The First Total Synthesis of (±)-γ-Herbertenol, a Herbertene Isolated from a Non-Herbertus Source

A. Srikrishna,* P. C. Ravikumar

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560012, India
Fax +91(80)23600529; E-mail: ask@orgchem.iisc.ernet.in

Received 7 August 2006; revised 14 September 2006

Abstract: The structure of the aromatic sesquiterpene, (±)-γ-herbertenol, the first herbertane to be isolated from a non-herbertus source, was confirmed by a total synthesis, employing a Claisen rearrangement and ring-closing metathesis.

Key words: natural products, total synthesis, rearrangement, ring closure, metathesis

Liverworts from the genus *Herbertus* contain herbertane sesquiterpenoids, which are considered to be chemical markers of the genus.[1] The herbertane group is a small group of aromatic sesquiterpenes, isomeric to cuparanes, containing a sterically crowded 1-aryl-1,2,2-trimethylcyclopentane carbon framework incorporating two vicinal quaternary carbon atoms on a cyclopentane ring. Though cuparene (**1**), isomeric to herbertane, has been known since 1958,[2] the herbertane family of sesquiterpenes was only reported in the 1980s. The first member of the family to be identified, herbertene (**2**), was isolated in 1981 by Matsuo and coworkers from an ethyl acetate extract of the liverwort *Herberta adunca* (Dicks) S. Gray, belonging to the family herbertaceae.[3] Subsequently, several other herbertenoids **3**–**16**, mostly phenolic herbertanes, were isolated from a variety of *Herbertus* sources (Figure 1). The herbertane sesquiterpenes (mainly the phenolic herbertanes) possess interesting biological properties, such as growth-inhibiting activity and antilipid peroxidation activity.[1,4]

Contrary to the assumption that herbertanes are chemical markers of liverwort belonging to the genus *Herbertus*,[1] Becker et al.[5] recently reported the isolation of two new herbertanes, herbertene-1,12-diol (**17**) and γ-herbertenol (**18**) (Figure 2), along with aromadendranes and α-herbertenol (**3**) from the liverwort *Tylimanthus renifolius*. For years, it was believed that herbertanes are restricted to *Herbertus* species and their potential as a chemical marker of these genera has been discussed. The occurrence of herbertene sesquiterpenes in *T. renifolius* is remarkable in that it questions the validity of this hypothesis.

The presence of a sterically crowded 1-aryl-1,2,2-trimethylcyclopentane carbon framework, the difficulty associated with the construction of vicinal quaternary carbon atoms on a cyclopentane ring and the significant biologi-

