Enantioselective total synthesis of plakotenin, a cytotoxic metabolite from *Plakortis sp*†

Stephanie Arzt, Emmanuel Bourcet, Thierry Muller and Stefan Bräse*

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The first total enantioselective synthesis of plakotenin is described. This marine natural product was isolated from an Okinawan sponge of the genus *Plakortis* and shows potent biological activity against several cancerous cell lines. A biomimetic intramolecular Diels–Alder reaction served as a key step in the total synthesis. The synthesis proves the relative and absolute stereochemistry of natural plakotenin.

Introduction

Nature provides a considerable number of highly functionalised natural products with great structural divergence. A particular interesting and biologically active group of natural products is derived from unsaturated polyketides and a subsequent Diels–Alder reaction.[1]

Plakotenin (**1**) was isolated from an Okinawan marine sponge of the genus *Plakortis* (Fig. 1).[2] It has a bicyclic system with six stereogenic centers, one of which is quaternary. *Homo*-plakotenin (**2**)[3] and *nor*-plakotenin (**3**)[3] are related carboxylic acids from the Palauan sponge *Plakortis lita* (Fig. 1). They are all optically active and their absolute stereochemistry was deduced from analogous compounds and from 2D-NMR analysis.[2,3] Compounds **1–3** were found to significantly reduce proliferation of rheumatoid synovial fibroblasts[3] and show moderate general cytotoxicity.[2] Spiculoic acid (**4**), a relative of plakotenin (**1**) with an additional carbonyl group isolated from *Plakortis angulospiculatus*,[4] was recently synthesised (Fig. 1).[5–7] Its absolute stereochemistry had to be revised after total synthesis and is shown in Fig. 1.

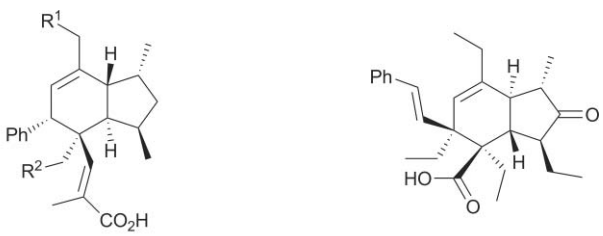
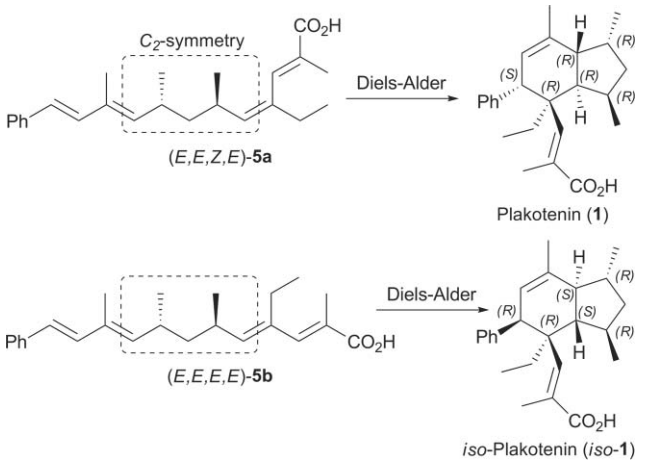


Fig. 1 Plakotenin (**1**) and related compounds.[2–4,8]

Based on precedence,[8,9] we hypothesised that plakotenin stems from a biosynthetic tetraene precursor **5** (Scheme 1). In contrast to spiculoic acid whose biosynthetic precursor has been shown to be a triene–ene, plakotenin needs a diene–diene system. Although, linear and/or oxidised all (*E*)-configurated polyketides (*e.g.* plakortin)[8,10] were often isolated from *Plakortis* strains and show interesting biological activity,[8] plakotenin (**1**) necessarily stems from a rather rare (*E*,*E*,***Z***,*E*)-tetraene precursor **5a** (Scheme 1).[10] In order to access plakotenin (**1**) as well as related diastereomers, both non linear and linear tetraene systems **5a** and **5b** have been considered. The challenge of a total synthesis of plakotenin (**1**) stays in the generation of the stereogenic centers and double bonds. In this manuscript we describe the total synthesis of plakotenin (**1**, Fig. 1).[11]



Scheme 1 Hypothetical ring closure of tetraenes (*E*,*E*,*Z*,*E*)-**5a** and (*E*,*E*,*E*,*E*)-**5b**.

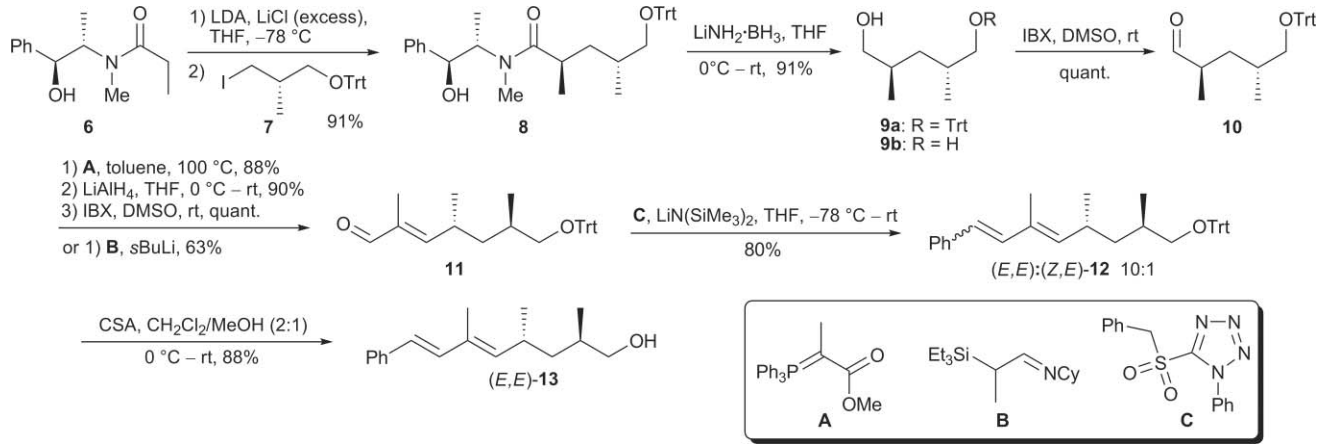
Results and discussion

Stereochemical analysis revealed that the tetraene **5** is perfectly suited for a bidirectional approach using a central C_2-symmetrical dimethyl building block (Scheme 1).

