide (KHMDS; 3.88 mL, 0.5 M in toluene, 1.94 mmol, 1.2 equiv.) was added by means of a syringe pump over 10 min. The mixture was stirred at –78 °C for 30 min and allowed to slowly warm to room temperature. Then a solution of tetra-*n*-butylammonium fluoride (TBAF; 3.67 mL, 1 M in THF, 3.67 mmol, 2.5 equiv.) was added, and the mixture was stirred for 1 h. Then water was added (20 mL), and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 20 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc, 1:1) to give allylic alcohol **25** (190 mg, 52 %, from **23b**) as a white solid. M.p. 128–130 °C. $[\alpha]_D^{20}$ = –36 (*c* = 0.5, $CHCl_3$); R_f = 0.23 (petroleum ether 40–60/EtOAc, 1:1). IR (neat): $\tilde{\nu}$ = 3483, 2924, 2868, 1769, 1716 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 7.4 Hz, 2 H), 5.00 (t, *J* = 7.3 Hz, 1 H), 7.39 (t, *J* = 7.8 Hz, 2 H), 5.85–5.74 (m, 2 H), 5.59 (s, 1 H), 4.89 (d, *J* = 4.0 Hz, 1 H), 4.79 (s, 1 H), 4.65 (s, 1 H), 4.13 (d, *J* = 3.9 Hz, 2 H), 2.26–2.15 (m, 3 H), 1.87 (dd, *J* = 14.5, 2.4 Hz, 1 H), 1.75–1.59 (m, 3 H), 1.54–1.45 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.8, 165.8, 152.6, 134.6, 133.1, 129.7 (3 C), 128.4 (2 C), 122.1, 96.3, 78.6, 65.8, 65.4, 62.6, 59.4, 55.4, 41.1, 26.4, 19.4, 16.3 ppm. HRMS (FAB): calcd. for $C_{22}H_{23}O_5$ $[MH]^+$ 367.1545; found 367.1548.

Cyclopropanation of 25: A solution of Et_2Zn (427 µL, 0.97 M in CH_2Cl_2, 0.41 mmol, 2.0 equiv.) was diluted with CH_2Cl_2 (427 µL) and cooled to 0 °C. Then chloro(iodo)methane (60 µL, 0.83 mmol, 4 equiv.) was added dropwise, and the mixture was stirred for 10 min. During this time a white precipitate was formed. Then a solution of allylic alcohol **25** (76 mg, 0.21 mmol) in CH_2Cl_2 (200 µL) was added, and the mixture was stirred at 0 °C for 2.5 h. The reaction was quenched by the addition of 10 % aqueous $KHSO_4$ (1 mL) and warmed to room temperature. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography (petroleum ether 40–60/EtOAc, 1:1) to give two chromatographic fractions. The first fraction contained methyl ether **26b** (38 mg, 46 %) as a 40:60 mixture of isomers and the second fraction contained alcohol **26a** (32 mg, 40 %) as a 90:10 mixture of isomers.

Data for 26b: $[\alpha]_D^{20}$ = –27.2 (*c* = 1.0, $CHCl_3$); R_f = 0.33 (petroleum ether 40–60/EtOAc, 1:1). IR (neat): $\tilde{\nu}$ = 2942, 2868, 1769, 1715 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.06–8.03 (m, 2 H), 7.59–7.56 (m, 1 H), 7.48–7.45 (m, 2 H), 5.65 (t, *J* = 2.4 Hz, 1 H), 4.99 (d, *J* = 1.2 Hz, 1 H), 4.48 (d, *J* = 4.0 Hz, 1 H), 4.71 (d, *J* = 1.2 Hz, 1 H), 3.39–3.21 (m, 5 H), 2.34–2.29 (m, 2 H), 1.98–1.92 (m, 2 H), 1.84–1.72 (m, 2 H), 1.60–1.56 (m, 2 H), 1.45–1.39 (m, 1 H), 1.27–1.07 (m, 1 H), 0.99–0.95 (m, 1 H), 0.74–0.69 (m, 0.3 H), 0.66–0.57 (m, 1 H), 0.50–0.46 (m, 0.7 H) ppm. HRMS (FAB): calcd. for $C_{24}H_{27}O_5$ $[MH]^+$ 395.1858; found 395.1855.

