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Total Synthesis of Isoprostanes Derived from Adrenic Acid and EPA

Camille Oger,^[a] Valérie Bultel-Poncé,^[a] Alexandre Guy,^[a] Thierry Durand,^[a] and Jean-Marie Galano*^[a]

Keywords: Biomarkers / Oxidation / Total synthesis / Natural products

Enantiomerically enriched F₂-dihomo-isoprostanes and F₃-isoprostanes have been synthesized. Such compounds are derived from the action of reactive oxygen species on the phospholipid-bound polyunsaturated fatty acids (PUFA), adrenic acid and eicosapentaenoic acid, respectively. Of special interest are the F₂-dihomo-isoprostanes because they could

represent potential biomarkers for myelin damage as its main PUFA constituent is adrenic acid. Our strategy, based on a pivotal enantiomerically enriched intermediate, has allowed access to F₂-dihomo-IsoP and both C5 epimers of 5-F_{3t}-IsoP for the first time.

Introduction

Discovered in 1990 by Morrow and co-workers, isoprostanes (IsoPs) are generated in vivo during the oxidative stress of phospholipid-bound arachidonic acid (AA, C20:4 ω6) by a free-radical-catalyzed mechanism.^[1] Oxidative stress has been implicated in a wide variety of human disorders, for example, diabetes, cardiovascular, and neurodegenerative diseases. Furthermore, IsoPs are commonly used in clinical trials as reliable oxidative stress biomarkers for many diseases and pathologies.^[2] But more than reliable markers, IsoPs are also biologically active.^[3]

In 1998, a novel class of IsoP, named neuroprostane (NeuroP), was discovered independently by two teams.^[4,5] The name of neuroprostane was adopted because of their polyunsaturated fatty acid source. Indeed, NeuroPs are generated from docosahexaenoic acid (DHA, C22:6 ω3), which is among the most abundant fatty acids in both the brain and retina and is essential for their development.^[6] Levels of F₄-NeuroP are 2.1-fold higher in the temporal lobe of Alzheimer's disease (AD) patients than in a control sample^[7] and are four-fold higher than F₂-IsoP levels.^[8] Recently, a high level of F₄-NeuroP in plasma was also found in Rett (RTT) syndrome patients (one order of magnitude higher than the control sample), thus providing a novel RTT marker related to neurological symptoms, severity, mutation type, and clinical presentation.^[9]

At the same time, novel IsoPs derived from eicosapentaenoic acid (EPA, C20:5 ω3) were discovered and named F₃-

IsoP.^[10] In addition, it was found that at least one F₃-IsoP could be generated from F₄-NeuroP by a β-oxidation process.^[11]

The last family of IsoPs to be discovered was from adrenic acid (AdA, C22:4 ω6) peroxidation.^[12] AdA is concentrated in the brain and especially in the myelin within the white matter. VanRollins and co-workers also showed that F₂-dihomo-IsoPs are significantly increased in samples of white matter taken from AD patients. Therefore, F₄-NeuroP and F₂-dihomo-IsoP could represent oxidative stress biomarkers for neuronal oxidative damage.

Having been interested for quite some time in the quantification of oxidative stress, we herein describe the syntheses of the most abundant series of F₂-dihomo-IsoP, *ent-7-epi-7-F_{2t}*-dihomo-IsoP (**1**) and both epimers of 17-F_{2t}-dihomo-IsoP (**2**; Figure 1). We also describe a novel access to both epimers of 5-F_{3t}-IsoP (**3**).

Results and Discussion

We recently described the synthesis of 4-F_{4t}-NeuroP and D₄-labeled 4-F_{4t}-NeuroP by a NiP2 skipped diyne deuteration strategy.^[13] Such complex isoprostanoid syntheses have been made easy by applying our previous approach, which proceeds through an enantiomerically enriched bicyclo[3.3.0]octene keto-epoxide intermediate **4**^[14,15] to give advanced intermediate **5**^[16] (up to 12 g in 10% overall yield from 1,3-COD) ready for the introduction of lateral chains (Scheme 1).

Synthesis of *ent-7-epi-7-F_{2t}*-Dihomo-IsoP (**1**)

The synthesis required the use of unreported β-keto phosphonate **6**, which was prepared in one step by condensation of the lithium salt of dimethyl methylphosphonate

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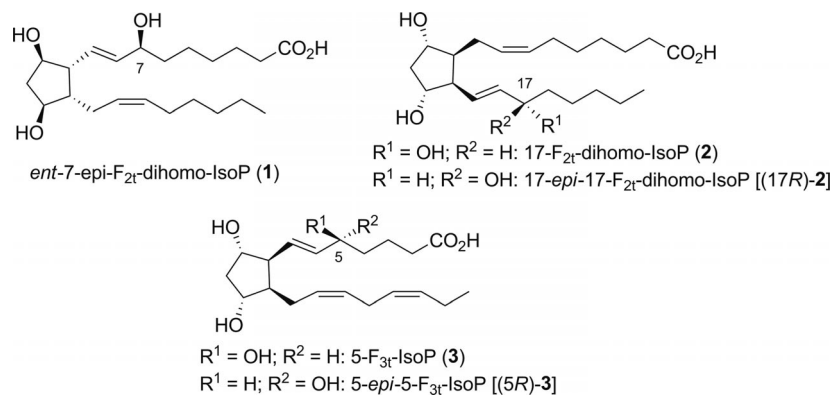
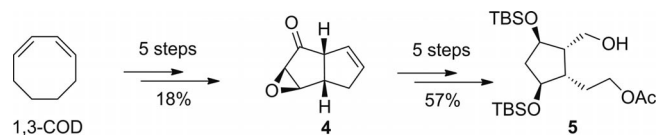
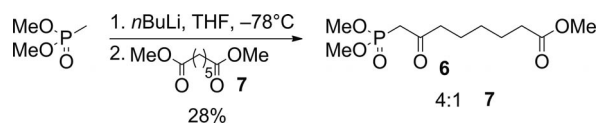


Figure 1. Isoprostanes synthesized in this work.



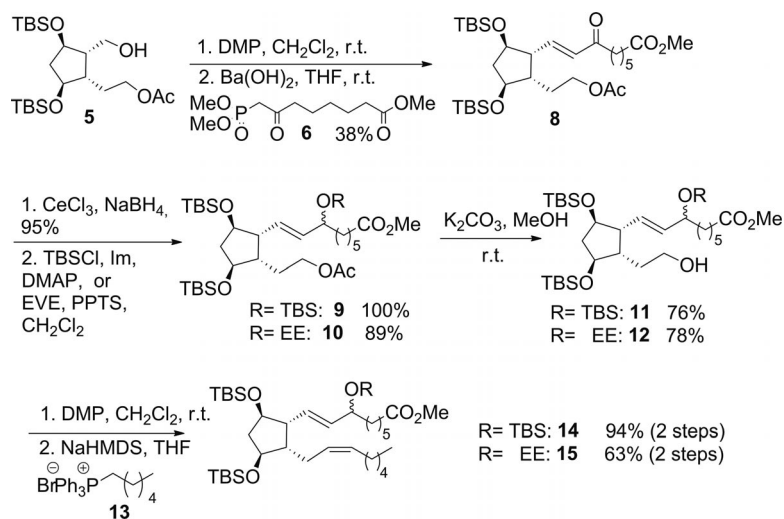
Scheme 1. Synthesis of bicyclo[3.3.0]octene keto-epoxide intermediate **4** and intermediate **5**.

with dimethyl pimelate **7**. Despite considerable effort, a yield of only 28% of a 4:1 mixture of novel β -keto phosphonate **6** and dimethyl pimelate **7** was recovered after purification (Scheme 2).



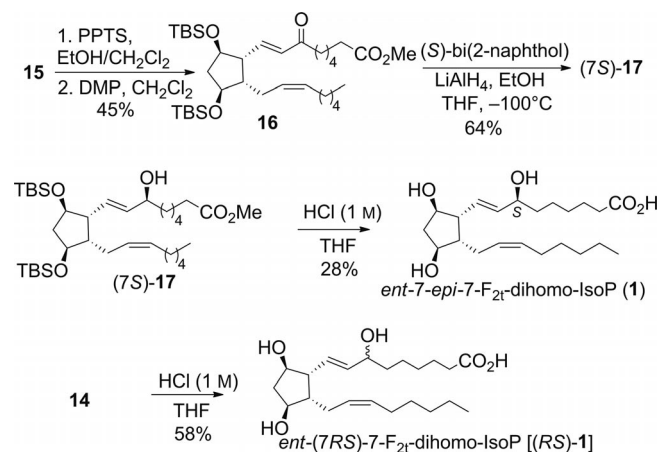
Scheme 2. Synthesis of methyl 8-(dimethoxyphosphoryl)-7-oxooctanoate (**6**).

With phosphonate **6** in hand, alcohol **5** was oxidized to the corresponding aldehyde by using the Dess–Martin periodinane reagent (DMP).^[17] Subsequent Horner–Wadsworth–Emmons (HWE) olefination in the presence of $\text{Ba}(\text{OH})_2$ gave enone **8** in 38% yield (unoptimized conditions, Scheme 3). The poor yield can be explained by the presence of the dimethyl pimelate in the reaction medium. Reduction of the keto group of **8** under Luche conditions^[18] led to a 1:1 epimeric mixture of the corresponding alcohol, which was protected either as the silylated ether (compound **9**) or the ethoxyethyl ether (EE, compound **10**). Saponification of the acetate group of **9** and **10** led to primary alcohols **11** and **12**, respectively. The ω chain was introduced after oxidation followed by Wittig reaction^[19] with the hexylphosphonium bromide **13** in the presence of NaHMDS to give compounds **14** and **15** in excellent to moderate yields (94 and 63%, respectively). At no stage of this procedure could the C7 epimeric mixture be separated by flash column chromatography.



Scheme 3. Lateral chain insertion towards *ent*-7-*epi*-7- F_{21} -dihomo-IsoP (**1**; Im = imidazole, EVE = ethyl vinyl ether, PPTS = pyridinium *p*-toluenesulfonate).

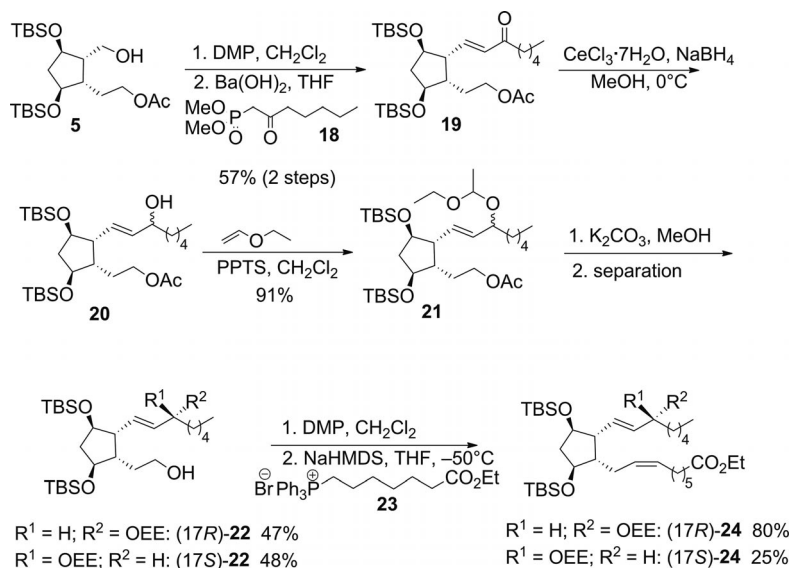
Therefore, a diastereoselective Noyori (*S*)-BINAL-H reduction^[20] was performed on compound **8**, but this gave low diastereoselectivity (approx. 2:1). The more advanced orthogonally protected compound **15** was then used to access enone **16** by a deprotection/oxidation two-step sequence (Scheme 4). (*S*)-BINAL-H reduction of **16** led to the allylic alcohol (*7S*)-**17** in 64% yield and with a good diastereomeric ratio (>95:5). Finally, one-pot silyl ether deprotection and methyl ester hydrolysis under acid conditions gave *ent*-7-*epi*-7-*F*₂₁-dihomo-IsoP (**1**) in 28% yield; *ent*-(*7RS*)-7-*F*₂₁-dihomo-IsoP [(*RS*)-**1**] could also be obtained from compound **14** by similar acidic treatment in 58% yield.



Scheme 4. Diastereoselective reduction and final deprotections in the synthesis of **1**.

Synthesis of 17-*F*₂₁-Dihomo-IsoP (**2**)

Starting from monoacetate **5**, HWE reaction (to the corresponding aldehyde) with commercially available β -keto phosphonate **18** gave enone **19** in 57% yield (Scheme 5).



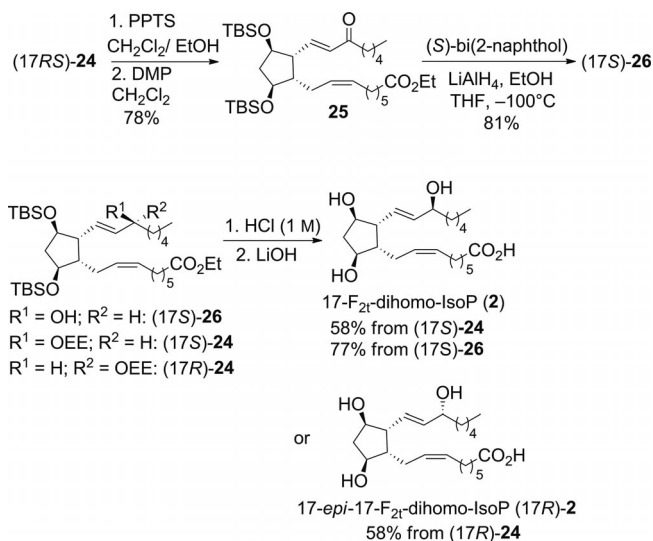
Scheme 5. Lateral chain insertion towards 17-*F*₂₁-dihomo-IsoP (**2**).

Luche reduction gave a 1:1 epimeric mixture of the allylic alcohol **20**, which was subsequently protected as the ethoxyethyl ether **21** in 91% yield over two steps. Acetate saponification led to primary alcohols (*17RS*)-**22** in 88% yield. Chromatographic separation of the two epimers led to (*17S*)-**22** and (*17R*)-**22** in 47 and 48% yields, respectively. The α chain was then introduced after primary alcohol oxidation by Wittig reaction with phosphonium salt **23** and NaHMDS to give compounds (*17S*)-**24** and (*17R*)-**24** in 80 and 25% yields, respectively.

As the first total synthesis of 17-*F*₂₁-dihomo-IsoP, we had to perform a diastereoselective reduction to assess the absolute configuration at C17. We consistently observed a low *dr* (2:1) after (*S*)-BINAL-H reduction to various enone systems with the acetoxyethyl moiety as the second lateral chain, and compound **19** suffered the same fate. Therefore, racemic **24** was converted into enone **25** in a two-step sequence in good yield. (*S*)-BINAL-H reduction afforded (*17S*)-**26** in 81% yield and with a good diastereomeric ratio (>95:5; Scheme 6). Finally, acid cleavage of the protecting groups followed by ethyl ester saponification of (*17S*)-**26** afforded 17-*F*₂₁-dihomo-IsoP (**2**) in 77% yield. Similarly, (*17S*)-**24** and (*17R*)-**24** gave access to 17-*F*₂₁-dihomo-IsoP (**2**) and 17-*epi*-17-*F*₂₁-dihomo-IsoP [(*17R*)-**2**] in good yields.

