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Synthesis of methyl epijasmonate and *cis*-3-(2-oxopropyl)-2-(pent-2*Z*-enyl)-cyclopentan-1-one

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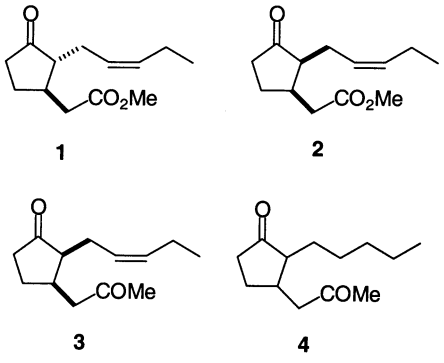
Abstract—A novel and efficient synthesis of both (±)-methyl epijasmonate and (±)-*cis*-3-(2-oxopropyl)-2-(pent-2*Z*-enyl)-cyclopentan-1-one is described. The key step to establish the *cis*-stereochemistry on the 5-membered ring is an ionic Diels–Alder reaction, which is high yielding and highly regioselective. Subsequent key steps include oxidative cleavage of the six-membered ring, Wittig coupling and for the synthesis of epijasmonate, the haloform reaction.

1. Introduction

The methyl jasmonates[1] (**1** and **2**) are key natural products occurring in *Jasminium grandiflorum* L. and the blossoms of many flowers, and are used widely in the formulation of many perfumes. Not only does (±)-methyl epijasmonate **2** possess superior olfactory properties compared to (±)-methyl jasmonate[2] **1**, but the *epi*-isomers have been shown to have greater biological activity for example, in tuber induction.[3] Other key biological roles include the induction of gene expression,[4] mediation in plant defence mechanisms[5,6] and signal transmission.[7] Although epijasmonate epimerises to the thermodynamically more stable *trans*-isomer **1**, its synthesis is of significant interest, since with its much greater odour characteristics it has potential for use in fragrance applications, particularly via a profragrance strategy. In addition, the numerous biological activities displayed in plants have generated a requirement for efficient, rapid routes to the *epi*-isomer alone. 3-(2-Oxopropyl)-2-(pent-2*Z*-enyl)-cyclopentan-1-one (*cis*-isomer **3** shown) is an unsaturated analogue of magnolia ketone **4**, and this group of compounds have also been reported to possess fragrant properties.[8,9] However, the synthesis of compounds possessing the *cis*-stereochemistry on the 5-membered ring has not been reported to date. Herein we report an efficient route to both (±)-methyl epijasmonate (**2**) and (±)-*cis*-3-(2-oxopropyl)-2-(pent-2*Z*-enyl)-cyclopentan-1-one (**3**) using a high yielding, regioselective Diels–Alder strategy and the low cost diene isoprene.



1 **2** **3** **4**

2. Results and discussion

Previous routes have been reported to the jasmonates, using cyclopentenone and a Diels–Alder strategy to establish the *cis*-stereochemistry on the 5-membered ring, notably Torii's synthesis[10] of methyl epijasmonate using butadiene and a hemiacetal strategy, and a patent describing the synthesis of methyl jasmonates using 2-alkoxybutadiene.[11] The key cycloaddition steps were not high yielding because isomers were generated.[10,12–14] In particular, a report has highlighted the difficulties of such a Diels–Alder strategy with butadienes where the cycloaddition reaction proceeds to give a mixture of cycloadducts including double bond shifted isomerised products.[12] Alternative synthetic approaches reported to epijasmonate include Knochels' free radical approach to establish the *cis*-stereochemistry[15] and Montforts'[16] and Bestmann's[17] enantioselective syntheses using enantiomerically pure starting materials. Bestmann also used a Diels–Alder strategy with 2-alkoxybutadiene but required several synthetic manipulations to remove the chiral directing group. We wished to develop a general route