Data for 26a: $[\alpha]_D^{20}$ = –38.2 (*c* = 1.0, $CHCl_3$); R_f = 0.17 (petroleum ether 40–60/EtOAc, 1:1). IR (neat): $\tilde{\nu}$ = 3469, 2927, 2868, 1766, 1715 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): major isomer: δ = 8.05–8.02 (m, 2 H), 7.59–7.56 (m, 1 H), 7.48–7.45 (m, 2 H), 5.65 (t, *J* = 2.4 Hz, 1 H), 4.96 (d, *J* = 1.2 Hz, 1 H), 4.89 (d, *J* = 4.0 Hz, 1 H), 4.71 (d, *J* = 1.2 Hz, 1 H), 3.61 (dd, *J* = 11.2, 6.4 Hz, 1 H), 3.49 (dd, *J* = 11.2, 6.9 Hz, 1 H), 2.32 (d, *J* = 14.0 Hz, 1 H), 2.01–1.92 (m, 2 H), 1.81–1.72 (m, 2 H), 1.63–1.54 (m, 2 H), 1.43 (d, *J* = 11.6 Hz, 1 H), 1.27–1.18 (m, 2 H), 1.02–0.96 (m, 1 H), 0.63–0.57 (m, 1 H), 0.51–0.46 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): major isomer: δ = 175.1, 165.9, 153.1, 133.2, 129.8 (3 C), 128.5 (2 C), 95.9, 78.3, 66.1, 65.8, 65.2, 59.8, 54.3, 38.7, 26.6, 19.3, 18.1, 16.9, 12.7, 6.3 ppm. HRMS (FAB): calcd. for $C_{23}H_{25}O_5$ $[MH]^+$ 381.1702; found 381.1705.

Cyclopropane 27: $Ba(OH)_2 \cdot 8H_2O$ (97 mg, 0.31 mmol, 4.0 equiv.) was added to a solution of **26a** (29 mg, 0.077 mmol) in MeOH (6.4 mL), and the mixture was stirred for 8 h. Then the reaction was quenched by the addition of excess solid NH_4Cl and diluted with diethyl ether (15 mL). The mixture was filtered through Celite and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc, 1:3) to give the corresponding alcohol (16 mg, *dr* 90:10, 75 %). This mixture was recrystallized from *n*-pentane/CH_2Cl_2 to afford pure **27** as a crystalline solid, which was suitable for an X-ray crystal structure determination (see the Supporting Information). M.p. 133–135 °C; R_f = 0.27 (petroleum ether 40–60/EtOAc, 1:3). IR (neat): $\tilde{\nu}$ = 3403, 2941, 1747 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.98 (d, *J* = 4.0 Hz, 1 H), 4.88 (s, 1 H), 4.58 (s, 1 H), 4.36 (br. s, 1 H), 3.59 (dd, *J* = 11.2, 6.8 Hz, 1 H), 3.49 (dd, *J* = 11.2, 6.8 Hz, 1 H), 2.23 (d, *J* = 13.6 Hz, 1 H), 1.97 (dd, *J* = 11.6, 4.0 Hz, 1 H), 1.72–1.63 (m, 3 H), 1.54–1.43 (m, 8 H), 1.23–1.18 (m, 1 H), 0.97–0.92 (m, 1 H), 0.60–0.56 (m, 1 H), 0.49–0.44 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3, 153.9, 95.3, 78.3, 66.6, 66.3, 63.4, 59.7, 54.0, 38.9, 29.7, 19.5, 18.1, 15.5, 12.7, 6.3 ppm. HRMS (FAB): calcd. for $C_{16}H_{21}O_4$ $[MH]^+$ 277.1440; found 277.1446.

Triol 28: A solution of $LiAlH_4$ (0.5 mL, 1 M in THF, 0.5 mmol, 5 equiv.) was cooled to 0 °C. Then a solution of **21** (43 mg, 0.1 mmol) in THF (1 mL) was added dropwise. After the addition was complete, the mixture was stirred at 0 °C for 2 h and the reaction quenched by the addition of a saturated aqueous solution of Na_2SO_4 (1 drop).