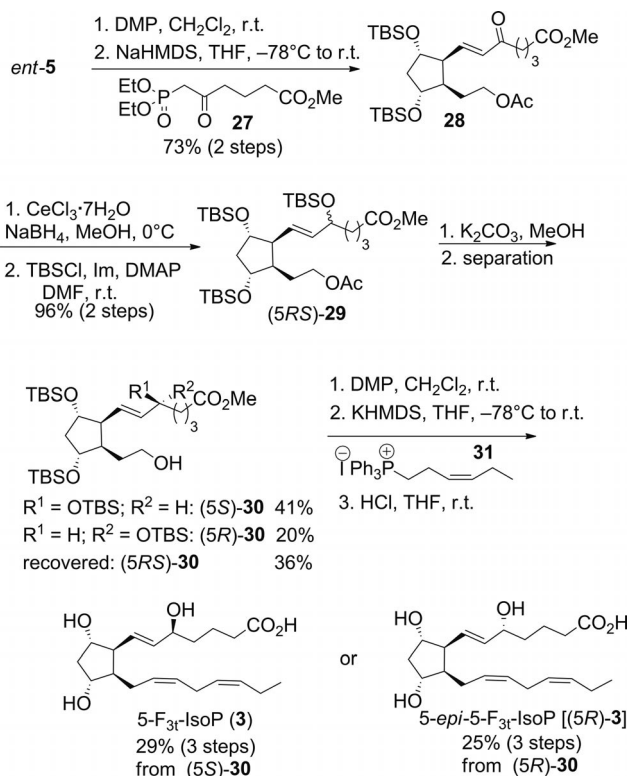
Synthesis of 5-*F*₃₁-IsoP (**3**)

Applying the same strategy, the α chain of 5-*F*₃₁-IsoP was introduced after oxidation of the primary alcohol of *ent*-**5** followed by HWE reaction with methyl 6-(diethoxyphosphoryl)-5-oxohexanoate (**27**)^[21] and NaHMDS as base to afford compound **28** (Scheme 7). Luche reduction and protection of the resulting allylic alcohol as a *tert*-butyldimethylsilyl ether furnished the protected compound (*5RS*)-**29** in excellent yield over two steps. Saponification of the acetate functionality allowed separation of the epimeric mixture, and pure epimers (*5R*)-**30** and (*5S*)-**30** were reco-



Scheme 6. Diastereoselective reduction and final deprotections to yield 17-*F*_{2*t*}-dihomo-IsoP (**2**) and its epimer.

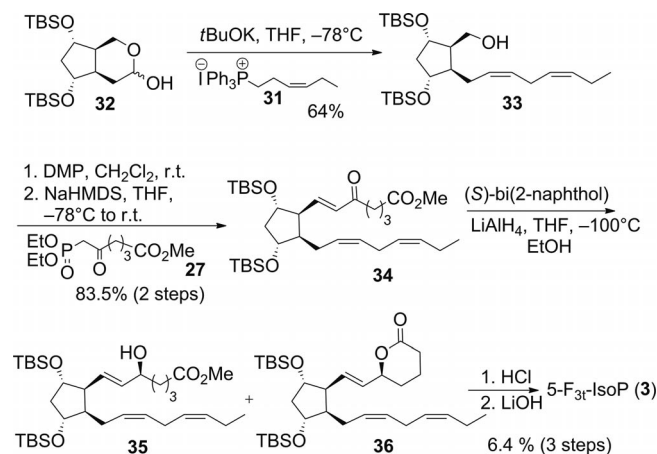
vered. The ω chain was inserted after oxidation of the primary alcohol functionality by Wittig reaction using phosphonium salt **31** and KHMDS in THF. Finally, one-pot silyl ether cleavage and methyl ester hydrolysis under acidic conditions led to 5-*F*_{3*t*}-IsoP (**3**) and 5-*epi*-5-*F*_{3*t*}-IsoP [(5*R*)-**3**] in 17 and 3.5% overall yields, respectively.



Scheme 7. Synthesis of 5-*F*_{3*t*}-IsoP (**3**) and its C5 epimer (5*R*)-**3**.

To confirm the configuration of the stereogenic center at C5, and because the 5-*F*_{3*t*}-IsoP previously synthesized has no reported ¹³C NMR data nor optical rotation value,^[11]

we had to perform a diastereoselective reduction to access the corresponding diastereomerically enriched allylic alcohol. As (*S*)-BINAL-H reduction of the enone **28** gave poor diastereoselectivity, we had to resort to the previously described lactol **32**^[14] to complete the diastereoselective synthesis of 5-*F*_{3*t*}-IsoP (**3**; Scheme 8).



Scheme 8. Synthesis of 5-*F*_{3*t*}-IsoP (**3**) by using (*S*)-BINAL-H reagent.

By applying a strategy similar to that of Rokach and co-workers,^[11] the upper chain was introduced into lactol **32** by Wittig reaction with phosphonium salt **31** and *t*BuOK in THF to give diene **33** in 64% yield. The α chain was subsequently attached by DMP oxidation followed by HWE reaction with β-keto phosphonate **27** and NaHMDS to give **34** in excellent yield. Diastereoselective reduction of the enone **34** with the Noyori (*S*)-BINAL-H reagent led to allylic alcohol **35** and lactone **36** in a 1:1 mixture with a good diastereomeric ratio (>95%). Hydrolysis of the terminal ester and TBS deprotection was achieved under acidic conditions. A poor overall yield was observed for this stereoselective synthesis of 5-*F*_{3*t*}-IsoP (**3**). The unequivocal determination of the C5 stereocenter was possible by comparison of the ¹³C NMR spectra.

Conclusions

We have described the enantioselective synthesis of the two most abundant cyclic metabolites of the free-radical-catalyzed peroxidation of adrenic acid, *ent*-7-*epi*-7-*F*_{2*t*}-dihomo-IsoP and 17-*F*_{2*t*}-dihomo-IsoP. These metabolites are of high interest in lipidomics as dihomo-IsoPs may represent very specific lipidic oxidative stress biomarkers of the brain's white matter. Validation of this hypothesis is underway in our laboratory and will be reported in due course.

Experimental Section

General: All reactions requiring anhydrous conditions were conducted in oven-dried glassware with magnetic stirring under nitrogen unless mentioned otherwise. Syringes and needles for the transfer of reagents were dried at 120 °C and allowed to cool in a desiccant.

cator over CaCl₂ before use. THF and Et₂O were redistilled from sodium diphenylketyl and CH₂Cl₂ from CaH₂. Other solvents and reagents were used as obtained from the supplier unless otherwise noted. Reactions were monitored by TLC using plates precoated with silica gel 60 (Merck). Reaction components were visualized by using a 254 nm UV lamp, treatment with acidic *p*-anisaldehyde stain followed by gentle heating. Organic layers were dried with MgSO₄ unless otherwise stated. Column chromatography was performed by using silica gel 40–63 μm, whereas spherical silica gel 30 μm was used for flash column chromatography. Concentrations *c* reported for the optical rotation data are given in g/100 mL. Infrared data are reported as wavenumbers (cm⁻¹). ES-MS data were obtained by ionization methods. ¹H NMR spectra were obtained at 300 or 400 MHz. The spectra were recorded in CDCl₃ (internal reference at δ = 7.26 ppm) unless otherwise noted. The ¹H NMR spectra are reported as follows: chemical shift in ppm [multiplicity, coupling constant(s) *J* in Hz, relative integral]. The multiplicities are defined as follows: br. = broad, m = multiplet, AB = AB system, s = singlet, d = doublet, t = triplet, or combinations thereof. Selected ¹³C NMR spectra were recorded by using a *J*-modulated sequence, and the central peak of the CDCl₃ triplet was used as the internal reference (δ = 77.16 ppm) and MeOD (fixed at δ = 49.0 ppm). The NMR spectra were assigned by homonuclear (¹H–¹H) and heteronuclear (¹H–¹³C) correlation spectroscopy (COSY45, HMQC, HMBC) and are reported as follows: CH₃, CH₂, CH, and Cq (for quaternary carbon atoms).

Synthesis of Methyl 8-(Dimethoxyphosphoryl)-7-oxooctanoate (6): *n*BuLi (2.4 mL, 2.5 M/hexanes, 6.0 mmol) was added dropwise to a solution of dimethyl methylphosphonate (600 μL, 5.62 mmol) in THF (50 mL) at –78 °C. After 30 min, the reaction mixture was added through a cannula to dimethyl pimelate **7** (1.5 mL, 8.3 mmol) in THF (50 mL) at –90 °C. After 3.5 h at –90 °C, AcOH (1.0 mL) and Et₂O (100 mL) were added, and the mixture was warmed to room temp. The mixture was extracted with CH₂Cl₂ (3 × 40 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure, and the residue was distilled under reduced pressure (0.5 mbar, approx. 120 °C). The crude from the distillation was purified by column chromatography (95:5 CH₂Cl₂/MeOH) to afford 440 mg of the β-keto phosphonate **6** as an 8:2 mixture with the dimethyl pimelate **7** (28%). ¹H NMR (300 MHz, CDCl₃): δ = 3.79 (d, *J* = 11.2 Hz, 6 H), 3.66 (s, 3 H), 3.09 (d, *J*_{PH} = 22.0 Hz, 2 H), 2.50–2.70 (m, 2 H), 2.20–2.40 (m, 2 H), 1.50–1.80 (m, 4 H), 1.20–1.50 (m, 2 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 201.0 (1 C, Cq), 174.5 (1 C, Cq), 173.1 (1 C, Cq), 52.3 (1 C, CH₃), 50.6 (2 C, CH₃), 42.9 (1 C, CH₂), 41.1 (1 C, CH₂), 39.4 (1 C, CH₂), 33.0 (1 C, CH₂), 27.6 (1 C, CH₂), 23.9 (1 C, CH₂), 22.3 (1 C, CH₂) ppm. ³¹P NMR (120 MHz, CDCl₃): δ = 23.4 ppm.

Methyl (E)-9-[(1*S*,2*R*,3*R*,5*S*)-2-(2-Acetoxyethyl)-3,5-bis(*tert*-butyldimethylsilyloxy)cyclopentyl]-7-oxonon-8-enoate (8): A Dess–Martin periodinane solution (1.5 mL of a 0.47 M solution in CH₂Cl₂, 0.70 mmol) was added dropwise to a solution of alcohol **5** (225 mg, 0.51 mmol) in CH₂Cl₂ (10 mL). After completion (TLC), 10% aq. NaHCO₃/Na₂S₂O₃ (1:1, 30 mL) was added. After stirring for 1.5 h, the mixture was extracted with CH₂Cl₂ (3 × 30 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The material was directly used in the next step without further purification. The β-keto phosphonate **6** (440 mg, 1.11 mmol) was added dropwise to a suspension of Ba(OH)₂ (70 mg, 0.41 mmol) in THF (10 mL). After 1 h, the aldehyde in THF (20 mL) was added through a cannula to the reaction mixture, which was stirred overnight. Then the reaction was quenched with H₂O (25 mL) and Et₂O (25 mL). The mix-

ture was extracted with Et₂O (3 × 30 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (7:3 pentane/Et₂O) to afford 115 mg of the enone **8** as a colorless oil (38% over two steps). *R*_f = 0.55 (5:5 cyclohexane/Et₂O). [*a*]_D²⁰ = +20.6 (*c* = 1, CHCl₃). IR: ν̄ = 2955, 2927, 2856, 1736, 1697, 1674, 1626, 1463, 1252, 1071 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 6.50–6.70 (m, 1 H), 6.10 (d, *J* = 15.6 Hz, 1 H), 3.80–4.20 (m, 4 H), 3.64 (s, 3 H), 2.65–2.85 (m, 1 H), 2.50 (t, *J* = 6.9 Hz, 2 H), 2.40 (m, 4 H), 2.00 (s, 3 H), 1.40–1.75 (m, 7 H), 1.20–1.40 (m, 2 H), 0.75–0.90 (m, 18 H), –0.01 (d, *J* = 13.0 Hz, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 199.7 (1 C, Cq), 174.1 (1 C, Cq), 171.0 (1 C, Cq), 144.5 (1 C, CH), 131.5 (1 C, CH), 76.1 (1 C, CH), 75.4 (1 C, CH), 63.2 (1 C, CH₂), 53.2 (1 C, CH), 51.5 (1 C, CH₃), 46.6 (1 C, CH), 44.3 (1 C, CH₂), 40.9 (1 C, CH₂), 33.9 (1 C, CH₂), 28.8 (1 C, CH₂), 28.0 (1 C, CH₂), 25.9 (6 C, CH₃), 24.8 (1 C, CH₂), 23.7 (1 C, CH₂), 21.0 (1 C, CH₃), 18.0 (2 C, Cq), –4.2 (1 C, CH₃), –4.6 (2 C, CH₃), –4.7 (1 C, CH₃) ppm. MS (ESI⁺): *m/z* = 541.4 [M + H – OAc]⁺, 409.3 [M – OTBS – OAc]⁺. HRMS (ESI⁺): calcd. for C₂₉H₅₇O₅Si₂ [M + H – OAc]⁺ 541.3745; found 541.3744.

Methyl (E)-9-[(1*S*,2*R*,3*R*,5*S*)-2-(2-Acetoxyethyl)-3,5-bis(*tert*-butyldimethylsilyloxy)cyclopentyl]-7-(*tert*-butyldimethylsilyloxy)non-8-enoate (9): CeCl₃·7H₂O (71 mg, 0.191 mmol) was added to a solution of the enone **8** (115 mg, 0.19 mmol) in MeOH (12 mL). The mixture was cooled to 0 °C and NaBH₄ was added (6.0 mg, 0.159 mmol). After 10 min, the reaction was quenched with a Et₂O/H₂O mixture (1:1, 20 mL). The reaction mixture was extracted with Et₂O (3 × 20 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (7:3 pentane/Et₂O) to afford 109 mg of the allylic alcohol as a colorless oil (95%). *R*_f = 0.37 (5:5 cyclohexane/Et₂O). [*a*]_D²⁰ = +23.9 (*c* = 1, CHCl₃). IR: ν̄ = 3508, 2953, 2930, 1732, 1250, 1056 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 5.45–5.55 (m, 1 H), 5.25–5.45 (m, 1 H), 4.15–4.40 (m, 0.5 H), 3.90–4.15 (m, 2 H), 3.70–3.90 (m, 2.5 H), 3.64 (s, 3 H), 2.40–2.65 (m, 1 H), 2.15–2.40 (m, 3 H), 2.05–2.20 (m, 1 H), 2.00 (s, 3 H), 1.00–1.90 (m, 10 H), 0.80–0.90 (m, 18 H), –0.10–0.10 (m, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 174.2 (1 C, Cq), 171.3 (1 C, Cq), 136.1 (1 C, CH), 129.8 (1 C, CH), 76.4 (1 C, CH), 72.8 (1 C, CH), 72.4 (1 C, CH), 63.5 (1 C, CH₂), 52.9 (1 C, CH), 51.5 (1 C, CH₃), 45.8 (1 C, CH), 44.3 (1 C, CH₂), 37.0 (1 C, CH₂), 34.0 (1 C, CH₂), 29.2 (1 C, CH₂), 28.0 (1 C, CH₂), 25.9 (6 C, CH₃), 25.2 (1 C, CH₂), 25.0 (1 C, CH₂), 21.1 (1 C, CH₃), 18.1 (2 C, Cq), –4.2 (1 C, CH₃), –4.5 (1 C, CH₃), –4.6 (1 C, CH₃), –4.7 (1 C, CH₃) ppm. MS (ESI⁺): *m/z* = 583.3 [M + H – H₂O]⁺, 451.2 [M + H – H₂O – OTBS]⁺, 319.1 [M + H – H₂O – 2 OTBS]⁺. HRMS (ESI⁺): calcd. for C₃₁H₅₉O₆Si₂ [M + H – H₂O]⁺ 583.3850; found 583.3849. Imidazole (50 mg, 0.73 mmol), DMAP (10 mg, 0.076 mmol), and TBSCl (55 mg, 0.37 mmol) were successively added to a solution of the allylic alcohol (147 mg, 0.25 mmol) in DMF (18 mL). After stirring overnight, the reaction was quenched with H₂O (40 mL) and Et₂O (30 mL). The mixture was extracted with Et₂O (3 × 15 mL), and the combined organic layers were washed with H₂O (3 × 15 mL) and brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (9:1 pentane/Et₂O) to afford 206 mg of **9** as a colorless oil (quantitative yield). *R*_f = 0.47 (8:2 cyclohexane/Et₂O). [*a*]_D²⁰ = +24.0 (*c* = 1, CHCl₃). IR: ν̄ = 2954, 2930, 1732, 1472, 1463, 1251, 1057 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 5.35–5.50 (m, 1 H), 5.20–5.35 (m, 1 H), 3.95–4.15 (m, 3 H), 3.75–3.90 (m, 2 H), 3.66 (s, 3 H), 2.40–2.60 (m, 1 H), 2.40 (m, 4 H), 2.02 (s, 3 H), 1.20–1.80 (m, 11 H), 0.75–1.00

(m, 27 H), -0.10–0.10 (m, 18 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 174.3 (1 C, Cq), 171.2 (1 C, Cq), 136.3 (1 C, CH), 127.5 (1 C, CH), 127.2 (1 C, CH), 76.3 (1 C, CH), 76.7 (1 C, CH), 73.1 (1 C, CH), 63.5 (1 C, CH_2), 53.0 (1 C, CH), 52.8 (1 C, CH), 51.5 (1 C, CH_3), 45.6 (1 C, CH), 44.3 (1 C, CH_2), 38.4 (1 C, CH_2), 34.2 (1 C, CH_2), 29.3 (1 C, CH_2), 27.8 (1 C, CH_2), 25.8 (9 C, CH_3), 25.0 (2 C, CH_2), 21.0 (1 C, CH_3), 18.3 (1 C, Cq), 18.1 (2 C, Cq), -4.2 (1 C, CH_3), -4.3 (1 C, CH_3), -4.5 (1 C, CH_3), -4.6 (2 C, CH_3), -4.7 (1 C, CH_3) ppm. MS (ESI $^+$): m/z = 715.5 [M + H] $^+$, 583.4 [M + H - OTBS] $^+$, 451.3 [M + H - 2 OTBS] $^+$, 319.2 [M + H - 3 OTBS] $^+$. HRMS (ESI $^+$): calcd. for $\text{C}_{37}\text{H}_{75}\text{O}_7\text{Si}_3$ [M + H] $^+$ 715.4821; found 715.4827.

