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A Concise Enantiospecific Synthesis of (-)-Invictolide

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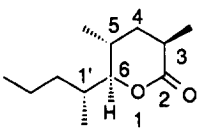
Absrtact: (-)-Invictolide, a component of the queen recognition pheromone of *Solenopsis invicta*, was stereoselectively synthesized starting from (-)-carvone, where the regioselective carbon-carbon bond cleavage reaction of γ-halo ester with samarium diiodide was successfully involved as an important reaction.

δ-Lactonic compounds with a wide range of structural feature are often observed in nature and also are of biologically significance. Invictolide **1** was isolated from the red imported fire ant queens, *Solenopsis invicta* (Buren),[1a] as a queen recognition pheromone and its relative stereochemistry was proposed by Tumlinson and co-workers[1b] based on spectroscopic analysis and synthesis. Although the absolute stereostructure of natural invictolide **1** was established to have (3*R*,5*R*,6*S*,1'*R*)-configuration by Mori and co-worker in 1986,[2] both the levorotatory and the racemic forms of invictolide exhibit pheromone activity.[1b] Whereas its dextrorotatory form, in admixture with its related pheromone, was inactive in surrogate queen field tests.[3] Owing to its interesting structural feature having the δ-lactone moiety with four chiral centers and also to the biological activity, several syntheses have been appeared in the literature.[4]

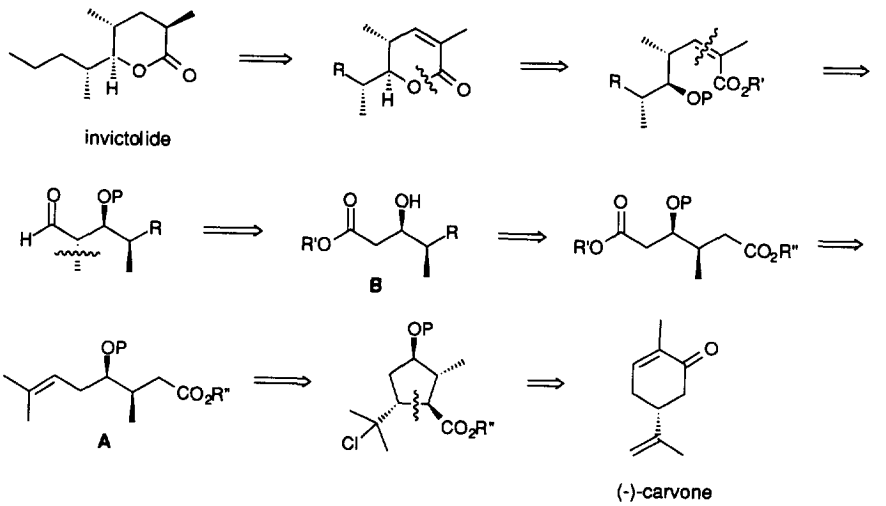


1 (-)-Invictolide

Figure 1.

During the course of our studies toward the total synthesis of natural products utilizing a monoterpene, carvone, as a chiral source,[5] we became interested in developing a new method for the stereoselective synthesis of invictolide with natural configuration. In searching the structure of **1** for retrosynthetic disconnections, we