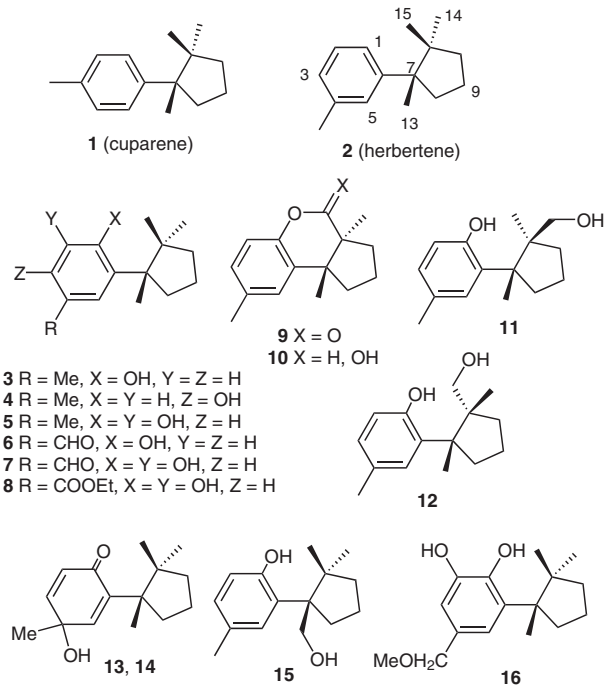


Figure 1

cal properties associated with the phenolic herbertanes, made herbertenoids interesting and challenging synthetic targets. Prior to 1999, only three reports appeared in the literature on the synthesis of phenolic herbertanes. However, since then, nearly forty reports have described the synthesis of phenolic herbertanes, making it a topic of contemporary interest.[6] We addressed the total synthesis of γ-herbertenol [(±)-**18**] in order to confirm the structure of the natural product. Herein, we wish to report the first total synthesis of **18** via a combination of Claisen rearrangement and ring-closing metathesis (RCM) reactions.[6b]

A retrosynthetic analysis is depicted in Scheme 1. It was anticipated that γ-herbertenol (**18**) could be obtained from the enone **19**, containing the requisite two quaternary car-

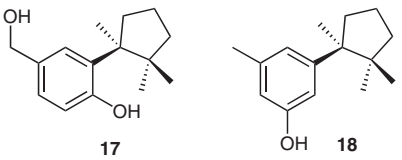
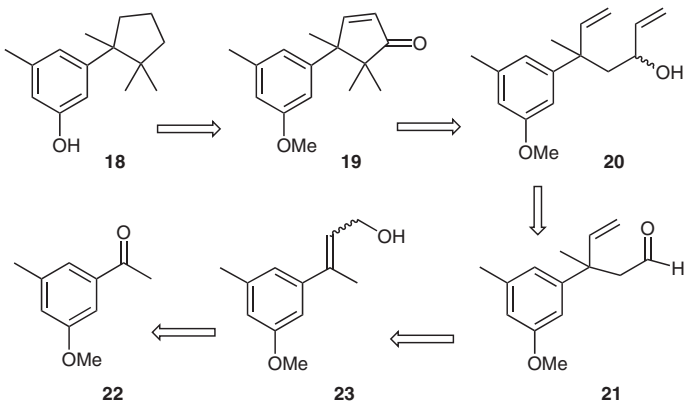


Figure 2

SYNTHESIS 2007, No. 1, pp 0065–0074
Advanced online publication: 02.11.2006
DOI: 10.1055/s-2006-950355; Art ID: P09606SS

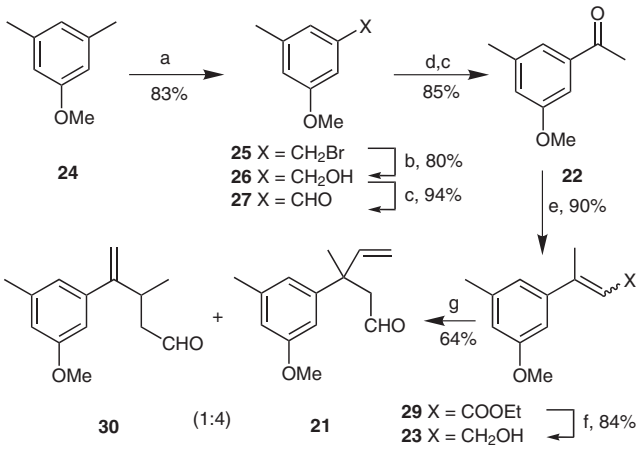


Scheme 1

bons, which in turn could be obtained from the hydroxydiene **20**, via an RCM reaction.[7] The hydroxydiene **20** could be prepared from the aldehyde **21**, which in turn could be obtained from the acetophenone **22** via the Claisen rearrangement of the cinnamyl alcohol **23**.