Methyl (E)-9-[(1S,2R,3R,5S)-2-(2-Acetoxyethyl)-3,5-bis(tert-butyl-dimethylsilyloxy)cyclopentyl]-7-(1-ethoxyethyl)non-8-enoate (10): Ethyl vinyl ether (2 mL, 20.9 mmol) and PPTS (10 mg, 0.040 mmol) were successively added to a solution of the allylic alcohol derived from enone **8** (109 mg, 0.18 mmol) in CH_2Cl_2 (7 mL) at 0 °C. The reaction mixture was warmed to room temp. overnight. Then 2 mL of a saturated aqueous solution of NaHCO_3 was added, and the reaction mixture was extracted with CH_2Cl_2 (3 \times 20 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (1% Et_3N deactivated SiO_2 , 8:2 pentane/ Et_2O) to afford 109 mg of **10** as a colorless oil (89%). R_f = 0.65 (5:5 cyclohexane/ Et_2O). $[\alpha]_D^{20}$ = +25.2 (c = 1, CHCl_3). IR: $\tilde{\nu}$ = 2956, 2930, 2858, 1743, 1249, 1056 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 5.20–5.60 (m, 2 H), 5.55–5.70 (m, 1 H), 3.75–4.20 (m, 4 H), 3.66 (s, 3 H), 3.25–3.60 (m, 2 H), 2.45–2.60 (m, 1 H), 2.40 (m, 4 H), 2.02 (s, 3 H), 1.50–1.85 (m, 4 H), 1.00–1.45 (m, 14 H), 0.70–1.00 (m, 18 H), -0.10–0.10 (m, 12 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 174.2 (1 C, Cq), 171.0 (1 C, Cq), 134.3 (1 C, CH, diast.), 133.6 (1 C, CH, diast.), 133.5 (1 C, CH, diast.), 131.5 (1 C, CH, diast.), 131.3 (1 C, CH, diast.), 129.9 (1 C, CH, diast.), 129.7 (1 C, CH, diast.), 98.7 (1 C, CH, diast.), 96.8 (1 C, CH, diast.), 96.7 (1 C, CH, diast.), 76.5 (3 C, CH), 63.5 (1 C, CH_2), 61.3 (1 C, CH_2), 59.0 (1 C, CH_2), 53.1 (1 C, CH), 51.5 (1 C, CH_3), 45.7 (1 C, CH), 44.3 (1 C, CH_2), 35.9 (1 C, CH_2), 34.1 (1 C, CH_2), 29.2 (1 C, CH_2), 28.0 (1 C, CH_2), 25.9 (6 C, CH_3), 25.3 (1 C, CH_2), 20.0–21.0 (2 C, CH_3 , diast.), 18.0 (2 C, Cq), 15.5 (1 C, CH_3), -4.2 (1 C, CH_3), -4.6 (2 C, CH_3), -4.7 (1 C, CH_3) ppm. MS (ESI $^+$): m/z = 583.4 [M + H - $\text{C}_4\text{H}_9\text{O}_2$] $^+$, 451.3 [M + H - $\text{C}_4\text{H}_9\text{O}_2$ - OTBS] $^+$, 319.2 [M + H - $\text{C}_4\text{H}_9\text{O}_2$ - 2 OTBS] $^+$, 259.2 [M + H - $\text{C}_4\text{H}_9\text{O}_2$ - 2 OTBS - OAc] $^+$. HRMS (ESI $^+$): calcd. for $\text{C}_{31}\text{H}_{59}\text{O}_6\text{Si}_2$ [M + H - $\text{C}_4\text{H}_9\text{O}_2$] $^+$ 583.3850; found 583.3844.

Methyl (E)-9-[(1S,2R,3R,5S)-3,5-Bis(tert-butyl-dimethylsilyloxy)-2-(2-hydroxyethyl)cyclopentyl]-7-(tert-butyl-dimethylsilyloxy)non-8-enoate (11): K_2CO_3 (110 mg, 0.8 mmol) was added to a solution of **9** (144 mg, 0.20 mmol) in MeOH (15 mL). After 2 h, a mixture of $\text{Et}_2\text{O}/\text{H}_2\text{O}$ (1:1, 20 mL) was added and stirred for 15 min. The reaction mixture was extracted with pentane/ Et_2O (1:1, 3 \times 20 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure and the residue purified by column chromatography (7:3 pentane/ Et_2O) to afford 125 mg of **11** as a colorless oil. R_f = 0.42 (5:5 cyclohexane/ Et_2O). $[\alpha]_D^{20}$ = +18.5 (c = 1, CHCl_3). IR: $\tilde{\nu}$ = 3462, 2953, 2929, 2857, 1741, 1252, 1055 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 5.15–5.60 (m, 2 H), 3.95–4.15 (m, 1 H), 3.75–3.95 (m, 2 H), 3.35–3.75 (m, 5 H), 2.45–2.65 (m, 1 H), 2.15–2.45 (m, 4 H), 2.00–2.15 (m, 1 H), 1.50–1.70 (m, 4 H), 1.20–1.50 (m, 6 H), 0.70–1.00 (m, 27 H), -0.2–0.2 (m, 18 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 174.2 (1 C, Cq), 136.0 (1 C, CH), 127.7 (1 C, CH), 77.1 (1 C, CH), 76.3 (1 C, CH), 73.0 (1 C, CH), 61.9 (1 C, CH_2), 54.0 (1 C, CH),

53.7 (1 C, CH), 51.4 (1 C, CH_3), 46.0 (1 C, CH), 44.4 (1 C, CH_2), 38.3 (1 C, CH_2), 34.0 (1 C, CH_2), 32.5 (1 C, CH_2), 30.4 (1 C, CH_2), 29.1 (1 C, CH_2), 25.8 (9 C, CH_3), 24.9 (1 C, CH_2), 18.2 (1 C, Cq), 18.0 (2 C, Cq), -4.1 (1 C, CH_3), -4.3 (1 C, CH_3), -4.4 (1 C, CH_3), -4.6 (1 C, CH_3), -4.7 (2 C, CH_3) ppm. MS (ESI $^+$): m/z = 673.5 [M + H] $^+$, 541.4 [M + H - OTBS] $^+$, 409.3 [M + H - 2 OTBS] $^+$, 277.2 [M + H - 3 OTBS] $^+$. HRMS (ESI $^+$): calcd. for $\text{C}_{35}\text{H}_{73}\text{O}_6\text{Si}_3$ [M + H] $^+$ 673.4715; found 673.4720.

Methyl (E)-9-[(1S,2R,3R,5S)-3,5-Bis(tert-butyl-dimethylsilyloxy)-2-(2-hydroxyethyl)cyclopentyl]-7-(1-ethoxyethoxy)non-8-enoate (12): K_2CO_3 (78 mg, 0.56 mmol) was added to a solution of **10** (109 mg, 0.16 mmol) in MeOH (11 mL). After 2 h, $\text{Et}_2\text{O}/\text{H}_2\text{O}$ (1:1, 20 mL) was added, and the mixture was stirred for 15 min. The mixture was then extracted with pentane/ Et_2O (3 \times 20 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (1% Et_3N deactivated SiO_2 , 7:3 pentane/ Et_2O) to afford 80 mg of **12** as a colorless oil (78%). R_f = 0.36 (5:5 cyclohexane/ Et_2O). $[\alpha]_D^{20}$ = +18.3 (c = 1, CHCl_3). IR: $\tilde{\nu}$ = 3484, 2930, 2857, 1739, 1253, 1055 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 5.15–5.60 (m, 2 H), 5.55–5.70 (m, 1 H), 3.75–4.00 (m, 3 H), 3.30–3.75 (m, 7 H), 2.45–2.60 (m, 1 H), 2.00–2.45 (m, 5 H), 1.00–1.85 (m, 16 H), 0.70–1.00 (m, 18 H), -0.10–0.10 (m, 12 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 174.3 (1 C, Cq), 134.2 (1 C, CH, diast.), 133.3 (1 C, CH, diast.), 131.9 (1 C, CH, diast.), 130.5 (1 C, CH, diast.), 130.2 (1 C, CH, diast.), 98.5 (1 C, CH, diast.), 96.8 (1 C, CH, diast.), 96.7 (1 C, CH, diast.), 76.2–77.0 (3 C, CH), 61.8 (1 C, CH_2), 61.1 (1 C, CH_2), 59.0 (1 C, CH_2), 54.0 (1 C, CH), 51.5 (1 C, CH_3), 46.1 (1 C, CH), 44.9 (1 C, CH_2), 35.2 (1 C, CH_2), 34.9 (1 C, CH_2), 34.1 (1 C, CH_2), 29.2 (1 C, CH_2), 26.0 (6 C, CH_3), 25.3 (1 C, CH_2), 20.5 (1 C, CH_3), 18.1 (2 C, Cq), 15.5 (1 C, CH_3), -4.0 (2 C, CH_3), -4.5 (2 C, CH_3) ppm. MS (ESI $^+$): m/z = 541.4 [M + H - $\text{C}_4\text{H}_9\text{O}_2$] $^+$, 409.3 [M + H - $\text{C}_4\text{H}_9\text{O}_2$ - OTBS] $^+$, 277.2 [M + H - $\text{C}_4\text{H}_9\text{O}_2$ - 2 OTBS] $^+$. HRMS (ESI $^+$): calcd. for $\text{C}_{29}\text{H}_{57}\text{O}_5\text{Si}_2$ [M + H - $\text{C}_4\text{H}_9\text{O}_2$] $^+$ 541.3745; found 541.3738.

Methyl (E)-9-[(1S,2R,3R,5S)-3,5-Bis(tert-butyl-dimethylsilyloxy)-2-[(Z)-oct-2-enyl]cyclopentyl]-7-(tert-butyl-dimethylsilyloxy)non-8-enoate (14): A Dess–Martin periodinane solution (600 μL of a 0.47 M solution in CH_2Cl_2 , 0.28 mmol) was added to a solution of **11** (110 mg, 0.16 mmol) in CH_2Cl_2 (11 mL). After 2 h and completion of the reaction (TLC), a 10% aq. $\text{NaHCO}_3/\text{Na}_2\text{S}_2\text{O}_3$ solution (1:1, 20 mL) was added. After stirring for 1.5 h, the mixture was extracted with CH_2Cl_2 (3 \times 10 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The material was directly used in the next step without further purification. NaHMDS (600 μL , 2 M in toluene, 1.2 mmol) was added dropwise to a suspension of dried phosphonium salt **13** (560 mg, 1.31 mmol) in degassed THF (10 mL) at 0 °C. After 1 h at 0 °C, the aldehyde in degassed THF (10 mL) was added by cannula to the reaction mixture. The reaction mixture was warmed to room temp. overnight. After 1 h, the reaction was quenched with a saturated aqueous solution of NH_4Cl (10 mL) and the mixture allowed to reach room temp. The mixture was extracted with Et_2O (3 \times 20 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (95:5 pentane/ Et_2O) to afford 114 mg of **14** as a colorless oil (94% over two steps). R_f = 0.79 (8:2 cyclohexane/ Et_2O). $[\alpha]_D^{20}$ = +16.2 (c = 1, CHCl_3). IR: $\tilde{\nu}$ = 2954, 2928, 2856, 1743, 1251, 1067 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 5.25–5.60 (m, 4 H), 4.00–4.15 (m, 1 H), 3.85–4.00 (m, 1 H), 3.70–3.85 (m, 1 H), 3.66 (s, 3 H), 2.50–2.70 (m, 1 H), 2.20–2.40 (m, 3 H), 1.85–2.15 (m, 4 H), 1.15–1.70 (m, 17 H), 0.70–1.00 (m, 30 H), -0.10–0.10 (m,

18 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 174.3 (1 C, Cq), 135.8 (1 C, CH), 130.6 (1 C, CH), 128.7 (1 C, CH), 128.0 (1 C, CH), 76.3 (2 C, CH), 73.3 (1 C, CH), 52.5 (1 C, CH), 51.5 (1 C, CH_3), 50.3 (1 C, CH), 44.5 (1 C, CH_2), 38.5 (1 C, CH_2), 34.2 (1 C, CH_2), 31.7 (1 C, CH_2), 29.5 (1 C, CH_2), 29.3 (1 C, CH_2), 27.5 (2 C, CH_2), 26.3 (1 C, CH_2), 26.0 (9 C, CH_3), 25.1 (1 C, CH_2), 22.7 (1 C, CH_2), 18.4 (2 C, Cq), 18.2 (1 C, Cq), 14.2 (1 C, CH_3), -4.1 (1 C, CH_3), -4.3 (1 C, CH_3), -4.4 (2 C, CH_3), -4.6 (2 C, Cq) ppm.

