Synthesis of the C1–C14 Fragment of Sarcoglaucol-16-one via *Z*-Selective Ando-Type Horner–Wadsworth–Emmons Olefination

Christoph Gastl, Sabine Laschat*

Institut für Organische Chemie, Universität Stuttgart, Pfaffenwaldring 55, 70569 Stuttgart, Germany
Fax +49(711)68564285; E-mail: sabine.laschat@oc.uni-stuttgart.de

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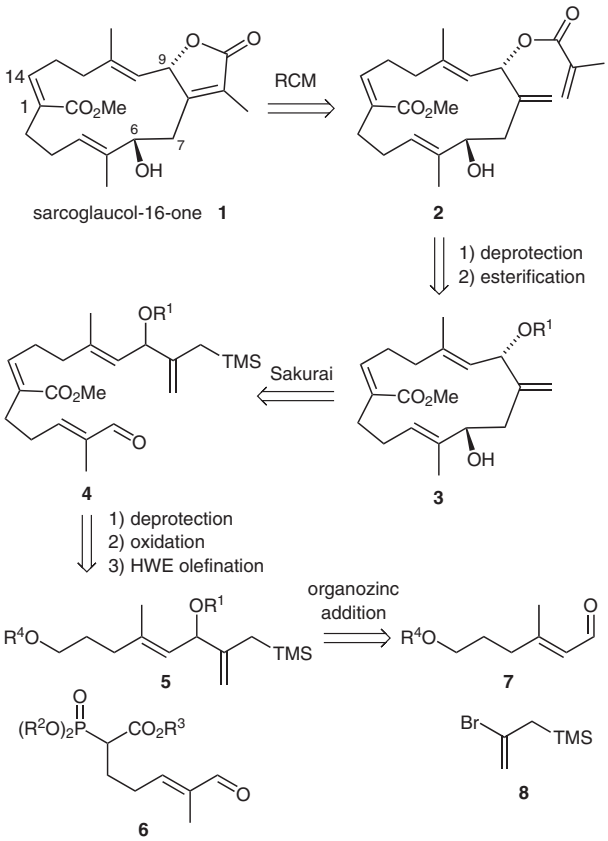
Abstract: A synthetic strategy involving a *Z*-selective Horner–Wadsworth–Emmons olefination was developed for the preparation of the sarcoglaucolone precursor methyl (2*Z*,6*E*)-8-(methoxymethoxy)-6-methyl-2-[(3*E*)-4-methyl-5-oxopent-3-enyl]-9-[(trimethylsilyl)methyl]deca-2,6,9-trienoate. The target compound was isolated in a *E*/*Z* ratio of 17:83

Key words: Ando-type reaction, olefination, cembranolide, natural product, macrocycles

Cembranolides are macrocyclic diterpenes of marine origin that possess a variety of interesting biological activities, such as cytotoxic, anti-inflammatory, anti-bacterial and anti-viral activities, which make these natural products promising targets for synthetic approaches[1–3] as pioneered by Marshall.[4] In 2004, Wright and König reported the isolation of the cembranolide sarcoglaucol-16-one (**1**) from a soft coral species belonging to the genus *Sarcophyton* (Scheme 1).[5] The structure of **1** was established by NMR analysis and the absolute stereochemistry was determined by the modified Mosher method. It was further shown that compound **1** displayed promising cytotoxic activity against MCF7 tumor cell lines.[5] From a synthetic point of view, sarcoglaucol-16-one (**1**) possesses the following structural features: (a) a 14-membered macrocycle with attached γ-butenolide unit,[6] (b) two stereogenic centres at C-6 and C-9 and (c) a methyl ester at a branching position of the diterpenoid, the latter being rather uncommon among the various cembranolides. Whereas the carbon skeleton of **1** can be biogenetically traced back to geranylacetone or geranylgeraniol,[1] results by Dorta on furanocembranolides revealed that a genus-specific oxidation cascade leads from a methyl group to a carboxylic acid or ester.[2e] However, the regioselective C–H oxidation of the branching methyl groups in a terpene precursor is rather difficult to achieve by chemical means,[7] and even treatment of terpene derivatives with isolated cytochrome P450 monooxygenases often yields complex product mixtures with competing or sometimes strongly favoured epoxide formation rather than allylic oxidation.[8,9] In order to develop a total synthesis of sarcoglaucol-16-one (**1**), we decided to first establish the C1–C14 carbon skeleton of the macrocycle **1** with correct configuration of the C=C double bonds, and to focus later on the installation of the stereogenic centres at C-6 and C-9. The results are reported below.

In our retrosynthetic approach, which is shown in Scheme 1, a ring-closing metathesis (RCM)[10,11] of macrocyclic methacrylate **2** was planned as the final step. Methacrylate **2** should be obtained from allylic alcohol derivative **3** via deprotection and esterification. Macrocyclization towards **3** should be achieved via intramolecular Sakurai reaction[12,13] of enal **4** which, in turn, could arise from the C7–C14 fragment **5** via deprotection of the primary alcohol, oxidation to the corresponding aldehyde, followed by Horner–Wadsworth–Emmons olefination with phosphonate **6** (i.e., C1–C6 fragment). We hoped to establish the stereogenic centre at C-9 via a Noyori-type addition[14] of an organozinc species derived from isopropenyl bromide **8** to the α,β-unsaturated aldehyde **7**.



Scheme 1

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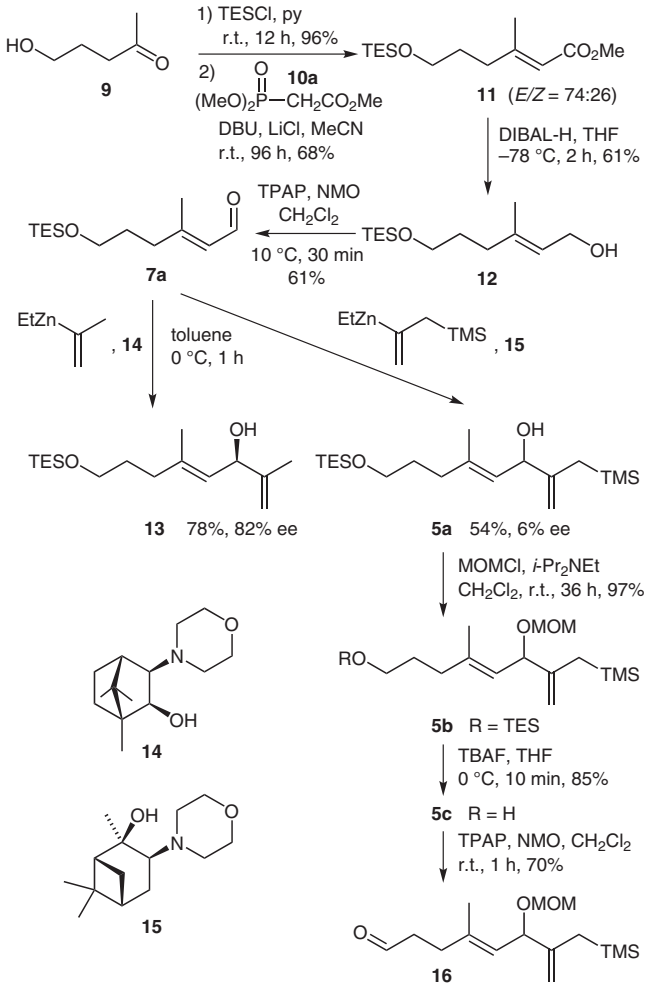
The synthesis of the C7–C14 fragment commenced with protection of 5-hydroxypentan-2-one (**9**) with triethylsilyl chloride (TESCl) in the presence of triethylamine at room temperature in 96% yield, followed by olefination with phosphonate **10a** in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and lithium chloride in acetonitrile at room temperature according to the procedure by Roush,[15] to yield the α,β-unsaturated ester **11** in 68% yield (*E*/*Z* = 74:26; Scheme 2). Reduction of **11** to the corresponding allylic alcohol **12** was achieved with diisobutylaluminum hydride (DIBAL-H)[16] in tetrahydrofuran (THF) at –78 °C, from which the pure *E*-isomer **12** could be obtained after flash chromatography in 61% yield.