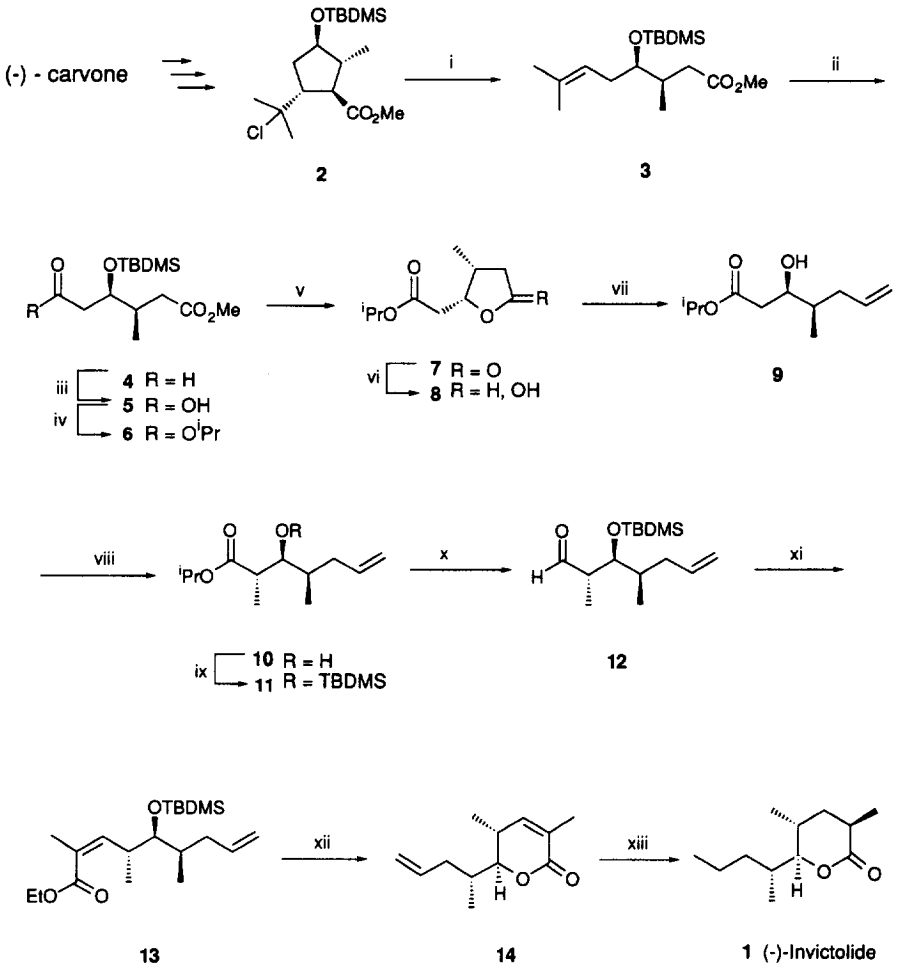
thought that the most straightforward way to achieve this goal was an exploitation of the ester **A** as a starting material, readily obtained from (-)-carvone, since the adjacent methyl and hydroxyl groups of natural product were already incorporated in **A** with correct stereochemistry and the 5*R*-methyl group could be constructed by chelation controlled alkylation of the corresponding β-hydroxy ester **B**.



Scheme 1.

Thus, the cyclopentane derivative **2**,[6] readily accessible from (-)-carvone, was subjected to the regioselective carbon-carbon fragmentation with samarium diiodide in THF-HMPA (10:1) at room temperature, recently developed by us,[6] to give the desired ester **3** in 89% yield. Ozonolysis of **3** and subsequent oxidation of the resulting aldehyde **4** with *m*-chloroperbenzoic acid (MCPBA)[7] afforded the acid **5**, which was further converted into the diester **6** on treatment with isopropyl iodide and sodium carbonate in dimethyl sulfoxide (DMSO) in 95% yield from **3**. Removal of the silyl group of **6** on exposure to 5% hydrochloric acid brought about a lactonization simultaneously to provide the γ-lactone **7** in 85% yield. Selective reduction of the γ-lactone ring with DIBAL in THF at -78°C, followed by Wittig reaction of the resulting lactol **8** with methyltriphenylphosphonium bromide and *n*-butyllithium gave the olefin **9** in 62% yield from **7**. Stereoselective construction of the 5*R*-methyl group was carried out at this stage by using the chelation controlled alkylation[8] affording the dimethyl compound **10** as the sole stereoisomer in 69% yield. After silylation of the hydroxyl group of **10** with *tert*-butyldimethylsilyl triflate in 94% yield, the ester **11** was reduced with DIBAL in toluene at -78°C to furnish the aldehyde **12** in quantitative yield. Based on the consideration of the previous report,[4h] the stereoselective construction of 3*R*-methyl group would be achieved without difficulties by a catalytic reduction of the α,β-unsaturated δ-lactone **14**. We therefore focused our attention on the synthesis of α,β-unsaturated δ-lactone.

Application of (Z)-selective Wittig-Horner reaction to **12**, developed by Still,[9] afforded the α,β-unsaturated ester **13** in 84% yield, which on acid treatment gave the expected δ-lactone **14** in 81% yield.