Methyl (*E*)-9-((1*S*,2*R*,3*R*,5*S*)-3,5-Bis(*tert*-butyldimethylsilyloxy)-2-[(*Z*)-oct-2-enyl]cyclopentyl)-7-(1-ethoxyethoxy)non-8-enoate (15): A Dess–Martin periodinane solution (600 μL of a 0.47 M solution in CH_2Cl_2 , 0.28 mmol) was added to a solution of alcohol **12** (80 mg, 0.13 mmol) in CH_2Cl_2 (8 mL). After 2 h, $\text{Na}_2\text{S}_2\text{O}_3/\text{NaHCO}_3$ (20 mL, 1:1, v/v, 10%) was added, and the mixture was stirred for 1 h. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3×15 mL). The organic layers were washed with brine (15 mL), dried with MgSO_4 , filtered, and the solvent was removed under reduced pressure. The resulting aldehyde was used directly in the next step without further purification. NaHMDS (330 μL , 2 M in toluene, 0.66 mmol) was added dropwise to a suspension of dried phosphonium salt **13** (296 mg, 0.69 mmol) in degassed THF (5 mL) at 0 °C. After 1 h at 0 °C, the aldehyde in degassed THF (4 mL) was added through a cannula to the ylide. The reaction mixture was warmed to room temp. overnight. Then the reaction was quenched with a saturated aqueous solution of NH_4Cl (10 mL), and the mixture was extracted with Et_2O (3×20 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (1% Et_3N deactivated SiO_2 , 95:5 pentane/ Et_2O) to afford 56 mg of diene **15** as a colorless oil (63% over two steps). R_f = 0.55 (8:2 cyclohexane/ Et_2O). $[\alpha]_D^{20}$ = +16.9 (c = 1, CHCl_3). IR: $\tilde{\nu}$ = 2954, 2928, 2857, 1740, 1251, 1059 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 5.15–5.60 (m, 4 H), 5.55–5.70 (m, 1 H), 4.00–4.15 (m, 1 H), 3.90–4.00 (m, 1 H), 3.75–3.90 (m, 1 H), 3.66 (s, 3 H), 3.30–3.65 (m, 2 H), 3.55–3.75 (m, 1 H), 2.15–2.45 (m, 3 H), 1.75–2.15 (m, 6 H), 1.00–1.75 (m, 23 H), 0.70–1.00 (m, 18 H), -0.10–0.10 (m, 12 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 174.3 (1 C, Cq), 133.5 (1 C, CH), 132.4 (1 C, CH), 131.0 (1 C, CH), 128.0 (1 C, CH), 97.1 (1 C, CH), 75.5 (3 C, CH), 63.7 (1 C, CH₂), 61.3 (1 C, CH₂), 59.0 (1 C, CH₂), 52.3 (1 C, CH), 51.3 (1 C, CH₃), 50.2 (1 C, CH), 38.1 (1 C, CH₂), 35.8 (1 C, CH₂), 32.5 (1 C, CH₂), 29.6 (1 C, CH₂), 28.6 (1 C, CH₂), 27.1 (1 C, CH₂), 26.0 (6 C, CH₃), 25.1 (1 C, CH₂), 23.5 (1 C, CH₂), 22.5 (1 C, CH₂), 20.3 (1 C, CH₃), 17.9 (2 C, Cq), 15.3 (1 C, CH₃), 14.0 (1 C, CH₃), -4.5 (1 C, CH₃), -4.6 (1 C, CH₃), -4.7 (1 C, CH₃), -4.8 (1 C, CH₃) ppm. MS (ESI⁺): m/z = 607.5 $[\text{M} + \text{H} - \text{C}_4\text{H}_9\text{O}_2]^+$, 475.4 $[\text{M} + \text{H} - \text{C}_4\text{H}_9\text{O}_2 - \text{OTBS}]^+$. HRMS (ESI⁺): calcd. for $\text{C}_{35}\text{H}_{67}\text{O}_4\text{Si}_2$ $[\text{M} + \text{H} - \text{C}_4\text{H}_9\text{O}_2]^+$ 607.4578; found 607.4575.

Methyl (*E*)-9-((1*S*,2*R*,3*R*,5*S*)-3,5-Bis(*tert*-butyldimethylsilyloxy)-2-[(*Z*)-non-2-enyl]cyclopentyl)-7-oxonon-8-enoate (16): PPTS (4 mg, 0.016 mmol) was added to a solution of **15** (50 mg, 0.072 mmol) in $\text{EtOH}/\text{CH}_2\text{Cl}_2$ (5:1, 4.8 mL). After 17 h at room temp., a saturated aqueous solution of NaHCO_3 (1 mL) was added, and the mixture was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (7:3 pentane/ Et_2O) to afford 35 mg of the allylic alcohol as a colorless oil (78%). R_f = 0.49 (7:3 cyclohexane/ Et_2O). $[\alpha]_D^{20}$ = +10.0 (c = 1, CHCl_3). IR: $\tilde{\nu}$ = 34.82, 2954, 2928, 2856, 1739, 1463, 1252, 1069 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 5.15–5.60 (m, 4 H), 4.00–4.15 (m, 1 H), 3.75–4.00 (m, 2 H), 3.66 (s, 3 H), 3.55–3.75 (m, 1 H), 2.15–2.45 (m, 3 H), 1.75–2.15 (m, 6 H), 1.00–1.75 (m, 18 H), 0.70–1.00 (m, 18 H), -0.10–0.10 (m, 12

H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 173.9 (1 C, Cq), 135.4 (1 C, CH), 130.4–130.7 (1 C, CH, epi), 130.2–130.4 (1 C, CH, epi), 128.3–128.5 (1 C, CH, epi), 76.3 (1 C, CH), 76.0 (1 C, CH), 73.0 (1 C, CH), 63.9 (1 C, CH₂), 52.5 (1 C, CH₂), 52.4 (1 C, CH₃), 51.6 (1 C, CH), 44.4 (1 C, CH₂), 37.3 (1 C, CH₂), 34.4 (1 C, CH₂), 31.6 (1 C, CH₂), 29.2 (2 C, CH₂), 27.3 (1 C, CH₂), 26.0 (6 C, CH₃), 25.1 (2 C, CH₂), 22.5 (1 C, CH₂), 17.1 (2 C, Cq), 14.2 (1 C, CH₃), -4.53 (1 C, CH₃), -4.4 (2 C, CH₃), -4.6 (1 C, CH₃) ppm. MS (ESI⁺): m/z = 625.5 $[\text{M} + \text{H}]^+$, 607.5 $[\text{M} + \text{H} - \text{H}_2\text{O}]^+$, 475.4 $[\text{M} + \text{H} - \text{H}_2\text{O} - \text{OTBS}]^+$, 343.3 $[\text{M} + \text{H} - \text{H}_2\text{O} - 2 \text{OTBS}]^+$. HRMS (ESI⁺): calcd. for $\text{C}_{35}\text{H}_{69}\text{O}_5\text{Si}_2$ $[\text{M} + \text{H}]^+$ 625.4684; found 625.4692. A Dess–Martin periodinane solution (150 μL of a 0.47 M solution in CH_2Cl_2 , 0.071 mmol) was added to a solution of the previous allylic alcohol (30 mg, 0.048 mmol) in CH_2Cl_2 (4 mL). After completion of the reaction (TLC), a 10% aq. $\text{NaHCO}_3/\text{Na}_2\text{S}_2\text{O}_3$ solution (1:1, 5 mL) was added. After stirring for 1.5 h, the mixture was extracted with CH_2Cl_2 (3×15 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure and the residue purified by column chromatography (9:1 pentane/ Et_2O) to afford 17 mg of the enone **16** as a colorless oil (57%). R_f = 0.55 (8:2 cyclohexane/ Et_2O). $[\alpha]_D^{20}$ = +0.8 (c = 1, CHCl_3). IR: $\tilde{\nu}$ = 2955, 2927, 2856, 1736, 1697, 1674, 1626, 1463, 1252, 1071 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 6.55–6.75 (m, 1 H), 6.15 (d, J = 15.2 Hz, 1 H), 5.15–5.50 (m, 2 H), 3.75–4.20 (m, 2 H), 3.65 (s, 3 H), 2.70–2.90 (m, 1 H), 2.20–2.70 (m, 5 H), 1.80–2.20 (m, 6 H), 1.50–1.80 (m, 6 H), 1.15–1.50 (m, 9 H), 0.70–1.00 (m, 18 H), -0.10–0.10 (s, 12 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 200.0 (1 C, Cq), 174.2 (1 C, Cq), 145.8 (1 C, CH), 131.5 (1 C, CH), 131.3 (1 C, CH), 127.8 (1 C, CH), 75.8 (1 C, CH), 75.6 (1 C, CH), 52.9 (1 C, CH), 51.6 (1 C, CH₃), 51.1 (1 C, CH), 44.5 (1 C, CH₂), 40.6 (1 C, CH₂), 34.0 (1 C, CH₂), 31.7 (1 C, CH₂), 30.3 (1 C, CH₂), 29.4 (1 C, CH₂), 27.6 (1 C, CH₂), 26.6 (1 C, CH₂), 25.9 (6 C, CH₃), 24.9 (1 C, CH₂), 23.9 (1 C, CH₂), 22.7 (1 C, CH₂), 18.1 (2 C, Cq), 14.2 (1 C, CH₃), -4.3 (1 C, CH₃), -4.4 (1 C, CH₃), -4.5 (1 C, CH₃), -4.6 (1 C, Cq) ppm.

Methyl (*S,E*)-9-((1*S*,2*R*,3*R*,5*S*)-3,5-Bis(*tert*-butyldimethylsilyloxy)-2-[(*Z*)-oct-2-enyl]cyclopentyl)-7-hydroxynon-8-enoate (17): LiAlH_4 (170 μL , 1 M in THF, 0.170 mmol) was added dropwise to a solution of dry (*S*)-binaphthol (49 mg, 0.171 mmol) in freshly distilled dry THF at room temp. After 5 min, freshly distilled dried EtOH (170 μL , 1 M in THF, 0.170 μL) was added dropwise. The reaction mixture was cooled to -100 °C, and the enone **16** (17 mg, 0.0273 mmol) was added through a cannula to the reaction mixture. The reaction mixture was slowly warmed to -30 °C. Then MeOH (500 μL) and H_2O (1.0 mL) were added, and the suspension was filtered through a plug of Celite, which had previously been washed with Et_2O . The filtrate was washed with H_2O (10 mL) and the mixture was extracted with Et_2O (3×15 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. Excess binaphthol was precipitated with hexanes, but traces of binaphthol remained. After concentration, the residue was purified by column chromatography (8:2 heptane/ Et_2O) to afford the alcohol **17** as a colorless oil (11 mg, 64% yield). R_f = 0.58 (5:5 cyclohexane/ Et_2O). $[\alpha]_D^{20}$ = +5.3 (c = 1, CHCl_3). ^1H NMR (300 MHz, CDCl_3): δ = 5.20–5.70 (m, 4 H), 3.75–4.20 (m, 3 H), 3.66 (s, 3 H), 2.55–2.75 (m, 1 H), 2.15–2.50 (m, 4 H), 1.80–2.15 (m, 6 H), 1.10–1.80 (m, 17 H), 0.70–1.00 (m, 18 H), -0.10–0.10 (s, 12 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 174.1 (1 C, Cq), 135.1 (1 C, CH), 130.5 (1 C, CH), 130.0 (1 C, CH), 128.2 (1 C, CH), 76.0 (1 C, CH), 75.7 (1 C, CH), 72.8 (1 C, CH), 52.3 (1 C, CH), 51.3 (1 C, CH₃), 51.3 (1 C, CH), 44.2 (1 C, CH₂), 37.1 (1 C, CH₂), 33.9 (1 C, CH₂), 31.5 (1 C, CH₂), 29.6 (1 C, CH₂), 29.2 (1 C, CH₂), 27.3 (1 C, CH₂), 26.1 (1 C, CH₂), 25.8

(6 C, CH₃), 25.0 (1 C, CH₂), 24.8 (1 C, CH₂), 22.5 (1 C, CH₂), 18.0 (2 C, Cq), 14.0 (1 C, CH₃), -4.5 (1 C, CH₃), -4.6 (2 C, CH₃), -4.8 (1 C, CH₃) ppm.

ent-7-epi-7-F_{2t}-Dihomo-IsoP (1): HCl (1 M in THF, 1.0 mL, 1.0 mmol) was added to a solution of **17** (11 mg, 0.018 mmol) in THF (1 mL). After 2 d at room temp., brine (5 mL) was added, and the mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried, and filtered, and the solvent was removed under reduced pressure. The residue was purified by column chromatography (9:1 EtOAc/MeOH) to afford 2.9 mg of *ent*-(7S)-F_{2t}-dihomo-IsoP (**1**) as a colorless oil (28% over two steps). *R*_f = 0.76 (9:1 EtOAc/MeOH + 1% AcOH). [*a*]_D²⁰ = +2.4 (*c* = 0.166, MeOH). IR: $\tilde{\nu}$ = 3343, 2483, 2071, 1704, 1120 cm⁻¹. ¹H NMR (300 MHz, [D₄]MeOH): δ = 5.20–5.60 (m, 4 H), 3.60–4.10 (m, 3 H), 2.65–2.75 (m, 1 H), 2.35–2.55 (m, 1 H), 2.15–2.35 (m, 3 H), 1.90–2.00 (m, 4 H), 1.20–1.70 (m, 15 H), 0.80–1.00 (m, 3 H) ppm. ¹³C NMR (75 MHz, [D₄]MeOH): δ = 136.8 (1 C, CH), 131.7 (1 C, CH), 130.6 (1 C, CH), 129.3 (1 C, CH), 76.4 (1 C, CH), 76.3 (1 C, CH), 76.7 (1 C, CH), 54.8 (1 C, CH), 53.8 (1 C, CH), 51.5 (1 C, CH₂), 43.6 (1 C, CH₂), 38.4 (1 C, CH₂), 35.4 (1 C, CH₂), 32.7 (1 C, CH₂), 30.5 (1 C, CH₂), 30.3 (1 C, CH₂), 28.4 (1 C, CH₂), 27.4 (1 C, CH₂), 26.3 (1 C, CH₂), 23.7 (1 C, CH₂), 14.4 (1 C, CH₃) ppm. MS (ESI⁺): *m/z* = 383.4 [M + H]⁺, 365.3 [M + H – H₂O]⁺, 347.3 [M + H – 2 H₂O]⁺, 329.3 [M + H – 3 H₂O]⁺. HRMS (ESI⁺): calcd. for C₂₂H₃₉O₅ [M + H]⁺ 383.2797; found 383.2794.

ent-(7RS)-7-F_{2t}-dihomo-IsoP [(RS)-1]: HCl (1 M in THF, 1.0 mL, 1.0 mmol) was added to a solution of **14** (110 mg, 0.15 mmol) in THF (5 mL). After 2 d at room temp., brine (10 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried, and filtered, and the solvent was removed under reduced. The residue was purified by column chromatography (9:1 EtOAc/MeOH) to afford 33 mg of *ent*-(7RS)-F_{2t}-dihomo-IsoP [(RS)-1] as a colorless oil (58%). *R*_f = 0.81 (9:1 EtOAc/MeOH + 1% AcOH). [*a*]_D²⁰ = +6.7 (*c* = 1 × 10⁻², MeOH). IR: $\tilde{\nu}$ = 3343, 2483, 2071, 1704, 1120 cm⁻¹. ¹H NMR (300 MHz, [D₄]MeOH): δ = 5.25–5.60 (m, 4 H), 3.80–4.15 (m, 3 H), 2.60–2.80 (m, 1 H), 2.40–2.60 (m, 1 H), 2.30 (t, *J* = 7.0 Hz, 2 H), 1.90–2.15 (m, 5 H), 1.20–1.70 (m, 15 H), 0.80–1.00 (m, 3 H) ppm. ¹³C NMR (75 MHz, [D₄]MeOH): δ = 177.7, (1 C, Cq), 136.7 (1 C, CH), 131.76 (1 C, CH), 130.6 (1 C, CH), 129.6 (1 C, CH), 76.3 (1 C, CH), 73.6 (1 C, CH), 73.3 (1 C, CH), 54.6 (1 C, CH), 51.4 (1 C, CH), 43.6 (1 C, CH₂), 38.3 (1 C, CH₂), 35.0 (1 C, CH₂), 32.7 (1 C, CH₂), 30.5 (1 C, CH₂), 30.2 (1 C, CH₂), 28.4 (1 C, CH₂), 27.4–26.3 (1 C, CH₂), 23.6 (1 C, CH₂), 14.4 (1 C, CH₃) ppm. MS (ESI⁺): *m/z* = 383.4 [M + H]⁺, 365.3 [M + H – H₂O]⁺, 347.3 [M + H – 2 H₂O]⁺, 329.3 [M + H – 3 H₂O]⁺. HRMS (ESI⁺): calcd. for C₂₂H₃₉O₅ [M + H]⁺ 383.2797; found 383.2805.