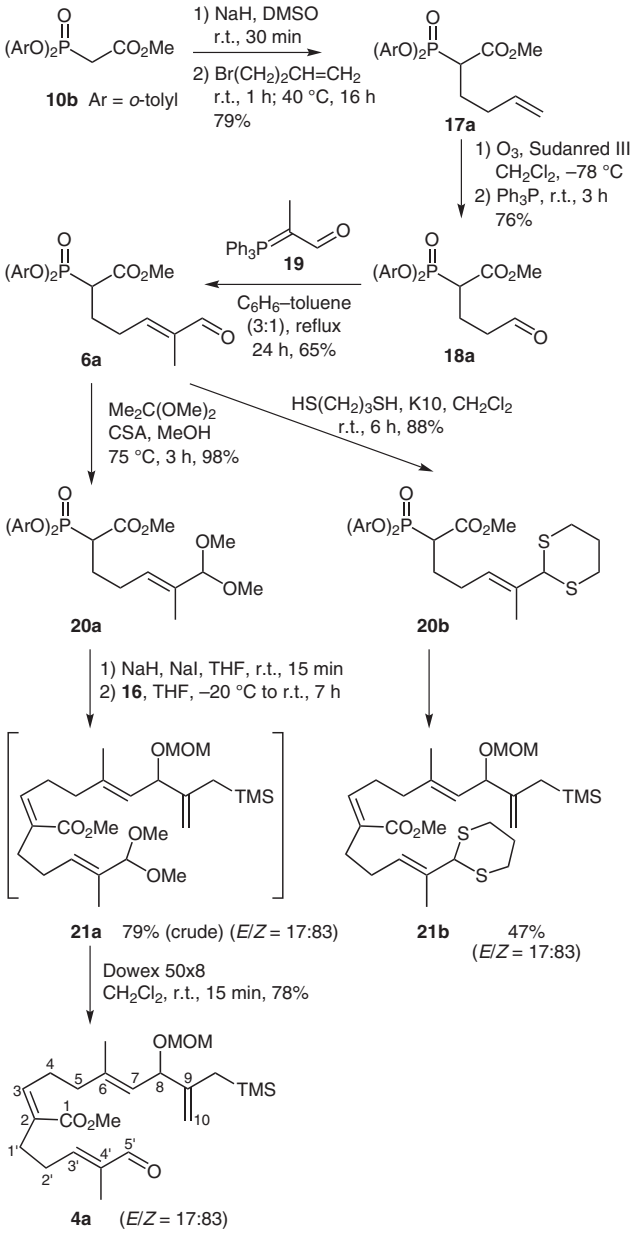
Scheme 2

Subsequent oxidation with tetrapropylammonium perruthenate (TPAP) and *N*-methylmorpholine *N*-oxide (NMO) in dichloromethane at 10 °C, yielded enal **7a** in 61% yield. Next, Noyori-type 1,2-additions[14,17] of an organozinc species to enal **7a** were investigated in order to establish the stereochemistry at C-9 of sarcoglaucol-16-one (**1**). In a preliminary experiment, when enal **7a** was treated with ethylisopropenylzinc,[18] employing *N*-morpholinoisoborneol **14**[19] as chiral ligand, in toluene at 0 °C, the desired allylic alcohol **13** was isolated in 78% yield and 82% ee. However, when enal **7a** was treated with ethyl{1-[(trimethylsilyl)methyl]vinyl}zinc[20] in the presence of ligand **14** under similar conditions, allylic alcohol **5a** was isolated in 54% yield in racemic form. Then, the addition was performed with ligand **15**[21] instead of *N*-morpholinoisoborneol **14**, yielding the allylic alcohol **5a** in 54% yield with a disappointing 6% ee (see also Supporting Information for further experiments). Due to these unexpected difficulties, we decided to continue the synthetic efforts with the racemic material **5a**, which was protected with chloromethyl methyl ether (MOMCl) in dichloromethane in the presence of Hünig's base at room temperature to give the *O*-MOM-derivative **5b** in 97% yield. Subsequent deprotection of the TES group with tetrabutylammonium fluoride (TBAF) in THF at 0 °C gave **5c** in 85% yield, which was oxidised with TPAP and NMO in dichloromethane at room temperature to yield aldehyde **16** in 70% yield.

For the synthesis of the C1–C6 fragment **6a**, the Ando phosphonate **10b**[22] was deprotonated with sodium hydride in dimethylsulfoxide (DMSO) at room temperature, followed by addition of 4-bromobut-1-ene at 40 °C to yield the phosphonate derivative **17a** in 79% based on recovered starting material **10b** (Scheme 3).

Compound **17a** was submitted to ozonolysis, the progress of which was monitored by addition of Sudanred III,[23] followed by reductive work-up with triphenylphosphane to give the aldehyde **18a** in 76% yield. Treatment with stabilized ylide **19**[24] in a (3:1) mixture of benzene and toluene under reflux gave the enal-substituted phosphonate **6a** in 65% yield. Compound **6a** was protected either with 2,2-dimethoxypropane in the presence of 10-camphorsulfonic acid (CSA) in methanol at room temperature to give the dimethylacetal **20a** in 98% yield, or with 1,3-propanedithiol and Montmorillonite K10 in dichloromethane at room temperature to give the corresponding dithioacetal **20b** in 88% yield. Phosphonate **20a** was deprotonated with sodium hydride in the presence of sodium iodide in THF at room temperature, followed by addition of the enal **16** in THF at –20 °C and warming to room temperature according to the procedure by Pikho,[25,26] to give the desired olefin **21a** in 79% crude yield, predominantly as the *Z*-isomer (*E*/*Z* = 17:83). Due to the fact that the crude product **21a** already contained 15% of enal **4a**, the mixture was treated with Dowex 50 × 8 ion-exchange resin in dichloromethane at room temperature in order to hydrolyze the dimethyl acetal; enal **4a** was isolated in 78% yield (*E*/*Z* = 17:83). Dithioacetal **20b** was treated in a similar manner with aldehyde **16** as described for phosphonate **20a**, and the corresponding olefin **21b** was isolated in 47% yield (*E*/*Z* = 17:83).

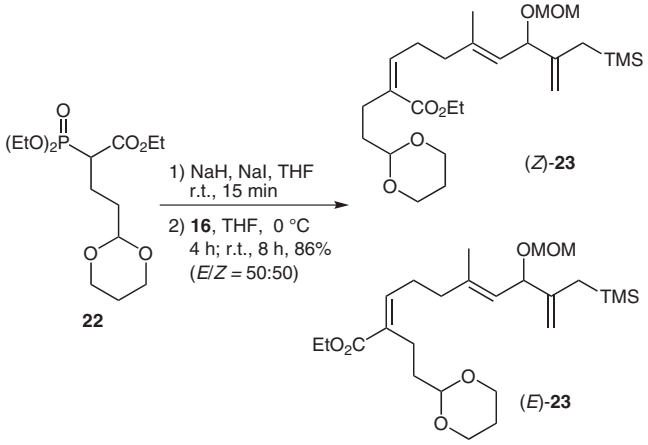
In order to check whether the Ando phosphonates **20a** and **20b** are required for the *Z*-selective Horner–Wadsworth–Emmons olefination, the structurally related diethyl phosphonate **22** was deprotonated with sodium hydride in the presence of sodium iodide in THF, followed by addition of aldehyde **16**, and the corresponding alkenes **23** were isolated in 80% yield as a mixture of *Z*- and *E*-isomers



Scheme 3

(50:50, Scheme 4). It should be noted that the Still–Gennari olefination[27] was not considered as an alternative method due to the use of expensive (bistrifluoroethyl)phosphonate and [18]crown-6-ether.

In conclusion, the acyclic C1–C14 carbon skeleton **4a** of sarcoglaucol-16-one (**1**) has been established by a convergent approach in ten steps (for the longest linear sequence) and 4.7% overall yield from hydroxyketone **9**, employing a *Z*-selective Ando-type Horner–Wadsworth–Emmons olefination of **20a** and aldehyde **16** as the key step. Attempts to improve the enantioselectivity of the 1,2-addition of isopropenylzinc derivatives to enal **7a** to gain access to the enantiomerically pure target molecule **4a** are currently in progress in our laboratories.



Scheme 4

Melting points were measured with a Mettler-Toledo DSC822e calorimeter and are uncorrected. IR spectra were recorded with a Bruker Vector 22 FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker Avance 300 or a Bruker Avance 500 spectrometer with TMS as an internal standard. Mass spectra were recorded with a Finnigan MAT 95 (CI) instrument with ammonia as reactant gas, a Varian MAT 711 (EI, 70 eV) and a Bruker Daltonics microTOF-Q (ESI) spectrometer with nitrogen as carrier gas. Flash chromatography was performed using Kieselgel 60, 40–63 μm (Fluka). All solvents were dried, and reactions were performed in dried glassware using standard Schlenk techniques. Reaction monitoring was performed with a Trace GC 2000 Ultra Optima 5-MS column (30 m × 0.25 mm) with hydrogen as carrier gas using different temperature programs. The enantioselectivity was detected by gas chromatography on chiral stationary phases.

The following compounds were prepared according to literature procedures: **10b**,[22] **11**,[4d] **19**,[24] diisopropenylzinc[18] and 2-bromo-3-trimethylsilylprop-1-ene.[20] For details of the preparation of ligand **15** and phosphonate **22**, see the Supporting Information.

(2*E*)-3-Methyl-6-[(triethylsilyl)oxy]hex-2-en-1-ol (12)

To a solution of **11** (4.27 g, 15.7 mmol) in THF (80 mL), was dropwise added DIBAL-H (52 mL, 62.7 mmol, 1.2 M in toluene) at –78 °C and the mixture was stirred for 2 h. Sat. Seignette salt solution (20 mL) was added at –78 °C, and the mixture was warmed to r.t., the layers were separated, the aqueous layer was extracted with Et_2O (5 × 100 mL) and the combined organic layers were dried over Na_2SO_4 and evaporated. The crude product was purified by flash chromatography on SiO_2 (hexanes–EtOAc, 5:1) to yield **12**.

Yield: 2.32 g (61%); pale-yellow oil; 100% *E* by ^{1}H NMR analysis; R_f = 0.34 (hexanes–EtOAc, 5:1).

FTIR (ATR): 3340 (w), 2952 (s), 2912 (s), 2876 (s), 1669 (w), 1458 (m), 1415 (m), 1382 (m), 1299 (w), 1238 (m), 1193 (w), 1095 (vs), 1003 (vs), 960 (s), 804 (s), 775 (m), 724 (vs), 669 (m) cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.58 (q, *J* = 7.9 Hz, 6 H, CH_2, TES), 0.96 (t, *J* = 7.9 Hz, 9 H, CH_3, TES), 1.34 (br s, OH), 1.59–1.72 (m, 2 H, H-4), 1.68 (d, *J* = 1.3 Hz, 3 H, CH_3), 2.03–2.11 (m, 2 H, H-5), 3.68 (t, *J* = 6.6 Hz, 2 H, H-6), 4.15 (dq, *J* = 6.9, 0.7 Hz, 2 H, H-1), 5.42 (tq, *J* = 6.9, 1.3 Hz, 1 H, H-2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 2.9 (CH_3, TES), 5.3 (CH_2, TES), 14.7 (C-4), 29.4 (C-5), 34.2 (CH_3), 57.9 (C-3), 60.9 (C-1), 121.8 (C-2), 138.1 (C-3).