The resulting mixture was stirred at room temperature for 1 h. Then solid Na_2SO_4 was added, and the mixture was filtered through Celite. The filter cake was washed with EtOAc (10 mL), and the filtrate was concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc, 1:2) to give triol **28** as a crystalline solid (29 mg, 88 %). M.p. 90–92 °C. $[\alpha]_D^{22}$ = +20.2 (*c* = 1.0, $CHCl_3$); R_f = 0.22 (petroleum ether 40–60/EtOAc, 1:2). IR (neat): $\tilde{\nu}$ = 3335, 2935, 2864, 1689 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.29 (m, 5 H), 4.57 (s, 2 H), 4.42–4.34 (m, 4 H), 4.30 (t, *J* = 2.4 Hz, 1 H), 3.64 (d, *J* = 12.0 Hz, 1 H) 3.57 (d, *J* = 9.6 Hz, 1 H), 3.48 (d, *J* = 9.6 Hz, 1 H), 3.36 (br. s, 3 H), 2.22 (dd, *J* = 12.0, 2.8 Hz, 1 H), 2.12–2.00 (m, 2 H), 1.79–1.62 (m, 3 H), 1.51–1.40 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.6, 137.2, 128.5, 127.9, 127.6, 94.2, 73.9, 73.6, 66.7, 65.7, 61.9, 59.9, 59.0, 47.4, 38.7, 30.7, 25.1, 15.7 ppm. HRMS (FAB): calcd. for $C_{20}H_{27}O_4$ $[MH]^+$ 331.1909; found 331.1913.

Acetonide 29: *p*TsOH (3 mg, 0.009 mmol, 0.1 equiv.) was added to a solution of triol **28** (29 mg, 0.09 mmol) in acetone (0.9 mL). The mixture was stirred at room temperature overnight. Then Et_3N was added (1 drop), and the mixture was concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc, 1:1) to give acetonide **29** (22 mg, 66 %) as a colorless oil. $[\alpha]_D^{22}$ = +41.4 (*c* = 1.85, $CHCl_3$); R_f = 0.38 (petroleum ether 40–60/EtOAc, 1:1). IR (neat): $\tilde{\nu}$ = 3472, 2990, 2938, 2868, 1691 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.29 (m, 5 H), 4.61 (d, *J* = 12.0 Hz, 1 H), 4.58 (d, *J* = 12.0 Hz, 1 H), 4.45–4.39 (m, 3 H), 4.29 (t, *J* = 2.8 Hz, 1 H), 4.19 (dd, *J* = 8.0, 2.4 Hz, 1 H), 3.62–3.52 (m, 3 H), 3.14 (d, *J* = 10.8 Hz, 1 H), 2.39 (dd, *J* = 12.0 2.4 Hz, 1 H), 2.19–2.15 (m, 1 H), 1.96 (dd, *J* = 12.0, 7.6 Hz, 1 H), 1.75–1.59 (m, 3 H), 1.52–1.42 (m, 5 H), 1.37 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9, 137.1, 128.5, 127.9, 127.7, 99.9, 94.3, 73.6, 69.8, 65.7, 64.6, 59.5, 59.2, 57.9, 47.6, 35.7, 29.4, 28.2, 23.7, 19.6, 16.3 ppm. HRMS (FAB): calcd. for $C_{23}H_{31}O_4$ $[MH]^+$ 371.2222; found 371.2219.

Tetramethylphosphordiamidate 30: A solution of acetonide **29** (24 mg, 0.065 mmol) in dimethoxyethane/tetramethylethylenediamine (DME/TMEDA, 3:1, 1.2 mL) was cooled to 0 °C. Then methyllithium (49 µL, 1.6 M in diethyl ether, 0.078 mmol, 1.2 equiv.) was added, and the mixture was stirred for 30 min. Then *N*,*N*,*N*′,*N*′-tetramethylphosphordiamidic chloride (56 µL, 0.39 mmol, 6 equiv.) was added, and the ice bath was removed. The mixture was stirred for 2 h. The reaction was quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (1 mL) and then stirred at room temperature for 1 h. Then the mixture was extracted with EtOAc (5 × 5 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by chromatography (EtOAc with 5 % MeOH) to give tetramethylphosphordiamidate **30** (30 mg, 93 %) as a colorless oil. R_f = 0.22 (EtOAc with 5 % MeOH). IR: $\tilde{\nu}$ = 984 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.24 (m, 5 H), 4.79–4.74 (m, 2 H), 4.54 (d, *J* = 12.0 Hz, 1 H), 4.50 (s, 1 H), 4.47 (d, *J* = 12.0 Hz, 1 H), 4.29 (br. s, 1 H), 4.17 (dd, *J* = 8.0, 2.4 Hz, 1 H), 4.08 (dd, *J* = 11.2, 5.2 Hz, 1 H), 3.71 (d, *J* = 10.0 Hz, 1 H), 3.67 (d, *J* = 10.0 Hz, 1 H), 2.60 (d, *J* = 9.6 Hz, 12 H), 2.30 (dd, *J* = 12.0, 8.0 Hz, 1 H), 2.06 (dd, *J* = 12.4, 2.4 Hz, 1 H), 1.99 (d, *J* = 10.4 Hz, 1 H), 1.78–1.62 (m, 4 H), 1.48 (s, 3 H), 146–1.41 (m, 1 H), 1.41 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.6, 138.6, 128.2, 127.3, 127.3, 99.9, 95.6, 73.4, 69.9, 67.9, 64.5, 62.5, 59.9, 57.9, 46.4 (d, J_{CP} = 8.9 Hz), 36.6 (d, J_{CP} = 4.1 Hz), 36.5 (d, J_{CP} = 3.8 Hz), 34.8, 29.5, 28.1, 24.9, 19.6, 16.1 ppm.