The required dimethyl precursor **9a** was synthesised by an asymmetric alkylation approach (Scheme 2). Commercially available Myers pseudo-ephedrine auxiliary **6**[12,13] was alkylated with iodide (*S*)-**7**[14]—prepared from Roche ester[15]—to give the amide **8** as a single diastereoisomer. The trityl group was chosen as the protecting group due to its stability during the reaction sequence as well as its facile introduction and removal.[16] Reduction of amide **8** using lithium amidotrihydroborate gave alcohol **9a**. In order to

Institut für Organische Chemie, Karlsruhe Institute of Technology (KIT), Fritz-Haber-Weg 6, 76131 Karlsruhe, Germany. E-mail: braese@kit.edu; Fax: + 49 721 608 8581

† Electronic Supplementary Information (ESI) available: Experimental procedures and characterisation for compounds **S1**, **S2** and copies of NMR spectra of compounds **1, 13, 14a, 15a, 16–19** are available. See DOI: 10.1039/c004199h/



Scheme 2 Sequence for the generation of alcohol (*E*,*E*)-**13**.

assure that the desired diastereochemistry was achieved during the asymmetric alkylation, alcohol **9a** was deprotected (formic acid) and the optical rotation of the obtained diol **9b** compared with literature values.[17] Oxidation of alcohol **9a** delivered aldehyde **10**. Wittig reaction sequence with subsequent leveling of the oxidation state gave aldehyde **11**. Latter was also directly accessible from aldehyde **10** in comparable yield (63%) in one step by using silylimine **B**.[18] Extension of **11** *via* a Julia–Kocienski olefination approach with tetrazole **C**[19] gave rise to a mixture of inseparable (*E*,*E*)/(*Z*,*E*)-dienes **12** in a 10 : 1 ratio. The undesired geometrical isomer could eventually be removed after cleavage of the trityl protecting group with camphorsulfonic acid, yielding alcohol (*E*,*E*)**-13** as pure isomer in good yield.

With (*E*,*E*)**-13** in hand, we first explored the route of linear tetraene precursor **5b**. Oxidation of (*E*,*E*)**-13** with Dess–Martin periodinane (DMP) furnished the corresponding aldehyde which was directly used in a classical Wittig reaction (Scheme 3). However, under the employed reaction conditions (**D**, toluene, 100 °C), cyclisation of intermediate (*E*,*E*,*E*)**-14b** took place to give the bicyclic product **15b**. The corresponding alcohol **16b** was obtained in good yield after subsequent reduction (43% over three steps). Its stereochemistry was deduced by 2D-NMR experiments (Fig. 2, see ESI†). The spectra showed prominent differences with plakotenin (**1**) and its congeners, which support the stereochemical assignment made for plakotenin (**1**).[2] Unfortunately, alcohol **16b**

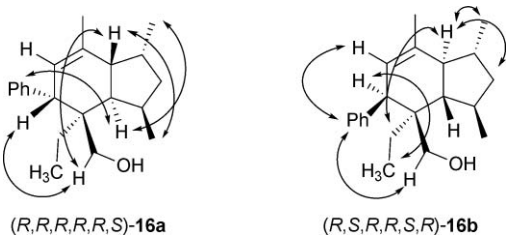
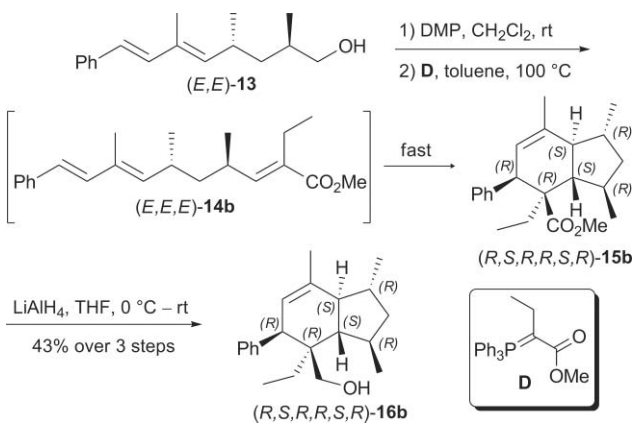


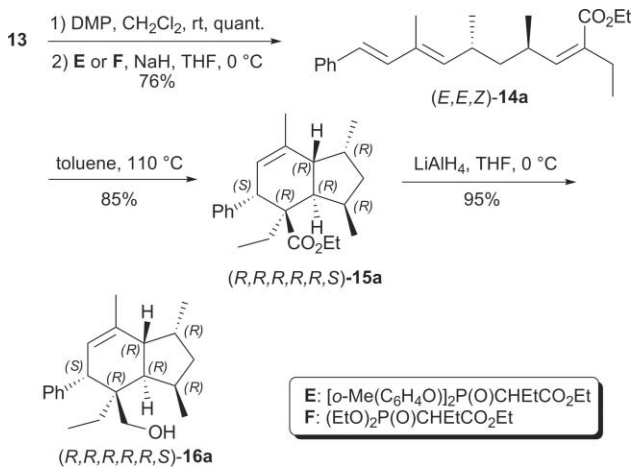
Fig. 2 NOESY correlations for compounds **16a** and **16b**.

was not suitable for direct extension to plaketonin isomers using classical olefination chemistry (results not shown).

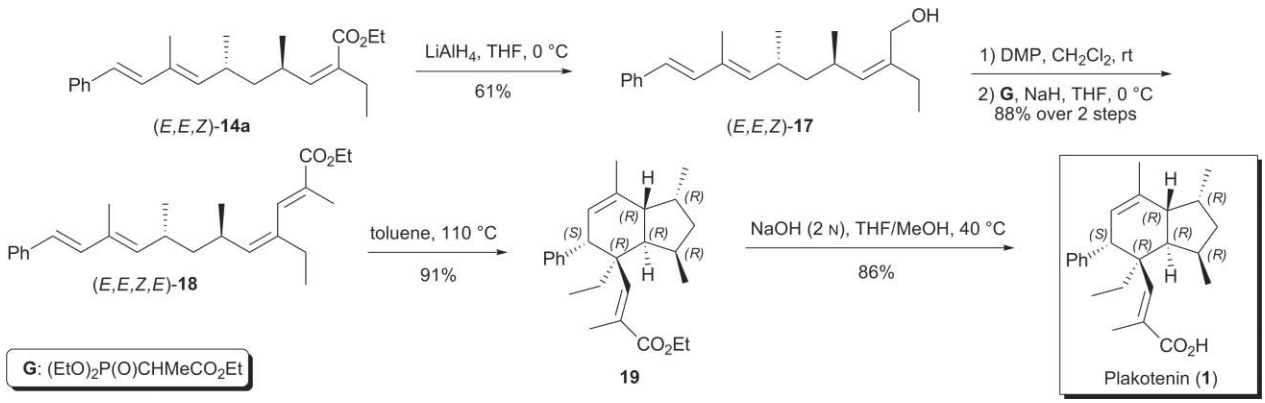
We then turned to the synthesis of non-linear tetraene precursor **5a**. In order to avoid *in situ* cyclisation of the generated triene, a mild (*Z*)-selective variation of the Horner–Wadsworth Emmons reaction, using phosphonate **E** (ethyl 2-((bis(*o*-tolyloxy))-phosphoryl)butanoate) was chosen to generate the triene ester (*E*,*E*,*Z*)**-14a** required for the plakotenin stereochemistry.[20] Thus, (*E*,*E*,*Z*)-isomer **14a** was obtained in 64% yield (over two steps) with a *Z* : *E* selectivity of 6 : 1. Both isomers could be separated by silica column chromatography. The classical HWE reaction conditions using phosphonate **F** also proceeded nicely and, surprisingly delivered again the (*E*,*E*,*Z*)**-14a** isomer as the major product with a 4 : 1 ratio in 76% yield over two steps



Scheme 3 Wittig and *in situ* Diels–Alder reaction yielded **16b**.