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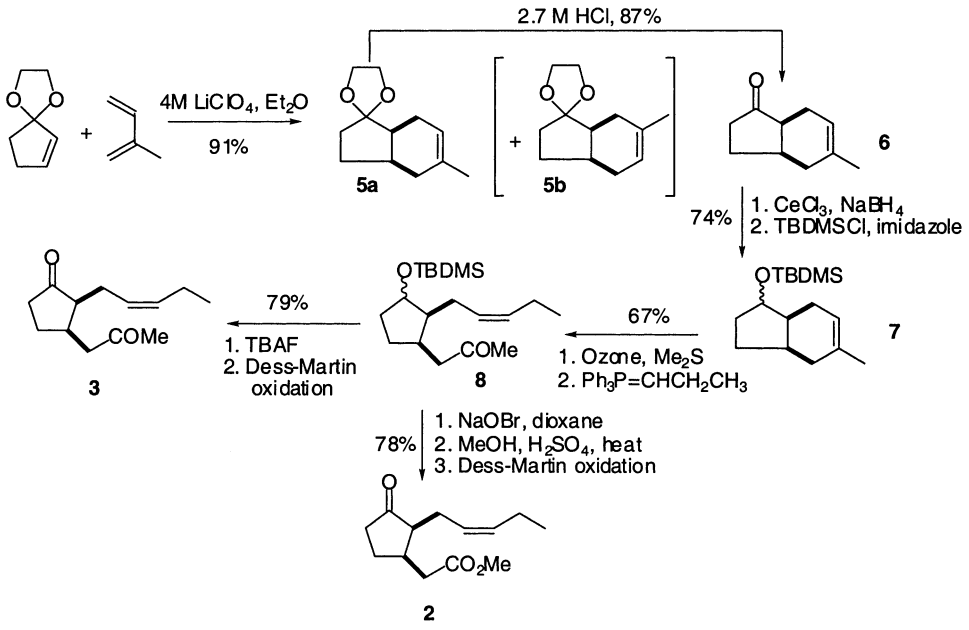

Scheme 1.

for the construction of *cis*-substituted cyclopentanones, avoiding the problems outlined earlier, but using readily available, low cost starting materials.

The synthetic route explored is outlined in Scheme 1. The use of isoprene as a diene was ideal due to its low cost, and compared to 2-alkoxybutadienes is less prone to polymerisation under Lewis acid conditions. It also enabled direct access to **3**, and via a haloform reaction methyl epijasmonate (**2**) could also be generated. Whilst the direct reaction between cyclopentenone and isoprene was considered it is well known to give, even under Lewis acid conditions, regioisomeric products.[14] However, Grieco has shown that Diels–Alder reactions can be carried out in high yield and regioselectivity by using the ethylene ketals of masked cyclohexenones as dieneophiles, in 4.0–5.0 M solutions of lithium perchlorate in diethyl ether, with 1 mol% of camphorsulfonic acid at ambient temperature.[18] We explored assembly of the bicyclic ring system using this method with the ethylene ketal of 2-cyclopenten-1-one.[19] The ionic Diels–Alder reaction using isoprene and lithium perchlorate in diethyl ether readily proceeded giving the adducts **5a** and **5b** in excellent yields (91%), and the isomer **5a** in greater than 95% regioselectivity (by ^{1}H NMR spectroscopy). The regioisomeric products were separated by column chromatography to give **5a** in an 85% isolated yield. We noted that this reaction has also been reported in lower yields by Vankar et al., who has performed the reaction with lithium perchlorate in nitromethane (73% yield),[20] Nafion-H as an acid catalyst (68% yield),[20] and also using indium trichloride (64% yield).[21]

The direct ozonolysis of **5** resulted in the formation of several components and was thought to be a result of the ketal breaking down during the ozonolysis. It was therefore decided to deprotect the ketal and convert the ketone into a protected alcohol to ensure that no epimerization would take place during the remaining synthetic steps. Initial attempts to deprotect the ketal using dilute sulfuric acid at 50°C for 2 h led to migration of the double bond and the formation of a mixture of inseparable isomers. However, the use of dilute hydrochloric acid (2.7 M) at room temperature overcame the bond isomerization problem and the desired ketone **6** was isolated in 87% yield. The ketone was then reduced using several standard reducing agents. The preferred method was using cerium(III) chloride heptahydrate[22] with sodium borohydride to generate two inseparable diastereoisomeric alcohols in 91% yield (and in a ratio of 10:1 by ^{1}H NMR spectroscopy). The material was carried through as a mixture since both would provide the required *epi*-isomer after a late stage oxidation.