(7-Ethoxy-7-oxoheptyl)triphenylphosphonium Bromide (23): Ph₃P (11.1 g, 42.2 mol) and a catalytic amount of K₂CO₃ were added to a solution of ethyl 7-bromoheptanoate (5.0 g, 21.1 mol) in CH₃CN (100 mL) at room temp. The reaction mixture was heated at reflux overnight, and the solvent was then removed under reduced pressure. The residue was purified by column chromatography (solid SiO₂ deposit, 9:1 CH₂Cl₂/MeOH) to afford 21.0 g of **23** as a white powder (87%). *R*_f = 0.33 (9:1 EtOAc/MeOH). M.p. 130 °C. IR: $\tilde{\nu}$ = 3254, 2875, 1706, 1471, 1253, 1051 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 4.40 (q, *J* = 6.1 Hz, 1 H), 3.90 (m, 1 H), 3.50–3.80 (m, 3 H), 3.20 (s, 1 H), 1.80–2.25 (m, 3 H), 1.30–1.80 (m, 5 H), 0.89 (d, *J* = 2.8 Hz, 9 H), 0.08 (d, *J* = 2.9 Hz, 6 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 135.0 (3 C, CH), 134.0 (3 C, Cq), 133.3 (6 C, CH), 130.4 (6 C, CH), 124.9 (1 C, CH), 124.7 (1 C, CH), 116.9–118.0 (d, *J*_{C-P} = 1.14 Hz, 1 C, CH₂), 23.4–22.0 (d, *J*_{C-P} = 0.65 Hz,

1 C, CH₂), 20.3–19.9 (d, *J*_{C-P} = 0.4 Hz, 1 C, CH₂), 13.7 (1 C, CH₃) ppm. ³¹P NMR (120 MHz, CDCl₃): δ = 24.5 ppm.

2-[(1S,2R,3R,5S)-3,5-Bis(*tert*-butyldimethylsilyloxy)-2-[(*E*)-3-oxooct-1-enyl]cyclopentyl]ethyl acetate (19): A Dess–Martin periodinane solution (1.5 mL of a 0.47 M solution in CH₂Cl₂, 0.61 mmol) was added to a solution of alcohol **5** (225 mg, 0.51 mmol) in CH₂Cl₂ (10 mL). After completion of the reaction (TLC, 10% aq. NaHCO₃/Na₂S₂O₃ (1:1, 50 mL) was added. After stirring for 1.5 h, the mixture was extracted with CH₂Cl₂ (3 × 30 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The material was directly used in the next step without further purification. β -Keto phosphonate **18** (440 mg, 1.11 mmol) was added dropwise to a suspension of dry Ba(OH)₂ (70 mg, 0.41 mmol) in THF (10 mL). After 1 h, the aldehyde in THF (20 mL) was added through a cannula to the reaction mixture and stirred overnight. Then the reaction was quenched with H₂O (25 mL) and Et₂O (25 mL). The mixture was extracted with Et₂O (3 × 30 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (9:1 pentane/Et₂O) to afford 155 mg of enone **19** as a colorless oil (57% over two steps). *R*_f = 0.50 (8:2 cyclohexane/Et₂O). [*a*]_D²⁰ = +23.4 (*c* = 1, CHCl₃). IR: $\tilde{\nu}$ = 2955, 2930, 2857, 1741, 1248, 1056 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 6.50 (dd, *J* = 10.5, 5.0 Hz, 1 H), 6.20 (d, *J* = 15.6 Hz, 1 H), 3.80–4.15 (m, 4 H), 2.65–2.90 (m, 1 H), 2.50 (t, *J* = 7.4 Hz, 2 H), 2.15–2.45 (m, 2 H), 2.03 (s, 3 H), 1.45–1.80 (m, 7 H), 1.15–1.45 (m, 5 H), 0.70–1.00 (m, 18 H), -0.10–0.10 (m, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 200.2 (1 C, Cq), 171.0 (1 C, Cq), 144.4 (1 C, CH), 131.6 (1 C, CH), 76.2 (1 C, CH), 75.4 (1 C, CH), 63.3 (1 C, CH₂), 53.1 (1 C, CH), 46.4 (1 C, CH), 44.4 (1 C, CH₂), 41.3 (1 C, CH₂), 31.6 (1 C, CH₂), 28.0 (1 C, CH₂), 25.9 (6 C, CH₃), 24.0 (1 C, CH₂), 22.6 (1 C, CH₂), 21.0 (1 C, CH₃), 18.0 (2 C, Cq), 14.0 (1 C, CH₃), -4.2 (1 C, CH₃), -4.5 (2 C, CH₃), -4.7 (1 C, CH₃) ppm. MS (ESI⁺): *m/z* = 599.4 [M + H]⁺, 467.3 [M – OTBS]⁺. HRMS (ESI⁺): calcd. for C₃₁H₅₉O₇Si₂ [M + H]⁺ 599.3799; found 599.3791.

2-[(1S,2R,3R,5S)-3,5-Bis(*tert*-butyldimethylsilyloxy)-2-[(*E*)-3-hydroxyoct-1-enyl]cyclopentyl]ethyl acetate (20): CeCl₃·7H₂O (240 mg, 0.64 mmol) in MeOH (30 mL) was added to a solution of enone **19** (350 mg, 0.65 mmol). The mixture was cooled to 0 °C, and then NaBH₄ was added (22.0 mg, 0.582 mmol). After 10 min, the reaction was quenched with H₂O (12 mL) and Et₂O (5 mL). The reaction mixture was extracted with Et₂O (3 × 15 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (8:2 pentane/Et₂O) to afford 326 mg of **20** as a colorless oil (98%). *R*_f = 0.66 (5:5 cyclohexane/Et₂O). [*a*]_D²⁰ = +25.9 (*c* = 1, CHCl₃). IR: $\tilde{\nu}$ = 3509, 2955, 2929, 2857, 1732, 1250, 1056 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 5.20–5.60 (m, 2 H), 3.60–4.35 (m, 5 H), 2.40–2.55 (m, 1 H), 1.85–2.40 (m, 7 H), 1.00–1.90 (m, 12 H), 0.70–1.00 (m, 18 H), -0.10–0.10 (m, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 171.3 (1 C, Cq), 136.2 (1 C, CH), 129.2 (1 C, CH), 76.4 (1 C, CH), 73.0 (1 C, CH), 72.6 (1 C, CH), 63.6 (1 C, CH₂), 52.9 (1 C, CH), 45.8 (1 C, CH), 44.4 (1 C, CH₂), 37.4 (1 C, CH₂), 37.2 (1 C, CH₂), 31.9 (1 C, CH₂), 28.0 (1 C, CH₂), 25.9 (6 C, CH₃), 25.3 (1 C, CH₂), 21.1 (1 C, CH₃), 18.1 (2 C, Cq), 14.1 (1 C, CH₃), -4.2 (1 C, CH₃), -4.5 (1 C, CH₃), -4.6 (1 C, CH₃), -4.7 (1 C, CH₃) ppm. MS (ESI⁺): *m/z* = 543.4 [M + H]⁺, 525.4 [M + H – H₂O]⁺, 393.3 [M + H – H₂O – OTBS]⁺, 261.2 [M + H – H₂O – 2 OTBS]⁺. HRMS (ESI⁺): calcd. for C₂₉H₅₉O₅Si₂ [M + H – H₂O]⁺ 543.3901; found 543.3910.

2-{{(1S,2R,3R,5S)-3,5-Bis(tert-butylidimethylsilyloxy)-2-[(E)-3-(1-ethoxyethoxy)oct-1-enyl]cyclopentyl}ethyl acetate (21): Ethyl vinyl ether (2 mL, 20.9 mmol) and PPTS (10 mg, 0.053 mmol) were successively added to a solution of **20** (140 mg, 0.27 mmol) in CH₂Cl₂ (7 mL) at 0 °C. The reaction mixture was allowed to warm to room temp. overnight. Then a saturated aqueous solution of NaHCO₃ (2 mL) was added, and the reaction mixture was extracted with CH₂Cl₂ (3 × 20 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (1% Et₃N deactivated SiO₂, 8:2 pentane/Et₂O) to afford 145 mg of **21** as a colorless oil (91%). *R*_f = 0.61 (5:5 cyclohexane/Et₂O). [α]_D²⁰ = +26.4 (*c* = 1, CHCl₃). IR: $\tilde{\nu}$ = 2953, 2930, 2858, 1741, 1248, 1056 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 5.20–5.40 (m, 2 H), 4.55–4.80 (m, 1 H), 3.75–4.20 (m, 6 H), 3.25–3.75 (m, 4 H), 2.50–2.70 (m, 1 H), 2.50 (m, 2 H), 2.02 (s, 3 H), 1.40–1.90 (m, 7 H), 1.05–1.40 (m, 14 H), 0.70–1.00 (m, 18 H), 0.02 (m, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 171.0 (1 C, Cq), 134.1 (1 C, CH), 130.5 (1 C, CH), 97.5 (1 C, CH), 76.5 (3 C, CH), 63.7 (1 C, CH₂), 61.5 (1 C, CH₂), 58.8 (1 C, CH₂), 53.1 (1 C, CH), 45.7 (1 C, CH), 43.5 (1 C, CH₂), 36.2 (1 C, CH₂), 32.5 (1 C, CH₂), 27.7 (1 C, CH₂), 25.9 (6 C, CH₃), 25.2 (1 C, CH₂), 22.5 (1 C, CH₂), 20.4–20.9 (2 C, CH₃), 18.0 (2 C, Cq), 15.5 (1 C, CH₃), 14.0 (1 C, CH₃), –4.2 (1 C, CH₃), –4.6 (2 C, CH₃), –4.7 (1 C, CH₃) ppm. MS (ESI⁺): *m/z* = 525.4 [M + H – C₄H₉O₂]⁺, 393.3 [M + H – C₄H₉O₂ – OTBS]⁺, 261.2 [M + H – C₄H₉O₂ – 2 OTBS]⁺, 201.2 [M + H – C₄H₉O₂ – 2 OTBS – OAc]⁺. HRMS (ESI⁺): calcd. for C₂₉H₅₇O₄Si₂ [M + H – C₄H₉O₂]⁺ 525.3795; found 525.3798.

2-{{(1S,2R,3R,5S)-3,5-Bis(tert-butylidimethylsilyloxy)-2-[(3S,E)-3-(1-ethoxyethoxy)oct-1-enyl]cyclopentyl}ethanol [(17S)-22] and 2-{{(1S,2R,3R,5S)-3,5-Bis(tert-butylidimethylsilyloxy)-2-[(3R,E)-3-(1-ethoxyethoxy)oct-1-enyl]cyclopentyl}ethanol [(17R)-22]: K₂CO₃ (85 mg, 0.62 mmol) was added to a solution of **21** (140 mg, 0.23 mmol) in MeOH (15 mL). After 2 h, the reaction was quenched with a solution of H₂O/Et₂O (20 mL). The mixture was extracted with a mixture of Et₂O/pentane (3 × 20 mL), washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (1% Et₃N deactivated SiO₂, 8:2 pentane/Et₂O) to afford 61 mg of (17S)-**22** and 63 mg of (17R)-**22** as colorless oils. (17S)-**22**: *R*_f = 0.56 (5:5 cyclohexane/Et₂O). [α]_D²⁰ = –2.2 (*c* = 1, CHCl₃). IR: $\tilde{\nu}$ = 3470, 2955, 2929, 2857, 1252, 1055 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 5.15–5.60 (m, 2 H), 4.60–4.90 (m, 1 H), 3.80–4.00 (m, 3 H), 3.75–3.90 (m, 2 H), 3.25–3.75 (m, 4 H), 2.45–2.65 (m, 1 H), 2.00–2.45 (m, 3 H), 1.50–1.75 (m, 4 H), 1.00–1.50 (m, 13 H), 0.60–1.00 (m, 18 H), –0.20–0.20 (m, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 134.0 (1 C, CH), 130.5 (1 C, CH), 97.0 (1 C, CH), 76.5 (3 C, CH), 61.9 (1 C, CH₂), 60.9 (1 C, CH₂), 59.0 (1 C, CH), 46.1 (1 C, CH), 44.6 (1 C, CH₂), 36.1 (1 C, CH₂), 32.7 (1 C, CH₂), 31.9 (1 C, CH₂), 26.0 (6 C, CH₃), 25.3 (1 C, CH₂), 22.7 (1 C, CH₂), 20.7 (1 C, CH₂), 18.2 (2 C, Cq), 15.5 (1 C, CH₃), 14.2 (1 C, CH₃), –3.9 (2 C, CH₃), –4.5 (2 C, CH₃) ppm. MS (ESI⁺): *m/z* = 483.4 [M + H – C₄H₉O₂]⁺, 351.3 [M + H – C₄H₉O₂ – OTBS]⁺, 219.2 [M + H – C₄H₉O₂ – 2 OTBS]⁺. HRMS (ESI⁺): calcd. for C₂₇H₅₅O₃Si₂ [M + H – C₄H₉O₂]⁺ 483.3683; found 483.3690. (17R)-**22**: *R*_f = 0.46 (5:5 cyclohexane/Et₂O). [α]_D²⁰ = +37.9 (*c* = 1, CHCl₃). IR: $\tilde{\nu}$ = 3470, 2955, 2929, 2857, 1252, 1055 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 5.15–5.60 (m, 2 H), 4.60–4.90 (m, 1 H), 3.80–4.00 (m, 3 H), 3.75–3.90 (m, 2 H), 3.25–3.75 (m, 4 H), 2.45–2.65 (m, 1 H), 2.00–2.45 (m, 3 H), 1.50–1.75 (m, 4 H), 1.00–1.50 (m, 13 H), 0.60–1.00 (m, 18 H), –0.20–0.20 (m, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 134.0 (1 C, CH), 130.5 (1 C, CH), 97.7 (1 C, CH), 76.8 (3 C, CH), 61.9 (1 C, CH₂), 61.3 (1 C, CH₂), 58.8 (1 C, CH), 46.2 (1 C,

CH₂), 44.5 (1 C, CH₂), 36.1 (1 C, CH₂), 32.8 (1 C, CH₂), 31.9 (1 C, CH₂), 25.8 (6 C, CH₃), 25.3 (1 C, CH₂), 22.7 (1 C, CH₂), 20.7 (1 C, CH₂), 18.1 (2 C, Cq), 15.5 (1 C, CH₃), 14.2 (1 C, CH₃), –3.9 (2 C, CH₃), –4.5 (2 C, CH₃) ppm. MS (ESI⁺): *m/z* = 483.4 [M + H – C₄H₉O₂]⁺, 351.3 [M + H – C₄H₉O₂ – OTBS]⁺, 219.2 [M + H – C₄H₉O₂ – 2 OTBS]⁺. HRMS (ESI⁺): calcd. for C₂₇H₅₅O₃Si₂ [M + H – C₄H₉O₂]⁺ 483.3683; found 483.3690.

Ethyl (Z)-9-{{(1S,2R,3R,5S)-3,5-Bis(tert-butylidimethylsilyloxy)-2-[(3R,E)-3-(1-ethoxyethoxy)oct-1-enyl]cyclopentyl}non-7-enoate [(17R)-24]: A Dess–Martin periodinane solution (400 μL of a 0.47 M solution in CH₂Cl₂) was added to a solution of (17R)-**22** (62 mg, 0.11 mmol) in CH₂Cl₂ (8 mL). After completion of the reaction (TLC), 10% aq. NaHCO₃/Na₂S₂O₃ (1:1, 15 mL) was added. After stirring for 1.5 h, the mixture was extracted with CH₂Cl₂ (3 × 20 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The material was directly used in the next step without further purification. NaHMDS (400 μL, 2 M THF, 0.8 mmol) was added dropwise to a suspension of dried phosphonium salt **23** (433 mg, 0.87 mmol) in degassed THF (10 mL) at –50 °C. After 1 h, the mixture was added through a cannula to the aldehyde in degassed THF (7 mL) at –78 °C. After 3 h at –50 °C, the reaction mixture was allowed to warm to room temp. overnight. The reaction was quenched with a saturated aqueous solution of NH₄Cl (20 mL). The mixture was extracted with Et₂O (3 × 10 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure and the residue purified by column chromatography (1% Et₃N deactivated SiO₂, 95:5 pentane/Et₂O) to afford 54 mg of (17R)-**24** as a colorless oil (81% over two steps). *R*_f = 0.51 (9:1 cyclohexane/Et₂O). [α]_D²⁰ = +35.2 (*c* = 1, CHCl₃). IR: $\tilde{\nu}$ = 2955, 2929, 2857, 1736, 1251, 1060 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 5.15–5.60 (m, 4 H), 4.55–4.80 (m, 1 H), 4.00–4.15 (m, 2 H), 3.75–4.00 (m, 2 H), 3.25–3.55 (m, 2 H), 2.50–2.75 (m, 1 H), 2.15–2.40 (m, 3 H), 1.90–2.15 (m, 4 H), 1.45–1.90 (m, 6 H), 1.00–1.45 (m, 21 H), 0.70–1.00 (m, 20 H), –0.10–0.10 (m, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 173.8 (1 C, Cq), 133.6 (1 C, CH), 132.3 (1 C, CH), 130.6 (1 C, CH), 128.6 (1 C, CH), 97.6 (1 C, CH), 77.1 (1 C, CH), 76.0 (1 C, CH), 76.3 (1 C, CH), 61.4 (1 C, CH₂), 60.2 (1 C, CH₂), 59.1 (1 C, CH₂), 52.5 (1 C, CH), 50.4 (1 C, CH), 44.5 (1 C, CH₂), 36.1 (1 C, CH₂), 34.4 (1 C, CH₂), 32.0 (1 C, CH₂), 29.4 (1 C, CH₂), 29.0 (1 C, CH₂), 27.3 (1 C, CH₂), 26.4 (1 C, CH₂), 25.9 (6 C, CH₃), 25.3 (1 C, CH₂), 25.0 (1 C, CH₂), 22.7 (1 C, CH₂), 20.6 (1 C, CH₃), 18.1 (2 C, Cq), 15.5 (1 C, CH₃), 14.2 (1 C, CH₃), –4.3 (1 C, CH₃), –4.4 (1 C, CH₃), –4.5 (1 C, CH₃), –4.6 (1 C, CH₃) ppm. MS (ESI⁺): *m/z* = 621.6 [M + H – C₄H₉O₂]⁺. HRMS (ESI⁺): calcd. for C₃₆H₆₉O₄Si₂ [M + H – C₄H₉O₂]⁺ 621.4734; found 621.4730.