Scheme 4 HWE reaction followed by Diels–Alder reaction yielded **16a**.



Scheme 5 Sequence to complete (*R*,*R*,*R*,*R*,*S*)-plakotenin (**1**).

(Scheme 4). NOESY experiments realised on alcohol **17** (see ESI†) permitted indeed the assignment of the geometry of the double bonds unambiguously. With the triene in hand, (*E*,*E*,*Z*)-**14a** was heated in toluene overnight and cyclisation took place to deliver the bicycle (*R*,*R*,*R*,*R*,*S*)-**15a** in very good yield (85%, Scheme 4).

The stereochemistry of the product was again deduced by 2D-NMR spectra (realised on alcohol **16a**, obtained by reduction of ester **15a** with $LiAlH_4$) and shows very similar NMR shifts compared to plakotenin (Fig. 2). Unfortunately, after subsequent oxidation of **16a**, as for **16b**, introduction of the last missing double bond for plakotenin could not be achieved by olefination reactions (results not shown). Since addition of other nucleophiles (*e.g.* Grignard reagents) proceeds smoothly on the corresponding aldehyde (results not shown), this failure might be attributed to steric hindrance. Hence, we focused on the strategy of the biomimetic Diels–Alder reaction of the corresponding tetraene.

Standard reduction of (*E*,*E*,*Z*)-**14a** using $LiAlH_4$ and subsequent oxidation with DMP provided the corresponding aldehyde, which was directly elongated to the tetraene (*E*,*E*,*Z*,*E*)-**18** using ester **G** (Scheme 5). It is noteworthy that compounds **14a**, **17** and **18** are very prone to cyclisation and great care must be taken to store and handle these sensitive compounds in a cold environment. Indeed, on heating, tetraene (*E*,*E*,*Z*,*E*)-**18** cyclises smoothly in excellent yield to ester (*R*,*R*,*R*,*R*,*S*)-**19** detected as single diastereoisomer. Saponification eventually yielded synthetic plakotenin (**1**, Scheme 5), which was extensively analysed by 2D-NMR (the same correlations as for compound **16a** are observed, see ESI†). The spectroscopic data (^{1}H-NMR, ^{13}C-NMR and mass) as well as the optical rotation of synthetic plakotenin (**1**) were identical with the reported data of the natural product (see ESI†).

Conclusions

In summary, we have developed a rapid and very efficient route to (*R*,*R*,*R*,*R*,*S*)-plakotenin (**1**) in 15 steps (14.7% overall yield from **6**) which should also be suitable for the syntheses of analogous compounds such as **2** and **3**. The biological assays and modelling studies to reveal the transition states are currently being pursued.

Experimental

General methods

^{1}H and ^{13}C NMR spectra were recorded on a *Bruker* AM 400 (400 MHz/100 MHz), *Bruker* DRX 500 (500 MHz/125 MHz) or *Bruker* Avance 600 (600 MHz/150 MHz) instrument using $CDCl_3$ as solvent. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to $CHCl_3$ (7.26 ppm) as internal standard. All coupling constants are absolute values and *J* values are expressed in Hertz (Hz). For assigning signal separation of ^{1}H NMR spectra the following abbreviations were used: *s* = singlet, bs = broad singlet, *d* = doublet, *t* = triplet, *q* = quartet, sext = sextet, *m* = multiplet, dd = doublet of doublets, dq = doublet of quartets, ddq = doublet of dq and $H_{arom.}$ = aromatic proton. For assigning signals of ^{13}C NMR spectra the following abbreviations were used: *p* = primary (RCH_3), *s* = secondary (R_2CH_2), *t* = tertiary (R_3CH), *q* = quaternary (R_4C). The assignment was supported by analysis of DEPT90 and DEPT135 spectra. MS (EI) (electron impact mass spectrometry), MS (FAB) (fast atom bombardment mass spectrometry) and HRMS: *Finnigan* MAT 90. The molecular fragments are quoted as the relation between mass and charge (*m*/*z*), the intensities as a percentage value relative to the intensity of the base signal (100%). The molecular ion obtains the abbreviation [M^+]. IR (infrared spectroscopy): FT-IR *Bruker* IFS 88. IR spectra of oils were recorded as thin films on KBr; in the case of solids the neat substance was used. The deposit of the absorption band is given in wave numbers in cm^{-1}. Solvents and chemicals used for reactions were purchased from commercial suppliers. Solvents were dried under standard conditions; chemicals were used without further purification. All the reactions were performed in standard glassware. All reactions were carried out under Argon in flame-dried glassware. Evaporation of solvents and concentration of reaction mixtures were performed *in vacuo* on a *Büchi* rotary evaporator. Column chromatography was performed using silica gel 60 (purchased from *Merck*) under flash conditions. For thin layer chromatography, aluminium foils layered with silica gel with fluorescence indicator (silica gel 60 F_{254}) produced by *Merck* were employed. The detection was carried out with an UV-lamp from *Heraeus*, model Fluotest. Seebach-reagent [molybdophosphoric acid (2.5 w%), cerium(IV) sulfate

tetrahydrate (1.0 w%), H_2SO_4 conc. (6.0 w%), water (90.5 w %)] was used as dipping reagent. Specific rotations were determined using the polarimeter *Perkin Elmer* 241. Melting points were registered on a Mel-Temp II melting point microscope from *Laboratory Devices Inc.* and are not corrected.

(2*R*,4*R*)-*N*-((1*S*,2*S*)-1-Hydroxy-1-phenylpropan-2-yl)-*N*,2,4-trimethyl-5-(trityloxy)pentanamide (8)