GC/MS (EI): *m*/*z* (%) = 340 (6), 307 (10), 294 (4), 266 (8), 262 (3), 239 (4), 220 (2), 215 (7), 199 (3), 191 (22), 180 (23), 165 (4), 153

(8), 147 (9), 134 (86), 119 (44), 106 (38), 103 (41), 93 (42), 90 (38), 87 (7), 73 (100, TMS), 67 (7), 59 (10), 51 (13).

Anal. Calcd for $C_{13}H_{28}O_2Si$: C, 63.87; H, 11.56. Found: C, 63.78; H, 11.45.

(2*E*)-3-Methyl-6-[(triethylsilyl)oxy]hex-2-enal (7a)

To a solution of **12** (500 mg, 2.04 mmol) in CH_2Cl_2 (30 mL), were added powdered molecular sieves 4 Å (1.00 g), NMO (1.44 g, 12.3 mmol) and TPAP (30 mg, 0.08 mmol) at 0 °C. After 10 min, the mixture was warmed to r.t., filtered through SiO_2, evaporated and purified by flash chromatography (hexanes–EtOAc, 2:1) to yield aldehyde **7a**.

Yield: 302 mg (61%); colourless oil; R_f = 0.30 (hexane–EtOAc, 10:1).

FTIR (ATR): 2953 (s), 2912 (s), 2876 (s), 1673 (vs), 1634 (m), 1458 (m), 1414 (m), 1383 (m), 1239 (m), 1192 (m), 1097 (vs), 1008 (s), 956 (m), 863 (m), 799 (s), 725 (vs), 670 (m), 599 (w), 551 (w), 516 (w) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.59 (q, *J* = 7.9 Hz, 6 H, CH_2, TES), 0.96 (t, *J* = 7.9 Hz, 9 H, CH_3, TES), 1.67–1.79 (m, 2 H, H-5), 2.18 (d, *J* = 1.2 Hz, 3 H, H-7), 2.25–2.33 (m, 2 H, H-4), 3.63 (t, *J* = 6.2 Hz, 2 H, H-6), 5.89 (ddd, *J* = 8.0, 2.3, 1.2 Hz, 1 H, H-2), 10.00 (d, *J* = 8.0 Hz, 1 H, H-1).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 4.5 (CH_3, TES), 6.8 (CH_2, TES), 16.5 (C-5), 31.5 (C-4), 41.9 (C-7), 59.6 (C-6), 125.2 (C-2), 135.1 (C-3), 202.2 (C-1).

GC/MS (EI): *m*/*z* (%) = 224 (3), 182 (4), 165 (3), 149 (8), 134 (12), 131 (7), 120 (10), 115 (22, TES), 108 (43), 105 (38), 102 (8), 92 (88), 83 (62), 75 (22), 73 (100, TMS), 59 (36), 50 (24).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{26}NaO_2Si^+$: 265.1594; found: 265.1587.

(3*R*,4*E*)-2,5-Dimethyl-8-[(triethylsilyl)oxy]octa-1,4-dien-3-ol (13)

To a solution of diethylzinc (127 µL, 1.24 mmol) in toluene (3 mL), were added at r.t. over 15 min, diisopropenylzinc (413 µL, 0.41 mmol, 1 M in toluene) and ligand **14** (165 µL, 16.5 µmol, 0.1 M in toluene) and the mixture was cooled to 0 °C. Then, **7a** (100 mg, 0.41 mmol) was added and the reaction mixture was stirred for 1 h at 0 °C, hydrolyzed with sat. NH_4Cl (10 mL) and diluted with Et_2O (10 mL). The organic layer was separated, dried (Na_2SO_4), evaporated and the crude product was purified by flash chromatography on SiO_2 (hexanes–EtOAc, 12:1) to give **13**.

Yield: 91 mg (78%); colourless oil; R_f = 0.26 (hexanes–EtOAc, 10:1); 82% ee (by GC on Bondex α un β); $[\alpha]_D^{20}$ –36 (*c* = 1, $CHCl_3$).

FTIR (ATR): 3340 (m), 2939 (m), 2903 (m), 2876 (m), 2702 (w), 2548 (w), 2346 (w), 2189 (w), 1942 (m), 1651 (m), 1465 (m), 1415 (m), 1382 (m), 1335 (w), 1232 (m), 1095 (s), 1005 (s), 960 (m), 895 (m), 832 (m), 725 (vs), 670 (m) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.61 (q, *J* = 7.9 Hz, 6 H, CH_2, TES), 0.96 (t, *J* = 7.9 Hz, 9 H, CH_3, TES), 1.54 (d, *J* = 3.9 Hz, 1 H, OH), 1.6–1.71 (m, 2 H, H-7), 1.65 (dd, *J* = 1.2, 0.8 Hz, 3 H, H-10), 1.73 (d, *J* = 1.4 Hz, 3 H, H-9), 1.97–2.13 (m, 2 H, H-6), 4.04–4.07 (m, 1 H, H-3), 4.17–4.19 (m, 2 H, H-8), 4.84–4.85 (m, 1 H, H^a-1), 4.94–4.95 (m, 1 H, H^b-1), 5.36 (tq, *J* = 6.5, 1.4 Hz, 1 H, H-4).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 4.5 (CH_3, TES), 6.8 (CH_2, TES), 16.4 (C-10), 17.6 (C-9), 32.9 (C-7), 35.5 (C-6), 59.7 (C-8), 75.6 (C-3), 111.2 (C-1), 124.5 (C-4), 136.9 (C-5), 147.4 (C-2).

HRMS (ESI, positive): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{32}O_2SiNa$: 307.2064; found: 307.2073.

(4*E*)-5-Methyl-8-[(triethylsilyl)oxy]-2-[(trimethylsilyl)methyl]octa-1,4-dien-3-ol (5a)

To a solution of 2-bromo-3-trimethylsilylprop-1-ene (80 mg, 0.41 mmol) in Et_2O (1 mL), was added *t*-BuLi (565 µL, 0.85 mmol, 1.5 M in toluene) at –78 °C. The mixture was warmed to –20 °C over 1 h and re-cooled to –78 °C. Then, $ZnCl_2$ (207 µL, 0.21 mmol, 1 M in Et_2O) was added and the mixture was warmed to r.t. over 3 h, followed by sequential addition of diethylzinc (22 µL, 0.21 mmol) and **7a** (97 mg, 0.4 mmol) in Et_2O (1 mL). After 1 h, the reaction mixture was hydrolyzed by addition of sat. NH_4Cl (10 mL). The layers were separated and the organic layers were extracted with EtOAc (3 × 10 mL), dried (Na_2SO_4) and evaporated. The crude product was purified by flash chromatography on SiO_2 (hexanes–EtOAc, 10:1) to give **5a**.

Yield: 38 mg (54%); pale-yellow oil; R_f = 0.55 (hexanes–EtOAc, 10:1); 6% ee (by GC on Bondex α un β).

FTIR (ATR): 3370 (w), 2952 (s), 2912 (s), 2877 (s), 2568 (w), 2373 (w), 2181 (w), 1973 (m), 1635 (w), 1458 (m), 1415 (m), 1382 (m), 1247 (s), 1157 (m), 1096 (s), 1005 (s), 962 (m), 882 (s), 839 (vs), 796 (s), 724 (vs), 693 (s), 670 (m), 633 (m) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.04 (s, 9 H, TMS), 0.58 (q, *J* = 7.9 Hz, 6 H, CH_2, TES), 0.95 (t, *J* = 7.9 Hz, 9 H, CH_3, TES), 1.38 (ddd, *J* = 14.0, 1.1, 0.3 Hz, 1 H, H^a-10), 1.45 (d, *J* = 3.5 Hz, 1 H, OH), 1.59 (dd, *J* = 14.0, 1.1 Hz, 1 H, H^b-10), 1.63–1.69 (m, 2 H, H-7), 1.73 (d, *J* = 1.4 Hz, 3 H, H-9), 2.06–2.09 (m, 2 H, H-6), 3.59 (t, *J* = 6.7 Hz, 2 H, H-8), 4.65 (dq, *J* = 1.3, 1.04 Hz, 1 H, H^a-1), 4.65–4.69 (m, 1 H, H-3), 4.98 (t, *J* = 1.4 Hz, 1 H, H^b-1), 5.15 (dq, *J* = 8.8, 1.4 Hz, 1 H, H-4).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 0.9 (TMS), 4.8 (CH_3, TES), 7.1 (CH_2, TES), 17.1 (C-9), 22.9 (C-10), 31.2 (C-7), 36.2 (C-6), 62.8 (C-8), 72.2 (C-3), 106.7 (C-1), 126.7 (C-4), 139.7 (C-5), 145.5 (C-2).

GC/MS (EI): *m*/*z* (%) = 338 (4) $[M^+ – H_2O]$, 206 (10), 191 (6), 180 (24), 165 (9), 134 (39), 119 (34), 117 (26), 115 (18) [TES], 106 (15), 103 (16), 93 (20), 79 (6), 73 (100) [TMS], 59 (12).

HRMS (EI, 70 eV): *m*/*z* $[M]^+$ calcd for $C_{19}H_{40}O_2Si_2$: 356.2567; found: 356.2578.

Anal. Calcd for $C_{19}H_{40}O_2Si_2$: C, 63.98; H, 11.30. Found: C, 63.97; H, 11.31.

Triethyl[{(4*E*)-6-(methoxymethoxy)-4-methyl-7-[(trimethylsilyl)methyl]octa-4,7-dienyl}oxy]silane (5b)

To an ice-cooled solution of alcohol **5a** (243 mg, 0.68 mmol) in CH_2Cl_2 (20 mL) were added sequentially DIPEA (2.56 mL, 14.3 mmol) and MOMCl (363 µL, 4.78 mmol). After 10 min, the mixture was warmed to r.t., stirred for 36 h and then diluted with H_2O (20 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with 1.5 N HCl (20 mL), sat. $NaHCO_3$ (20 mL), dried (Na_2SO_4) and the solvent was evaporated. The crude product was purified by flash chromatography on SiO_2 (hexanes–EtOAc, 10:1) to give **5b**.