The alcohols were protected with *t*-butyldimethylsilyl chloride (in 81% yield) and the silyl ether **7** was then subjected to ozone treatment followed by a reductive work-up of the ozonide with dimethyl sulfide to afford the methyl ketone intermediate. The use of non-stabilised ylids under 'salt-free' conditions are known to give rise to predominately *Z*-alkenes and therefore the unstabilised ylid was generated in situ by the treatment of *n*-propyltriphenylphosphonium bromide with sodium hexamethyldisilazide in tetrahydrofuran.[23] To the resulting supernatant ylid solution was added freshly prepared aldehyde to generate **8** in 67% yield over two steps.

The methyl ketone **8** was then successfully converted to the corresponding acid by the haloform reaction with sodium hypobromite in a dioxane/water mixture. This also brought about the deprotection of the silyl protecting group to give the acid in 89% yield. The acid was methylated to afford the methyl cucurbate diastereoisomers in 92% yield. The cucurbate was oxidised, under mild conditions utilising freshly prepared Dess–Martin periodinane,[24] to readily generate methyl epijasmonate (**2**) (in 95% yield) with its characteristic strong sweet jasmine odour.

Alternatively, the deprotection of **8** with TBAF, and oxidation of the resulting alcohol with Dess–Martin periodinane gave

3, in 79% yield over the two steps, possessing a sweet floral odour.

In summary, we have investigated the use of the ionic Diels–Alder reaction to establish the *cis*-stereochemistry on the 5-membered rings of two important fragrance compounds, (±)-methyl epijasmonate (**2**) and (±)-*cis*-3-(2-oxopropyl)-2-(pent-2*Z*-enyl)-cyclopentan-1-one (**3**) in overall yields of 29%.

3. Experimental

3.1. General

Unless otherwise indicated, reagents were obtained from commercial suppliers and were used without further purification. THF was freshly distilled from sodium/benzophenone. Toluene was freshly distilled from sodium. Triethylamine was distilled from and stored over potassium hydroxide. Methanol was distilled from magnesium turnings and stored over 3 Å molecular sieves. 'Ethanol' refers to absolute ethanol (>99.7%) and was used as received. Flash column chromatography[25] was carried out using silica gel (particle size 40–63 μm) purchased from BDH.

^{1}H NMR spectra were recorded at 400 MHz on a Varian VXR-400 instrument or at 200 MHz, on a Varian XL-200 instrument. ^{13}C NMR spectra were recorded at 100.6 MHz on a Varian VXR-400 instrument. Residual protic solvent was taken as internal standard, with $CDCl_3$ as solvent unless otherwise stated, stored over 4 Å molecular sieves and filtered through basic alumina prior to use. Coupling constant (*J*) values are given in Hz.

Mass spectra were taken on an Autospec Q, VG 7070, or VG 7070B instrument with sources for EI. Infra red spectra were recorded on a Perkin–Elmer FT-IR 1605 spectrometer. CHN analyses were carried out on a Perkin–Elmer 2400 CHN Elemental Analyzer. Melting points were taken on a Reichert hot stage instrument and are uncorrected.