Scheme 2. *Reagents and conditions*; i) SmI_2, THF-HMPA, r.t.; ii) O_3, MeOH, -78°C, then PPh_3; iii) MCPBA, CH_2Cl_2, r.t., then Me_2S; iv) ^iPrI, Na_2CO_3, DMSO, r.t.; v) 5% HCl, ^iPrOH, reflux; vi) DIBAL, THF, -78°C; vii) $Ph_3P^+MeBr^-$, BuLi, THF, r.t.; viii) LDA, MeI, THF, -30 to -10°C; ix) TBDMSOTf, 2,6-lutidine, CH_2Cl_2, 0°C; x) DIBAL, toluene, -78°C; xi) $(CF_3CH_2O)_2P(O)CH(Me)CO_2Et$, $(TMS)_2NK$, 18-c-6, THF, -78°C; xii) 10% HCl, MeOH, r.t.; xiii) 10% Pd-C, H_2, EtOAc

Scheme 2.

Finally catalytic reduction of **14** over 10% palladium on carbon provided (-)-invictolide **1** and its 3-epimer in quantitative yield in a ratio of 6:1. Pure invictolide, m.p. <26°C (lit.,[2] 28-28.5°C), was obtained by recrystallization from *n*-hexane at -78°C. Spectroscopic data including specific optical rotation of the synthetic compound, $[\alpha]_D$ -99.2° (c=0.7, $CHCl_3$) {lit.,[2] $[\alpha]_D$ -101° (c=0.45, $CHCl_3$)}, were identical with those reported.[2,4h]

In summary we have presented a stereoselective synthesis of invictolide in optically pure form and the methodology developed here would be applicable to the synthesis of other structurally similar δ-lactonic natural products, such as Prelog-Djerassi lactone.

Experimental

General Procedures. Melting points were measured with a Yanaco MP apparatus and are uncorrected. IR spectra were recorded on $CHCl_3$ solutions with a Hitachi 260-10 spectrophotometer. ^{1}H-NMR spectra were obtained for $CDCl_3$ solutions on a JEOL GSX-270 instrument. Mass spectra were measured using a JEOL JMS D-300 spectrometer. Optical rotations were taken using $CHCl_3$ solutions in a JASCO DIP-360 polarimeter.

Methyl (3*R*, 4*R*)-4-(*tert*-Butyldimethylsiloxy)-3-methyl-5-oxoheptanoate (4). A stirred solution of the olefin (**3**) (2.3 g, 7 mmol) in MeOH (100 ml) was saturated with ozone at -78°C. The solution was stirred for 30 min, the ozone removed by exchange with argon, and the mixture treated with triphenylphosphine (2.9 g, 11 mmol) then warm to room temperature. Removal of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-ethyl acetate(12:1, v/v) afforded the aldehyde (**4**) (2.1 g, quant.) as a colorless oil; $[\alpha]_D$ +16.4° (c = 1.5, $CHCl_3$); νmax ($CHCl_3$) 1725 cm^{-1}; δ 0.44-0.09 (6H, m, 2×SiMe), 0.87 (9H, br s, *tert*-Bu), 0.92 (3H, d, J=6.7 Hz, Me), 2.06 (1H, dd, J=9.8 and 15.3 Hz, 2-H), 2.16-2.20 (1H, m, 3-H), 2.47-2.51 (2H, m, 5-H_2), 2.58 (1H, dd, J=4.3 and 15.3 Hz, 2-H), 3.68 (3H, s, OMe), 4.21-4.27 (1H, m, 4-H), 9.79 (1H, t, J=2.4 Hz, CHO).

