Stereoselective Synthesis of 7-Substituted Jasmonic Acid Derivatives and Investigation of their Biological Activity

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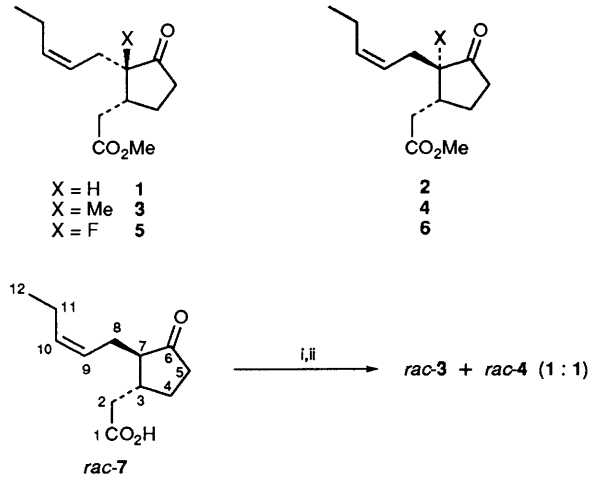
Racemic 7-substituted derivatives of methyl jasmonate have been synthesized. Methyl 7-*epi*-methyljasmonate **3** was also synthesized in enantiomerically pure form in 7 steps from the Hajos–Wichert ketone **8**. In addition the biological activity of the prepared compounds has been investigated for the induction of tendril coiling in *Bryonia dioica* and the elicitation of the phytoalexin production in *Eschscholtzia californica*. All the synthesized compounds showed poor activity in the bioassays. The specificity of the investigated species towards methyl 7-*epi*-jasmonate **1** seems to be very high.

Compounds related to jasmonic acid have recently gained attention due to their common occurrence in the plant kingdom.[1] They have biological activity as plant-growth regulators[2,3] and signal transmitters in interplant communication.[4] In addition, many other physiological effects on a variety of different plant species[5] have been reported to be induced by methyl jasmonate **2** and jasmonic acid, which led to the conclusion that they can be classified as phytohormones.[6] It has been shown that only compounds with *cis*-stereochemistry in relation to the (*Z*)-pent-2-enyl and the acetic acid moiety arise from the biochemical pathway starting off from (*Z*,*Z*,*Z*)-octadeca-9,12,15-trienoic acid (linolenic) acid.[7] Nevertheless methyl 7-*epi*-jasmonate **1** cannot be isolated in diastereoisomerically pure form due to *in vivo* and *in vitro* epimerisation to the more stable *trans*-diastereoisomer **2**. Since it has been assumed that only the resulting methyl 7-*epi*-jasmonate **1** is responsible for the physiological activity,[8] synthetic compounds which cannot epimerise at C-7 are important as objects of study for structure–activity relationships.



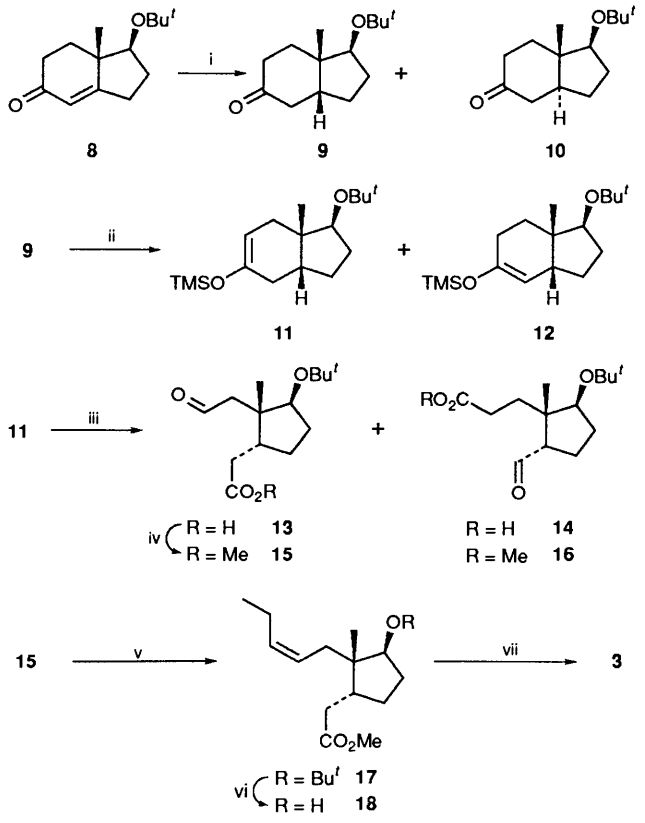
Scheme 1 *Reagents and conditions:* i, KH, MeI, THF, 0 °C; ii, CH_2N_2, TBME, 0 °C