Yield: 265 mg (97%); pale-yellow oil; R_f = 0.60 (hexanes–EtOAc, 10:1).

FTIR (ATR): 2952 (s), 2912 (m), 2877 (s), 1665 (w), 1637 (w), 1459 (m), 1416 (m), 1383 (m), 1247 (s), 1213 (m), 1149 (s), 1094 (vs), 1035 (vs), 958 (s), 917 (m), 884 (s), 840 (vs), 797 (s), 740 (vs), 726 (vs), 694 (s), 671 (m), 633 (m) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.04 (s, 9 H, TMS), 0.59 (q, *J* = 7.9 Hz, 6 H, CH_2, TES), 0.96 (t, *J* = 7.9 Hz, 9 H, CH_3, TES), 1.39 (dd, *J* = 14, 1 Hz, 1 H, H^a-3′), 1.57 (dd, *J* = 14, 1 Hz, 1 H, H^b-3′), 1.64–1.70 (m, 2 H, H-9), 1.72 (d, *J* = 1.3 Hz, 3 H, CH_3), 2.06–2.1 (m, 2 H, H-8), 3.36 (s, 3 H, H-1), 3.58 (t, *J* = 6.9 Hz, 2 H, H-10),

4.56 (dd, J = 6.7, 0.3 Hz, 1 H, H^a-3), 4.61 (d, J = 6.7 Hz, 1 H, H^b-3), 4.62–4.65 (m, 1 H, H-5), 4.68 (ddd, J = 3.7, 1.8, 1.1 Hz, 1 H, H^a-1′), 4.96–4.97 (m, 1 H, H^b-1′), 5.07 (dq, J = 9.1, 1.3 Hz, 1 H, H-6).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –1.1 (TMS), 4.4 (CH_3-TES), 6.8 (CH_2-TES), 16.7 (CH_3), 22.6 (C-3′), 31.0 (C-9), 35.9 (C-8), 55.4 (C-1), 62.6 (C-10), 74.6 (C-5), 93.1 (C-3), 108.1 (C-1′), 124.1 (C-6), 140.2 (C-7), 146.4 (C-2′).

GC/MS (EI): m/z (%) = 338 (2) [M$^+$ – OMOM], 309 (2), 266 (2), 237 (6), 210 (4), 206 (8), 179 (14), 165 (7), 148 (4), 146 (9), 133 (72), 118 (43), 115 (21) [TES], 105 (34), 92 (46), 90 (37), 88 (32), 75 (26), 73 (100) [TMS], 59 (28).

HRMS (EI, 70 eV): m/z [M]$^+$ calcd for $C_{21}H_{44}O_3Si_2$: 400.2829; found: 400.2810.

(4*E*)-6-(Methoxymethoxy)-4-methyl-7-[(trimethylsilyl)methyl]octa-4,7-dienal (16)

To a solution of **5b** (151 mg, 0.38 mmol) in THF (2 mL) was added dropwise a solution of TBAF·H_2O (125 mg, 0.39 mmol) in THF (1 mL) at 0 °C, and the reaction mixture was stirred for 10 min. Then, sat. NH_4Cl (10 mL) was added, the mixture was warmed to r.t. and the organic layer was extracted with EtOAc (3 × 10 mL), dried (Na_2SO_4) and evaporated. The crude product was purified by flash chromatography on SiO_2 (hexanes–EtOAc, 10: 1) to give **5c**.

Yield: 98 mg (90%); pale-yellow oil; R_f = 0.35 (hexanes–EtOAc, 10:1).

FTIR (ATR): 3346 (w), 2949 (m), 2884 (m), 2554 (w), 2367 (w), 1996 (w), 1636 (w), 1442 (w), 1417 (w), 1383 (w), 1247 (m), 1213 (w), 1145 (m), 1094 (m), 1033 (s), 957 (w), 917 (w), 884 (m), 839 (s), 771 (w), 726 (w), 694 (m), 634 (w) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.04 (s, 9 H, TMS), 1.38 (dd, J = 14.1, 1.0 Hz, 1 H, CH_2TMS^a), 1.58 (dd, J = 14.1, 1.0 Hz, 1 H, CH_2TMS^b), 1.68–1.76 (m, 2 H, H-2), 1.73 (d, J = 1.4 Hz, 3 H, CH_3), 2.13 (td, J = 7.6, 1.3 Hz, 2 H, H-3), 3.36 (s, 3 H, OCH_3), 3.62–3.66 (m, 2 H, H-1), 4.58 (dd, J = 6.7, 0.3 Hz, 1 H, H^a-2′), 4.62 (d, J = 6.7 Hz, 1 H, H^b-2′), 4.63–4.65 (m, 1 H, H-6), 4.68 (ddd, J = 3.7, 1.8, 1.1 Hz, 1 H, H^a-8), 4.96 (dd, J = 1.8, 1.1 Hz, 1 H, H^b-8), 5.08 (dq, J = 9.2, 1.3 Hz, 1 H, H-5).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –1.1 (TMS), 16.6 (CH_3), 22.5 (CH_2TMS), 30.6 (C-2), 36.1 (C-3), 55.4 (OCH_3), 62.7 (C-1), 74.8 (C-6), 93.3 (C-2′), 108.2 (C-8), 124.5 (C-5), 139.9 (C-4), 146.3 (C-7).

MS (EI): m/z (%) = 225 (3) [M$^+$ – OMOM], 180 (4), 165 (3), 152 (5), 141 (6), 136 (12), 126 (5), 118 (36), 110 (14), 106 (25), 96 (16), 93 (58), 90 (48), 88 (18), 84 (12), 73 (100) [TMS], 66 (10), 58 (17).

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{15}H_{30}O_3SiNa^+$: 309.1856; found: 309.1858.

To a solution of **5c** (72 mg, 0.24 mmol) in CH_2Cl_2 (10 mL) were sequentially added powered 4 Å molecular sieves (250 mg), NMO (170 mg, 1.43 mmol) and TPAP (6 mg, 0.02 mmol) at 0 °C. The reaction mixture was stirred for 1.5 h then warmed to r.t., filtered over a plug of SiO_2 and evaporated. The crude product was purified by flash chromatography (hexane–EtOAc, 7:1) to yield **16**.

Yield: 50 mg (70%); colourless oil; R_f = 0.35 (hexanes–EtOAc, 6:1).

FTIR (ATR): 2952 (m), 2890 (m), 2821 (w), 2721 (w), 2563 (w), 2367 (w), 2181 (w), 1965 (w), 1725 (s), 1668 (m), 1636 (m), 1444 (m), 1416 (m), 1386 (m), 1348 (w), 1247 (s), 1212 (w), 1148 (s), 1093 (s), 1031 (vs), 976 (m), 957 (m), 916 (m), 883 (s), 838 (vs), 772 (m), 723 (w), 693 (m), 621 (m) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.04 (s, 9 H, TMS), 1.36 (dd, J = 14.1, 1.0 Hz, 1 H, CH_2TMS^a), 1.57 (dd, J = 14.1, 1.1 Hz, 1 H, CH_2TMS^b), 1.74 (d, J = 1.4 Hz, 3 H, CH_3), 2.38 (td, J = 7.5, 1.4 Hz, 2 H, H-3), 2.56–2.60 (m, 2 H, H-2), 3.35 (s, 3 H, OCH_3), 4.57 (dd, J = 6.5, 6.0 Hz, 2 H, H-2′), 4.68–4.69 (m, 1 H, H^a-8), 4.95 (dt, J = 2.9, 1.0 Hz, 1 H, H^b-8), 5.1 (dq, J = 9.0, 1.4 Hz, 1 H, H-5), 9.77 (t, J = 1.7 Hz, 1 H, H-1).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –1.1 (TMS), 16.8 (CH_3), 22.4 (CH_2TMS), 31.7 (C-3), 41.9 (C-2), 55.4 (OCH_3), 74.6 (C-6), 93.2 (C-2′), 108.5 (C-8), 125.1 (C-5), 138.2 (C-4), 146 (C-7), 201.9 (C-1).

GC/MS (EI): m/z (%) = 222 (5), 204 (5), 187 (5), 181 (6), 165 (4), 149 (7), 135 (14), 132 (10), 117 (48), 106 (53), 95 (10), 93 (30), 92 (84), 90 (62), 88 (28), 79 (13), 74 (33), 73 (100) [TMS], 64 (8), 58 (33).

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{15}H_{28}O_3SiNa^+$: 307.1700; found: 307.1702.

Methyl 2-[Di(*o*-tolyl)oxyphosphoryl]hex-5-enoate (17a)

NaH (216 mg, 8.98 mmol, 60% suspension in mineral oil) was added to a solution of phosphonate **10b** (3.00 g, 8.98 mmol) in DMSO (5 mL). After stirring for 30 min at r.t., 4-bromobut-1-ene (1.05 μL, 10.3 mmol) was added dropwise and stirring was continued for 1 h. The mixture was warmed to 40 °C and stirred for 16 h. After cooling to r.t., sat. NH_4Cl (50 mL) was added, the layers were separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The organic layer was dried (Na_2SO_4), evaporated and the residue was purified by flash chromatography on SiO_2 (hexanes–EtOAc, 2:1) to yield **10b** (705 mg, 2.11 mmol, 24%) and **17a** (2.08 g, 79% based on recovered **10b**).

Yellow oil; R_f = 0.35 (hexanes–EtOAc, 2:1).