1,4-Dioxaspiro[4.4]non-6-ene (2-cyclopenten-1-one ethylene ketal) was prepared as previously reported.[19] 1,1,1,-Triacetoxy-1,1-dihydro-1,2-benziodoxol-3-1*H*-one was prepared as previously reported.[24]

3.1.1. 2,3,3a,4,7,7a-Hexahydro-5-methyl-ind-5-en-1-one ethylene ketal (5a).[20] To a solution of 2-cyclopenten-1-one ethylene ketal (1.26 g, 10 mmol) in lithium perchlorate-diethyl ether (4.0 M, 40 ml, 160 mmol) was added isoprene (4.0 ml, 40 mmol) and camphorsulfonic acid in tetrahydrofuran (0.5 M, 46 μl, 1 mol%). After stirring for 40 min, triethylamine (25 μl, 0.18 mmol) was added. The mixture was diluted with water (20 ml) and extracted with diethyl ether (4×30 ml). The organic layer was dried ($MgSO_4$) and concentrated in vacuo to give **5a** and **5b** in a 91% combined yield and **5a** in greater than 95% regioselectivity by ^{1}H NMR (a trace of **5b** was detectable by ^{1}H NMR spectroscopy). The oil containing the regioisomers **5a** and **5b** was purified by flash column chromatography (petroleum ether 40–60°C/ethyl acetate, 25:1) to yield the title compound **5a** as a colourless oil (1.65 g, 85%). ν_{max}(film)/cm^{-1} 2879s, 2827s and 1684s; δ_H (400 MHz; $CDCl_3$) 1.42–1.51 (1H, m), 1.63 (3H, s, CH_3), 1.68–2.05 (7H, m), 2.07–2.16 (1H, m), 2.28–2.36 (1H, m), 3.81–3.95 (4H, m, 2×CH_2O) and 5.33–5.40 (1H, m, C=C*H*); δ_C (100 MHz; $CDCl_3$) 22.5, 24.1, 27.3, 32.1, 34.2, 34.8, 41.7, 64.1 and 65.1 (2×CH_2O), 118.9 (C=*C*H), 119.4 (O–C–O) and 132.1 (*C*=CH); *m/z* (EI) 194.1314 (M^+, 2%. $C_{12}H_{18}O_2$ requires 194.1307), 150 (M−OCH_2CH_2, 25), 135 (15), 105 (100).

3.1.2. *cis*-5-Methyl-2,3,3a,4,7,7a-hexahydro-inden-1-one (6).[14] To a solution of the ketal **5a** (194 mg, 1.0 mmol) in methanol (5 ml) at 0°C was added slowly (over 5 min) a solution of hydrochloric acid (2.7 M, 310 μl). After 2 h the reaction was poured into saturated sodium hydrogen carbonate solution (10 ml) and extracted with petroleum spirits 30–40°C (3×20 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated. The crude oil was purified by flash column chromatography (petroleum ether 40–60°C/diethyl ether, 15:1) yielding the title ketone as a colourless oil (130 mg, 87%). ν_{max}(film)/cm^{-1} 2924s, 1739s and 1684w; δ_H (400 MHz; $CDCl_3$) 1.62 (3H, s, CH_3), 1.75–1.85 (1H, m), 1.97–2.10 (2H, m), 2.12–2.42 (6H, m), 2.47–2.55 (1H, m, C*H*CO) and 5.31 (1H, br s, C=C*H*); δ_C (100 MHz; $CDCl_3$) 21.7, 23.9, 26.6, 30.8, 32.8, 34.2, 46.5, 118.7 (C=*C*H), 132.2 (*C*=CH) and 219.7 (C=O); *m/z* (EI) 150.1041 (M^+, 30%. $C_{10}H_{14}O$ requires 150.1045) and 135 (M−CH_3, 25).