Results and Discussion

A recent publication[9] on the synthesis of the 7-methyl epimers *rac*-**3** and *rac*-**4** prompted us to report our own results on the synthesis of these types of compounds. In our laboratories *rac*-**3** and *rac*-**4** were synthesized by potassium hydride-induced alkylation of jasmonic acid *rac*-**7** with methyl iodide and subsequent esterification with diazomethane (Scheme 1). The corresponding esters could be isolated as a 1:1 mixture of diastereoisomers in 68% yield. In order to prepare enantiomerically pure compounds with the naturally occurring (3*R*,7*S*)-configuration (jasmonic acid numbering) we started off from the readily available hydrindanone derivative **8**[10] (Scheme 2).

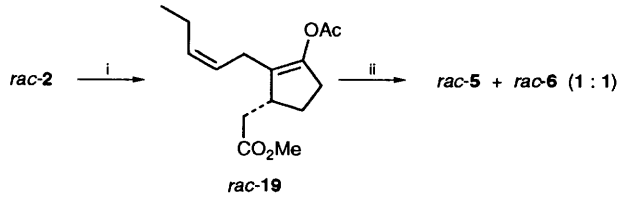
Reduction of the unsaturated ketone under modified Birch conditions[11] with lithium–ethylamine in the presence of *tert*-butyl alcohol afforded a 9:1 mixture of the diastereoisomers **9** and **10** in 86% yield from which compound **9** could be isolated in diastereoisomerically pure form by simple recrystallisation from pentane. Deprotonation with lithium diisopropylamide (LDA) at −78 °C and subsequent treatment with trimethylsilyl chloride (TMSCl) led to a 2.1:1 mixture (determined by GLC) of the corresponding silyl enol ethers **11** and **12** in 94% yield. Ozonolysis[12] of that mixture in CH_2Cl_2–MeOH (9:1) followed by reductive work-up with acetic acid and zinc dust at −78 °C led to the cleavage products **13** and **14** in quantitative yield. Esterification with diazomethane and Wittig olefination with the ylide prepared from triphenyl(propyl)phosphonium bromide and butyllithium at −30 °C yielded compound **17** in 65%. Finally, cleavage of the *tert*-butyl ether with trimethylsilyl iodide (TMSI) in CCl_4[13] and subsequent oxidation with pyridinium dichromate (PDC) gave rise to the enantiomerically pure compound **3** in 67% yield.

As the methyl group at C-7 in the synthesized compound **3** represents a drastic change in steric demand compared with naturally occurring methyl 7-*epi*-jasmonate **1**, we also investigated the α-fluorinated compounds *rac*-**5** and *rac*-**6**. This change of functionality should lead to a compound with comparable steric demand but drastically modified electronic properties. In order to evaluate this effect, a systematic conformational analysis of 7-*epi*-jasmonates **1**, **3** and **5** was performed using the empirical force field MM3. The revealing global minima were reoptimised on the semiempirical MNDO level and dipole moments as well as the electrostatic properties and the van der Waals radii were calculated. Whereas the calculated dipole moments of compounds **1** and **3** are rather similar (2.7 D and 2.6 D, respectively), compound **5** possesses a dipole moment of 3.1 D. In addition the plot of the calculated electrostatic potential of compound **5** differs strongly from the calculated plots for compounds **1** and **3** (Fig. 1). Nevertheless,



Scheme 2 *Reagents and conditions:* i, Li, $EtNH_2$, ^{t}BuOH, THF, −78 °C; ii, LDA, THF, −78 °C; then TMSCl; iii, O_3, CH_2Cl_2–MeOH (9:1); then Zn, AcOH, −78 °C; iv, CH_2N_2, TBME, 0 °C; v, Me-$[CH_2]_2{}^+$–PPh_3 Br^-, BuLi, −30 °C, inverse addition; vi, TMSI; then MeOH, CCl_4, room temp.; vii, PDC, CH_2Cl_2, room temp.