1-Isopropyl 6-Methyl (3*R*, 4*S*)-3-(*tert*-Butyldimethylsiloxy)-4-methyladipate (6). To a stirred solution of the aldehyde (**4**) (1.2 g, 4 mmol) in CH_2Cl_2 (12 ml) was added *m*-chloroperbenzoic acid (1.0 g, 6 mmol) at room temperature under argon and the resulting solution was further stirred for overnight at ambient temperature. The mixture was cooled to 0°C and methyl sulfide (0.73 ml, 10 mmol) was added to this solution. The solution was stirred for 1 h at ambient temperature and the solvent was evaporated to give crude carboxylic acid (**5**), which was dissolved in DMSO (12 ml). To this solution, were added sodium carbonate (2.8 g, 20 mmol) and isopropyl iodide (2.7 g, 16 mmol) and the resulting mixture was further stirred for 1 h at ambient temperature. The mixture was treated with saturated aqueous ammonium chloride solution and extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-ethyl acetate (25:1, v/v) afforded the diester (**6**) (1.4 g, 2 steps overall yield 95.1%) as a colorless oil; $[\alpha]_D$ +25.3° (c = 0.5,

$CHCl_3$); (Found: C, 58.71; H, 9.87. $C_{17}H_{34}O_5Si$ requires C, 58.92; H, 9.89); vmax ($CHCl_3$) 1723 cm^{-1}; δ 0.04-0.08 (6H, m, 2×SiMe), 0.87 (9H, br s, *tert*-Bu), 0.91 (3H, d, J=6.7 Hz, Me), 1.23 and 1.25 (each 3H, each br s, 2×Me), 2.05 (1H, dd, J=9.8 and 14.6 Hz, 2-H), 2.12-2.17 (1H, m, 3-H), 2.32-2.37 (2H, m, 5-H_2), 2.56 (1H, dd, J=4.3 and 14.6 Hz, 2-H), 3.67 (3H, s, OMe), 4.12-4.18 (1H, m, 4-H), 4.97-5.02 (1H, m, OCH).

(3*R*, 4*R*)-4-Isopropyloxycarbonylmethyl-3-methyl-γ-butyrolactone (7). To a stirred solution of the diester (**6**) (5 g, 15 mmol) in isopropyl alcohol (50 ml), was added 5% aqueous hydrochloric acid (7.5 ml) and the resulting mixture was heated at reflux for 3 h. After being cooled to 0°C, the solution was neutralized with aqueous saturated sodium hydrogen carbonate and extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4. Removal of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-ethyl acetate (2:1, v/v) afforded γ-butyrolactone (**7**) (2.5 g, 84.8%) as a colorless oil; $[\alpha]_D$ +48.2° (c = 1.4, $CHCl_3$); (Found: C, 59.74; H, 7.91. $C_{10}H_{16}O_4$ requires C, 59.98; H, 8.05); vmax ($CHCl_3$) 1723, 1775 cm^{-1}; δ 1.03 (3H, d, J=7.3 Hz, Me), 1.26 (6H, d, J=6.1 Hz, 2×Me), 2.17-2.79 (5H, m, 2-H_2, 3-H, $^iPrOCOCH_2$), 4.81-4.97 (1H, m, 4-H), 5.01-5.13 (1H, m, OCH).

(1*R*/*S*, 3*R*, 4*R*)-1-Hydroxy-4-isopropyloxycarbonylmethyl-3-methyltetrahydrofuran (8). To a stirred solution of the lactone (**7**) (1.5 g, 7.5 mmol) in THF (150 ml), was added hexane solution of 0.98M DIBAL (9.2 ml, 9 mmol) over the period of 1 h at -78°C. After being stirred for overnight, methanol-water (20 ml, 1:1, v/v) was added to the mixture at -78°C and warmed to room temperature. The solution was further stirred for 2 h and the insoluble material was filtered off by filtration through Celite pad, and the filtrate was concentrated to leave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-ethyl acetate (2:1, v/v) afforded the lactol (**8**) (1.3 g, 87.8%) as a colorless oil; vmax ($CHCl_3$) 1730, 3500 cm^{-1}; δ 0.93 (1.8H, d, J=6.7 Hz, Me), 1.05 (1.2H, d, J=6.7 Hz, Me), 1.24 (6H, d, J=6.1 Hz, 2×Me), 1.71-2.80 (6H, m, 2-H_2, 3-H, $^iPrOCOCH_2$, OH), 4.47 (0.4H, m, 4-H), 4.64 (0.6H, m, 4-H), 5.00-5.10 (1H, m, OCH), 5.46 (0.4H, m, OCHO), 5.57 (0.6H, m, OCHO). HRMS *m/z* calcd for $C_{10}H_{16}O_3$ (M^+-18) 184.1098. Found (M^+-18) 184.1098.