A solution of *n*-butyllithium in hexanes (2.5 M, 10.8 mL, 27.0 mmol) was slowly added to a suspension of lithium chloride (3.64 g, 85.9 mmol) and diisopropylamine (4.10 mL, 3.00 g, 29.0 mmol) in THF (15 mL) at –78 °C. The resulting suspension was warmed to 0 °C briefly and was then cooled to –78 °C again. An ice-cooled solution of *N*-((1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl)-*N*-methylpropionamide (3.14 g, 14.2 mmol) in THF (35 mL) was added. The mixture was stirred at –78 °C for 2 h, at 0 °C for 15 min and at rt for 5 min. The mixture was cooled to 0 °C and iodide **7** (2.99 g, 6.76 mmol) in THF (35 mL) was added. After being stirred for 2 d at 45 °C the reaction mixture was treated with half saturated aqueous NH_4Cl (70 mL) and the resulting mixture was extracted with EtOAc (3 × 40 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified by column chromatography on silica using cyclohexane/ethyl acetate 2 : 1 to give amide **8** (3.31 g, 91%) as white foam. R_f 0.22 (cyclohexane/EtOAc 2 : 1). – mp 50 °C. – $[\alpha]_D^{20}$ = +33.5 (0.99 g/100 mL, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (d, J = 2.7 Hz, 3 H), 0.94 (d, J = 2.7 Hz, 3 H), 1.00 (d, J = 6.9 Hz, 3 H), 1.31–1.44 (m, 2 H), 1.50–1.61 (m, 1 H), 2.35–2.43 (m, 1 H), 2.50 (s, 3 H), 2.70 (dd, J = 8.8 Hz, J = 6.0 Hz,1 H), 2.88 (dd, J = 8.8 Hz, J = 4.7 Hz, 1 H), 4.24 (bs, 1 H), 4.49 (t, J = 7.2 Hz, 1 H), 7.11–7.24 (m, 14 H), 7.33–7.39 (m, 6 H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3 (p), 17.5 (p), 18.2 (p), 31.7 (t), 34.1 (t), 37.8 (s), 67.4 (s), 76.4 (t), 86.0 (q), 126.1 (t), 126.8 (t), 127.5 (t), 127.6 (t), 128.2 (t), 128.7 (t), 142.5 (q), 144.3 (q), 179.0 (q) (The ^{1}H- and ^{13}C NMR spectra are complex due to amide geometrical isomerism). – IR (neat): $\tilde{\nu}$ = 3382, 3059, 3030, 2969, 2930, 2871, 1620, 1490, 1449, 1410, 1373, 1318, 1221, 1155, 1070, 988, 926, 899, 839, 764, 747, 705, 648, 633, 506 cm^{-1}. – MS (FAB, Matrix: 3-NBA) m/z (%): 558 [M+Na]$^+$, 536 [M+H]$^+$, 243 (100). – HRMS (FAB, Matrix: 3-NBA) ($C_{36}H_{42}NO_3$): calc. 536.3165, found 536.3167.

(2*R*,4*R*)-2,4-Dimethyl-5-(trityloxy)pentan-1-ol (9a)

A solution of *n*-butyllithium in hexanes (2.5 M, 9.30 mL, 23.0 mmol) was added to a solution of diisopropylamine (3.50 mL, 2.50 g, 25.0 mmol) in THF (30 mL) at –78 °C. The resulting solution was stirred at –78 °C for 10 min, was then warmed to 0 °C and held at that temperature for 20 min. Lithium amidotrihydroborate (819 mg, 23.9 mmol) was added in one portion. The suspension was stirred at 0 °C for 15 min and then was warmed to rt. After 15 min, the suspension was cooled to 0 °C. A solution of amide **8** (3.20 g, 5.97 mmol) in THF (30 mL) was slowly added. The reaction mixture was warmed to rt, held at that temperature for 2 h and was then cooled to 0 °C where excess hydride was quenched by careful addition of 3 M aqueous HCl (70 mL). The mixture was stirred for 10 min at 0 °C and was then extracted with Et_2O (3 × 50 mL). The combined extracts were washed sequentially with 3 M aqueous HCl (10 mL), 2 M aqueous NaOH (10 mL) and brine (50 mL). The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified by column chromatography on silica using cyclohexane/ethyl acetate 9 : 1 to give alcohol **9a** (2.03 g, 91%) as a white solid. R_f 0.18 (cyclohexane/EtOAc 6 : 1). – mp 72 °C. – $[\alpha]_D^{20}$ = +13.0 (0.81 g/100 mL, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (d, J = 6.6 Hz, 3 H, CH_3), 0.93 (d, J = 6.7 Hz, 3 H, CH_3), 1.10–1.23 (m, 2 H, CHCH_2CH), 1.31 (t, J = 5.5 Hz, 1 H, OH), 1.61–1.69 (m, 1 H, HOCH$_2$CH), 1.79–1.87 (m, 1 H, TrtOCH$_2$CH), 2.89–2.96 (m, 2 H, TrtOCH_2), 3.34–3.46 (m, 2 H, HOCH_2), 7.20–7.31 (m, 9 H, $H_{arom.}$), 7.43–7.46 (m, 6 H, $H_{arom.}$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.3 (p), 17.1 (p), 31.2 (t), 33.0 (t), 37.2 (s), 68.9 (s), 69.0 (s), 86.2 (q), 126.8 (t), 127.6 (t), 128.7 (t), 144.4 (q). – IR (neat): $\tilde{\nu}$ = 3299, 3056, 3031, 2958, 2925, 2871, 1595, 1491, 1449, 1387, 1323, 1220, 1177, 1151, 1062, 1033, 985, 949, 931, 897, 821, 765, 752, 709, 697, 648, 632, 540, 484, 422 cm^{-1}. – MS (EI, 70 eV) m/z (%): 374 (1) [M$^+$], 259 (12), 243 (100), 183 (17), 165 (35), 105 (11), 77 (4). – HRMS ($C_{26}H_{30}O_2$): calc. 374.2246, found 374.2249.

((((2*R*,4*R*,5*E*,7*E*)-2,4,6-Trimethyl-8-phenylocta-5,7-dien-1-yl)oxy)methanetriyl)tribenzene (12)

To a solution of alcohol (4*R*,6*R*,*E*)-2,4,6-trimethyl-7-(trityloxy)hept-2-en-1-ol (**S2**) (201 mg, 485 µmol) in DMSO (10 mL) was added 2-iodoxybenzoic acid (340 mg, 1.21 mmol). The reaction mixture was stirred at rt for 1 h, after which it was diluted with H_2O (50 mL) and the resulting precipitate was filtered off. The aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to yield the crude aldehyde **11** (200 mg, 485 µmol, assumed to be quantitative) as colourless oil, which was used without further purification for the following olefination reaction.

To a solution of 5-(benzylsulfonyl)-1-phenyl-1*H*-tetrazole (218 mg, 728 µmol) in THF (5 mL) was slowly added lithium bis(trimethylsilyl)amide (1 M in THF, 600 µL, 600 µmol) at 0 °C. After stirring for 20 min at rt, it was cooled to –78 °C and a solution of crude aldehyde **11** (200 mg, 0.485 mmol) in THF (5 mL) was added. The reaction mixture was stirred overnight while slowly warming up to rt. It was diluted with Et_2O (5 mL) and the reaction quenched by addition of saturated aqueous $NaHCO_3$ (5 mL). The aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified by column chromatography on silica using cyclohexane/ethyl acetate 50 : 1 to give compound **12** (190 mg, 80%) as colourless oil. A 10 : 1 ratio of *E*/*Z* products was obtained. R_f 0.30 (cyclohexane/EtOAc 50 : 1). – $[\alpha]_D^{20}$ = –75.0 (0.71 g/100 mL, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (d, J = 6.6 Hz, 3 H, TrtOCH$_2$CHCH_3), 1.03 (d, J = 6.7 Hz, 3 H, C=CHCHCH_3), 1.09–1.16 (m, 1 H, CHCH_AH$_B$CH), 1.45–1.49 (m, 1 H, CHCH$_A$$H_B$CH), 1.63 (s, 3 H, PhCH=CHCCH_3), 1.70–1.80 (m, 1 H, TrtOCH$_2$CH), 2.36–2.47 (m, 1 H, C=CHCH), 2.81 (dd, J = 8.6 Hz, J = 6.7 Hz, 1 H, TrtOCH_AH$_B$), 3.02 (dd, J = 8.7 Hz, J = 4.7 Hz, 1 H, TrtOCH$_A$$H_B$), 5.36 (d, J = 9.6 Hz, 1 H, PhCH=CHC=CH), 6.38 (d, J = 16.1 Hz, 1 H, PhCH), 6.74 (d, J = 15.6 Hz, 1 H, PhCH=CH), 7.16–7.24 (m, 5 H, $H_{arom.}$), 7.26–7.32 (m, 9 H, $H_{arom.}$), 7.40–7.46 (m, 6 H,