the van der Waals radii for compounds **1** and **5** are quite similar. Therefore we also decided to synthesize compounds *rac*-**5** and *rac*-**6**. Methyl jasmonate *rac*-**2** was converted into its thermodynamic enol acetate *rac*-**19** in 88% yield by treatment with acetic anhydride and catalytic amounts of *p*-TosOH at 120 °C, with removal of the acetic acid thus formed with a Hickmann–Still condenser.[14] Compound *rac*-**19** was treated with the electrophilic fluorinating reagent Selectfluor™* in acetonitrile. After 30 min reaction at room temperature, aqueous work-up and chromatographic separation, a mixture of the two resulting diastereoisomers *rac*-**5** and *rac*-**6** (ratio 1 : 1) was isolated in 84% yield (Scheme 3). The two diastereoisomers



Scheme 3 *Reagents and conditions:* i, Ac_2O, *p*-TosOH (cat.), 120 °C; ii, Selectfluor™, MeCN, room temp.

could be separated by repeated MPLC chromatography but the stereochemistry could not be assigned by NMR spectroscopy.

The biological activity of the synthesized compounds was investigated as described before[3,15] by analysing the induction

* Selectfluor™: registered trademark for *N*-fluorotriethylenediamine compounds by Air Products and Chemicals, Inc., Allenton, PA, USA. In our case the *N'*-chloromethyl bistetrafluoroboranuide derivative was used.

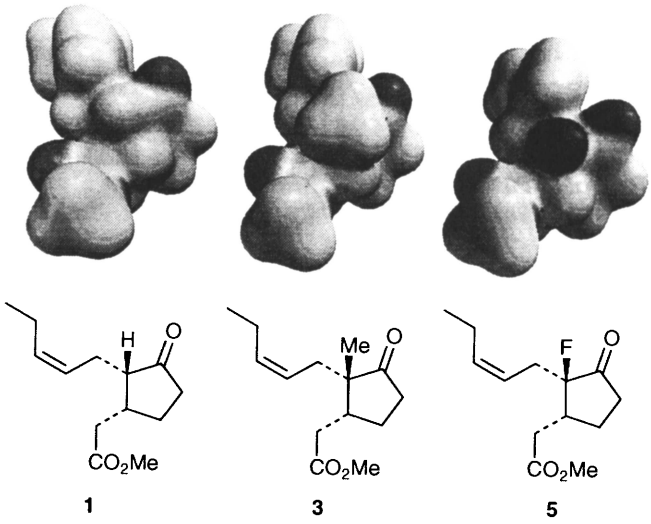


Fig. 1 Calculated electrostatic potential projected on the van der Waals radii for compounds **1**, **3** and **5**. The dark regions represent high electronic density.

of free tendril coiling of shoots of the species *Bryonia dioica*. For this purpose the compounds were purified by column or MPLC chromatography prior to the performance of the tests in order to insure that they were free from methyl jasmonate (all compounds synthesized from *rac*-**2** were >99.5% pure by GLC). None of the synthesized compounds *rac*-**3**–*rac*-**6**, nor the enantiomerically pure compound **3**, showed any induction of tendril coiling. Control experiments with methyl jasmonate *rac*-**2** showed the described biological activity.[3] The results are in contradiction to the observation of a strong biological activity induced by compound *rac*-**3** in the same bioassay made by Beale and co-workers.[9] In addition we also performed bioassays in order to investigate the elicitation of the phytoalexin production at cell suspension cultures of *Eschscholtzia californica*. As described previously,[16] methyl jasmonate *rac*-**2** has been shown to be a potent elicitor of phytoalexin production in this species. Compared with methyl jasmonate **2**, the synthesized compounds were unable to induce the described effect. Only *rac*-**5** and *rac*-**6** showed weak activity as elicitors for phytoalexin production in *E. californica* when applied in higher concentrations (>50 μmol dm^{-3}). The formed benzo-[*c*]phenanthrolidine alkaloids were detected by UV spectroscopy and HPLC. A change in steric demands and/or electronic properties of the substrate led to a complete loss of biological activity. This agrees with preliminary tests performed with other analogues of methyl jasmonate which we hope will be published soon.

Experimental

NMR spectra were taken on Bruker AM 400 and 270 spectrometers. *J* Values are given in Hz. IR spectra were taken on a Nicolet FTIR 750 spectrometer. Mass spectra were recorded on Varian MAT 711 and 44 S spectrometers. TLC analyses were performed on Merck 60 F 254 silica gel plates. Silica gel 60 (240–400 mesh) was used for silica gel chromatography. MPLC was performed on a Büchi 680 system. All reactions were carried out under dry and oxygen-free argon. All reagents and solvents were dried and purified before use. Light petroleum was the fraction boiling at 40–60 °C.