Lithium Reduction of 30: Lithium (20 mg, 3.3 mmol, 24 equiv.) was added at 0 °C to ethylamine (ca. 25 mL) freshly distilled from lithium. When the lithium was completely dissolved (blue color), a solution of **30** (72 mg, 0.14 mmol) in THF/*t*BuOH (1:1, 3 mL) was added dropwise. The mixture was stirred for 30 min, and the reaction was quenched by the addition of solid NH_4Cl. The ice bath was removed, and the ethylamine was allowed to evaporate. Then water was added (5 mL) and the aqueous layer extracted with EtOAc (3 × 5 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. Analysis of the oily residue (29 mg) by ^1H NMR spectroscopy (400 MHz, $CDCl_3$) showed that a mixture of compounds had formed. The distinct signals expected for the exocyclic methylene protons, present in the spectrum of **31**, were not observed. Instead, a clear doublet in the aliphatic region was observed, which led us to conclude that reduction of the exocyclic methylene group had occurred to the corresponding methyl group.

Diol 32: Pyridine (240 µL) was added to a solution of **21** (130 mg, 0.3 mmol) in *t*BuOH (3.6 mL), and the solution was purged with argon for 20 min. Then a solution of OsO_4 (2.75 mL, 4 % in H_2O, 0.45 mmol, 1.5 equiv.) was added, and the mixture was warmed to 40 °C. The mixture was stirred for 2.5 h and was quenched by the addition of a 20 % aqueous solution of $NaHSO_3$ (5 mL). The mixture was stirred at room temperature for 1 h. Then the mixture was extracted with EtOAc (5 × 20 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc, 1:3) to give diol **32** (140 mg, 98 %) as a colorless oil. $[\alpha]_D^{22}$ = +15.2 (*c* = 1.0, $CHCl_3$); R_f = 0.34 (petroleum ether 40–60/EtOAc, 1:3). IR (neat): $\tilde{\nu}$ = 3470, 2946, 2866, 1770, 1715 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 7.6 Hz, 2 H), 7.56 (t, *J* = 7.2 Hz, 1 H), 7.46–7.30 (m, 7 H), 5.53 (br. s, 1 H), 4.93 (d, *J* = 4.4 Hz, 1 H), 4.59–4.47 (m, 3 H), 3.89–3.82 (m, 2 H), 3.76 (d, *J* = 11.2 Hz, 1 H), 3.67 (d, *J* = 11.2 Hz, 1 H), 3.29 (d, *J* = 6.4 Hz, 1 H), 2.86 (dd, *J* = 11.6, 4.4 Hz, 1 H), 2.49 (d, *J* = 14.4 Hz, 1 H), 2.24–2.16 (m, 1 H), 1.92 (dd, *J* = 14.4, 2.0 Hz, 1 H), 1.66–1.42 (m, 3 H), 1.29 (d, *J* = 11.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.3, 165.8, 136.6, 133.1, 129.7 (3 C), 128.7 (2 C), 128.4 (2 C), 128.2, 127.7 (2 C), 81.3, 80.1, 73.9, 67.8, 65.1, 64.0, 62.9, 58.0, 51.3, 38.1, 27.1, 21.0, 16.5 ppm. HRMS (FAB): calcd. for $C_{27}H_{29}O_7$ $[MH]^+$ 465.1913; found 465.1920.