H_{arom}.). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.4 (p), 18.5 (p), 21.0 (p), 30.2 (t), 31.8 (t), 41.7 (s), 67.6 (s), 86.0 (q), 125.6 (t), 126.1 (t), 126.7 (t), 126.8 (t), 127.7 (t), 128.5 (t), 128.8 (t), 132.1 (q), 134.2 (t), 138.0 (q), 140.9 (t), 144.5 (q). – IR (film): $\tilde{\nu}$ = 3084, 3058, 3025, 2957, 2924, 2866, 2851, 1597, 1560, 1542, 1491, 1448, 1386, 1314, 1220, 1182, 1155, 1070, 1031, 959, 926, 899, 826, 774, 763, 746, 706, 647, 632, 530 cm^{-1}. – MS (EI, 70 eV) *m*/*z* (%): 486 (50) [M$^+$], 374 (73), 414 (100), 485 (95). – HRMS ($C_{36}H_{38}O$): calc. 486.2922, found 486.2917.

(2*R*,4*R*,5*E*,7*E*)-2,4,6-Trimethyl-8-phenylocta-5,7-dien-1-ol (13)

To a solution of **12** (3.01 g, 6.19 mmol) in CH_2Cl_2–MeOH (200/100 mL) at 0 °C camphorsulfonic acid (2.44 g, 10.5 mmol) was added in one portion. The mixture was stirred at rt for 90 min and was then neutralized by the addition of saturated aqueous $NaHCO_3$ (60 mL). The layers were separated and the aqueous layer extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and then concentrated. The crude product was then purified by flash chromatography using cyclohexane/ethyl acetate 6 : 1 to yield alcohol **13** (1.33 g, 88%) as colourless solid. R_f 0.16 (cyclohexane/EtOAc 6 : 1). – mp 43 °C. – $[\alpha]_D^{20}$ = –44.5 (0.92 g/100 mL, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (d, *J* = 6.7 Hz, 3 H, $HOCH_2CHCH_3$), 0.99 (d, *J* = 6.6 Hz, 3 H, $C{=}CHCHCH_3$), 1.11–1.19 (m, 1 H, $CHCH_AH_BCH$), 1.27 (bs, 1 H, O*H*), 1.39–1.45 (m, 1 H, $CHCH_AH_BCH$), 1.63–1.71 (m, 1 H, $HOCH_2CH$), 1.88 (s, 3 H, $PhCH{=}CHCCH_3$), 2.61–2.72 (m, 1 H, $C{=}CHCH$), 3.42 (dd, *J* = 10.5 Hz, *J* = 6.5 Hz, 1 H, $HOCH_AH_B$), 3.53 (dd, *J* = 10.5 Hz, *J* = 5.2 Hz, 1 H, $HOCH_ACH_B$), 5.43 (d, *J* = 9.5 Hz, 1 H, $PhCH{=}CHC{=}CH$), 6.45 (d, *J* = 16.1 Hz, 1 H, PhC*H*), 6.79 (d, *J* = 16.1 Hz, 1 H, $PhCH{=}CH$), 7.17–7.21 (m, 1 H, H_{arom}.), 7.29–7.32 (m, 2 H, H_{arom}.), 7.39–7.41 (m, 2 H, H_{arom}.). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.6 (p), 17.2 (p), 20.8 (p), 30.3 (t), 33.5 (t), 41.0 (s), 68.1 (s), 125.8 (t), 126.1 (t), 126.9 (t), 128.5 (t), 132.1 (q), 134.1 (t), 137.9 (q), 140.8 (t). – IR (neat): $\tilde{\nu}$ = 3307, 3078, 3055, 3028, 2959, 2921, 2870, 1658, 1630, 1596, 1575, 1492, 1447, 1370, 1269, 1232, 1153, 1074, 1037, 990, 961, 924, 909, 883, 830, 747, 690, 647, 532, 456, 438, 427, 409 cm^{-1}. – MS (EI, 70 eV) *m*/*z* (%): 244 (47) [M$^+$], 171 (100), 143 (29), 129 (31), 99 (37), 91 (31). – HRMS ($C_{17}H_{24}O$): calc. 244.1827, found 244.1829.

(2*Z*,4*R*,6*R*,7*E*,9*E*)-Ethyl 2-ethyl-4,6,8-trimethyl-10-phenyldeca-2,7,9-trienoate (14a)

Dess–Martin periodinane (3.56 mL, 1.65 mmol) was added at 0 °C to a solution of alcohol **13** (310 mg, 1.27 mmol) in CH_2Cl_2 (15 mL). After stirring for 2 h at rt, the reaction mixture was quenched by adding saturated aqueous $Na_2S_2O_3$ (5 mL) and saturated aqueous $NaHCO_3$ (5 mL). The layers were separated and the aqueous layer extracted with CH_2Cl_2 (4 × 10 mL). The organic layer was dried ($MgSO_4$) and concentrated to yield the crude aldehyde (310 mg, 1.27 mmol, assumed to be quantitative) as colourless oil, which was used without further purification for the following olefination reaction.