{2-Methyl-3-oxo-2-[(Z)-pent-2-enyl]cyclopentyl}acetate rac-**3** *and* rac-**4**.—A stirred suspension of KH (1.32 g; 30% dispersion in mineral oil, washed with pentane) in tetrahydrofuran (THF) (50 cm^3) was cooled to 0 °C and a solution of

jasmonic acid *rac*-**7** (1.05 g) in THF (10 cm^3) was added. After being stirred for 1.5 h at room temperature the solution was cooled again to 0 °C and methyl iodide (10.2 cm^3 of a 1 mol dm^{-3} solution in THF) was added over a period of 10 min. After being stirred for a further 8 h while the mixture warmed up to room temperature the reaction mixture was quenched with saturated aq. NH_4Cl (10 cm^3), extracted 5 times with 20 cm^3 *tert*-butyl methyl ether (TBME), dried over $MgSO_4$, and concentrated. The resulting acid was dissolved in TBME (25 cm^3), cooled to 0 °C, treated with a 0.7 mol dm^{-3} solution of CH_2N_2 in TBME (8 cm^3) and stirred for 1 h. The reaction mixture was washed successively with saturated aq. NH_4Cl (5 cm^3), aq. $NaHCO_3$, and brine, then was concentrated, and purified by silica gel chromatography with TBME–light petroleum (1 : 5) to yield a 1.3 : 1 mixture of the diastereoisomeric compounds *rac*-**3** and *rac*-**4** as an oil (812 mg, 68%) with R_f 0.39 and 0.43; $\nu_{max}(CCl_4)/cm^{-1}$ 3035, 3030–2860, 1740, 1435, 1195 and 1175; δ_H(400 MHz; $CDCl_3$) *rac*-**3**: (jasmonic acid numbering) 0.96 (3 H, t, *J* 7.5, 12-H_3), 1.02 (3 H, s, 7-Me), 1.63–1.70 (1 H, m, 4-H), 1.95–2.43 (9 H, m), 2.56 (1 H, dd, *J* 9.5 and 20, 2-H), 3.71 (3 H, s, OMe), 5.13–5.30 (1 H, m, 9-H) and 5.38–5.52 (1 H, m, 10-H); δ *rac*-**4**: 0.85 (3 H, s, 7-Me), 0.95 (3 H, t, *J* 7.5, 12-H_3), 1.41–1.55 (1 H, m, 4-H), 1.83–2.40 (9 H, m), 2.69 (1 H, dd, *J* 8 and 19, 2-H), 3.68 (3 H, s, OMe), 5.13–5.30 (1 H, m, 9-H) and 5.38–5.52 (1 H, m, 10-H); δ_C(67.9 MHz; $CDCl_3$) *rac*-**3**: 14.00 (q, C-12), 20.35 (q, 7-Me), 20.51, 25.39, 27.11, 37.65, 39.01 (each t, C-2, -4, -5, -8, -11), 37.95 (d, C-3), 50.80 (s, C-7), 51.63 (q, OMe) 124.90 and 133.96 (each d, C-9, -10), 172.00 (s, C-1) and 218.89 (s, C-6); δ_C *rac*-**4**: 14.04 (q, C-12), 20.61 (q, 7-Me), 20.52, 24.86, 29.44, 34.60 and 35.95 (each t, C-2, -4, -5, -8, -11), 44.02 (d, C-3), 50.89 (s, C-7), 51.76 (q, OMe), 122.84 and 134.43 (d, C-9, -10), 172.96 (s, C-1) and 220.87 (s, C-6); *m/z* (EI, 70 eV) 55 (65%), 97 (100), 207 (10), 220 (10) and 238 (10) (Found: M^+, 238.1569. Calc. for $C_{14}H_{22}O_3$: *M*, 238.1569).