Acetonide 33: Dimethoxypropane (714 µL, 5.8 mmol, 20 equiv.) and a catalytic amount of pyridinium *p*-toluenesulfonate (PPTS) was added to a solution of diol **32** (136 mg, 0.29 mmol) in acetone (17 mL). The mixture was stirred at room temperature for 48 h. Then the reaction mixture was concentrated in vacuo and the residue purified by chromatography (petroleum ether 40–60/EtOAc, 3:1) to give acetonide **33** (145 mg, 99 %) as a colorless oil. $[\alpha]_D^{22}$ = –10.7 (*c* = 1.0, $CHCl_3$); R_f = 0.21 (petroleum ether 40–60/EtOAc, 3:1). IR (neat): $\tilde{\nu}$ = 2986, 2941, 2868, 1774, 1716 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 6.8 Hz, 2 H), 7.57 (t, *J* = 7.6 Hz, 1 H), 7.46 (t, *J* = 8.0 Hz, 2 H), 7.39–7.29 (m, 5 H), 5.51 (br. s, 1 H), 4.89 (d, *J* = 4.4 Hz, 1 H), 4.59 (d, *J* = 9.2 Hz, 1 H), 4.55 (d, *J* = 12.0 Hz, 1 H), 4.49 (d, *J* = 12.0 Hz, 1 H), 2.22 (d, *J* = 9.2 Hz, 1 H), 3.71 (d, *J* = 10.8 Hz, 1 H), 3.64 (d, *J* = 11.2 Hz, 1 H), 2.69 (dd, *J* = 11.6, 4.4 Hz, 1 H), 2.41 (d, *J* = 14.4 Hz, 1 H), 2.00–1.97 (m, 1 H), 1.75–1.57 (m, 3 H), 1.51–1.46 (m, 2 H), 1.41 (s, 3 H), 1.35 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.4, 165.7, 137.7, 133.1, 129.8 (2 C), 128.4 (2 C), 128.3 (2 C), 127.6, 127.4 (2 C; signal of one aromatic C missing due to overlap), 107.5, 86.8, 79.9, 73.4, 66.5, 64.2, 64.8, 62.6, 58.5, 50.7, 37.1, 28.2, 26.4, 25.8, 20.5, 16.8 ppm. HRMS (FAB): calcd. for $C_{30}H_{33}O_7$ $[MH]^+$ 505.2226; found 505.2221.

Bis(acetonide) 34: A solution of $LiAlH_4$ (430 µL, 1 M solution in THF, 0.43 mmol, 5 equiv.) was diluted with THF (1.7 mL) and cooled to 0 °C. Then a solution of **33** (43 mg, 0.086 mmol) was added. After the addition was complete, the ice bath was removed, and the mixture was stirred at room temperature for 1 h. The reaction was quenched by the addition of a saturated aqueous solution of Na_2SO_4 (1 drop), and the mixture was stirred at room temperature