To a solution of sodium hydride (60% in mineral oil, 152 mg, 3.87 mmol) in THF (15 mL) at 0 °C was added dropwise ethyl 2-(diethoxyphosphoryl)butanoate (960 mg, 3.87 mmol) (or ethyl 2-((bis(*o*-tolyloxy))phosphoryl)acetate for method according to ANDO *et al.*). The solution was stirred at rt for 1 h before cooling to 0 °C and addition of the crude aldehyde (310 mg, 1.27 mmol, from previous reaction) in THF (5 mL). The solution was stirred for 1 h at 0 °C, warmed slowly to rt and stirred for an additional 3 h. The reaction was quenched by pouring on to saturated aqueous NH_4Cl (80 mL). The product was extracted with Et_2O and the combined extracts were dried ($MgSO_4$) and concentrated. The crude product was then purified by column chromatography on silica using *n*-pentane–Et_2O 30 : 1 to yield ester **14a** (328 mg, 76%) as a colourless oil. A 4 : 1 ratio of *Z*/*E* products was obtained. R_f 0.50 (cyclohexane/EtOAc = 18 : 1). – $[\alpha]_D^{20}$ = –10.0 (1.36 g/100 mL, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (d, *J* = 6.4 Hz, 3 H, $PhCH{=}CHC{=}CHCHCH_3$), 1.00 (d, *J* = 7.2 Hz, 3 H, $EtCO_2C{=}CHCHCH_3$), 1.04 (t, *J* = 7.2 Hz, 3 H, $EtCO_2CCH_2CH_3$), 1.21 (t, *J* = 6.8 Hz, 3 H, $CO_2CH_2CH_3$), 1.29–1.36 (m, 2 H, $CHCH_2CH$), 1.79 (s, 3 H, $PhCH{=}CHCCH_3$), 2.22–2.33 (m, 2 H, $EtCO_2CCH_2CH_3$), 2.43–2.59 (m, 1 H, $PHCH{=}CHC{=}CHCH$), 2.98–3.01 (m, 1 H, $EtCO_2C{=}CHCH$), 4.01–4.15 (m, 2 H, $CO_2CH_2CH_3$), 5.34 (d, *J* = 9.6 Hz, 1 H, $PhCH{=}CHC{=}CH$), 5.58 (d, *J* = 9.6 Hz, 1 H, $EtCO_2C{=}CH$), 6.41 (d, *J* = 16.0 Hz, 1 H, PhC*H*), 6.77 (d, *J* = 16.0 Hz, 1 H, $PhCH{=}CH$), 7.17–7.21 (m, 1 H, H_{arom}.), 7.28–7.32 (m, 2 H, H_{arom}.), 7.38–7.40 (m, 2 H, H_{arom}.). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.6 (p), 13.9 (p), 14.3 (p), 21.1 (p), 21.5 (p), 27.8 (s), 31.3 (t), 32.0 (t), 45.8 (s), 60.2 (s), 125.7 (t), 126.2 (t), 126.9 (t), 128.6 (t), 132.6 (q), 132.9 (q), 134.3 (t), 138.2 (q), 140.5 (t), 145.9 (t), 168.3 (q). – IR (film): $\tilde{\nu}$ = 3027, 2961, 2868, 1727, 1599, 1493, 1450, 1381, 1211, 1180, 1030, 1029, 704 cm^{-1}. – MS (EI, 70 eV) *m*/*z* (%): 340 (6) [M$^+$], 267 (14), 171 (8), 91 (6), 43 (100). – HRMS ($C_{23}H_{32}O_2$): calc. 340.2402, found 340.2400.

Compound 15a

A solution of linear ester **14a** (100 mg, 294 μmol) in toluene (30 mL) was heated to reflux and stirred in a sealed vial for 20 h. The mixture was concentrated. The crude product was purified by column chromatography on silica using *n*-pentane–Et_2O 40 : 1 to yield cyclic ester **15a** (85.0 mg, 85%) as colourless oil. R_f 0.40 (cyclohexane/EtOAc = 18 : 1). – $[\alpha]_D^{20}$ = +173.5 (0.34 g/100 mL, $CHCl_3$). – (NMR assignment according to numbering system of plakotenin, see ESI†) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.78 (t, *J* = 7.2 Hz, 3 H, 17-H), 0.94 (d, *J* = 6.4 Hz, 3 H, 14-H), 1.00–1.06 (m, 1 H, 11-H), 1.14 (d, *J* = 6.0 Hz, 3 H, 13-H), 1.19–1.24 (m, 1 H, 11-H), 1.31 (t, *J* = 7.5 Hz, 3 H, 17-H), 1.52–1.62 (m, 3 H, 3-H and 5-H), 1.80 (bs, 3 H, 15-H), 1.83–1.92 (m, 2 H, 4-H and 7-H), 2.43–2.51 (m, 1 H, 6-H), 4.12 (bs, 1 H, 10-H), 4.22 (ddq, *J* = 24, 9.6, 7.2 Hz, 2 H, 16-H), 5.28 (s, 1 H, 9-H), 7.22–7.25 (m, 1 H, H_{arom}.), 7.26–7.30 (m, 4 H, H_{arom}.). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.4 (p), 14.6 (p), 21.6 (p), 22.3 (p), 24.1 (p), 26.8 (s), 31.2 (t), 35.4 (t), 45.0 (s), 48.0 (t), 53.1 (t), 53.6 (t), 54.6 (q), 60.2 (s), 126.2 (t), 126.6 (t), 127.9 (t), 130.8 (t), 136.2 (q), 141.9 (q), 175.7 (q).

Compound 16a

To a solution of ester **15a** (85.0 mg, 250 μmol) in THF (3 mL) at 0 °C was slowly added lithium aluminium hydride (9.70 mg, 255 μmol). After stirring at 0 °C to rt overnight the mixture was quenched carefully at 0 °C with H_2O followed by Rochelle's salt solution. The aqueous layer was extracted with EtOAc (4 × 5 mL), the combined organic extracts were dried ($MgSO_4$) and

concentrated. The crude product was purified by column chromatography on silica using *n*-pentane–Et_2O 9 : 1 to yield alcohol **16a** (71.0 mg, 95%) as colourless oil. R_f 0.38 (cyclohexane/EtOAc = 6 : 1). – $[\alpha]_D^{20}$ = +184.6 (0.28 g/100 mL, $CHCl_3$). – (NMR assignment according to numbering system of plakotenin, see ESI†) ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.82 (t, J = 7.2 Hz, 3 H, 12-H), 0.93 (d, J = 6.6 Hz, 3 H, 14-H), 1.04 (sext, J = 7.2 Hz, 1 H, 11-H), 1.20 (d, J = 5.4 Hz, 3 H, 13-H), 1.28 (bs, 1 H, OH), 1.35 (sext, J = 7.2 Hz, 1 H, 11-H), 1.50–1.54 (m, 1 H, 5-H), 1.57–1.62 (m, 1 H, 5-H), 1.71 (t, J = 10.8 Hz, 1 H, 3-H), 1.83 (s, 3 H, 15-H), 1.86–1.90 (m, 2 H, 4-H and 7-H), 2.17–2.23 (m, 1 H, 6-H), 4.12 (d, J = 4.2 Hz, 1 H, 10-H), 3.60 (d, J = 11.4 Hz, 1 H, 1-H), 3.84 (d, J = 10.8 Hz, 1 H, 1-H), 5.19 (d, J = 3.6 Hz, 1 H, 9-H), 7.20–7.23 (m, 1 H, $H_{arom.}$), 7.25–7.29 (m, 4 H, $H_{arom.}$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.8 (p), 21.6 (p), 22.5 (p), 24.0 (p), 25.7 (s), 31.4 (t), 35.2 (t), 43.4 (q), 45.3 (s), 49.8 (t), 51.7 (t), 54.3 (t), 65.2 (s), 126.1 (t), 126.3 (t), 127.7 (t), 130.7 (t), 136.5 (q), 141.3 (q).