FTIR (ATR): 3064 (w), 2952 (w), 1966 (m), 1737 (s), 1641 (w), 1585 (m), 1490 (s), 1461 (m), 1435 (m), 1336 (m), 1274 (s), 1222 (s), 1182 (s), 1163 (s), 1106 (s), 1043 (m), 929 (vs), 833 (m), 843 (m), 756 (vs), 708 (m), 601 (m) cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.07–2.48 (m, 4 H, H-2, H-4), 2.18 (s, 3 H, $ArCH_3$), 2.24 (s, 3 H, $ArCH_3$′), 3.34 (ddd, J = 23.4, 10.8, 3.3 Hz, 1 H, H-2), 3.76 (s, 3 H, OCH_3), 5.02 (dd, J = 1.2, 0.3 Hz, 1 H, H^a-6), 5.05–5.11 (m, 1 H, H^b-6), 5.68–5.85 (m, 1 H, H-5), 7.05–7.11 (m, 4 H, H-4′, H-5′, H-4″, H-5″), 7.11–7.2 (m, 2 H, H-3′), 7.21–7.35 (m, 2 H, H-6′).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.3 ($ArCH_3$), 26.2 (d, J = 3.9 Hz, C-4), 32.3 (d, J = 16 Hz, C-3), 45.2 (d, J = 135.3 Hz, C-2), 52.6 (OCH_3), 116.62 (C-5), 120.16 (d, J = 2.5 Hz, C-6′), 120.24 (d, J = 2.5 Hz, C-9′), 125.15 (C-4′), 125.17 (C-4″), 127.04 (d, J = 1.3 Hz, C-5′), 127.06 (d, J = 1.3 Hz, C-5″), 129.22 (d, J = 1.3 Hz, C-2′), 129.32 (d, J = 1.3 Hz, C-2″), 131.41 (C-3), 131.43 (C-3″), 136.3 (d, J = 0.5 Hz, C-6), 148.9 (d, J = 1 Hz, C-1′), 149.1 (d, J = 1 Hz, C-1″), 168.3 (d, J = 5.5 Hz, C-1).

^{31}P NMR (202 MHz, $CDCl_3$): δ = 15.17–15.38 (m).

GC/MS (EI): m/z (%) = 388 (14) [M]$^+$, 357 (16), 347 (100), 334 (8), 315 (43), 302 (16), 287 (19), 249 (11), 227 (15), 192 (10), 180 (23), 165 (9), 153 (10), 133 (7), 115 (11), 108 (48) [*o*-cresyl], 107 (22), 91 (78) [tolyl], 77 (21), 64 (19), 55 (22).

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{21}H_{25}O_5PNa^+$: 411.1332; found: 411.1337.

Methyl 2-[Di(*o*-tolyl)oxyphosphoryl]-5-oxopentanoate (18a)

A solution of **17a** (768 mg, 1.98 mmol) and Sudanred III (3 mg) in CH_2Cl_2 (70 mL) was cooled to –78 °C. Then, ozone was bubbled through the solution until it turned colourless, followed by bubbling argon through the solution for 5 min. Ph_3P (648 mg, 2.47 mmol) was added and the reaction mixture was warmed to r.t. over 7 h. Evaporation of the solvent followed by flash chromatography on SiO_2 (hexanes–EtOAc, 1:1) yielded **18a**.

Yield: 586 mg (76%); yellow oil; R_f = 0.30 (hexanes–EtOAc, 1:1).

FTIR (ATR): 2953 (w), 2728 (w), 1965 (w), 1735 (s), 1585 (m), 1490 (s), 1461 (m), 1436 (m), 1385 (w), 1328 (w), 1271 (s), 1222 (s), 1181 (m), 1162 (s), 1106 (s), 1043 (m), 930 (vs), 852 (m), 806 (m), 757 (s), 708 (m), 599 (m), 562 (m), 530 (m), 518 (m) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.2 (s, 3 H, $ArCH_3$), 2.24 (s, 3 H, $ArCH_3'$), 2.45–2.55 (m, 2 H, H-4), 2.63–2.8 (m, 2 H, H-3), 3.44 (ddd, *J* = 29.9, 8.8, 5.6 Hz, 1 H, H-2), 3.76 (s, 3 H, OCH_3), 7.03–7.17 (m, 4 H, H-5′, H-5″, H-4′, H-4″), 7.15–7.20 (m, 2 H, H-3′, H-3″), 7.22–7.25 (m, 1 H, H-6′), 7.28–7.32 (m, 1 H, H-6″), 9.75 (s, 1 H, H-5).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 16.3 ($ArCH_3$), 19.7 (d, *J* = 4.8 Hz, C-4), 41.8 (d, *J* = 13.1 Hz, C-3), 44.8 (d, *J* = 134.6 Hz, C-2), 52.8 (OCH_3), 120.1 (d, *J* = 2.4 Hz, C-6′), 120.2 (d, *J* = 2.1 Hz, C-6″), 125.3 (C-4′), 127.1 (C-5′), 129.2 (d, *J* = 4.3 Hz, C-2′), 129.3 (d, *J* = 4.3 Hz, C-2″), 131.5 (d, *J* = 3.9 Hz, C-3′), 148.8 (d, *J* = 9.6 Hz, C-1′), 168.3 (d, *J* = 5.5 Hz, C-1), 203 (C-5).

^{31}P NMR (202 MHz, $CDCl_3$): δ = 14.03–14.38 (m).

GC/MS (EI): *m*/*z* (%) = 391 (2) $[M + H]^+$, 359 (6), 335 (11), 315 (24), 302 (18), 283 (100), 273 (5), 252 (26), 244 (7), 227 (28), 212 (14), 195 (10), 179 (23), 165 (12), 153 (15), 131 (12), 120 (6), 108 (61) [*o*-cresyl], 105 (13), 91 (74) [tolyl], 77 (32), 65 (26), 55 (17).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{23}O_6PH^+$: 391.1305; found: 391.1301.

Anal. Calcd for $C_{20}H_{23}O_6P$: C, 61.54; H, 5.94. Found: C, 61.62; H, 5.89.

Methyl (5*E*)-2-[Di(*o*-tolyl)oxyphosphoryl]-6-methyl-7-oxohept-5-enoate (6a)

A solution of **18a** (200 mg, 0.51 mmol) and ylide **19** (236 mg, 0.72 mmol) in benzene (3 mL) and toluene (1 mL) was heated at reflux for 15 h. Evaporation of the solvent followed by flash chromatography (hexanes–EtOAc, 1:1) yielded **6a**.

Yield: 144 mg (65%); pale-yellow oil; R_f = 0.50 (hexanes–EtOAc, 1:1).

FTIR (ATR): 3060 (w), 2952 (w), 2864 (w), 2825 (w), 2714 (w), 2359 (w), 2339 (w), 1736 (s), 1683 (s), 1645 (m), 1585 (m), 1490 (s), 1460 (m), 1436 (m), 1382 (w), 1336 (m), 1273 (s), 1223 (s), 1164 (vs), 1107 (vs), 1042 (s), 934 (vs), 853 (m), 806 (s), 759 (vs), 708 (m), 602 (m), 561 (m), 520 (s), 507 (s) cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 1.74 (d, *J* = 1.4 Hz, 3 H, CH_3), 2.19 (s, 3 H, $ArCH_3$), 2.25 (s, 3 H, $ArCH_3'$), 2.45–2.68 (m, 4 H, H-2, H-4), 3.35 (ddd, *J* = 23.9, 10.2, 4 Hz, 1 H, H-2), 3.78 (d, *J* = 0.6 Hz, 3 H, OCH_3), 6.42 (tq, *J* = 7.2, 1.4 Hz, 1 H, H-5), 7.04–7.12 (m, 4 H, H-5′, H-5″, H-4′, H-4″), 7.13–7.22 (m, 2 H, H-3′, H-3″), 7.23–7.32 (m, 2 H, H-6′, H-6″), 9.42 (s, 1 H, H-7).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 9.3 (CH_3), 16.31 ($ArCH_3$), 16.33 ($ArCH_3'$), 25.8 (d, *J* = 4.5 Hz, C-4), 27.5 (d, *J* = 15.9 Hz, C-3), 45.4 (d, *J* = 134.9 Hz, C-2), 52.8 (OCH_3), 120.1 (d, *J* = 2.5 Hz, C-6′), 120.2 (d, *J* = 2.5 Hz, C-6″), 125.34 (d, *J* = 1 Hz, C-4′), 125.35 (d, *J* = 1 Hz, C-4″), 127.11 (d, *J* = 1.4 Hz, C-5′), 127.14 (d, *J* = 1.4 Hz, C-5″), 129.18 (d, *J* = 5.9 Hz, C-2′), 129.24 (d, *J* = 5.9 Hz, C-2″), 131.51 (d, *J* = 0.7 Hz, C-3′), 131.53 (d, *J* = 0.7 Hz, C-3″), 140.79 (C-6), 148.82 (d, *J* = 1.3 Hz, C-1′), 148.9 (d, *J* = 1.3 Hz, C-1″), 151.1 (C-5), 168.4 (d, *J* = 5.8 Hz, C-1), 194.9 (d, *J* = 2.2 Hz, C-7).

^{31}P NMR (202 MHz, $CDCl_3$): δ = 14.35–14.65 (m).

GC/MS (EI): *m*/*z* (%) = 431 (22) [M + H], 412 (8), 402 (10), 365 (7), 347 (51), 335 (12), 315 (33), 303 (16), 287 (8), 263 (72), 253 (12), 241 (28), 209 (26), 190 (14), 184 (27), 178 (28), 168 (21), 152 (12), 137 (25), 126 (32), 124 (14), 108 (32) [*o*-cresyl], 91 (100) [tolyl], 71 (28), 65 (18), 55 (38).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{27}O_6PH^+$: 431.1618; found: 431.1614.

Methyl (5*E*)-2-[Di(*o*-tolyl)oxyphosphoryl]-7,7-dimethoxy-6-methylhept-5-enoate (20a)

To a solution of **6a** (250 mg, 0.53 mmol) in MeOH (8 mL) were added dimethoxypropane (1 mL, 8.16 mmol) and CSA (12 mg, 0.05 mmol) and the mixture was distilled to remove MeOH and acetone. Filtration through basic Al_2O_3 and evaporation gave **20a**.

Yield: 257 mg (98%); pale-yellow oil.