3.1.3. [(*cis*-5-Methyl-2,3,3a,4,7,7a-hexahydro-1*H*-1-inden-1-yl)oxy]-*tert*-butyldimethylsilane (7). To a solution of **6** (1.75 g, 11.7 mmol) in methanol (100 ml) was added cerium(III) chloride heptahydrate (4.47 g, 12.0 mmol). The reaction mixture was cooled to 0°C and sodium borohydride (460 mg, 12.0 mmol) was added. The reaction was stirred for 1 h and then diluted with brine (20 ml). The mixture was concentrated in vacuo then diluted with diethyl ether (50 ml) and, after separation of the layers, the aqueous phase was extracted with diethyl ether (5×30 ml). The organic layer was dried ($MgSO_4$) and concentrated. The crude alcohol was purified by column chromatography (eluent: petroleum spirits 40–60°C/ethyl acetate, 10:1) yielding the *cis*-ring fused diastereoisomeric alcohols *5-methyl-2,3,3a,4,7,7a-hexahydro-1H-inden-1-ol* as a colourless viscous oil (1.61 g, 91% yield). ν_{max}(film)/cm^{-1} 3324s, 2955s, 2940s, 2883s and 1638m; major diastereoisomer δ_H (400 MHz; $CDCl_3$) 1.54–1.64 (2H, m), 1.66 (3H, s, CH_3), 1.70–1.90 (3H, m), 1.93–2.16 (6H, m), 4.25 (1H, ddd, *J*=7.9, 5.2 and 5.2 Hz, C*H*OH) and 5.46 (1H, br s, C=CH); δ_C (100 MHz; $CDCl_3$) 21.6, 23.9, 28.9, 31.9, 32.7, 34.7, 39.9, 76.5 (C–OH), 119.6 (C=*C*H) and 133.5 (*C*=CH); *m/z* (EI) 152.1203 (M^+, 15%. $C_{10}H_{16}O$ requires 152.1201), 136 (M−CH_3, 17) and 84 (100).

A solution of the diastereoisomeric alcohols (1.80 g, 11.8 mmol), imidazole (1.21 g, 17.8 mmol) and *t*-butyldimethylsilyl chloride (2.68 g, 17.8 mmol) in dichloromethane (25 ml) was stirred at rt for 18 h. The reaction mixture was diluted with dichloromethane (30 ml) and water (30 ml), the organic layer extracted with dichloromethane (3×30 ml), dried ($MgSO_4$) and concentrated in vacuo. The crude silyl ether was purified by column

chromatography (eluent: petroleum spirits 30–40°C/diethyl ether, 20:1) yielding the *cis*-ring fused *title compound* **7**, a colourless oil, as a mixture of inseparable diastereoisomers (2.55 g, 81%). ν_{max}(film)/cm^{-1} 2961s, 2956s and 1638w; major diastereoisomer δ_H (400 MHz; $CDCl_3$) 0.03 (6H, s, 2×Si–Me), 0.87 (9H, s, ^{t}Bu), 1.56–1.63 (2H, m), 1.65 (3H, s, C=CCH_3), 1.80–2.10 (8H, m), 4.23 (1H, ddd, J=6.4, 5.6 and 5.6 Hz, CHOSi) and 5.41 (1H, s, C=CH); δ_C (100 MHz; $CDCl_3$) −4.9 (Si–Me), −4.7 (Si–Me), 18.1 (C(CH$_3$)$_3$), 21.5, 23.9, 25.8 (C(CH$_3$)$_3$), 28.1, 32.0, 32.8, 34.7, 40.1, 76.5 (COSi), 119.3 (C=CH) and 131.9 (C=CH); m/z (EI) 266 (M$^+$, 5%), 209 (M−C(CH$_3$)$_3$, 40), 133 (50) and 75 (100).