Compound 16b

To a solution of ester **15b** (85.0 mg, 250 µmol) in THF (3 mL) at 0 °C was slowly added lithium aluminium hydride (9.70 mg, 255 µmol). After stirring at 0 °C to rt overnight the mixture was quenched carefully at 0 °C with H_2O followed by Rochelle's salt solution. The aqueous layer was extracted with EtOAc (4 × 5 mL), dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography on silica using n-pentane–Et_2O 9 : 1 to yield alcohol **16b** (71.0 mg, 95%) as colourless oil. R_f 0.38 (cyclohexane/EtOAc = 6 : 1). – $[\alpha]_D^{20}$ = +160.3 (0.72 g/100 mL, $CHCl_3$). – (NMR assignment according to numbering system of plakotenin, see ESI†) ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.91 (d, J = 6.6 Hz, 3 H, 14-H), 1.03 (t, J = 7.2 Hz, 3 H, 12-H), 1.19 (d, J = 5.4 Hz, 3 H, 13-H), 1.55 (t, J = 8.4 Hz, 1 H, 5-H), 1.55–1.60 (m, 1 H, 11-H), 1.61 (sext, J = 7.2 Hz, 1 H, 11-H), 1.61 (t, J = 10.8 Hz, 1 H, 3-H), 1.82–1.87 (m, 4 H, 7-H and 15-H), 1.88–1.92 (m, 1 H, 4-H), 1.96–2.02 (m, 1 H, 6-H), 3.23 (d, J = 8.4 Hz, 1 H, 1-H), 3.33 (d, J = 2.4 Hz, 1 H, 10-H), 3.39 (d, J = 11.4 Hz, 1 H, 1-H), 5.15 (s, 1 H, 9-H), 7.22–7.25 (m, 1 H, $H_{arom.}$), 7.30–7.31 (m, 4 H, $H_{arom.}$). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 8.8 (p), 22.0 (p), 22.5 (p), 22.6 (p), 24.4 (s), 31.1 (t), 34.8 (t), 43.2 (q), 45.2 (s), 50.5 (t), 51.0 (t), 52.1 (t), 66.2 (s), 125.0 (t), 126.7 (t), 128.3 (t), 130.2 (t), 136.9 (q), 142.5 (q), 175.7 (q). – IR (film): $\tilde{\nu}$ = 3471, 3059, 3024, 2930, 2880, 1598, 1490, 1452, 1376, 1032, 702 cm^{-1}. – MS (EI, 70 eV) *m/z* (%): 298 (26) [M$^+$], 267 (51), 225 (25), 171 (100), 91 (15).

(2*Z*,4*R*,6*R*,7*E*,9*E*)-2-Ethyl-4,6,8-trimethyl-10-phenyldeca-2,7,9-trien-1-ol (17)

To a solution of ester **14a** (325 mg, 954 µmol) in THF (10 mL) at 0 °C was slowly added lithium aluminium hydride (37.0 mg, 974 µmol). After stirring at 0 °C for 2 h the reaction mixture was quenched carefully at 0 °C with H_2O followed by Rochelle's salt solution. The aqueous layer was extracted with Et_2O (4 × 10 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. The crude product was then purified by column chromatography on silica using n-pentane–Et_2O 9 : 1 to yield alcohol **17** (175 mg, 61%). R_f 0.52 (cyclohexane/EtOAc = 6 : 1). – $[\alpha]_D^{20}$ = –102.6 (0.61 g/100 mL, $CHCl_3$). – ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.94 (d, J = 6.5 Hz, 3 H, $HOCH_2C$=CHCHCH_3), 0.97 (d, J = 6.5 Hz, 3 H, PhCH=CHC=CHCHCH_3), 1.05 (t, J = 7.5 Hz, 3 H, $HOCH_2CCH_2CH_3$), 1.14 (bs, 1 H, OH), 1.27–1.38 (m, 2 H, $CHCH_2CH$), 1.80 (s, 3 H, PhCH=CHCCH_3), 2.14 (q, J = 7.5 Hz, 2 H, $HOCH_2CCH_2CH_3$), 2.41–2.56 (m, 2 H, $CHCH_2CH$), 4.02 (s, 2 H, $HOCH_2$), 5.05 (d, J = 10.0 Hz, 1 H, $HOCH_2C$=C*H*), 5.41 (d, J = 9.5 Hz, 1 H, PhCH=CHC=C*H*), 6.44 (d, J = 16.0 Hz, 1 H, PhC*H*), 6.79 (d, J = 16.0 Hz, 1 H, PhCH=C*H*), 7.19 (t, J = 7.5 Hz, 1 H, $H_{arom.}$), 7.29–7.32 (m, 2 H, $H_{arom.}$), 7.40 (d, J = 7.5 Hz, 2 H, $H_{arom.}$). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.7 (p), 13.2 (p), 21.7 (p), 22.7 (p), 28.0 (s), 30.5 (t), 31.2 (t), 46.0 (s), 60.7 (s), 126.2 (t), 126.3 (t), 127.1 (t), 128.7 (t), 133.0 (q), 133.7 (t), 133.9 (t), 138.0 (q), 139.3 (q), 140.8 (t). – IR (film): $\tilde{\nu}$ = 3343, 3027, 2959, 2923, 1598, 1493, 1450, 1385, 1016, 958, 747, 692 cm^{-1}. – MS (EI, 70 eV) *m/z* (%): 298 (67) [M$^+$], 171 (100), 153 (69), 107 (60). – HRMS ($C_{21}H_{30}O$): calc. 298.2297, found 298.2296.

(2*E*,4*Z*,6*R*,8*R*,9*E*,11*E*)-Ethyl 4-ethyl-2,6,8,10-tetramethyl-12-phenyldodeca-2,4,9,11-tetraenoate (18)

Dess–Martin periodinane (1.41 mL, 653 µmol) was added at 0 °C to a solution of alcohol **17** (150 mg, 503 µmol) in CH_2Cl_2 (10 mL). After stirring for 2 h at rt, the reaction mixture was quenched by adding saturated aqueous $Na_2S_2O_3$ (5 mL) and saturated aqueous $NaHCO_3$ (5 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (4 × 10 mL). The organic layer was dried ($MgSO_4$) and concentrated to yield the crude aldehyde (150 mg, 503 µmol, assumed to be quantitative) as colourless oil, which was used without further purification for the following olefination reaction.