for 1 h. Then solid Na_2SO_4 was added, and the mixture was filtered through Celite. The filter cake was washed with EtOAc (10 mL), and the filtrate was concentrated in vacuo. The residue was purified by chromatography (EtOAc) to give the expected triol (32 mg, 92 %) as a crystalline solid. M.p. 154–155 °C. $[\alpha]_D^{22}$ = –4.2 (*c* = 0.5, $CHCl_3$); R_f = 0.36 (EtOAc). IR (neat): $\tilde{\nu}$ = 3211 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.29 (m, 5 H), 4.73 (dd, *J* = 7.6, 2.4 Hz, 1 H), 4.59–4.48 (m, 3 H), 4.38 (d, *J* = 9.6 Hz, 1 H), 4.22 (br. s, 1 H), 3.98 (d, *J* = 9.6 Hz, 1 H), 3.57 (d, *J* = 9.6 Hz, 1 H), 3.52 (d, *J* = 12.0 Hz, 1 H), 3.37 (d, *J* = 9.2 Hz, 1 H), 2.27 (dd. *J* = 11.6, 7.2 Hz, 1 H), 2.19–2.11 (m, 2 H), 1.89–1.79 (m, 1 H), 1.71–1.67 (m, 2 H), 1.52–1.49 (m, 1 H), 1.27 (s, 3 H), 1.25 (s, 3 H), 1.29–1.22 (m, 1 H) ppm; signal of 3 OH very broad. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.0, 128.5, 127.9, 127.7, 105.4, 87.7, 74.7, 73.7, 66.4, 66.3, 65.4, 61.3, 59.5, 57.2, 45.0, 37.4, 30.8, 26.2, 25.9, 22.8, 15.1 ppm. HRMS (FAB): calcd. for $C_{23}H_{33}O_6$ $[MH]^+$ 405.227; found 405.2280. A catalytic amount of *p*TsOH was added to a solution of this triol (98 mg, 0.24 mmol) in acetone (9 mL), and the mixture was stirred at room temperature overnight. The reaction was quenched by the addition of Et_3N (1 drop) and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc, 1:1) to give bis(acetonide) **34** (100 mg, 93 %) as a colorless oil. $[\alpha]_D^{22}$ = –16.3 (*c* = 1.0, $CHCl_3$); R_f = 0.41 (petroleum ether 40–60/EtOAc, 1:1). IR (neat): $\tilde{\nu}$ = 3471, 2989, 2936, 2868 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.29 (m, 5 H), 4.58 (d, *J* = 12.0 Hz,1 H), 4.45 (d, *J* = 12.0 Hz, 1 H), 4.49–4.47 (m, 2 H), 4.20 (br. s, 1 H), 4.08 (d, *J* = 9.2 Hz, 1 H), 3.60 (d, *J* = 9.2 Hz, 1 H), 3.49–3.41 (m, 2 H), 3.09 (d, *J* = 9.2 Hz, 1 H), 2.30–2.16 (m, 3 H), 1.84–1.58 (m, 3 H), 1.49–1.47 (m, 4 H), 1.35 (s, 3 H), 1.29 (s, 3 H), 1.28 (s, 3 H), 1.19–1.09 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.0, 128.5, 12709, 127.6, 105.5, 98.9, 87.3, 73.7, 69.4, 66.5, 65.3, 64.4, 60.8, 58.2, 55.1, 45.1, 34.1, 29.3, 28.3, 25.9, 25.5, 22.1, 19.4, 15.6 ppm. HRMS (FAB): calcd. for $C_{26}H_{37}O_6$ $[MH]^+$ 445.2590; found 445.2585.

Tetramethylphosphordiamidate 35: A solution of bis(acetonide) **34** (100 mg, 0.225 mmol) in DME/TMEDA (4:1, 875 µL) was cooled to 0 °C followed by the addition of methyllithium (421 µL, 1.6 M in diethyl ether, 0.675 mmol, 3 equiv.). The mixture was stirred for 30 min, *N*,*N*,*N*′,*N*′-tetramethylphosphordiamidic chloride (165 µL, 1.13 mmol, 5 equiv.) was added, the ice bath was removed, and the mixture was stirred for 2 h. The reaction was quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (1 mL), and the mixture was stirred at room temperature for 1 h. Then the mixture was extracted with EtOAc (5 × 5 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by chromatography (EtOAc with 5 % MeOH) to give tetramethylphosphordiamidate **35** (121 mg, 93 %) as a light-yellow oil. $[\alpha]_D^{22}$ = –21.8 (*c* = 1.0, $CHCl_3$); R_f = 0.2 (EtOAc with 5 % MeOH). IR: $\tilde{\nu}$ = 2933, 976 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.22 (m, 5 H), 4.86 (d, *J* = 11.2 Hz, 1 H), 4.57 (d, *J* = 8.8 Hz, 1 H), 4.48–4.44 (m, 2 H), 4.39 (s, 1 H), 4.36 (d, *J* = 3.6 Hz, 1 H), 4.19 (s, 1 H), 4.01 (dd, *J* = 11.2, 5.2 Hz, 1 H), 3.71 (d, *J* = 10.4 Hz, 1 H), 3.65 (d, *J* = 10.4 Hz, 1 H), 2.63–2.59 (m, 12 H), 2.29 (dd, *J* = 12.0, 8.0 Hz, 1 H), 2.08 (d, *J* = 15.2 Hz, 1 H), 1.94 (dd, *J* = 12.0, 2.0 Hz, 1 H), 1.75–1.68 (m, 3 H), 1.54–1.44 (m, 5 H), 1.33 (s, 3 H), 1.29 (s, 3 H), 1.28 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.4, 128.1, 127.2, 127.1, 105.4, 98.9, 88.0, 73.3, 69.3, 68.6, 67.0, 64.4, 64.3, 64.2, 58.6, 55.2, 43.8 (d, J_{CP} = 9.1 Hz), 36.6 (d, J_{CP} = 4.0 Hz), 36.5 (d, J_{CP} = 3.9 Hz) 34.0, 29.4, 28.0, 25.9, 25.8, 23.8, 19.4, 15.4 ppm. HRMS (FAB): calcd. for $C_{30}H_{48}N_2O_7P$ $[MH]^+$ 579.3199; found 579.3206.