Ethyl (Z)-9-{{(1S,2R,3R,5S)-3,5-Bis(tert-butylidimethylsilyloxy)-2-[(3S,E)-3-(1-ethoxyethoxy)oct-1-enyl]cyclopentyl}non-7-enoate [(17S)-24]: The same procedure as described for the synthesis of (17R)-**24** was applied to 35 mg of (17S)-**22** to give 11 mg of (17S)-**24** (25% over two steps, non-optimized). *R*_f = 0.55 (8:2 cyclohexane/Et₂O). [α]_D²⁰ = +25.0 (*c* = 1, CHCl₃). IR: $\tilde{\nu}$ = 2954, 2928, 2856, 1738, 1251, 1060 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 5.15–5.60 (m, 4 H), 4.55–4.80 (m, 1 H), 4.00–4.15 (m, 2 H), 3.75–4.00 (m, 2 H), 3.25–3.55 (m, 2 H), 2.50–2.75 (m, 1 H), 2.15–2.40 (m, 3 H), 1.90–2.15 (m, 4 H), 1.45–1.90 (m, 6 H), 1.00–1.45 (m, 21 H), 0.70–1.00 (m, 20 H), –0.10–0.10 (m, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 173.8 (1 C, Cq), 133.6 (1 C, CH), 132.1 (1 C, CH), 130.5 (1 C, CH), 128.6 (1 C, CH), 97.5 (1 C, CH), 77.0 (1 C, CH), 76.3 (1 C, CH), 76.0 (1 C, CH), 61.4 (1 C, CH₂), 60.2 (1 C, CH₂), 58.9 (1 C, CH₂), 52.5 (1 C, CH), 50.3 (1 C, CH), 44.5 (1 C, CH₂), 36.1 (1 C, CH₂), 34.4 (1 C, CH₂), 31.9 (1 C, CH₂), 29.4 (1 C, CH₂),

29.0 (1 C, CH₂), 27.3 (1 C, CH₂), 26.4 (1 C, CH₂), 25.9 (6 C, CH₃), 25.3 (1 C, CH₂), 25.0 (1 C, CH₂), 22.7 (1 C, CH₂), 20.6 (1 C, CH₃), 18.1 (2 C, Cq), 15.4–15.6 (1 C, CH₃), 14.1–14.4 (1 C, CH₃), –4.3 (1 C, CH₃), –4.4 (1 C, CH₃), –4.5 (1 C, CH₃), –4.6 (1 C, CH₃) ppm. MS (ESI⁺): *m/z* = 621.6 [M + H – C₄H₉O₂]⁺. HRMS (ESI⁺): calcd. for C₃₆H₆₉O₄Si₂ [M + H – C₄H₉O₂]⁺ 621.4734; found 621.4725.

Ethyl (Z)-9-((1S,2R,3R,5S)-3,5-Bis(*tert*-butyldimethylsilyloxy)-2-[(*E*)-3-oxooct-1-enyl]cyclopentyl)non-7-enoate (25): PPTS (5 mg, 0.02 mmol) was added to a solution of racemic **24** (142 mg, 0.2 mmol) in EtOH/CH₂Cl₂ (5:1, 12 mL). After 24 h at room temp., the reaction was quenched with a saturated aqueous solution of NaHCO₃ (5 mL), and the mixture was extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (7:3 pentane/Et₂O) to afford 90 mg of the corresponding allylic alcohol as a colorless oil (80%). *R*_f = 0.78 (5:5 cyclohexane/Et₂O). [*a*]_D²⁰ = +10.0 (*c* = 1, CHCl₃). IR: $\tilde{\nu}$ = 3458, 2954, 2929, 2856, 1738, 1251, 1066 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 5.20–5.70 (m, 4 H), 4.00–4.20 (m, 3 H), 3.70–4.00 (m, 2 H), 2.50–3.80 (m, 1 H), 2.20–2.40 (m, 3 H), 1.80–2.15 (m, 5 H), 1.00–1.75 (m, 21 H), 0.70–1.00 (m, 18 H), –0.10–0.10 (m, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 173.9 (1 C, Cq), 135.5 (1 C, CH), 130.2 (1 C, CH), 129.8 (1 C, CH), 128.7 (1 C, CH), 76.2 (1 C, CH), 76.0 (1 C, CH), 73.0 (1 C, CH), 60.3 (1 C, CH₂), 52.4 (1 C, CH), 50.4 (1 C, CH), 44.4 (1 C, CH₂), 37.5 (1 C, CH₂), 34.4 (1 C, CH₂), 29.8 (1 C, CH₂), 29.4 (1 C, CH₂), 28.9 (1 C, CH₂), 27.3 (1 C, CH₂), 26.4 (2 C, CH₂), 25.9 (6 C, CH₃), 25.9 (1 C, CH₂), 25.4 (1 C, CH₂), 22.7 (1 C, CH₂), 18.3 (2 C, Cq), 14.2 (1 C, CH₃), –4.3 (1 C, CH₃), –4.4 (2 C, CH₃), –4.6 (1 C, CH₃) ppm. MS (ESI⁺): *m/z* = 621.6 [M + H – H₂O]⁺, 489.5 [M + H – OTBS]⁺, 357.4 [M + H – 2 OTBS]⁺. HRMS (ESI⁺): calcd. for C₃₆H₆₉O₄Si₂ [M + H – H₂O]⁺ 621.4734; found 621.4738. A Dess–Martin periodinane solution (500 μ L of a 0.47 M solution in CH₂Cl₂, 0.24 mmol) was added to a solution of the alcohol (89 mg, 0.14 mmol) in CH₂Cl₂ (10 mL). After completion of the reaction (TLC), 10% aq. NaHCO₃/Na₂S₂O₃ (1:1, 15 mL) was added. After stirring for 1.5 h, the mixture was extracted with CH₂Cl₂ (3 × 15 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (9:1 pentane/Et₂O) to afford 86 mg of the enone **25** as a colorless oil (97%). *R*_f = 0.78 (5:5 cyclohexane/Et₂O). [*a*]_D²⁰ = +0.5 (*c* = 1, CHCl₃). IR: $\tilde{\nu}$ = 2954, 2929, 2857, 1736, 1697, 1674, 1626, 1251, 1067 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 6.65 (dd, *J* = 9.8, 5.7 Hz, 1 H), 6.13 (d, *J* = 15.5 Hz, 1 H), 5.15–5.45 (m, 2 H), 4.10 (q, *J* = 7.0 Hz, 2 H), 3.90–4.00 (m, 1 H), 3.75–3.90 (m, 1 H), 2.70–2.90 (m, 1 H), 2.48 (t, *J* = 7.1 Hz, 2 H), 2.30–2.40 (m, 1 H), 2.26 (t, *J* = 7.3 Hz, 2 H), 1.80–2.20 (m, 5 H), 1.50–1.80 (m, 5 H), 1.15–1.50 (m, 14 H), 0.70–1.00 (m, 18 H), –0.10–0.10 (m, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 200.3 (1 C, Cq), 173.8 (1 C, Cq), 145.5 (1 C, CH), 131.5 (1 C, CH), 130.8 (1 C, CH), 128.1 (1 C, CH), 75.8 (1 C, CH), 75.5 (1 C, CH), 60.2 (1 C, CH₂), 52.9 (1 C, CH), 51.0 (1 C, CH), 44.5 (1 C, CH₂), 40.9 (1 C, CH₂), 34.4 (1 C, CH₂), 31.6 (1 C, CH₂), 29.4 (1 C, CH₂), 29.0 (1 C, CH₂), 27.4 (1 C, CH₂), 26.6 (1 C, CH₂), 25.9 (6 C, CH₃), 25.0 (1 C, CH₂), 24.1 (1 C, CH₂), 22.6 (1 C, CH₂), 18.1 (2 C, Cq), 14.4 (1 C, CH₃), 14.0 (1 C, CH₃), –4.3 (1 C, CH₃), –4.5 (2 C, CH₃), –4.6 (1 C, Cq) ppm. MS (ESI⁺): *m/z* = 637.6 [M + H]⁺. HRMS (ESI⁺): calcd. for C₃₆H₆₉O₃Si₂ [M + H]⁺ 637.4684; found 637.4692.

Ethyl (Z)-9-((1S,2R,3R,5S)-3,5-Bis(*tert*-butyldimethylsilyloxy)-2-[(*E*)-3-hydroxyoct-1-enyl]cyclopentyl)non-7-enoate [(17S)-26]: LiAlH₄ (820 μ L, 1 M in THF, 0.82 mmol) was added dropwise to a solution of dry (*S*)-binaphthol (235 mg, 0.83 mmol) in freshly dis-

tilled THF at room temp. After 5 min, a solution of freshly distilled dried EtOH (820 μ L, 1 M in THF, 0.820 mmol) was added dropwise. The reaction mixture was cooled to –100 °C, and enone **25** (85 mg, 0.134 mmol) was added through a cannula to the reaction mixture. Then MeOH (1 mL) and H₂O (2.5 mL) were added, and the suspension was filtered through a plug of Celite that had been previously washed with Et₂O. The filtrate was washed with H₂O (10 mL). The mixture was extracted with Et₂O (3 × 15 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. Excess binaphthol was precipitated with hexanes. The crude residue was purified by column chromatography (9:1 heptane/Et₂O) to afford 69 mg of (17S)-**26** as a colorless oil (81%). *R*_f = 0.60 (7:3 cyclohexane/Et₂O). [*a*]_D²⁰ = +15.0 (*c* = 1, CHCl₃). IR: $\tilde{\nu}$ = 3485, 2954, 2928, 2856, 1738, 1251, 1065 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 5.25–5.70 (m, 4 H), 4.00–4.20 (m, 3 H), 3.70–4.00 (m, 2 H), 2.50–2.80 (m, 1 H), 2.20–2.40 (m, 3 H), 1.80–2.15 (m, 5 H), 1.10–1.75 (m, 20 H), 0.70–1.00 (m, 18 H), –0.10–0.10 (m, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 173.9 (1 C, Cq), 135.5 (1 C, CH), 130.2 (1 C, CH), 129.9 (1 C, CH), 128.8 (1 C, CH), 76.2 (1 C, CH), 76.0 (1 C, CH), 73.0 (1 C, CH), 60.3 (1 C, CH₂), 52.6 (1 C, CH), 50.4 (1 C, CH), 44.4 (1 C, CH₂), 37.6 (1 C, CH₂), 34.5 (1 C, CH₂), 31.9 (1 C, CH₂), 29.4 (1 C, CH₂), 29.0 (1 C, CH₂), 27.3 (1 C, CH₂), 26.4 (1 C, CH₂), 26.0 (6 C, CH₃), 25.3 (1 C, CH₂), 25.0 (1 C, CH₂), 22.7 (1 C, CH₂), 18.1 (2 C, Cq), 14.4 (1 C, CH₃), 14.1 (1 C, CH₃), –4.3 (1 C, CH₃), –4.4 (2 C, CH₃), –4.6 (1 C, CH₃) ppm. MS (ESI⁺): *m/z* = 639.5 [M + H]⁺, 621.6 [M + H – H₂O]⁺, 489.5 [M + H – OTBS]⁺, 357.4 [M + H – 2 OTBS]⁺. HRMS (ESI⁺): calcd. for C₃₆H₇₁O₅Si₂ [M + H]⁺ 639.4840; found 639.4840.

17-F_{2t}-Dihomo-IsoP (2): HCl (500 μ L, 1 M in THF, 0.50 mmol) was added to a solution of (17S)-**24** (11 mg, 0.015 mmol) in THF (1 mL). After stirring at room temp. overnight, brine (5 mL) was added and the mixture extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried, and filtered, and the solvent was removed under reduced pressure. The residue was directly used in the next step without further purification. LiOH (1.5 mg, 0.05 mmol) was added to a solution of the previous material in THF/H₂O (1:1, 1 mL). After stirring overnight at room temp., the mixture was cooled to 0 °C, and a solution of HCl (1 M) was added until pH = 1. The mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried, and filtered, the solvent was removed under reduced pressure, and the residue purified by flash chromatography (9:1 EtOAc/MeOH) to afford 3.5 mg of 17-F_{2t}-dihomo-IsoP (**2**) as a yellow oil (58% over two steps). *R*_f = 0.64 (9:1 EtOAc/MeOH + 1% AcOH). [*a*]_D²⁰ = +12.0 (*c* = 1, MeOH). ¹H NMR (300 MHz, [D₄]MeOH): δ = 5.25–5.65 (m, 4 H), 3.80–4.10 (m, 3 H), 2.55–2.80 (m, 1 H), 2.40–2.55 (m, 1 H), 2.27 (t, *J* = 7.0 Hz, 2 H), 1.90–2.20 (m, 5 H), 1.20–1.80 (m, 17 H), 0.80–1.00 (m, 3 H) ppm. ¹³C NMR (75 MHz, [D₄]MeOH): δ = 177.9 (1 C, Cq), 136.9 (1 C, CH), 131.3 (1 C, CH), 130.6 (1 C, CH), 129.5 (1 C, CH), 76.4 (1 C, CH), 76.3 (1 C, CH), 73.8 (1 C, CH), 53.8 (1 C, CH), 51.4 (1 C, CH), 43.5 (1 C, CH₂), 38.4 (1 C, CH₂), 35.2 (1 C, CH₂), 33.0 (1 C, CH₂), 30.4 (1 C, CH₂), 29.9 (1 C, CH₂), 28.3 (1 C, CH₂), 27.4 (1 C, CH₂), 26.3 (1 C, CH₂), 26.1 (1 C, CH₂), 23.7 (1 C, CH₂), 14.4 (1 C, CH₃) ppm. MS (ESI⁺): *m/z* = 365.3 [M + H – H₂O]⁺, 347.3 [M + H – 2 H₂O]⁺, 329.3 [M + H – 3 H₂O]⁺. HRMS (ESI⁺): calcd. for C₂₂H₃₇O₄ [M + H – H₂O]⁺ 365.2692; found 365.2684.