To a solution of sodium hydride (60% in mineral oil, 66.0 mg, 1.66 mmol) in THF (10 mL) at 0 °C was added dropwise ethyl 2-(diethoxyphosphoryl)propanoate (350 µL, 1.61 mmol). The solution was stirred at rt for 1 h before cooling to 0 °C and addition of crude aldehyde (150 mg, 503 µmol, from previous reaction) in THF (5 mL). The solution was warmed slowly to rt and after stirring overnight the reaction was quenched by pouring on to saturated aqueous NH_4Cl (10 mL). The product was extracted with Et_2O and the combined extracts were dried ($MgSO_4$) and concentrated. The crude product was then purified by column chromatography on silica using *n*-pentane–Et_2O 40 : 1 to yield ester **18** (169 mg, 88%) as colourless oil. R_f 0.44 (cyclohexane/EtOAc = 18 : 1). – $[\alpha]_D^{20}$ = +17.3 (0.84 g/100 mL, $CHCl_3$). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (d, J = 6.4 Hz, 3 H, PhCH=CHC=CHCHCH_3), 0.93 (d, J = 6.8 Hz, 3 H, $EtCO_2C$=CHC=CHCHCH_3), 0.99 (t, J = 7.6 Hz, 3 H, $EtCO_2C$=CHCCH_2CH_3), 1.13 (t, J = 7.2 Hz, 3 H, $CO_2CH_2CH_3$), 1.30–1.34 (m, 2 H, $CHCH_2CH$), 1.80 (s, 3 H, $EtCO_2CCH_3$), 1.83 (s, 3 H, PhCH=CHCCH_3), 2.13 (q, J = 7.6 Hz, 2 H, $EtCO_2C$=CHCCH_2CH_3), 2.17–2.23 (m, 1 H, $EtCO_2C$=CHC=CHC*H*), 2.44–2.55 (m, 1 H, PhCH=CHC=CHC*H*), 3.94–4.08 (m, 2 H, $CO_2CH_2CH_3$), 5.12 (d, J = 10.0 Hz, 1 H, $EtCO_2C$=CHC=C*H*), 5.35 (d, J = 9.6 Hz, 1 H, PhCH=CHC=C*H*), 6.41 (d, J = 16.0 Hz, 1 H, PhC*H*), 6.76 (d, J = 16.0 Hz, 1 H, PhCH=C*H*), 7.05 (s, 1 H, $EtCO_2C$=C*H*), 7.15 (t, J = 7.2 Hz, 1 H, $H_{arom.}$) 7.28 (d, J = 8.0 Hz, 2 H, $H_{arom.}$), 7.39 (d, J = 7.2 Hz, 2 H, $H_{arom.}$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.7 (p), 13.4 (p), 14.3 (p), 14.4 (p), 21.1 (p), 21.5 (p), 30.0 (s), 30.9 (t), 31.9 (t), 45.9 (s), 60.7 (s), 125.6 (t), 126.2 (t), 126.9 (t), 128.5 (q), 128.6 (t), 132.6 (q), 134.3 (t), 134.9 (t), 136.3 (q), 138.2

(q), 139.1 (t), 141.0 (t), 168.4 (q). – IR (film): $\tilde{\nu}$ = 3027, 2962, 2926, 2869, 1711, 1631, 1598, 1493, 1450, 1368, 1254, 1115, 1034, 959, 747, 692 cm^{-1}. – MS (EI, 70 eV) *m/z* (%): 380 (4) [M$^+$], 225 (4), 171 (4), 91 (3), 43 (100). – HRMS ($C_{26}H_{36}O_2$): calc. 380.2715, found 380.2717.

Plakotenin ethyl ester (19)

A solution of linear ester **18** (85.0 mg, 223 µmol) in toluene (20 mL) was heated to reflux and stirred in a sealed vial for 20 h. The mixture was concentrated. The crude product was purified by column chromatography on silica using *n*-pentane–Et_2O 40 : 1 to yield plakotenin ethyl ester **19** (77.0 mg, 91%) as colourless oil. R_f 0.42 (cyclohexane/EtOAc = 18 : 1). – $[\alpha]_D^{20}$ = +203.8 (1.46 g/100 mL, $CHCl_3$). – (NMR assignment according to numbering system of plakotenin, see ESI†) ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.77 (t, *J* = 7.2 Hz, 3 H, 18-H), 0.98 (d, *J* = 6.0 Hz, 3 H, 15-H), 1.00–1.10 (m, 1 H, 17-H), 1.15 (d, *J* = 6.0 Hz, 3 H, 14-H), 1.32 (t, *J* = 7.5 Hz, 3 H, 20-H), 1.54 (t, *J* = 8.2 Hz, 2 H, 7-H), 1.72–1.78 (m, 3 H, 5-H, 9-H and 17-H), 1.82 (s, 3 H, 16-H), 1.85–1.92 (m, 2 H, 6-H and 8-H), 2.05 (s, 3 H, 13-H), 3.69 (d, *J* = 4.0 Hz, 1 H, 12-H), 4.22 (q, *J* = 7.2 Hz, 2 H, 19-H), 5.23 (d, *J* = 4.0 Hz, 1 H, 11-H), 6.86 (s, 1 H, 3-H), 7.20–7.24 (m, 1 H, $H_{arom.}$), 7.28–7.31 (m, 4 H, $H_{arom.}$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.4 (p), 14.3 (p), 14.4 (p), 21.9 (p), 22.5 (p), 23.3 (p), 27.2 (s), 31.7 (t), 34.7 (t), 45.1 (s), 47.9 (q), 52.3 (t), 52.4 (t), 55.5 (t), 60.8 (s), 125.4 (t), 126.6 (t), 127.8 (t), 128.1 (q), 131.0 (t), 137.1 (q), 142.3 (q), 146.6 (t), 169.5 (q). – MS (EI, 70 eV) *m/z* (%): 380 (22) [M$^+$], 225 (16), 171 (13), 91 (12), 43 (100). – HRMS ($C_{26}H_{36}O_2$): calc. 380.2715, found 380.2714.

Plakotenin (1)

To a solution of plakotenin ethyl ester **19** (25.0 mg, 66.0 µmol) in THF–MeOH (1.6/0.8 mL) was added NaOH (2 M) (160 µL, 328 µmol) and the resulting mixture was heated to 40 °C and stirred for 20 h. After cooling to rt, the mixture was acidified with aqueous HCl (1 M) and then extracted with EtOAc. The combined organic extracts were backwashed with brine, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography on silica using *n*-pentane–Et_2O 2 : 1 to yield plakotenin **1** (20.0 mg, 86%) as colourless oil. R_f 0.40 (cyclohexane/EtOAc = 2 : 1). – $[\alpha]_D^{20}$ = +212 (0.24 g/100 mL, $CHCl_3$). – (NMR assignment according to numbering system shown in ESI†) ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.78 (t, *J* = 7.0 Hz, 3 H, 18-H), 0.98 (d, *J* = 6.5 Hz, 3 H, 15-H), 1.03–1.12 (m, 1 H, 17-H), 1.16 (d, *J* = 6.5 Hz, 3 H, 14-H), 1.56 (t, *J* = 8.5 Hz, 3 H, 7-H), 1.73–1.80 (m, 3 H, 5-H, 9-H and 17-H), 1.83 (s, 3 H, 16-H), 1.86–1.95 (m, 2 H, 6-H and 8-H), 2.07 (s, 3 H, 13-H), 3.71 (d, *J* = 4.0 Hz, 1 H, 12-H), 5.23 (s, 1 H, 11-H), 7.03 (s, 1 H, 3-H), 7.21–7.25 (m, 1 H, $H_{arom.}$), 7.29–7.30 (m, 4 H, $H_{arom.}$). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 9.4 (p), 14.0 (p), 21.9 (p), 22.5 (p), 23.3 (p), 27.1 (s), 31.7 (t), 34.7 (t), 45.1 (s), 48.2 (q), 52.2 (t), 52.5 (t), 55.4 (t), 125.3 (t), 126.6 (t), 127.3 (q), 127.9 (t), 131.0 (t), 137.2 (q), 142.1 (q), 149.7 (t), 174.8 (q). – IR (film): $\tilde{\nu}$ = 2929, 2868, 1683, 1629, 1492, 1451, 1419, 1377, 1281, 877, 762, 745, 703 cm^{-1}. – MS (EI, 70 eV) *m/z* (%): 352 (100) [M$^+$], 261 (48), 225 (84), 171 (70). – HRMS ($C_{24}H_{32}O_2$): calc. 352.2402, found 352.2401.

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