Isopropyl (3*R*,4*R*)-3-Hydroxy-4-methyl-6-heptenoate (9). To a stirred solution of methyltriphenylphosphonium bromide (0.27 g, 0.7 mmol) in THF (5 ml), was added 1.68 M *n*-BuLi (0.41 ml, 0.7 mmol) in hexane at 0°C. After being stirred for 30 min, a solution of the lactol (**8**) (0.05 g, 0.2 mmol) in THF (1 ml) was added, and the resulting mixture was futher stirred for overnight at ambient temperature. The mixture was treated with saturated aqueous ammonium chloride, and extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-ethyl acetate (9:1, v/v) afforded the olefin (**9**) (35 mg, 70.7%) as a colorless oil; $[\alpha]_D$ +22.8° (c = 0.7, $CHCl_3$); (Found: C, 65.84; H, 10.10. $C_{11}H_{20}O_3$ requires C, 65.97; H, 10.07); vmax ($CHCl_3$) 1720, 3550 cm^{-1}; δ 0.93 (3H, d, J=6.7 Hz, Me), 1.25 (6H, d, J=6.1 Hz, 2×Me), 1.59-1.88 (1H, m, 4-H), 1.91-2.37 (2H, m, 5-H_2), 2.42-2.51 (2H, m, 2-H_2), 2.87 (1H, br s, OH), 3.96 (1H, m, 3-H), 5.01-5.10 (3H, m, 7-H_2, OCH), 5.74-5.84 (1H, m, 6-H).

Isopropyl (2*R*, 3*S*, 4*S*)-3-Hydroxy-2,4-dimethyl-6-heptenoate (10). To a stirred solution of diisopropylamine (0.8 ml, 0.7 mmol) in THF (1 ml), was added 1.68M of *n*-BuLi (0.5 ml, 0.87 mmol) in hexane at -30°C. After being stirred for 30 min, the ester (**9**) (0.05 g, 0.3 mmol) in THF (1 ml) was added at the same temperature, and the mixture was allowed to warm to 0°C. The mixture was again cooled to -10°C, and methyl iodide (0.16 ml, 2.5 mmol) was added. After being stirred for 3 h at the same temperature, the solution was treated with saturated aqueous ammonium chloride, and extracted with ethyl acetate. The extract was washed with brine, and dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-ether (4:1, v/v) afforded the methylated compound (**10**) (0.04 g, 69.2%) as a colorless oil; $[\alpha]_D$ +2.0° (c = 1.7, $CHCl_3$); (Found: C, 66.95; H, 10.27. $C_{12}H_{22}O_3$ requires C, 67.24; H, 10.35); νmax ($CHCl_3$) 1718, 3520 cm^{-1}; δ 0.90 (3H, d, J=6.7 Hz, Me), 1.15 (3H, d, J=6.7 Hz, Me), 1.25 and 1.26 (each 3H, each d, J=6.7 Hz, 2×Me), 1.66-1.71 (1H, m, 4-H), 1.99-2.28 (2H, m, 5-H_2), 2.53-2.63 (2H, m, 2-H, OH), 3.60 (1H, m, 3-H), 5.00-5.08 (3H, m, 7-H_2, OCH), 5.79 (1H, ddt, J=7.3, 10.4, 24.4 Hz, 6-H). HRMS *m/z* calcd for $C_{12}H_{22}O_3$ (M^+) 214.1565. Found (M^+) 214.1566.