3.1.4. 1-[3-(*tert*-Butyldimethylsilyl)oxy-2-pent-2*Z*-enyl-cyclopentyl]-propan-2-one (8). Molecular oxygen was bubbled though a stirred solution of the silylether (1.00 g, 3.70 mmol) in dichloromethane (20 ml) at −78°C. After 5 min ozone was bubbled through the reaction mixture until a faint blue colouration persisted (ca. 30 min). Nitrogen was then bubbled through the mixture for 30 min, dimethyl sulfide (2 ml, 21.1 mmol) was added at −78°C and the mixture stirred for 3 h, gradually increasing the temperature to rt. The mixture was concentrated in vacuo and the crude viscous oil of *[2-(*tert*-butyldimethylsilyl)oxy-5-(2-oxopropyl)-cyclopentyl]acetaldehyde* was used without further purification. ν_{max}(film)/cm^{-1} 2979s, 2955s, 2890s, 1734s and 1718m; major diastereoisomer δ_H (400 MHz; $CDCl_3$) 0.03 (6H, s, 2×Si–Me), 0.88 (9H, s, C(CH_3)$_3$), 1.25–1.28 (1H, m), 1.44–1.89 (5H, m), 2.12 (3H, s, COCH_3), 2.13–2.20 (1H, m), 2.21–2.35 (1H, m), 2.48–2.65 (2H, m), 4.23–4.25 (1H, m, CHOSi) and 9.53 (1H, m, CHO).

To a solution of sodium bis(trimethylsilyl)amide (1.0 M, 2.4 ml, 2.4 mmol) in tetrahydrofuran (10 ml), was added *n*-propyltriphenylphosphonium bromide (925 mg, 2.40 mmol). The reaction mixture was cooled to −30°C and a solution of the crude aldehyde from above in tetrahydrofuran (2 ml) added dropwise. The reaction mixture was maintained at −30°C for further 2 h before it was warmed to rt. After a further 1 h of stirring the reaction mixture was diluted with methanol (1 ml) and brine (5 ml). The product was extracted with ether (3×20 ml), dried over ($MgSO_4$) and concentrated in vacuo. The crude oil was purified by column chromatography (eluent: petroleum spirits 40–60°C/ethyl acetate, 20:1) yielding the *methyl ketone* **8** (0.773 g, 67% over two steps). ν_{max}(film)/cm^{-1} 2997s, 2956s, 1714s and 1711m; major diastereoisomer δ_H (400 MHz; $CDCl_3$) −0.05 (6H, s, 2×Si–Me), 0.89 (9H, s, C(CH_3)$_3$), 0.96 (3H, t, J=6.3 Hz, CH$_2$CH_3), 1.25–1.95 (6H, m), 2.00–2.12 (4H, m), 2.10 (3H, s, COCH$_3$), 2.41–2.49 (1H, m), 2.52–2.58 (1H, m), 4.10–4.14 (1H, m, CHOSi) and 5.31–5.38 (2H, m, CH=CH); δ_C (100 MHz; $CDCl_3$) −5.1 (Si–Me), −4.6 (Si–Me), 14.2 (CH$_2$$CH_3$), 18.0 ($C$(CH$_3$)$_3$), 20.8, 23.3, 25.9 (C($CH_3$)$_3$), 29.6, 30.4, 34.1, 34.9, 46.5, 48.5, 75.3 (C–OSi), 128.3 (CH=CHCH$_2$CH$_3$), 131.9 (CHCH$_2$CH$_3$) and 209.7 (COMe); m/z (EI) 324 (M$^+$, 2%), 281 (24), 210 (25) and 147 (100).