(1S,3aR,7aS)-1-(tert-*Butoxy*)-7a-*methyl*-3a,4,5,6,7,7a-*hexahydroindan*-5-*one* **9**.—Lithium shots (0.8 g) were dissolved in ethylamine (125 cm^3) at −78 °C and the solution was stirred for 20 min until it turned deep blue. A solution of (1*S*,7a*S*)-1-(*tert*-butoxy)-7-7,7a-dihydro-7a-methylindan-5(6*H*)-one **8** (1.11 g) and *tert*-butyl alcohol (3.7 g) in THF (25 cm^3) was added over a period of 45 min while the temperature was kept below −70 °C. Stirring was continued for 1 h and the reaction mixture was quenched with small portions of solid NH_4Cl (3.8 g) and of water (15 cm^3) under rigorous stirring while the temperature was allowed to rise to 17 °C and the solvents were distilled off. The mixture was extracted 5 times with TBME (20 cm^3). The combined organic layers were subsequently washed successively with 20 cm^3 aliquots of saturated aq. NH_4Cl, aq. $NaHCO_3$, and brine, then was concentrated and purified by crystallisation from pentane to give ketone **9** as needles (968 mg, 86%); $\nu_{max}(CCl_4)/cm^{-1}$ 2990–2845, 1712, 1367, 1205 and 1070; δ_H(400 MHz; $CDCl_3$) 1.08 (3 H, s, 7a-Me), 1.17 (9 H, s, OBu^t), 1.50–2.47 (11 H, m) and 3.61 (1 H, t, *J* 6, 1-H); δ_C(100.6 MHz; $CDCl_3$) 20.73 (q, 7a-Me), 28.44, 32.30, 32.47, 36.86 and 42.52 (each t, C-2, -3, -4, -6, -7), 28.48 (q, $OCMe_3$), 42.43 (s, C-7a), 43.87 (d, C-3a), 72.67 (s, $OCMe_3$), 77.98 (d, C-1) and 213.11 (s, C-5); *m/z* (EI, 70 eV) 57 (95%), 111 (65), 168 (100) and 224 (1) (Found: C, 74.3; H, 11.0. Calc. for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78%).

(1S,3aR,7aS)-1-(tert-*Butoxy*)-7a-*methyl*-5-*trimethylsiloxy*-3a,4,7,7a-*tetrahydroindane* **11**.—Ketone **9** (750 mg) was dissolved in THF (3 cm^3) and the solution was added to a solution of LDA (3.5 mmol) in THF (10 cm^3) at −78 °C. After the mixture had been stirred for 45 min, a solution of trimethylsilyl chloride (TMSCl) (378 mg) in THF (2 cm^3) was slowly added, with the temperature kept below −70 °C, and then the mixture was stirred for a further 4 h while the temperature rose to 0 °C. The mixture then was partitioned between pentane (150 cm^3) and saturated aq. $NaHCO_3$ (20 cm^3). The organic layer was washed with brine and evaporated. Column chromatography with TBME–light petroleum–triethylamine (1:8:0.01) finally yielded a 2.4:1 mixture of the regioisomeric silyl enol ethers **11** and **12** (determined by GLC) (928 mg, 94%), δ_H(400 MHz; $CDCl_3$) 0.19 (9 H, s, $SiMe_3$), 0.92 (3 H, s, 7a-Me), 0.95–2.22 (9 H, m), 1.14 (9 H, s, OBu^t), 3.51 (1 H, dd, *J* 3 and 7, 1-H) and 4.70–4.75 (1 H, m, 4-H); δ_C(67.9 MHz; $CDCl_3$) 0.29 (q, $SiMe_3$), 20.47 (q, 7a-Me), 26.80, 30.39, 31.67 and 32.65 (t, C-2, -3, -6, -7), 28.53 (q, $OCMe_3$), 41.93 (s, C-7a), 41.86 (d, C-3a), 72.52 (d, C-1), 80.16 (s, $OCMe_3$), 101.91 (d, C-4) and 148.14 (s, C-5); *m/z* (EI, 70 eV) 57 (80%), 73 (100), 97 (80), 143 (80), 239 (95) and 296 (3) (Found: M^+, 296.2172. Calc. for $C_{17}H_{32}O_2Si$; *M*, 296.2172).