17-*epi*-17-F_{2t}-Dihomo-IsoP [(17R)-2]: The previous procedure as described for the synthesis of 17-F_{2t}-dihomo-IsoP (**2**) was applied to 54 mg of (17R)-**24** to give 17 mg of 17-*epi*-17-F_{2t}-dihomo-IsoP [(17R)-**2**] (58% over two steps). *R*_f = 0.71 (9:1 EtOAc/MeOH + 1% AcOH). [*a*]_D²⁰ = +4.4 (*c* = 1, MeOH). ¹H NMR (300 MHz, [D₄]-

MeOH): δ = 5.25–5.65 (m, 4 H), 3.80–4.20 (m, 3 H), 2.60–2.80 (m, 1 H), 2.40–2.60 (m, 1 H), 2.27 (t, J = 7.0 Hz, 2 H), 1.90–2.20 (m, 5 H), 1.20–1.80 (m, 16 H), 0.80–1.00 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $[\text{D}_4]\text{MeOH}$): δ = 177.0 (1 C, Cq), 136.6 (1 C, CH), 131.4 (1 C, CH), 129.8 (1 C, CH), 129.6 (1 C, CH), 76.2 (2 C, CH), 73.4 (1 C, CH), 53.4 (1 C, CH), 51.4 (1 C, CH), 43.6 (1 C, CH_2), 38.5 (1 C, CH_2), 35.2 (1 C, CH_2), 33.0 (1 C, CH_2), 30.5 (1 C, CH_2), 29.9 (1 C, CH_2), 28.2 (1 C, CH_2), 27.3 (1 C, CH_2), 26.3 (1 C, CH_2), 26.1 (1 C, CH_2), 23.7 (1 C, CH_2), 14.4 (1 C, CH_3) ppm. MS (ESI⁺): m/z = 365.3 $[\text{M} + \text{H} - \text{H}_2\text{O}]^+$, 347.3 $[\text{M} + \text{H} - 2 \text{H}_2\text{O}]^+$, 329.3 $[\text{M} + \text{H} - 3 \text{H}_2\text{O}]^+$. HRMS (ESI⁺): calcd. for $\text{C}_{22}\text{H}_{37}\text{O}_4$ $[\text{M} + \text{H} - \text{H}_2\text{O}]^+$ 365.2692; found 365.2700.

17-F₂-Dihomo-IsoP (2) Derived from (17S)-26: The same procedure described for the synthesis of (17S)-F₂-dihomo-IsoP (2) was applied to 69 mg of alcohol (17S)-26 to give 32 mg of 17-F₂-dihomo-IsoP (2; 77% over two steps) with similar spectral data.

(Z)-Hex-3-enyltriphenylphosphonium Iodide (31): A solution of 3-hexyn-1-ol (6.0 mL, 50.9 mol) in CH_2Cl_2 (100 mL) was added through a cannula to a solution of Ph_3P (19.8 g, 75.5 mol), imidazole (10.2 g, 150 mol), and iodine (19.0 g, 74.8 mol) in CH_2Cl_2 (200 mL) at 0 °C. The reaction mixture was warmed to room temp. over 2.5 h, and a solution of $\text{Na}_2\text{S}_2\text{O}_3$ (25%, 300 mL) was added. After stirring for 15 min, the mixture was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (100% pentane) to afford 10.7 g of the iodide as a colorless oil (100%). R_f = 0.90 (5:5 cyclohexane/Et₂O). IR: $\tilde{\nu}$ = 2961, 1454, 1238, 1168 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 5.40–5.65 (m, 1 H), 5.15–5.35 (m, 1 H), 3.12 (t, J = 7.3 Hz, 2 H), 2.60 (q, J = 7.2 Hz, 2 H), 1.90–2.20 (m, 2 H), 0.97 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 134.3 (1 C, CH), 127.2 (1 C, CH), 31.5 (1 C, CH_2), 20.8 (1 C, CH_2), 14.3 (1 C, CH_3), 5.8 (1 C, CH_2) ppm. Ph_3P (20.0 g, 76.3 mol) and a catalytic amount of K_2CO_3 were added to a solution of this iodide (10.7 g, 50.9 mol) in CH_3CN (300 mL). The reaction mixture was heated at reflux overnight, then cooled, and the solvent was removed under reduced pressure. The residue was purified by column chromatography (solid SiO_2 deposit, 9:1 $\text{CH}_2\text{Cl}_2/\text{MeOH}$) to afford 21.0 g of the phosphonium salt **31** as a white powder (87% yield over two steps). R_f = 0.30 (9:1 EtOAc/MeOH). M.p. 120 °C. IR: $\tilde{\nu}$ = 3254, 2875, 1706, 1471, 1253, 1051 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 7.55–7.90 (m, 15 H), 5.20–5.50 (m, 2 H), 3.50–3.75 (m, 2 H), 2.25–2.55 (m, 2 H), 1.75–1.90 (m, 2 H), 0.80 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 135.0 (3 C, CH), 134.1 (3 C, Cq), 133.2 (6 C, CH), 130.3 (6 C, CH), 124.9 (1 C, CH), 124.7 (1 C, CH), 117.5 (d, $J_{\text{C-P}}$ = 85.4 Hz, 1 C, CH_2), 22.9 (d, $J_{\text{C-P}}$ = 48.5 Hz, 1 C, CH_2), 20.1 (d, $J_{\text{C-P}}$ = 30.0 Hz, 1 C, CH_2), 13.7 (1 C, CH_3) ppm. ^{31}P NMR (120 MHz, CDCl_3): δ = 24.5 ppm.

Methyl (E)-7-[(1S,2R,3R,5S)-2-(2-Acetoxyethyl)-3,5-bis(tert-butyl-dimethylsilyloxy)cyclopentyl]-5-oxohept-6-enoate (28): A Dess–Martin periodinane solution (5.0 mL of a 0.47 M solution in CH_2Cl_2 , 2.35 mmol) was added dropwise to a solution of *ent*-**5** (305 mg, 0.68 mmol) in CH_2Cl_2 (15 mL). After completion of the reaction (TLC), 10% aq. $\text{NaHCO}_3/\text{Na}_2\text{S}_2\text{O}_3$ (1:1, 40 mL) was added. After stirring for 1.5 h, the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The material was directly used in the next step without further purification. NaHMDS (2.0 mL, 2 M in THF, 4.0 mmol) was added dropwise to a solution of the β -keto phosphonate **27** (1.15 g, 4.11 mmol) in THF (15 mL) at 0 °C. After 1 h

at 0 °C, the reaction mixture was added through a cannula to the aldehyde THF (15 mL) at –78 °C. The reaction mixture was allowed to warm to room temp. overnight. Then the reaction was quenched with H_2O (10 mL) and Et_2O (10 mL). The mixture was extracted with Et_2O (3 × 40 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (7:3 pentane/Et₂O) to afford 286 mg of the enone **28** as a colorless oil (73% over two steps). R_f = 0.48 (5:5 cyclohexane/Et₂O). $[\alpha]_{\text{D}}^{20}$ = –23.0 (c = 1, CHCl_3). IR: $\tilde{\nu}$ = 2929, 1737, 1247, 1055 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 6.60 (dd, J = 10.4, 5.0 Hz, 1 H), 6.10 (d, J = 15.6 Hz, 1 H), 3.95–4.10 (m, 2 H), 3.75–3.95 (m, 2 H), 3.64 (s, 3 H), 2.65–2.80 (m, 1 H), 2.60 (t, J = 7.1 Hz, 2 H), 2.30–2.45 (m, 3 H), 2.30 (m, 1 H), 2.00 (s, 3 H), 1.80–2.00 (m, 2 H), 1.35–1.75 (m, 3 H), 0.83 (d, J = 7.4 Hz, 18 H), –0.01 (d, J = 12.0 Hz, 12 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 199.0 (1 C, Cq), 173.7 (1 C, Cq), 171.1 (1 C, Cq), 144.9 (1 C, CH), 131.4 (1 C, CH), 76.1 (1 C, CH), 75.3 (1 C, CH), 63.2 (1 C, CH_2), 53.2 (1 C, CH), 51.6 (1 C, CH_3), 46.4 (1 C, CH), 44.3 (1 C, CH_2), 39.8 (1 C, CH_2), 33.1 (1 C, CH_2), 28.0 (1 C, CH_2), 25.8 (6 C, CH_3), 21.1 (1 C, CH_3), 19.2 (1 C, CH_2), 18.0 (2 C, Cq), –4.3 (1 C, CH_3), –4.3 (2 C, CH_3), –4.8 (1 C, CH_3) ppm. MS (ESI⁺): m/z = 571.4 $[\text{M} + \text{H}]^+$, 439.3 $[\text{M} - \text{OTBS}]^+$, 307.2 $[\text{M} - 2 \text{OTBS}]^+$. HRMS (ESI⁺): calcd. for $\text{C}_{29}\text{H}_{55}\text{O}_7\text{Si}_2$ $[\text{M} + \text{H}]^+$ 571.3486; found 571.3486.

Methyl (E)-7-[(1S,2R,3R,5S)-2-(2-Acetoxyethyl)-3,5-bis(tert-butyl-dimethylsilyloxy)cyclopentyl]-5-(tert-butyl dimethylsilyloxy)hept-6-enoate [(5RS)-29]: $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (98 mg, 0.26 mmol) was added to a solution of enone **28** (150 mg, 0.26 mmol) in MeOH (15 mL). The mixture was cooled to 0 °C, and NaBH_4 was added (7.6 mg, 0.20 mmol). After 10 min, the reaction was quenched with H_2O (12 mL) and Et_2O (5 mL). The reaction mixture was extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (8:2 pentane/Et₂O) to afford 145 mg of the allylic alcohol (96%). R_f = 0.22 (5:5 cyclohexane/Et₂O). $[\alpha]_{\text{D}}^{20}$ = –27.2 (c = 1, CHCl_3). IR: $\tilde{\nu}$ = 3480, 2929, 1738, 1248, 1056 cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ = 5.45–5.60 (m, 1 H), 5.25–5.45 (m, 1 H), 4.15–4.35 (m, 1 H), 3.90–4.15 (m, 2 H), 3.70–3.90 (m, 2 H), 3.64 (s, 3 H), 2.40–2.65 (m, 1 H), 2.20–2.40 (m, 3 H), 2.05–2.20 (m, 1 H), 2.00 (s, 3 H), 1.92 (s, 1 H), 1.60–1.80 (m, 3 H), 1.45–1.60 (m, 4 H), 0.85 (d, J = 6.0 Hz, 18 H), –0.00 (d, J = 8.8 Hz, 12 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 174.2 (1 C, Cq), 171.5 (1 C, Cq), 135.7 (1 C, CH), 130.0 (1 C, CH), 76.2 (1 C, CH), 72.6 (1 C, CH), 72.0 (1 C, CH), 63.5 (1 C, CH_2), 52.8 (1 C, CH), 51.6 (1 C, CH_3), 45.7 (1 C, CH), 44.3 (1 C, CH_2), 36.6 (1 C, CH_2), 33.9 (1 C, CH_2), 28.0 (1 C, CH_2), 25.9 (6 C, CH_3), 21.2 (1 C, CH_3), 21.0 (1 C, CH_2), 18.1 (2 C, Cq), –4.2 (1 C, CH_3), –4.5 (1 C, CH_3), –4.6 (1 C, CH_3), –4.7 (1 C, CH_3) ppm. MS (ESI⁺): m/z = 555.4 $[\text{M} + \text{H} - \text{H}_2\text{O}]^+$, 423.2 $[\text{M} + \text{H} - \text{H}_2\text{O} - \text{OTBS}]^+$, 291.2 $[\text{M} + \text{H} - \text{H}_2\text{O} - 2 \text{OTBS}]^+$. HRMS (ESI⁺): calcd. for $\text{C}_{29}\text{H}_{55}\text{O}_6\text{Si}_2$ $[\text{M} + \text{H} - \text{H}_2\text{O}]^+$ 555.3537; found 555.3534. Imidazole (70 mg, 1.0 mmol), DMAP (10 mg, 0.08 mmol), and TBSCl (78 mg, 0.52 mmol) were successively added to a solution of the allylic alcohol (197 mg, 0.34 mmol) in DMF (15 mL). After stirring overnight, the reaction was quenched with H_2O (30 mL) and Et_2O (15 mL). The mixture was extracted with Et_2O (3 × 20 mL), and the combined organic layers were washed with H_2O (3 × 20 mL) and brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (9:1 pentane/Et₂O) to afford 235 mg of **29** as a colorless oil (100%). R_f = 0.77 (5:5 cyclohexane/Et₂O). $[\alpha]_{\text{D}}^{20}$ = –29.4 (c = 1, CHCl_3). IR: $\tilde{\nu}$ = 2952, 2928, 2856, 1741, 1248, 1055 cm^{-1} . ^1H NMR (300 MHz, CDCl_3):

$\delta = 5.47$ (dd, $J = 10.0, 5.5$ Hz, 1 H), 5.20–5.40 (m, 1 H), 3.95–4.20 (m, 3 H), 3.75–3.95 (m, 2 H), 3.66 (s, 3 H), 2.45–2.60 (m, 1 H), 2.25–2.40 (m, 3 H), 2.20 (m, 1 H), 2.02 (s, 3 H), 1.30–1.85 (m, 7 H), 0.70–1.00 (m, 27 H), 0.02 (d, $J = 8.4$ Hz, 18 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): $\delta = 174.1$ (1 C, Cq), 171.2 (1 C, Cq), 135.8 (1 C, CH), 127.9 (1 C, CH), 127.5 (1 C, CH), 76.6 (1 C, CH), 76.3 (1 C, CH), 72.8 (1 C, CH), 63.5 (1 C, CH_2), 53.0 (1 C, CH), 52.8 (1 C, CH), 51.6 (1 C, CH_3), 45.5 (1 C, CH), 44.3 (1 C, CH_2), 37.8 (1 C, CH_2), 34.0 (1 C, CH_2), 27.7 (1 C, CH_2), 25.9 (9 C, CH_3), 21.1 (1 C, CH_3), 20.8 (1 C, CH_2), 18.3 (2 C, Cq), 18.1 (1 C, Cq), -4.2 (1 C, CH_3), -4.3 (1 C, CH_3), -4.4 (1 C, CH_3), -4.5 (1 C, CH_3), -4.6 (1 C, CH_3), -4.7 (1 C, CH_3) ppm. MS (ESI $^+$): $m/z = 788.6$ [$\text{M} + \text{H} + \text{Et}_3\text{N}$] $^+$, 555.4 [$\text{M} - \text{OTBS}$] $^+$, [$\text{M} - 2 \text{OTBS}$] $^+$, 291.2 [$\text{M} - 3 \text{OTBS}$] $^+$. HRMS (ESI $^+$): calcd. for $\text{C}_{41}\text{H}_{86}\text{NO}_7\text{Si}_3$ [$\text{M} + \text{H} + \text{Et}_3\text{N}$] $^+$ 788.5712; found 788.5732.