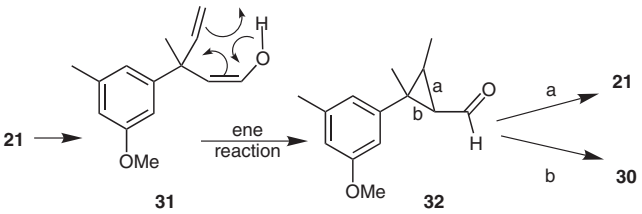
Since no reports on the synthesis of 3-methoxy-5-methylacetophenone **22** could be found in the literature, we first focused our attention on the synthesis of this starting material (Scheme 2). Reaction of the anisole **24** with one equivalent of *N*-bromosuccinimide (NBS) and a catalytic amount of benzoyl peroxide in refluxing carbon tetrachloride for one hour, furnished 3-methoxy-5-methylbenzyl bromide **25** in 83% yield. Solvolysis of the benzyl bromide **25** in refluxing aqueous acetone, in the presence of sodium bicarbonate, furnished the benzyl alcohol **26** in 80% yield. Oxidation of this alcohol with pyridinium chlorochromate (PCC) and silica gel in dichloromethane furnished the aldehyde **27** in 94% yield.[8] Grignard reaction of the aldehyde **27** with methylmagnesium iodide, followed by oxidation of the resultant benzyl alcohol **28** with PCC and silica gel, furnished the acetophenone **22**, the structure of which was established from spectral data. Horner–Wadsworth–Emmons reaction of the acetophenone **22** with sodium hydride and triethyl phosphonoacetate in refluxing THF, furnished a 12:1 *E*:*Z* mixture of the cinnamate **29**, which, on regioselective reduction at low temperature (–50 °C) with lithium aluminium hydride (LAH), gave an *E*/*Z*-mixture of the allyl alcohol **23**.

Attention was then focused on the creation of the first quaternary carbon atom. Thomas' one-pot variant[9] of the Claisen rearrangement was explored for the direct conversion of the allyl alcohol **23** into the γ,δ-unsaturated aldehyde **21**. Thus, reaction of the allyl alcohol **23** and ethyl vinyl ether, in the presence of a catalytic amount of mercuric acetate at 175 °C in a sealed tube, furnished an inseparable ~7:2 mixture of the γ,δ-unsaturated aldehyde **21** and the abnormal Claisen rearrangement product **30** in 64% overall yield. Structures of the two aldehydes **21** and **30** were assigned based on the ^{1}H NMR spectrum of the mixture. The formation of the abnormal Claisen rearrangement product **30** could be explained by an enolene rearrangement as depicted in Scheme 3.[10] An intramolec-



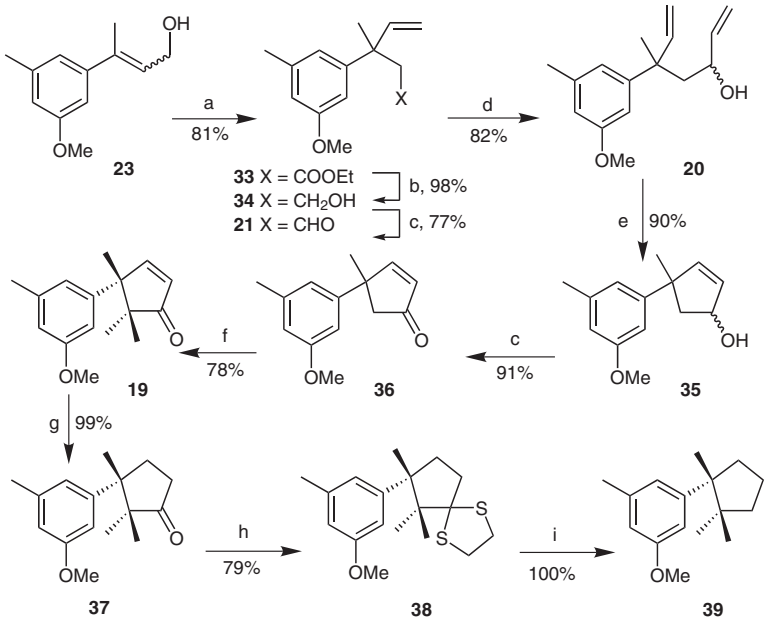
Scheme 2 *Reagents and conditions*: (a) NBS, $(PhCO_2)_2$, CCl_4; (b) H_2O, Me_2CO; (c) PCC, silica gel, CH_2Cl_2; (d) MeMgI, Et_2O; (e) $(EtO)_2P(O)CH_2CO_2Et$, NaH, THF; (f) LAH, Et_2O; (g) CH_2=CHOEt, $Hg(OAc)_2$, Δ.