3.1.5. Methyl 2-(2-pent-2*Z*-enyl)-3-oxo-cyclopentyl acetate (methyl epijasmonate) (2).[26–28] A stirred solution of sodium hypobromite was prepared by the addition of molecular bromine (0.50 g, 3.1 mmol) to aqueous sodium hydroxide solution (3.1 M, 4 ml). The solution was then added dropwise to **8** (193 mg, 0.596 mmol) in dioxane (3 ml), and the mixture left to stand overnight at rt. A solution of sodium sulfite (130 mg, 1.03 mmol) in water (1 ml) was added and the dioxane removed in vacuo. The crude mixture was then extracted with diethyl ether (1×30 ml). The aqueous phase was acidified with sulfuric acid (25%, 3 ml, to pH 2–3) and extracted with diethyl ether (3×30 ml). These extracts were dried ($MgSO_4$) and concentrated in vacuo. The acid was purified by column chromatography (eluent: petroleum spirits 40–60°C/ethyl acetate, 10:1) to afford 3-hydroxy-2-(pent-2*Z*-enyl-cyclopentyl)-acetic acid (epicucurbic acid) as a colourless oil (112 mg, 89%).[27,28] ν_{max}(film)/cm^{-1} 3520br s, 2956s, 1712s and 1651w; major *epi*-diastereoisomer δ_H (400 MHz; $CDCl_3$) 0.97 (3H, t, J=6.6 Hz, CH$_2$CH_3), 1.41–1.49 (1H, m), 1.60–1.68 (2H, m), 1.80–2.00 (5H, m), 2.08–2.18 (1H, m), 2.20–2.48 (4H, m), 4.14–4.22 (1H, m, 1-H), 5.32–5.38 (2H, m, CH=CH) and 8.70 (1H, br s, COOH); m/z (EI) 212.1408 (M$^+$, 4%. $C_{12}H_{20}O_3$ requires 212.1412), 210 (25) and 184 (22).

To a stirred solution of *epi*-cucurbic acid (120 mg, 0.566 mmol) in methanol (10 ml) was added sulpuric acid (14 M, 0.5 ml) and the mixture was heated at reflux for 12 h. The mixture was diluted with diethyl ether (30 ml) and brine (10 ml) added. The product was then extracted with diethyl ether (3×20 ml), dried ($MgSO_4$) and evaporated in vacuo. The crude oil was purified by column chromatography (eluent: petroleum spirits 40–60°C/ethyl acetate, 10:1), to afford methyl (3-hydroxy-2-pent-2*Z*-enylcyclopentyl)-acetate (methyl epicucurbate) as a colourless oil (118 mg, 92%).[27,28] ν_{max}(film)/cm^{-1} 3418br s, 2956s, 1732s and 1641w; major *epi*-diastereoisomer δ_H (400 MHz; $CDCl_3$) 0.98 (3H, t, J=7.2 Hz, CH$_2$CH_3), 1.42–1.46 (1H, m), 1.59–1.65 (2H, m), 1.81–1.95 (3H, m), 2.05–2.13 (3H, m), 2.21–2.30 (1H, m), 2.36–2.50 (3H, m), 3.68 (3H, s, OMe), 4.11–4.19 (1H, m, CHOH), 5.38–5.50 (2H, m, CH=CH); m/z (EI) 227.1660 (M$^+$+H, 18%. $C_{13}H_{23}O_3$ requires 227.1647), 209 (42) and 135 (100).

To a stirred solution of methyl epicucurbate (150 mg, 0.664 mmol) in dichloromethane (5 ml) was added 1,1,1,-triacetoxy-1,1-dihydro-1,2-benziodoxol-3-1*H*-one[24] (400 mg, 0.942 mmol). The reaction was stirred for 30 min, the white solid removed by filtration and the filtrate concentrated in vacuo to give a pale yellow oil. The oil was purified by chromatography (eluent: petroleum spirits 40–60°C/ethyl acetate, 10:1), to afford methyl epijasmonate (**2**) as a colourless oil (141 mg, 94%). ν_{max}(film)/cm^{-1} 2959s, 1735s, and 1642w; δ_H (400 MHz; $CDCl_3$) 0.94 (3H, t, J=7.4 Hz, CH$_2$CH_3), 1.78–1.86 (1H, m), 2.01–2.07 (2H, m, CH_2CH$_3$), 2.09–2.44 (8H, m), 2.72–2.95 (1H, m), 3.65 (3H, s, OCH_3), 5.19–5.29 (1H, m, HC=CHCH$_2$CH$_3$), 5.40–5.50 (1H, m, HC=CHCH$_2$CH$_3$); δ_C (100 MHz; $CDCl_3$) 14.0 (CH$_2$$CH_3$), 20.6 ($CH_2CH_3$), 22.8, 25.5, 33.5, 35.0 (CHCHCO), 35.7, 51.5 (O–CH$_3$), 52.2 (CHCO), 125.3 (CH=CHCH$_2$CH$_3$), 134.1 (CH=CHCH$_2$CH$_3$), 172.5 (COOMe) and 218.9 (C=O); m/z (EI) 224.1408 (M$^+$, 25%. $C_{13}H_{20}O_3$ requires 224.1412), 194 (M−OCH$_2$, 22), 151 (M−CH$_2$CO$_2$Me, 40) and 83 (100).