Methyl (S,E)-7-[(1S,2R,3R,5S)-3,5-Bis(tert-butylidimethylsilyloxy)-2-(2-hydroxyethyl)cyclopentyl]-5-(tert-butylidimethylsilyloxy)hept-6-enoate [(5S)-30] and Methyl (R,E)-7-[(1S,2R,3R,5S)-3,5-Bis(tert-butylidimethylsilyloxy)-2-(2-hydroxyethyl)cyclopentyl]-5-(tert-butylidimethylsilyloxy)hept-6-enoate [(5R)-30]: K_2CO_3 (47 mg, 0.36 mmol) was added to a solution of acetate **29** (66 mg, 0.096 mmol) in MeOH (5 mL). After 2 h, the reaction was quenched with a solution of $\text{H}_2\text{O}/\text{Et}_2\text{O}$ (15 mL). The mixture was extracted with pentane/ Et_2O (3×15 mL), washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (7:3 pentane/ Et_2O) to afford 25 mg of (S)-**30** and 12 mg of (R)-**30** as colorless oils, together with 22 mg of racemic **30**. (5S)-**30**: $R_f = 0.45$ (5:5 cyclohexane/ Et_2O). $[\alpha]_D^{20} = -14.8$ ($c = 1$, CHCl_3). IR: $\tilde{\nu} = 3289, 2954, 2930, 2857, 1742, 1472, 1253, 1062 \text{ cm}^{-1}$. ^1H NMR (300 MHz, CDCl_3): $\delta = 5.20$ –5.65 (m, 2 H), 4.00–4.20 (m, 1 H), 3.75–3.95 (m, 2 H), 3.50–3.75 (m, 5 H), 2.60 (m, 6 H), 1.30–1.75 (m, 7 H), 0.70–1.00 (m, 27 H), -0.20 – 0.20 (m, 18 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): $\delta = 174.2$ (1 C, Cq), 135.2 (1 C, CH), 128.0 (1 C, CH), 76.8 (1 C, CH), 76.2 (1 C, CH), 72.2 (1 C, CH), 61.7 (1 C, CH_2), 53.6 (1 C, CH), 51.5 (1 C, CH_3), 45.9 (1 C, CH), 44.3 (1 C, CH_2), 37.4 (1 C, CH_2), 33.9 (1 C, CH_2), 32.4 (1 C, CH_2), 25.8 (9 C, CH_3), 20.4 (1 C, CH_2), 18.1 (1 C, Cq), 18.0 (1 C, Cq), 17.9 (1 C, Cq), -4.2 (1 C, CH_3), -4.6 (1 C, CH_3), -4.7 (1 C, CH_3), -4.8 (2 C, CH_3), -4.9 (1 C, CH_3) ppm. MS (ESI $^+$): $m/z = 645.3$ [$\text{M} + \text{H}$] $^+$, 513.2 [$\text{M} + \text{H} - \text{OTBS}$] $^+$, 381.3 [$\text{M} + \text{H} - 2 \text{OTBS}$] $^+$, 249.2 [$\text{M} + \text{H} - 3 \text{OTBS}$] $^+$. HRMS (ESI $^+$): calcd. for $\text{C}_{33}\text{H}_{69}\text{O}_6\text{Si}_3$ [$\text{M} + \text{H}$] $^+$ 645.4402; found 645.4408. (5R)-**30**: $R_f = 0.49$ (5:5 cyclohexane/ Et_2O). $[\alpha]_D^{20} = -15.5$ ($c = 1$, CHCl_3). IR: $\tilde{\nu} = 3289, 2954, 2930, 2857, 1742, 1472, 1253, 1062 \text{ cm}^{-1}$. ^1H NMR (300 MHz, CDCl_3): $\delta = 5.35$ –5.50 (m, 1 H), 5.15–5.35 (m, 1 H), 4.00–4.15 (m, 1 H), 3.80–3.95 (m, 2 H), 3.50–3.80 (m, 5 H), 2.60 (m, 6 H), 1.45–1.65 (m, 7 H), 0.70–1.00 (m, 27 H), -0.20 – 0.20 (m, 18 H) ppm. ^{13}C NMR (75 MHz, CDCl_3): $\delta = 174.4$ (1 C, Cq), 135.7 (1 C, CH), 128.3 (1 C, CH), 76.2 (2 C, CH), 73.1 (1 C, CH), 61.9 (1 C, CH_2), 54.1 (1 C, CH), 51.7 (1 C, CH_3), 46.0 (1 C, CH), 44.5 (1 C, CH_2), 37.8 (1 C, CH_2), 34.0 (1 C, CH_2), 32.7 (1 C, CH_2), 26.0 (9 C, CH_3), 20.8 (1 C, CH_2), 18.3 (1 C, Cq), 18.1 (2 C, Cq), -4.0 (1 C, CH_3), -4.1 (1 C, CH_3), -4.6 (4 C, CH_3) ppm. MS (ESI $^+$): $m/z = 645.3$ [$\text{M} + \text{H}$] $^+$, 513.2 [$\text{M} + \text{H} - \text{OTBS}$] $^+$, 381.3 [$\text{M} + \text{H} - 2 \text{OTBS}$] $^+$, 249.2 [$\text{M} + \text{H} - 3 \text{OTBS}$] $^+$. HRMS (ESI $^+$): calcd. for $\text{C}_{33}\text{H}_{69}\text{O}_6\text{Si}_3$ [$\text{M} + \text{H}$] $^+$ 645.4402; found 645.4398.

5-F_{3t}-IsoP (3): A Dess–Martin periodinane solution (1.0 mL of a 0.47 M solution in CH_2Cl_2 , 0.47 mmol) was added to a solution of alcohol (5S)-**30** (102 mg, 0.158 mmol) in CH_2Cl_2 (5 mL). After completion of the reaction (TLC), a 10% aq. $\text{NaHCO}_3/\text{Na}_2\text{S}_2\text{O}_3$ solution (1:1, 20 mL) was added. After stirring for 1.5 h, the mixture was extracted with CH_2Cl_2 (3×10 mL). The combined or-

ganic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The material was directly used in the next step without further purification. KHMDS (1 mL, 0.5 M in toluene, 0.50 mmol) was added dropwise to a suspension of the dried phosphonium salt **17** (238 mg, 0.51 mmol) in THF (8 mL) at -78°C . After 1 h, the mixture was added through a cannula to the aldehyde (0.158 mmol) in THF (8 mL) at -78°C . The reaction mixture was allowed to warm to room temp. overnight. The reaction was then quenched with a saturated aqueous solution of NH_4Cl (15 mL) and the mixture warmed to room temp. The mixture was extracted with Et_2O (3×10 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (95:5 cyclohexane/ Et_2O) to afford 66.3 mg of the triene as a colorless oil (59% over two steps). HCl (370 μL , 1 M, 0.37 mmol) was added to a solution of the triene (60 mg, 0.084 mmol) in THF (4 mL). After 2.5 d at room temp., brine (10 mL) was added, and the mixture was extracted with EtOAc (3×15 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (92:8 EtOAc/MeOH) to afford 8.5 mg of 5-F_{3t}-IsoP (**3**) as a colorless oil (29%). $R_f = 0.55$ (8:2 AcOEt/MeOH + 1% AcOH). $[\alpha]_D^{20} = -6.8$ ($c = 0.5$, MeOH). ^1H NMR (300 MHz, $[\text{D}_4]\text{MeOH}$): $\delta = 5.50$ –5.70 (m, 2 H), 5.15–5.70 (m, 4 H), 3.80–4.10 (m, 3 H), 2.60–2.90 (m, 3 H), 2.40–2.60 (m, 1 H), 2.20–2.35 (m, 2 H), 1.90–2.20 (m, 5 H), 1.45–1.85 (m, 5 H), 0.97 (t, $J = 7.5$ Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $[\text{D}_4]\text{MeOH}$): $\delta = 177.5$ (1 C, Cq), 136.5 (1 C, CH), 132.7 (1 C, CH), 130.1 (1 C, CH), 129.9 (1 C, CH), 129.6 (1 C, CH), 128.4 (1 C, CH), 76.2 (1 C, CH), 76.1 (1 C, CH), 73.0 (1 C, CH), 53.5 (1 C, CH), 51.3 (1 C, CH), 43.6 (1 C, CH_2), 37.8 (1 C, CH_2), 34.8 (1 C, CH_2), 27.3 (1 C, CH_2), 26.6 (1 C, CH_2), 22.3 (1 C, CH_2), 21.5 (1 C, CH_2), 14.7 (1 C, CH_3) ppm. HRMS (ESI $^+$): calcd. for $\text{C}_{20}\text{H}_{31}\text{O}_4$ [$\text{M} - \text{H}_2\text{O}$] $^+$ 335.2222; found 335.2213.

5-epi-5-F_{3t}-IsoP (5R-3): The same procedure as described for the synthesis of 5-F_{3t}-IsoP (**3**) was applied to 47 mg of alcohol (5R)-**30** to give 7.4 mg of 5-epi-5-F_{3t}-IsoP [(5R)-**3**] (25% over three steps). $R_f = 0.50$ (8:2 EtOAc/MeOH + 1% AcOH). $[\alpha]_D^{20} = -7.4$ ($c = 0.4$, MeOH). ^1H NMR (300 MHz, $[\text{D}_4]\text{MeOH}$): $\delta = 5.50$ –5.70 (m, 2 H), 5.15–5.70 (m, 4 H), 3.80–4.10 (m, 3 H), 2.60–2.90 (m, 3 H), 2.40–2.60 (m, 1 H), 2.20–2.35 (m, 2 H), 1.90–2.20 (m, 5 H), 1.45–1.85 (m, 5 H), 0.97 (t, $J = 7.5$ Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $[\text{D}_4]\text{MeOH}$): $\delta = 177.5$ (1 C, Cq), 136.6 (1 C, CH), 132.7 (1 C, CH), 130.6 (1 C, CH), 129.9 (1 C, CH), 129.6 (1 C, CH), 128.3 (1 C, CH), 76.3 (1 C, CH), 76.2 (1 C, CH), 73.3 (1 C, CH), 53.8 (1 C, CH), 51.4 (1 C, CH), 43.5 (1 C, CH_2), 37.8 (1 C, CH_2), 34.9 (1 C, CH_2), 27.4 (1 C, CH_2), 26.6 (1 C, CH_2), 22.2 (1 C, CH_2), 21.5 (1 C, CH_2), 14.7 (1 C, CH_3) ppm. HRMS (ESI $^+$): calcd. for $\text{C}_{20}\text{H}_{31}\text{O}_4$ [$\text{M} - \text{H}_2\text{O}$] $^+$ 335.2222; found 335.2216.

{(1R,2R,3R,5S)-3,5-Bis(tert-butylidimethylsilyloxy)-2-[(2Z,5Z)-octa-2,5-dienyl]cyclopentyl}methanol (33): $t\text{BuOK}$ (68 mg, 0.606 mmol) was added to a suspension of the dried phosphonium salt **31** (313 mg, 0.663 mmol) in THF (5 mL) at -78°C . After 1 h at -78°C , the mixture was added through a cannula to the lactol **32** (40 mg, 0.0995 mmol) in THF (5 mL) at -78°C . After 2.5 h at -78°C , the reaction mixture was allowed to warm to room temp. overnight. The reaction was then quenched with a 10% NH_4Cl solution (20 mL) and the mixture stirred for 15 min. The mixture was extracted with Et_2O (3×20 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (9:1 cyclohexane/ Et_2O) to afford 30 mg of **33** (64%). $R_f = 0.38$ (8:2 cyclohexane/ Et_2O). $[\alpha]_D^{20} = -1.4$ ($c = 1$,

CHCl₃). IR: $\tilde{\nu}$ = 3495, 2957, 2930, 2857, 1472, 1253, 1069 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 5.20–5.60 (m, 4 H), 3.90–4.20 (m, 1 H), 3.60–3.80 (m, 3 H), 2.70–2.90 (m, 2 H), 2.20–2.45 (m, 2 H), 1.90–2.20 (m, 5 H), 1.70–2.00 (m, 1 H), 0.98 (t, J = 7.4 Hz, 3 H), 0.88 (s, 18 H), 0.08 (d, J = 9.6 Hz, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 132.2 (1 C, CH), 130.1 (1 C, CH), 129.3 (1 C, CH), 127.0 (1 C, CH), 75.7 (1 C, CH), 75.2 (1 C, CH), 62.8 (1 C, CH₂), 50.2 (1 C, CH₂), 48.2 (1 C, CH), 44.6 (1 C, CH), 30.4 (1 C, CH₂), 25.9 (6 C, CH₃), 25.8 (1 C, CH₂), 20.7 (1 C, CH₂), 18.0 (2 C, Cq), 14.4 (1 C, CH₃), -4.1 (1 C, CH₃), -4.3 (1 C, CH₃), -4.6 (1 C, CH₃), -4.7 (1 C, CH₃) ppm. MS (ESI⁺): m/z = 469.4 [M + H]⁺. HRMS (ESI⁺): calcd. for C₂₆H₅₃O₅Si₂ [M + H]⁺ 469.3533; found 469.3538.

Methyl (E)-7-((1S,2R,3R,5S)-3,5-Bis(tert-butylidimethylsilyloxy)-2-[(2Z,5Z)-octa-2,5-dienyl]cyclopentyl)-5-oxohept-6-enoate (34): A Dess–Martin periodinane solution (600 μ L of a 0.47 M solution in CH₂Cl₂, 0.28 mmol) was added dropwise to a solution of **33** (30 mg, 0.066 mmol) in CH₂Cl₂ (5 mL). After completion of the reaction (TLC), 10% aq. NaHCO₃/Na₂S₂O₃ (1:1, 10 mL) was added. After stirring for 1.5 h, the mixture was extracted with CH₂Cl₂ (3 \times 15 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The material was directly used in the next step without further purification. NaHMDS (200 μ L, 2 M in THF, 0.40 mmol) was added dropwise to a solution of the β -keto phosphonate **27** (200 mg, 0.71 mmol) in THF (5 mL) at 0 °C. After 1 h at 0 °C, the mixture was added through a cannula to the aldehyde in THF (5 mL) at -78 °C. Then the reaction mixture was allowed to warm to room temp. overnight. The reaction was then quenched with H₂O (10 mL) and Et₂O (10 mL). The mixture was extracted with Et₂O (3 \times 20 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (9:1 pentane/Et₂O) to afford 31.7 mg of enone **34** (83.5% over two steps). R_f = 0.40 (8:2 cyclohexane/Et₂O). [α]_D²⁰ = -1.0 (c = 1, CHCl₃). IR: $\tilde{\nu}$ = 2955, 2930, 2857, 1738, 1253, 1064 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 6.60–6.80 (m, 1 H), 6.13 (d, J = 15.6 Hz, 1 H), 5.15–5.50 (m, 4 H), 3.95–4.05 (m, 1 H), 3.80–3.95 (m, 1 H), 3.66 (s, 3 H), 2.65–2.90 (m, 3 H), 2.58 (t, J = 7.1 Hz, 2 H), 1.80–2.25 (m, 8 H), 1.50–1.80 (m, 2 H), 0.96 (t, J = 7.5 Hz, 3 H), 0.86 (d, J = 8.4 Hz, 18 H), -0.10–0.10 (m, 12 H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 199.1 (1 C, Cq), 173.8 (1 C, Cq), 146.1 (1 C, CH), 132.2 (1 C, CH), 131.4 (1 C, CH), 129.3 (1 C, CH), 128.1 (1 C, CH), 127.0 (1 C, CH), 75.7 (1 C, CH), 75.4 (1 C, CH), 52.9 (1 C, CH), 51.7 (1 C, CH₃), 50.9 (1 C, CH), 44.5 (1 C, CH₂), 39.6 (1 C, CH₂), 33.2 (1 C, CH₂), 26.6 (1 C, CH₂), 25.9 (6 C, CH₃), 25.8 (1 C, CH₂), 19.3 (1 C, CH₂), 18.1 (2 C, Cq), 14.4 (1 C, CH₃), -4.3 (1 C, CH₃), -4.4 (1 C, CH₃), -4.5 (2 C, CH₃), -4.6 (1 C, CH₃) ppm. MS (ESI⁺): m/z = 593.4 [M + H]⁺. HRMS (ESI⁺): calcd. for C₃₃H₆₁O₅Si₂ [M + H]⁺ 593.4058; found 593.4060.

5-F_{3t}-IsoP (3): LiAlH₄ (330 μ L, 1 M/THF, 0.330 mmol) was added dropwise to a solution of dry (*S*)-binaphthol (96 mg, 0.335 mmol) in freshly distilled dry THF (1.4 mL) at room temp. After 5 min, freshly distilled dry EtOH (330 μ L, 1 M in THF, 0.330 μ L) was added dropwise. The reaction mixture was cooled to -100 °C, and the enone **34** (31.7 mg, 0.054 mmol) was added through a cannula. The reaction mixture was slowly warmed to -30 °C. MeOH (500 μ L) and H₂O (1.0 mL) were added, and the suspension was filtered through a plug of Celite, which had previously been washed with Et₂O. The filtrate was washed with H₂O (10 mL). The mixture was extracted with Et₂O (3 \times 15 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The excess of binaphthol was precipitated with hexanes, but traces of binaphthol remained. After con-

centration, the residue was purified by column chromatography (8:2 heptane/Et₂O). Unfortunately, the excess binaphthol could not be completely removed. Therefore, the mixture of allylic alcohol **35**, lactone **36**, and binaphthol was used directly in the next step. HCl (1 M, 140 μ L, 0.14 mmol) was added to a solution of the previous material in THF (2 mL). After 2 d at room temp., brine (10 mL) was added. The mixture was extracted with EtOAc (3 \times 15 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure. The residue was directly used in the next step without further purification. LiOH (5 mg) was added to a solution of the previous material in THF/H₂O (1:1; 5 mL). After 4 h, a solution of HCl (1 M, 5 mL) was added until an acidic pH was obtained. The mixture was extracted with EtOAc (3 \times 10 mL). The combined organic layers were washed with brine, dried, and filtered. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (9:1 EtOAc/MeOH) to afford 1.2 mg of 5-F_{3t}-IsoP (**3**; 6.4% over three steps). The ¹³C NMR spectrum shows characteristic peaks at δ = 130.1, 76.2, 73.0, and 53.5 ppm, similar to the data obtained above for compound **3**.

Supporting Information (see footnote on the first page of this article): ¹H and ¹³C NMR spectra of all new products.

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