Lithium Reduction of 35: Lithium (27 mg, 4.5 mmol, 90 equiv.) at 0 °C was added to ethylamine (ca. 15 mL) freshly distilled from lithium. When the lithium was completely dissolved (blue color), a solution of **35** (30 mg, 0.05 mmol) in THF/*t*BuOH (1:1, 1.1 mL) was added dropwise. The mixture was stirred for 30 min and the reaction quenched by the addition of solid NH_4Cl. The ice bath was removed, and the ethylamine was allowed to evaporate. Then water was added (5 mL) and the aqueous layer extracted with EtOAc (5 × 5 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by chromatography (PE/EtOAc, 1:2) to provide two chromatographic fractions. The first fraction provided alcohol **36** (4 mg, 20 %), and the second fraction provided diol **37** (12 mg, 67 %) both as colorless oils.

Data for 36: $[\alpha]_D^{22}$ = –8.5 (*c* = 0.41, $CHCl_3$); R_f = 0.44 (PE/EtOAc, 1:2). ^1H NMR (400 MHz, $CDCl_3$): δ = 4.51 (dd, *J* = 7.7, 2.3 Hz, 1 H), 4.42 (d, *J* = 9.1 Hz, 1 H), 4.35 (d, *J* = 9.1 Hz, 1 H), 4.25 (t, *J* = 2.7 Hz, 1 H), 3.82 (d, *J* = 12.0 Hz, 1 H), 3.76 (d, *J* = 12.0 Hz, 1 H), 2.29 (dd, *J* = 12.0, 8.0 Hz, 1 H), 1.93 (dd, *J* = 11.6, 2.4 Hz, 1 H), 1.86–1.53 (m, 5 H), 1.50 (s, 3 H), 1.50–1.45 (m, 1 H), 1.39 (s, 3 H), 1.37 (s, 3 H), 1.34 (s, 3 H), 1.31 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 105.4, 99.0, 88.4, 69.5, 66.8, 64.8, 59.6, 59.4, 53.9, 39.9, 34.0, 30.4, 29.3, 29.0, 26.2, 25.6, 19.8, 19.6, 16.2 ppm. HRMS (FAB): calcd. for $C_{19}H_{31}O_5$ $[MH]^+$ 339.2171; found 339.2189.

Data for 37: M.p. 175–176 °C. $[\alpha]_D^{22}$ = –7.1 (*c* = 1.0, $CHCl_3$); R_f = 0.21 (PE/EtOAc, 1:2). IR (neat): $\tilde{\nu}$ = 3298, 2990, 2937 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.56–4.51 (m, 2 H), 4.34 (d, *J* = 9.2 Hz, 1 H), 4.22 (s, 1 H), 4.10 (d, *J* = 9.2 Hz, 1 H), 3.73 (d, *J* = 11.2 Hz, 1 H), 3.60 (d, *J* = 11.6 Hz, 1 H), 3.54 (d, *J* = 11.2 Hz, 1 H), 3.49 (br. s, 2 H), 2.24–2.23 (m, 2 H), 2.06 (d, *J* = 14.8 Hz, 1 H), 1.77–1.64 (m, 3 H), 1.53–1.48 (m, 4 H), 1.35 (s, 3 H), 1.32 (s, 3 H), 1.28–1.27 (4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 105.5, 99.1, 87.2, 69.5, 66.4, 64.4, 60.8, 59.9, 57.3, 54.9, 44.6, 33.5, 29.4, 25.9, 25.7, 22.5, 19.4, 15.5 ppm. HRMS (FAB): calcd. for $C_{19}H_{31}O_6$ $[MH]^+$ 355.2121; found 355.2119.

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Keywords: Terpenoids · Total synthesis · Asymmetric catalysis · Photolysis · Cycloaddition · Allenes

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