[(1R,2S,3S)-3-(tert-*Butoxy*)-2-(*formylmethyl*)-2-*methylcyclopentyl*]*acetic Acid* **13**.—A solution of the mixture of silyl enol ethers **11** and **12** (888 mg) in CH_2Cl_2–methanol (9 : 1) was treated with an excess of ozone at −78 °C until a light blue colour persisted. After being purged with argon the solution was treated with zinc dust (250 mg) and acetic acid (1 cm^3) and was stirred for a further 45 min while the temperature rose to ambient. The solid residue was filtered off and the filtrate was concentrated to yield a mixture of acids **13** and **14** in analytically pure form (763 mg, 99%); $\nu_{max}(CCl_4)/cm^{-1}$ 3450–2450, 2990–2850, 1710, 1365 and 1197; δ_H(270 MHz; $CDCl_3$) (jasmonic acid numbering) 1.15 (9 H, s, Bu^t), 1.21 (3 H, s, 7-Me), 1.05–2.68 (9 H, m), 3.76 (1 H, dd, *J* 5 and 7, 6-H) and 9.88 (1 H, t, *J* 3, 9-H); δ_C(67.9 MHz; $CDCl_3$) 20.74 (q, 7-Me), 27.53, 31.19, 35.51 and 43.01 (t, C-2, -4, -5, -8), 28.55 (q, CMe_3), 46.70 (d, C-3), 48.29 (s, C-7), 73.38 (s, CMe_3), 77.21 (d, C-6), 177.39 (s, C-1) and 203.11 (d, C-9); *m/z* (EI, 70 eV) 57 (100%), 152 (50), 198 (12) and 216 (15) (Found: C, 65.4; H, 9.3. Calc. for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44%).

Methyl [(1R,2S,3S)-3-(tert-*Butoxy*)-2-*formylmethyl*)-2-*methylcyclopentyl*]*acetate* **15**.—A mixture of acids **13** and **14** (620 mg) was dissolved in TBME (30 cm^3), cooled to 0 °C, and treated with a 0.7 mol dm^{-3} solution of CH_2N_2 in TBME (6 cm^3). After being stirred for 1 h at room temperature, the mixture was evaporated and the residue was purified by silica gel chromatography with ethyl acetate–light petroleum (1 : 5) to afford ester **15** (418 mg) as an oil with R_f 0.48; δ_H(200 MHz; $CDCl_3$) (jasmonic acid numbering) 1.04 (3 H, s, 7-Me), 1.11 (9 H, s, OBu^t), 0.75–2.44 (9 H, m), 3.63 (3 H, s, CO_2Me), 3.72 (1 H, dd, *J* 4 and 6, 6-H) and 9.86 (1 H, dd, *J* 1.5 and 3, 9-H); δ_C(50.3 MHz; $CDCl_3$) 19.66 (q, 7-Me), 20.59, 26.79, 31.20 and 35.57 (t, C-2, -4, -5, -8), 28.55 (q, $OCMe_3$), 43.16 (d, C-3), 45.97 (s, C-7), 51.55 (q, OMe), 73.24 (s, $OCMe_3$), 77.88 (d, C-6), 173.46 (s, C-1) and 202.98 (d, C-9); *m/z* (EI, 70 eV) 57 (100%), 74 (35), 139 (35) and 212 (5).

Methyl{(1R,2S,3S)-3-(tert-*Butoxy*)-2-*methyl*-2-[(Z)-*pent*-2-*enyl*]*cyclopentyl*}*acetate* **17**.—To a stirred suspension of triphenyl(propyl)phosphonium bromide (573 mg) in toluene (10 cm^3) was added BuLi (1.6 mol dm^{-3} in hexane; 0.93 cm^3) at room temperature. After being stirred for 45 min the solution of the ylide was slowly added to a solution of aldehyde **15** (400 mg) in toluene (20 cm^3) at −30 °C. The mixture was stirred for a further 12 h while the temperature rose to 0 °C. Saturated aq. $NaHCO_3$ (4 cm^3) was added and the mixture was vigorously stirred for 15 min. The organic layer was separated, concentrated, and then filtered on silica gel (10 g) with CH_2Cl_2 in order to separate product from triphenylphosphine oxide. After concentration of the solution the residue was purified by silica gel chromatography with TBME–light petroleum (1 : 5) to yield the alkene **17** (237 mg, 65%) as an oil with R_f 0.66;

$\nu_{max}(CCl_4)/cm^{-1}$ 2995–2865, 1740, 1462, 1436, 1362 and 1197; δ_H(400 MHz; $CDCl_3$) (jasmonic acid numbering) 0.92 (3 H, s, 7-Me), 0.94 (3 H, t, *J* 7.5, 12-H_3), 1.06–2.48 (11 H, m), 1.14 (9 H, s, OBu^t), 3.58 (1 H, t, *J* 8, 6-H), 3.65 (3 H, s, OMe) and 5.32–5.52 (2 H, m, 9- and 10-H); δ_C(100.6 MHz; $CDCl_3$) 13.85 (q, C-12), 18.73 (q, 7-Me), 20.43, 22.47, 27.69, 31.89 and 34.69 (t, C-2, -4, -5, -8, -11), 28.31 (q, $OCMe_3$), 43.37 (d, C-3), 47.23 (s, C-7), 51.04 (q, OMe), 72.68 (s, $OCMe_3$), 76.96 (d, C-6), 124.74 and 133.25 (d, C-9, -10) and 173.84 (s, C-1); *m/z* (EI, 70 eV) 57 (100%), 148 (20), 166 (10), 222 (10) and 240 (2); *m/z* (CI, isobutane) 223 (100%) and 297 (25, $[M + H]^+$) (Found: *m/z*, 240.1726. Calc. for $C_{14}H_{24}O_3$: *m/z*, 240.1725).