FTIR (ATR): 3475 (w), 2974 (m), 2932 (m), 2829 (m), 1962 (w), 1738 (s), 1651 (m), 1585 (m), 1491 (s), 1453 (m), 1438 (m), 1382 (w), 1333 (m), 1273 (m), 1223 (s), 1181 (s), 1163 (s), 1106 (vs), 1071 (s), 1042 (s), 931 (vs), 859 (m), 806 (m), 757 (vs), 708 (m), 601 (m), 561 (m) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.58 (d, *J* = 1.4 Hz, 3 H, CH_3), 2.14–2.40 (m, 3 H, H-2, H-4), 2.19 (s, 3 H, $ArCH_3$), 2.24 (s, 3 H, $ArCH_3'$), 3.27 (s, 3 H, OCH_3), 3.28 (s, 3 H, OCH_3'), 3.35 (ddd, *J* = 23.2, 11.2, 3.2 Hz, 1 H, H-2), 3.77 (d, *J* = 0.7 Hz, 3 H, CO_2CH_3), 4.45 (d, *J* = 0.6 Hz, 1 H, H-7), 5.53 (t, *J* = 6.7 Hz, 1 H, H-5), 7.02–7.12 (m, 4 H, H-5′, H-5″, H-4′, H-4″), 7.14–7.19 (m, 2 H, H-3′, H-3″), 7.21–7.24 (m, 1 H, H-6′), 7.27–7.30 (m, 1 H, H-6″).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.2 (CH_3), 16.3 ($ArCH_3$), 16.4 ($ArCH_3'$), 26.1 (d, *J* = 16.1 Hz, C-3), 26.6 (d, *J* = 4.8 Hz, C-4), 45.5 (d, *J* = 133.9 Hz, C-2), 52.7 (CO_2CH_3), 53.5 (OCH_3), 53.6 (OCH_3'), 107.4 (C-7), 120.1 (d, *J* = 2.6 Hz, C-6′), 120.2 (d, *J* = 2.1 Hz, C-6″), 125.1 (C-4′), 125.2 (C-4″), 126.8 (C-5), 127.0 (d, *J* = 1.3 Hz, C-5′), 127.1 (d, *J* = 1.3 Hz, C-5″), 129.3 (d, *J* = 4.5 Hz, C-2′), 129.3 (d, *J* = 4.4 Hz, C-2″), 131.4 (C-3′), 131.5 (C-3″), 134.2 (C-6), 148.9 (d, *J* = 1.5 Hz, C-1′), 149 (d, *J* = 1.4 Hz, C-1″), 168.6 (d, *J* = 5.8 Hz, C-1).

^{31}P NMR (202 MHz, acetonitrile-d_3): δ = 15.77–16.14 (m).

GC/MS (EI): *m*/*z* (%) = 444 (12), 405 (3), 386 (2), 354 (3), 293 (4), 285 (2), 222 (7), 198 (3), 182 (36), 171 (5), 166 (5), 150 (12), 137 (3), 123 (100), 111 (22), 91 (22) [tolyl], 79 (18), 77 (17), 65 (4), 55 (6), 53 (10).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{25}H_{33}O_7PNa^+$: 499.1856; found: 499.1849.

Methyl (5*Z*)-2-[Di(*o*-tolyl)oxyphosphoryl]-6-(1,3-dithian-2-yl)hept-5-enoate (20b)

To a solution of **6a** (100 mg, 0.21 mmol) in CH_2Cl_2 (10 mL), was added 1,3-propanedithiol (64 μL, 0.63 mmol) and Montmorillonite K10 (20 mg) and the mixture was stirred at r.t. for 6 h. Evaporation of the solvent yielded **20b**.

Yield: 96 mg (88%); pale-yellow oil.

FTIR (ATR): 2948 (w), 2898 (w), 1738 (s), 1491 (s), 1461 (m), 1435 (m), 1274 (s), 1226 (s), 1166 (s), 1108 (s), 947 (s), 633 (s), 607 (w) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.78 (s, 3 H, CH_3), 1.84 (dtt, *J* = 14, 12.2, 3.2 Hz, 1 H, H^a-2′), 2.10 (dtt, *J* = 14, 4.4, 2.5 Hz, 1 H, H^b-2′), 2.15–2.26 (m, 2 H, H^a-1′), 2.19 (d, *J* = 0.4 Hz, 3 H, Ar-CH_3), 2.24 (d, *J* = 0.4 Hz, 3 H, Ar-CH_3'), 2.3–2.38 (m, 2 H, H^b-1′), 2.82–2.88 (m, 2 H, H-3), 2.90–2.98 (m, 2 H, H-4), 3.36 (ddd, *J* = 23.4, 11, 3.1 Hz, 1 H, H-2), 3.77 (d, *J* = 0.4 Hz, 3 H, OCH_3), 4.56 (d, *J* = 0.4 Hz, 1 H, H-7), 5.31 (tdd, *J* = 6.3, 1.3, 0.4 Hz, 1 H, H-5), 7.02–7.07 (m, 2 H, H-5″, H-5‴), 7.08–7.13 (m, 2 H, H-4″, H-4‴), 7.14–7.18 (m, 2 H, H-3″, H-3‴), 7.22–7.24 (m, 1 H, H-6″), 7.27–7.29 (m, 1 H, H-6‴).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.1 (CH_3), 16.4 (Ar-CH_3), 16.4 (Ar-CH_3'), 25.4 (C-2′), 26.5 (d, *J* = 4.8 Hz, C-4), 26.6 (d, *J* = 16.2 Hz, C-3), 31.5 (C-1′), 45.2 (d, *J* = 132 Hz, C-2), 52.7 (OCH_3), 55.1 (C-7), 120.2 (d, *J* = 2.6 Hz, C-6″), 120.3 (d, *J* = 2.6 Hz, C-6‴), 125.15 (d, *J* = 1.3 Hz, C-4″), 125.16 (d, *J* = 1.3 Hz, C-4‴), 127.05 (d, *J* = 1.1 Hz, C-5″), 127.06 (d, *J* = 1.1 Hz, C-5‴), 127.24 (C-5), 129.29 (d, *J* = 1.4 Hz, C-2″), 129.34 (d, *J* = 1.1 Hz, C-2‴), 131.41

(C-3″, C-3‴), 135.42 (C-6), 148.92 (d, J = 3.0 Hz, C-1″), 148.99 (d, J = 3.0 Hz, C-1‴), 168.6 (d, J = 5.5 Hz, C-1).

^{31}P NMR (202 MHz, $CDCl_3$): δ = 14.91–15.43 (m).

GC/MS (EI): m/z (%) = 520 (2) $[M]^+$, 461 (88), 445 (3), 413 (6), 401 (4), 381 (24), 353 (8), 315 (5), 303 (2), 273 (2), 245 (2), 230 (3), 227 (5), 197 (3), 183 (5), 167 (8), 151 (11), 147 (4), 127 (100), 111 (13), 99 (23), 91 (42), 79 (54), 77 (16), 65 (12), 60 (10), 55 (14).

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{26}H_{33}O_5PS_2H^+$: 521.1589; found: 521.1580.

Methyl (2*Z*,6*E*)-8-(Methoxymethoxy)-6-methyl-2-[(3*E*)-4-methyl-5-oxopent-3-enyl]-9-[(trimethylsilyl)methyl]deca-2,6,9-trienoate (4a)

To a solution of **20a** (109 mg, 0.23 mmol) in THF (8 mL) were added NaI (45 mg, 0.29 mmol) and NaH (8 mg, 0.34 mmol) at 0 °C and the mixture was stirred at r.t. for 15 min. The yellow solution was cooled to –20 °C and a solution of **16** (65 mg, 0.23 mmol) in THF (2 mL) was added dropwise. The reaction mixture was warmed to r.t. over 7 h and quenched by addition of aqueous NaH_2PO_4/NaOH buffer (0.1 M, 5 mL, pH 7). The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL) and the combined organic layers were washed with brine (50 mL), dried (Na_2SO_4) and evaporated. The crude product was purified by flash chromatography on Florisil (hexanes–EtOAc, 6:1) to yield **21a** (86 mg, 79% crude) as a colourless oil (E/Z = 17:83 by ^{1}H NMR analysis), which contained **4a** (15% assessed by ^{1}H NMR analysis). The product mixture was dissolved in CH_2Cl_2 (10 mL), Dowex 50 × 8 (30 mg) was added and the mixture was stirred at r.t. for 10 min to give **4a** after filtration and evaporation.

Yield: 78 mg (78%); colourless oil.

FTIR (ATR): 2951 (m), 2927 (m), 2709 (w), 2571 (w), 2365 (w), 2187 (w), 1967 (w), 1714 (s), 1686 (vs), 1643 (m), 1506 (w), 1436 (m), 1378 (m), 1246 (s), 1195 (s), 1149 (s), 1117 (s), 1093 (s), 1035 (s), 975 (m), 959 (m), 917 (w), 839 (vs), 770 (m), 694 (m), 634 (w), 525 (w) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.04 (s, 9 H, TMS), 1.38 (dd, J = 5.0, 1.1 Hz, 1 H, CH_2TMS-H^a), 1.57 (dd, J = 5.0, 1.1 Hz, 1 H, CH_2TMS-H^b), 1.71 (d, J = 1.4 Hz, 3 H, 4′-CH_3), 1.72 (d, J = 1.4 Hz, 3 H, 6-CH_3), 2.15 (td, J = 7.5, 0.9 Hz, 2 H, H-5), 2.41–2.39 (m, 4 H, H-1′, H-2′), 2.58–2.63 (m, 2 H, H-4), 3.36 (s, 3 H, OCH_3), 3.75 (s, 3 H, CO_2CH_3), 4.58 (dd, J = 25.1, 6.6 Hz, 2 H, H-2″), 4.67–4.68 (m, 1 H, H-8), 4.96 (dd, J = 1.9, 1.2 Hz, 2 H, H-10), 5.08 (dq, J = 9.2, 1.4 Hz, 1 H, H-7), 5.93 (tt, J = 7.3, 2.1 Hz, 1 H, H-3), 6.44 (tq, J = 7.3, 1.4 Hz, 1 H, H-3′), 9.39 (s, 1 H, H-5′).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –1.2 (TMS), 9.2 (CH_3′), 16.5 (CH_3), 22.6 (CH_2TMS), 27.8 (C-1′), 28.7 (C-4), 33.4 (C-2′), 39.1 (C-5), 51.4 (CO_2CH_3), 55.3 (OCH_3), 74.5 (C-8), 93.1 (C-2″), 108.2 (C-10), 124.9 (C-7), 130.5 (C-2), 139.3 (C-6), 139.9 (C-4′), 143.2 (C-3), 146.2 (C-9), 153.2 (C-3′), 167.8 (C-1), 195.2 (C-5′).