3.1.6. *cis*-3-(2-Oxo-propyl)-2-pent-2*Z*-enyl-cyclopentan-1-one (3). To a solution of **8** (65 mg, 0.20 mmol) in tetrahydrofuran (1 ml) was added a solution of tetra *n*-butylammonium fluoride in tetrahydrofuran (1 M, 0.4 ml). The reaction was stirred for 2 h and then diluted with diethyl ether (10 ml) and brine (2 ml). The reaction mixture was extracted with diethyl ether (3×10 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The crude material was purified by chromatography (eluent: petroleum spirits 40–60°C/diethyl ether, 8:1) to yield the deprotected diastereoisomers *cis-1-(3-hydroxy-2-pent-2Z-enyl-cyclopentyl)-propan-2-one* which were isolated as a colourless oil (35 mg, 84%). ν_{max}(film)/cm^{-1} 3612br s, 2986s, 2936s, 2896s, 1714s and 1645w; major diastereoisomer δ_H (400 MHz; $CDCl_3$) 0.98 (3H, t, J= 6.5 Hz, CH_2CH_3), 1.35–1.48 (1H, m), 1.59–1.67 (2H, m), 1.80–2.14 (8H, m), 2.21 (3H, s, COMe), 2.31–2.39 (1H, m), 2.43–2.58 (1 H, m), 4.12–4.36 (1H, m, C*H*OH) and 5.34–5.39 (2H, m, CH=CH); δ_C (100 MHz; $CDCl_3$) 14.2 (CH_2CH_3), 21.5, 23.8, 31.7, 34.3, 37.7, 38.7, 46.7, 48.5, 74.2 (*C*HOH) 127.4 (C=CH), 132.9 (C=CH), 210.2 (*C*OMe); *m/z* (EI) 209.1557 (M^+-H. $C_{13}H_{21}O_2$ requires 209.1542).

To a stirred solution of the diastereoisomeric alcohols (35 mg, 0.167 mmol) in dichloromethane (2 ml) was added 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3-1*H*-one[24] (100 mg, 0.236 mmol). The reaction was stirred for 30 min, the solid generated filtered and the filtrate concentrated in vacuo. The crude material was purified by silica chromatography (eluent: petroleum spirits 40–60°C/ethyl acetate, 10:1) to yield *cis-3-(2-oxo-propyl)-2-pent-2Z-enyl-cyclopentan-1-one* **3** as a colourless oil (33 mg, 94%). ν_{max} (film)/cm^{-1} 2984s, 1743s, 1717s and 1641w; δ_H (400 MHz; $CDCl_3$) 0.99 (3H, t, J=7.2 Hz, CH_2CH_3), 1.32–1.48 (1H, m), 1.60–1.68 (2H, m), 1.80–2.14 (7H, m), 2.21 (3H, s, COMe), 2.33–2.40 (1H, m), 2.44–2.61 (1H, m), 5.20–5.30 (1H, m, C*H*=C) and 5.40–5.50 (1H, m, C*H*=C); δ_C (100 MHz; $CDCl_3$) 14.2, 20.3, 24.8, 34.8, 37.7, 38.7, 39.7, 45.0, 46.3, 127.1, 133.9, 210.2 (*C*OMe) and 218.9 (C=O); *m/z* (EI) 208.1460 (M^+. $C_{13}H_{20}O_2$ requires 208.1463).

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