Methyl{1R,2S,3S)-3-*Hydroxy*-2-*methyl*-2-[(Z)-*pent*-2-*enyl*]-*cyclopentyl*}*acetate* **18**.—*tert*-Butyl ether **17** (196 mg) was dissolved in CCl_4 (4 cm^3) and treated with TMSI (132 mg) (1 cm^3) at room temperature. After 1 min MeOH (0.4 cm^3) was added and the mixture was stirred for 10 min. After evaporation of the volatile compounds at 0.1 mmHg the crude residue was purified by silica gel chromatography with TBME–light petroleum (1 : 2) to give alcohol **18** (146 mg, 92%) as an oil with R_f 0.22; $\nu_{max}(CCl_4)/cm^{-1}$ 3650–3350, 3630, 3010, 2995–2865, 1741, 1465, 1436, 1200 and 1172; δ_H(400 MHz; $CDCl_3$) (jasmonic acid numbering) 0.95 (3 H, t, *J* 7.5, 12-H_3), 1.00 (3 H, s, 7-Me), 1.22–2.38 (6 H, m), 1.85 (2 H, ABX-system, 8-H_2), 2.15 (1 H, dd, *J* 10 and 14, 2-H), 2.42 (1 H, dd, *J* 4 and 14, 2-H), 3.67 (3 H, s, OMe), 3.87–3.94 (1 H, m, 6-H) and 5.30–5.53 (2 H, m, 9- and 10-H); δ_C(67.9 MHz; $CDCl_3$) 14.10 (q, C-12), 18.08 (q, 7-Me), 20.75, 28.26, 29.39, 32.01 and 34.89 (t, C-2, -4, -5, -8, -11), 43.33 (d, C-3), 48.28 (s, C-7), 51.57 (q, OMe), 78.67 (d, C-6), 124.31 and 134.01 (d, C-9, -10) and 174.69 (s, C-1); *m/z* (EI, 70 eV) 97 (100%), 121 (8), 153 (6), 170 (7) and 222 (1) (Found: M^+, 222.1620. Calc. for $C_{14}H_{22}O_2$: *M*, 222.1620).

Methyl{(1R,2S)-2-*Methyl*-3-*oxo*-2-[(Z)-*pent*-2-*enyl*]*cyclopentyl*}*acetate* **3**.—Alcohol **18** (132 mg) was dissolved in CH_2Cl_2 (6 cm^3) and the solution was treated with PDC (608 mg). After being stirred for 16 h the mixture was treated with TBME (50 cm^3) and filtered through silica gel (4 g). After evaporation of the solvents the crude product was purified by silica gel chromatography with TBME–light petroleum (1 : 3) to yield compound **3** (88 mg, 67%) as an oil with R_f 0.43, and starting material **18** (24 mg recovery). Spectroscopic data were identical with those of compound *rac*-**3**.