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{24}H_{40}NaO_5Si^+$: 459.6467; found: 459.6470.

Methyl (2*Z*,6*E*)-2-[(3*E*)-4-(1,3-Dithian-2-yl)pent-3-enyl]-8-(methoxymethoxy)-6-methyl-9-[(trimethylsilyl)methyl]deca-2,6,9-trienoate (21b)

To a solution of **20b** (56 mg, 0.09 mmol) in THF (5 mL) were added NaI (12 mg, 0.08 mmol) and NaH (2 mg, 0.09 mmol) at 0 °C and the mixture was stirred for 10 min. After warming to r.t. for 20 min, the yellow solution was cooled to –20 °C and a solution of **16** (23 mg, 0.09 mmol) in THF (3 mL) was added dropwise. The mixture was warmed to r.t. over 7 h and diluted with sat. NH_4Cl (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried (Na_2SO_4) and evaporated. The crude product was purified by flash chromatography on SiO_2 (hexanes–EtOAc, 5: 1) to yield **21b**.

Yield: 20 mg (47%); colourless oil (E/Z = 17:83 by ^{1}H NMR analysis); R_f = 0.50 (hexanes–EtOAc, 5:1).

FTIR (ATR): 2949 (m), 2897 (m), 2559 (w), 2371 (w), 2184 (w), 1966 (w), 1715 (s), 1683 (m), 1637 (w), 1506 (w), 1435 (m), 1379 (w), 1246 (s), 1195 (m), 1148 (s), 1093 (m), 1033 (vs), 977 (m), 957 (m), 914 (m), 881 (m), 839 (vs), 770 (m), 693 (m), 634 (w), 621 (w), 528 (w), 511 (w) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.04 (s, 9 H, TMS), 1.38 (ddd, J = 13.9, 1.1, 0.3 Hz, 1 H, CH_2TMS-H^a), 1.58 (ddd, J = 14.1, 1.1, 0.3 Hz, 1 H, CH_2TMS-H^b), 1.71 (d, J = 1.4 Hz, 3 H, CH_3′), 1.75 (dt, J = 1.4, 0.8 Hz, 3 H, CH_3), 1.78–1.87 (m, 1 H, H^a-8′), 2.07–2.13 (m, 1 H, H^b-8′), 2.14–2.18 (m, 4 H, H-5, H-1′), 2.26–2.30 (m, 2 H, H-2′), 2.56–2.62 (m, 2 H, H-4), 2.82–2.87 (m, 2 H, H-7′), 2.91–2.98 (m, 2 H, H-7′), 3.36 (s, 3 H, OCH_3), 3.74 (s, 3 H, CO_2CH_3), 4.55 (s, 1 H, H-5′), 4.59 (dd, J = 26.2, 7.1 Hz, 2 H, H-2″), 4.62–4.65 (m, 1 H, H-8), 4.68 (dd, J = 1.8, 0.8 Hz, 1 H, H-10a), 4.97 (dd, J = 1.8, 1.1 Hz, 1 H, H-10b), 5.09 (dq, J = 9.2, 1.3 Hz, 1 H, H-7), 5.6 (tdd, J = 7.2, 1.4, 0.7 Hz, 1 H, H-3′), 5.87 (tt, J = 7.3, 1 Hz, 1 H, H-3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = –1.1 (TMS), 15.1 (CH_3′), 16.5 (CH_3), 22.5 (CH_2TMS), 25.5 (C-8′), 27.7 (C-1′), 27.8 (C-4), 31.6 (C-7′), 34.1 (C-2′), 39.2 (C-5), 51.2 (CO_2CH_3), 55.3 (C-5′), 74.5 (C-8), 93.1 (C-2″), 108.1 (C-10), 124.7 (C-7), 128.7 (C-3′), 131.1 (C-4′), 133.8 (C-2), 139.6 (C-6), 142.6 (C-3), 146.3 (C-9), 168.2 (C-1).

GC/MS (CI, CH_4): m/z (%) = 526 (5) $[M]^+$, 495 (4), 481 (12), 465 (32), 375 (6), 359 (8), 285 (5), 225 (4), 179 (24), 173 (11), 149 (6), 119 (10), 106 (25), 89 (34), 73 (100) [TMS], 61 (32), 45 (62).

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{27}H_{46}O_4S_2Si^+$: 527.2680; found: 527.2670.

Ethyl (2*Z*,6*E*)-2-[2-(1,3-Dioxan-2-yl)ethyl]-8-(methoxymethoxy)-6-methyl-9-[(trimethylsilyl)methyl]deca-2,6,9-trienoate (23)

A solution of **22** (43 mg, 0.16 mmol) in THF (1 mL) was added dropwise to a suspension of NaH (4 mg, 0.16 mmol) in THF (3 mL) at 0 °C and the mixture was stirred for 30 min. Then **16** (50 mg, 0.18 mmol) in THF (50 μL) was added and the mixture was kept at 0 °C for 4 h, then warmed to 15 °C over 8 h, hydrolyzed with sat. NH_4Cl (10 mL) and diluted with EtOAc (20 mL). After warming to r.t. and extracting with EtOAc (3 × 20 mL), the organic layer was washed with brine (20 mL), dried (Na_2SO_4) and evaporated. The crude product was purified by flash chromatography (hexanes–EtOAc, 3:1) to yield **23**.

Yield: 59 mg (86%); colourless oil (E/Z = 50:50 by ^{1}H NMR analysis); R_f = 0.48 (hexanes–EtOAc, 3:1).

FTIR (ATR): 2953 (m), 2849 (m), 1960 (w), 1708 (s), 1638 (m), 1447 (m), 1378 (m), 1243 (s), 1192 (s), 1138 (vs), 1091 (s), 1032 (vs), 976 (m), 945 (m), 917 (m), 885 (m), 839 (vs), 769 (m), 724 (w), 694 (m), 634 (m), 588 (w), 565 (w), 546 (m), 526 (m) cm^{-1}.

(2*Z*)-**23**

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.4 (s, 9 H, TMS), 1.28 (t, J = 7.1 Hz, 3 H, $CO_2CH_2CH_3$), 1.33 (dq, J = 13.5, 1.3 Hz, 1 H, H^a-6′), 1.39 (ddd, J = 14.1, 5.1, 1.0 Hz, 1 H, CH_2TMS-H^a), 1.58 (dd, J = 14.1, 1.0 Hz, 1 H, CH_2TMS-H^b), 1.68–1.71 (m, 2 H, H-2′), 1.71 (d, J = 1.3 Hz, 3 H, CH_3), 2.02–2.11 (m, 1 H, H^b-6′), 2.12–2.2 (m, 2 H, H-5), 2.56–2.61 (m, 4 H, H-1′, H-4), 3.36 (s, 3 H, OCH_3), 3.70–3.77 (m, 2 H, H^a-5a′, H^a-5b′), 4.06–4.11 (m, 2 H, H^b-5a′, H^b-5b′), 4.18 (q, J = 7.1 Hz, 2 H, CO_2CH_2), 4.47 (t, J = 5.3 Hz, 1 H, H-3′), 4.56 (dd, J = 6.7, 1.7 Hz, 1 H, H^a-2″), 4.62 (dd, J = 6.7, 4.1 Hz, 1 H, H^b-2″), 4.62–4.66 (m, 1 H, H-8), 4.68 (dd, J = 1.9, 0.8 Hz, 1 H, H-10a), 4.96 (dd, J = 1.9, 1.2 Hz, 1 H, H-10b), 5.11 (dq, J = 9.2, 1.3 Hz, 1 H, H-7), 5.86 (tt, J = 7.4, 1.1 Hz, 1 H, H-3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.3 ($CO_2CH_2CH_3$), 16.5 (CH_3), 22.6 (C-10), 25.8 (C-6′), 26.6 (C-1′), 27.8 (C-4), 34.3 (C-18), 39.3 (C-5), 55.4 (OCH_3), 60.4 (CO_2CH_2), 66.9 (C-20, C-22), 74.5 (C-8), 93.2 (C-12), 101.7 (C-19), 108.3 (C-11), 124.7 (C-7), 131.7 (C-2), 139.6 (C-6), 141.5 (C-3), 146.3 (C-9), 167.8 (C-1).

MS (ESI): *m/z* = 486.21, 407.26, 361.22, 331.21, 305.19, 285.17, 259.16, 213.13, 185.13, 159.12, 131.09, 113.06.

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{25}H_{44}O_6SiNa^+$: 491.2799; found: 491.2800.