Isopropyl (2*R*,3*S*,4*S*)-3-(*tert*-Butyldimethylsiloxy)-2,4-dimethyl-6-heptenoate (11). To a stirred solution of the alcohol (**10**) (0.27 g, 1.3 mmol) and 2,6-lutidine (0.43 g, 4.0 mmol) in CH_2Cl_2 (6 ml), was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.53 g, 2.0 mmol) at 0°C. After being stirred for 1 h at the same temperature, the mixture was treated with brine, and extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-ether (4:1, v/v) afforded the silyl ether (**11**) (0.39 g, 94.2%) as a colorless oil; $[\alpha]_D$ +13.3° (c = 0.6, $CHCl_3$); νmax ($CHCl_3$) 1735 cm^{-1}; δ 0.01-0.11 (6H, m, 2×SiMe), 0.83-0.92 (12H, m, *tert*-Bu and Me), 1.08 (3H, d, J=7.3 Hz, Me), 1.23 (6H, d, J=6.7 Hz, 2×Me), 1.62-1.71 (1H, m , 4-H), 1.85-2.19 (2H, m, 5-H_2), 2,58 (1H, quint., J=6.7 Hz, 2-H), 3.92 (1H, dd, J=3.1, 6.7 Hz, 3-H), 4.94-5.04 (3H, m, OCH and 7-H_2), 5.78 (1H, ddt, J=7.3, 10.4, 24.4 Hz, 6-H). HRMS *m/z* calcd for $C_{17}H_{33}O_3Si$ (M^+-15) 313.2199. Found (M^+-15) 313.2199.

(2*R*,3*S*,4*S*)-3-(*tert*-Butyldimethylsiloxy)-2,4-dimethyl-6-hepten-1-al (12). To a stirred solution of the ester (**11**) (0.1 g, 0.3 mmol) in dry toluene (7.5 ml) was added 0.93 M of DIBAL (0.52 ml, 0.5 mmol) in hexane at -78°C under argon and the resulting mixture was stirred for further 30 min at the same temperature. Methanol-water (1ml, 1:1, v/v) was added to the solution and the mixture was allowed to warm to room temperature and stirred for 2 h. Insoluble material was filtered off by filtration through Celite pad and the filtrate was concentrated to leave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-dichloromethane (9:1, v/v) afforded the aldehyde (**12**) (0.08 g, 100%) as a colorless oil; $[\alpha]_D$ +19.2° (c = 0.1, $CHCl_3$); νmax ($CHCl_3$) 1722 cm^{-1}; δ 0.08 (6H, s, 2×SiMe), 0.89-0.92 (12H, m, *tert*-Bu and Me), 1.09 (3H, d, J=7.3 Hz, Me), 1.68-1.79 (1H, m, 4-H), 1.82-1.90 (1H, m, 5-H), 2.20-2.29 (1H, m, 5-H), 2.51-2.60 (1H, m, 2-H), 3.80 (1H, dd, J=4.1, 4.5 Hz, 3-H), 5.00-5.07 (2H, m, 7-H_2), 5.66-5.82 (1H, m, 6-H), 9.77 (1H, d, J=3.1 Hz, CHO). HRMS *m/z* calcd for $C_{14}H_{27}O_2Si$ (M^+-15) 255.1778. Found (M^+-15) 255.1773.

Ethyl (2*Z*)-(4*R*, 5*S*, 6*R*)-5-(*tert*-Butyldimethylsiloxy)-2,4,6-trimethylnona-2,8-dienoate (13). To a stirred solution of ethyl bis(trifluoroethyl)phosphonopropionate (72 mg, 0.2 mmol) and 18-crown-6 (0.14

g, 0.5 mmol) in THF (5 ml) was added 0.5 M of potassium hexamethyldisilazide (0.42 ml, 0.21 mmol) in toluene at -78°C under argon. A solution of the aldehyde (**12**) (47 mg, 0.17 mmol) in THF (2 ml) was added to this solution at the same temperature and the resulting mixture was stirred for further 1 h. After addition of saturated aqueous ammonium chloride, the mixture was extracted with ether and ethereal layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-dichloromethane (15:1, v/v) afforded the unsaturated ester (**13**) (52 mg, 84.4%) as a colorless oil; $[\alpha]_D$ -11.3° (c = 0.6, $CHCl_3$); (Found: C, 67.66; H, 10.55. $C_{20}H_{38}O_3Si$ requires C, 67.74; H, 10.80); νmax ($CHCl_3$) 1719 cm^{-1}; δ 0.07 (6H, s, 2×SiMe), 0.85 (3H, d, J=6.7 Hz, Me), 0.92 (9H, m, *tert*-Bu), 0.99 (3H, d, J=6.7 Hz, Me), 1.29 (3H, t, J=6.7 Hz, CH_2CH_3), 1.56-1.69 (1H, m, 6-H), 1.70-1.83 (1H, m, 7-H), 1.89 (3H, br s, Me), 2.15-2.28 (1H, m, 7-H), 3.36-3.51 (2H, m, 4-H and 5-H), 4.18 (2H, q, J=6.7 Hz, CH_2CH_3), 4.91-5.02 (2H, m, 9-H_2), 5.62-5.82 (1H, m, 8-H), 6.03 (1H, dd, J=9.8, 1.2 Hz, 3-H). HRMS *m/z* calcd for $C_{19}H_{35}O_3Si$ (M^+-15) 339.2353. Found (M^+-15) 339.2353.