Methyl{3-*Acetoxy*-2-[(Z)-*pent*-2-*enyl*]*cyclopentyl*}*acetate* rac-**19**.—Methyl jasmonate *rac*-**2** (1.12 g) was dissolved in acetic anhydride (1.5 cm^3) then the solution was treated with *p*-TosOH (2 mg) and refluxed for 4 h with the formed acetic acid being distilled off. After cooling to room temperature the mixture was neutralised with saturated aq. $NaHCO_3$ and extracted three times with light petroleum (15 cm^3). After evaporation of the solvent the crude residue was purified by silica gel chromatography with TBME–light petroleum (1 : 5) to afford enol acetate *rac*-**19** (1.17 g, 88%) as an oil with R_f 0.47; $\nu_{max}(CCl_4)/cm^{-1}$ 3025, 2995–2850, 1765, 1745, 1450, 1220 and 1205; δ_H(400 MHz; $CDCl_3$) (jasmonic acid numbering) 0.90 (3 H, t, *J* 7.5, 12-H_3), 1.55 (1 H, tdd, *J* 5, 9 and 12, 4-H), 2.00 (2 H, br dq, *J* 7 and 7.5, 11-H_2), 2.07–2.16 (1 H, m, 4-H), 2.07 (3 H, s, OAc), 2.14 (1 H, dd, *J* 10 and 15, 2-H), 2.29–2.55 (2 H, m, 5-H_2), 2.52 (1 H, dd, *J* 4 and 15, 2-H), 2.55 (1 H, br dd, *J* 8 and 15, 8-H), 2.77 (1 H, dd, *J* 7 and 15, 8-H), 2.97 (1 H, m, 3-H), 3.61 (3 H, s, OMe), 5.16–5.22 (1 H, m, 10-H) and 5.32–5.38 (1 H, m, 9-H); δ_C(100.6 MHz; $CDCl_3$) 13.93 (q, C-12), 20.55 (q, OCO*Me*), 20.45, 22.83, 26.74, 29.46 and 38.24 (t, C-2, -4, -5, -8, -11), 39.75 (d, C-3), 51.32 (q, CO_2Me), 124.54 and 132.79 (d, C-9, -10), 126.67 (s, C-7), 145.16 (s, C-6), 168.27 (s, O*C*OMe) and 172.90 (s, C-1), *m/z* (EI, 70 eV) 55 (95%), 151 (100), 206 (75), 224 (75) and 266 (2) (Found: M^+, 266.1518. Calc. for $C_{15}H_{22}O_4$: *M*, 266.1518).

Methyl{2-*Fluoro*-3-*oxo*-2-[(Z)-*pent*-2-*enyl*]*cyclopentyl*}*acetate* rac-**5** *and* rac-**6**.—A solution of enol acetate *rac*-**19** (135 mg) in MeCN (25 cm^3) was treated with the fluorinating reagent Selectfluor™ (209 mg) and was stirred for 30 min at room temperature. The mixture was then partitioned between ethyl acetate (35 cm^3) and saturated aq. $NaHCO_3$ (20 cm^3). The organic layer was then washed successively with water and brine (each 20 cm^3). After evaporation of the solvents the residue was purified by MPLC to yield a mixture of both diastereoisomers *rac*-**5** and *rac*-**6** (102 mg, 84%) as an oil (R_f 0.31 and 0.24) which could be separated by repeated MPLC (TBME–light petroleum; gradient from 0:1 to 1:3); $\nu_{max}(CCl_4)/cm^{-1}$ 3050–2865, 1775, 1755 and 1460; δ_H(400 MHz; $CDCl_3$) (jasmonic acid numbering; values for the second diastereoisomer in square brackets) 0.92 (3 H, t, *J* 7.5, 12-H_3), 1.48–2.84 (11-H, m), 3.67 (3 H, s, OMe) and 5.10–5.65 (2 H, m, 9- and 10-H) [0.93 (3 H, t, *J* 7.5, 12-H_3), 1.48–2.84 (11 H, m), 3.68 (3 H, s, OMe) and 5.10–5.65 (m, 2 H, 9- and 10-H)]; δ_C(100.6 MHz; $CDCl_3$) (values for the second diastereoisomer in square brackets) 13.81 (q, C-12), 20.75 (td, $^3J_{CF}$ 6, C-4), 33.38 (dt, $^3J_{CF}$ 16, C-5), 24.24 and 34.93 (t, C-2, -11), 29.20 (dt, $^2J_{CF}$ 24.8, C-8), 39.19 (dd, $^2J_{CF}$ 19.3, C-3), 51.74 (q, OMe), 98.71 (d, $^1J_{CF}$ 142, C-7), 119.66 (dd, $^3J_{CF}$ 9.8, C-9), 136.67 (d, C-10) and 171.84 (s, C-1) [13.81 (q, C-12), 22.68 (dt, $^3J_{CF}$ 8.2, C-4), 32.81 (dt, $^3J_{CF}$ 7, C-5), 24.24 and 34.93 (t, C-2, -11), 27.70 (dt, $^2J_{CF}$ 25.4, C-8), 41.25 (dd, $^2J_{CF}$ 20.7, C-3), 51.85 (q, OMe), 96.93 (d, $^1J_{CF}$ 131, C-7), 119.05 (dd, $^3J_{CF}$ 6.4, C-9), 136.05 (d, C-10) and 172.39 (s, C-1)]; *m/z* (EI, 70 eV) 55 (80%), 193 (100) and 222 (5).

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