(2*E*)-**23**

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.42 (s, 9 H, TMS), 1.28 (t, *J* = 7.1 Hz, 3 H, $CO_2CH_2CH_3$), 1.33 (dq, *J* = 13.5, 1.3 Hz, 1 H, H^a-6′), 1.39 (ddd, *J* = 14.1, 5.1, 1.0 Hz, 1 H, CH_2TMS-H^a), 1.58 (dd, *J* = 14.1, 1.0 Hz, 1 H, CH_2TMS-H^b), 1.68–1.71 (m, 2 H, H-2′), 1.73 (d, *J* = 1.3 Hz, 3 H, CH_3), 2.02–2.11 (m, 1 H, H^b-6′), 2.12–2.2 (m, 2 H, H-5), 2.30–2.37 (m, 2 H, H-4), 2.39 (t, *J* = 0.8 Hz, 2 H, H-1′), 3.37 (s, 3 H, OCH_3), 3.7–3.77 (m, 2 H, H^a-5a′, H^a-5b′), 4.06–4.11 (m, 2 H, H^b-5a′, H^b-5b′), 4.19 (q, *J* = 7.1 Hz, 2 H, CO_2CH_2), 4.49 (t, *J* = 5.3 Hz, 1 H, H-3′), 4.56 (dd, *J* = 6.7, 1.7 Hz, 1 H, H-2a″), 4.62 (dd, *J* = 6.7, 4.1 Hz, 1 H, H-2b″), 4.62–4.66 (m, 1 H, H-8), 4.68 (dd, *J* = 1.9, 0.8 Hz, 1 H, H-10a), 4.97 (dd, *J* = 1.9, 1.2 Hz, 1 H, H-10b), 5.08 (dq, *J* = 9.2, 1.3 Hz, 1 H, H-7), 6.73 (tt, *J* = 7.4, 1.1 Hz, 1 H, H-3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.3 ($CO_2CH_2CH_3$), 16.6 (CH_3), 21.4 (C-1′), 22.5 (CH_2TMS), 25.8 (C-6′), 29.1 (C-4), 34.5 (C-2′), 38.6 (C-5), 55.3 (OCH_3), 60.2 (CO_2CH_2), 66.9 (C-5′^{a}, C-5′^{b}), 74.5 (C-8), 93.1 (C-2″), 101.7 (C-3′), 108.1 (C-10), 124.9 (C-7), 132.1 (C-2), 139.2 (C-6), 142.0 (C-3), 146.2 (C-9), 167.6 (C-1).

Supporting Information for this article is available online at http://www.thieme-connect.de/ejournals/toc/synthesis.

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References

(1) For reviews, see: (a) Hanson, J. R. *Nat. Prod. Rep.* **2006**, *23*, 875. (b) Hanson, J. R. *Nat. Prod. Rep.* **2005**, *22*, 594. (c) Uyehara, T.; Yamamoto, Y. *Chemtracts: Org. Chem.* **1988**, *1*, 273. (d) Tius, M. A. *Chem. Rev.* **1988**, *88*, 719.

(2) For recent isolations, see: (a) Cheng, S.-Y.; Wen, Z.-H.; Wang, S.-K.; Chiou, S.-F.; Hsu, C.-H.; Dai, C.-F.; Chiang, M. Y.; Duh, C.-Y. *J. Nat. Prod.* **2009**, *72*, 152. (b) Cheng, S.-Y.; Wen, Z.-H.; Chiou, S.-F.; Hsu, C.-H.; Wang, S.-K.; Dai, C.-F.; Chiang, M. Y.; Duh, C.-Y. *Tetrahedron* **2008**, *64*, 9698. (c) Chen, S.-H.; Guo, Y.-W.; Huang, H.; Cimino, G. *Helv. Chim. Acta* **2008**, *91*, 873. (d) Marrero, J.; Benitez, J.; Rodriguez, A. D.; Zhao, H.; Raptis, R. G. *J. Nat. Prod.* **2008**, *71*, 381. (e) Dorta, E.; Diaz-Morrero, A. R.; Brito, I.; Cueto, M.; D'Croz, L.; Darias, J. *Tetrahedron* **2007**, *63*, 9057. (f) Desoubzdanne, D.; Marcourt, L.; Raux, R.; Chevalley, S.; Dorin, D.; Doerig, C.; Valentin, A.; Ausseil, F.; Debitus, C. *J. Nat. Prod.* **2008**, *71*, 1189. (g) Kamel, H. N.; Ferreira, D.; Garcia-Fernandez, L. F.; Slattery, M. *J. Nat. Prod.* **2007**, *70*, 1223. (h) Wang, L.-T.; Wang, S.-K.; Soong, K.; Duh, C.-Y. *Chem. Pharm. Bull.* **2007**, *55*, 766. (i) Yan, X.-H.; Gavagnin, M.; Cimino, G.; Guo, Y.-W. *Tetrahedron Lett.* **2007**, *48*, 5313. (j) Nieto, M. I.; Gonzalez, N.; Rodriguez, J.; Kerr, R. G.; Jimenez, C. *Tetrahedron* **2006**, *62*, 11747. (k) Su, J.-H.; Ahmed, A. F.; Sung, P.-J.; Chao, C.-H.; Shen, J.-H. *J. Nat. Prod.* **2006**, *69*, 1134. (l) Jia, R.; Guo, Y.-W.; Mollo, E.; Gavagnin, M.; Cimino, G. *J. Nat. Prod.* **2006**, *69*, 819.

(3) For recent synthetic approaches, see: (a) Tietze, L. F.; Brazel, C. C.; Hölsken, S.; Magull, J.; Ringe, A. *Angew. Chem. Int. Ed.* **2008**, *47*, 5246; *Angew. Chem.* **2008**, *120*, 5324. (b) Schweizer, E.; Gaich, T.; Brecker, L.; Mulzer, J. *Synthesis* **2007**, 3807. (c) Wipf, P.; Grenon, M. *Can. J. Chem.* **2006**, *84*, 1226. (d) Katsuyama, I.; Fahmy, H.; Zjawiony, J. K.; Khalifa, S. I.; Kilada, R. W.; Konoshima, T.; Takasahi, M.; Tokuda, H. *J. Nat. Prod.* **2002**, *65*, 1809.

(4) (a) Marshall, J. A.; Van Devender, E. A. *J. Org. Chem.* **2001**, *66*, 8037. (b) Marshall, J. A.; Gung, B. W. *Isr. J. Chem.* **1991**, *31*, 199. (c) Marshall, J. A.; Markwalder, J. A. *Tetrahedron Lett.* **1988**, *29*, 4811. (d) Marshall, J. A.; DeHoff, B. S. *J. Org. Chem.* **1986**, *51*, 863.

(5) Gross, H.; Wright, A. D.; Beil, W.; König, G. M. *Org. Biomol. Chem.* **2004**, *2*, 1133.

(6) For an excellent review on α-methylene-γ-butyrolactones, see: Kitson, R. R. A.; Millemaggi, A.; Taylor, R. J. K. *Angew. Chem. Int. Ed.* **2009**, *48*, 9426; *Angew. Chem.* **2009**, *121*, 9590.

(7) Umbreit, M. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 5526.

(8) Watanabe, Y.; Laschat, S.; Budde, M.; Affolter, O.; Shimada, Y.; Urlacher, V. B. *Tetrahedron* **2007**, *63*, 9413.

(9) Seifert, A.; Vormund, S.; Grohmann, K.; Kriening, S.; Urlacher, V. B.; Laschat, S.; Pleiss, J. *ChemBioChem* **2009**, *10*, 853.

(10) For reviews, see: (a) Hoveyda, A. H.; Malcolmson, S. J.; Meek, S. J.; Zhugralin, A. R. *Angew. Chem. Int. Ed.* **2010**, *49*, 434; *Angew. Chem.* **2010**, *122*, 38. (b) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4490; *Angew. Chem.* **2005**, *117*, 4564. (c) Fürstner, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 3012; *Angew. Chem.* **2000**, *112*, 3140.

(11) For a recent example, see: Fuwa, H.; Naito, S.; Goto, T.; Sasaki, M. *Angew. Chem. Int. Ed.* **2008**, *47*, 4737; *Angew. Chem.* **2008**, *120*, 4815.

(12) For a review, see: Hosomi, A. *Acc. Chem. Res.* **1988**, *21*, 200.

(13) (a) Ishihara, K.; Mouri, M.; Gao, Q.; Maruyama, T.; Furuta, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 11490. (b) Hosomi, A.; Hashimoto, H.; Kobayashi, H.; Sakurai, H. *Chem. Lett.* **1979**, *8*, 245. (c) Hosomi, A.; Sakurai, H. *Tetrahedron Lett.* **1976**, *17*, 1295.

(14) Kitamura, M.; Suga, S.; Kawai, K.; Noyori, R. *J. Am. Chem. Soc.* **1986**, *108*, 6072.

(15) Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A.; Masamune, S.; Roush, W. R.; Sakui, T. *Tetrahedron Lett.* **1984**, *25*, 2183.

(16) Daniewski, A. R.; Wojceichowska, W. *J. Org. Chem.* **1982**, *47*, 2993.

(17) For reviews, see: (a) Marshall, J. A. *J. Org. Chem.* **2007**, *72*, 8153. (b) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 34; *Angew. Chem.* **1991**, *103*, 34. (c) Tomioka, K. *Synthesis* **1990**, 541.

(18) Petrier, C.; Barbosa, J. D. S.; Dupuy, C.; Luche, J. L. *J. Org. Chem.* **1985**, *50*, 5761.

(19) Nugent, W. A. *Chem. Commun.* **1999**, 1369.
(20) Trost, B. M.; Greve, T. A.; Chan, D. M. T. *J. Am. Chem. Soc.* **1991**, *113*, 7350.
(21) Masui, M.; Shiori, T. *Tetrahedron* **1995**, *51*, 8363.
(22) (a) Ando, K. *J. Org. Chem.* **1999**, *64*, 8406. (b) Ando, K. *J. Org. Chem.* **1997**, *62*, 1934.
(23) Veysoglu, T.; Mitscher, L. A.; Swayze, J. K. *Synthesis* **1980**, 807.
(24) Phoenix, S.; Bourque, E.; Deslongchamps, P. *Org. Lett.* **2000**, *2*, 4149.
(25) Pihko, P. M.; Saloa, T. M. *Tetrahedron Lett.* **2003**, *44*, 4361.
(26) Ando, K.; Oishi, T.; Hirama, M.; Ohno, H.; Ibuha, T. *J. Org. Chem.* **2000**, *65*, 4745.
(27) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.