(4*R*, 5*S*)-5-[(1*R'*)-Methylbut-3'-enyl]-2,4-dimethyl-2-penten-5-olide (14). A solution of the ester (**13**) (50 mg, 0.14 mmol) and 10% HCl (0.05 ml) in MeOH (1 ml) was stirred at ambient temperature for 2 h. After neutralization with saturated aqueous sodium hydrogen carbonate, the mixture was extracted with ethyl acetate and the extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-ethyl acetate (14:1, v/v) afforded the unsaturated lactone (**14**) (20 mg, 81.4%) as a colorless oil; $[\alpha]_D$ -51.5° (c = 1.7, $CHCl_3$); νmax ($CHCl_3$) 1710 cm^{-1}; δ 0.97 (3H, d, J=7.3 Hz, Me), 1.04 (3H, d, J=7.3 Hz, Me), 1.81 (1H, ddt, J=2.4, 6.7, 7.3 Hz, CH_2=CHC*H*H), 1.90 (3H, br s, Me), 2.13-2.35 (2H, m, CH_2C*H*MeCHO- and CH_2=CHC*H*H), 2.58-2.65 (1H, m, C=CHC*H*MeCHO-), 4.00 (1H, dd, J=2.4, 11.0 Hz, C*H*O-), 5.02-5.11 (2H, m, CH_2=CH), 5.75 (1H, ddt, J=7.3, 14.0, 17.1 Hz, CH_2=C*H*), 6.30 (1H, m, *CH*=CMeCO). HRMS *m/z* calcd for $C_{12}H_{18}O_2$ (M^+) 194.1306. Found (M^+) 194.1306.

Invictolide (1). A solution of the unsaturated ester (**14**) (0.1 g, 0.5 mmol) and a catalytic amount of 10% Pd on carbon in ethanol (1 ml) was stirred at room temperature for 12 h under an atmosphere of hydrogen. After removal of the insoluble material by filtration through Celite pad, the filtrate was concentrated to leave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-ethyl acetate (15:1, v/v) afforded a mixture of invictolide (**1**) and its 3-epimer (102 mg, 99.5%) as a colorless oil. Pure invictolide (71 mg, 69.5%) was isolated from the mixture by crystallization from *n*-hexane at -78°C; m.p. <26°C (lit.,[2] 28-28.5°C); $[\alpha]_D$ -99.2° (c=0.7, $CHCl_3$) {lit.,[2] $[\alpha]_D$ -101° (c=0.45, $CHCl_3$)}; νmax ($CHCl_3$) 1740 cm^{-1}; δ 0.89 (3H, t, J=6.7 Hz, Me), 0.91 (3H, d, J=6.7 Hz, Me), 0.97 (3H, d, J=6.7 Hz, Me), 1.23 (3H, d, J=6.7 Hz, Me), 1.25-1.51 (5H, m, C*H*(Me)C*H*$_2$C*H*$_2$Me), 1.67 (2H, t, J=7.9 Hz, CH_2), 1.85-2.08 (1H, m, CH_2C*H*MeCHO-), 2.56-2.72 (1H, m, C*H*(Me)C=O), 3.90 (1H, dd, J=1.8, 10.4 Hz, C*H*O-). HRMS *m/z* calcd for $C_{12}H_{22}O_2$ (M^+) 198.1619. Found (M^+) 198.1619.

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