ular ene reaction of the enol tautomer **31** of the aldehyde **21**, generates the cyclopropyl aldehyde **32**. A retroene reaction (or 1,5 hydrogen transfer) of the cyclopropyl aldehyde **32** would then generate either the starting aldehyde **21** or the rearranged aldehyde **30** via the cleavage of the cyclopropane bonds 'a' or 'b', respectively.



Scheme 3

In order to overcome the problems associated with the isolation and low yield of the desired aldehyde **21**, an alternative three-step sequence via Johnson's orthoester variant[11] of the Claisen rearrangement was investigated (Scheme 4). Thus, reaction of the allyl alcohol **23** with tri-

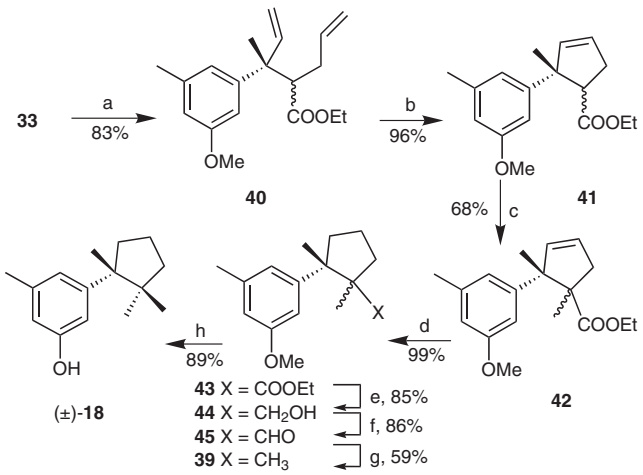


Scheme 4 *Reagents and conditions*: (a) $MeC(OEt)_3$, $EtCO_2H$, Δ; (b) LAH, Et_2O; (c) PCC, silica gel, CH_2Cl_2; (d) CH_2=CHMgBr, THF; (e) $PhCH=Ru(PCy_3)_2Cl_2$, CH_2Cl_2; (f) NaH, THF, DMF, MeI; (g) H_2, 10% Pd/C, EtOH; (h) I_2, $(CH_2SH)_2$, CH_2Cl_2; (i) Raney Ni, EtOH.

ethyl orthoacetate, in the presence of a catalytic amount of propionic acid in a sealed tube at 180 °C for 48 hours, generated the γ,δ-unsaturated ester **33** in 81% yield. Reduction of this ester with LAH in ether at 0 °C, furnished the primary alcohol **34** in 98% yield, which on oxidation with PCC and silica gel furnished the aldehyde **21** in 77% yield. Grignard reaction of the aldehyde **21** with vinylmagnesium bromide in dry THF at room temperature generated, as expected, a 1:1 epimeric mixture of the hydroxydiene **20** in 82% yield. Treatment of **20** with 5 mol% of Grubbs' first-generation catalyst [$PhCH=Ru(PCy_3)_2Cl_2$] in anhydrous dichloromethane at room temperature for one hour furnished a 1:1 diastereomeric mixture of the cyclopentenol **35** in 90% yield. Oxidation of **35** with PCC and anhydrous sodium acetate furnished the cyclopentenone **36** in 91% yield. Reaction of the cyclopentenone **36** with sodium hydride and methyl iodide in dry tetrahydrofuran and *N*,*N*-dimethylformamide at room temperature generated the enone **19**, containing the complete carbon framework of herbertanes, in 78% yield. Hydrogenation of the enone **19**, using 10% palladium over carbon as the catalyst at atmospheric hydrogen pressure, furnished the cyclopentanone **37**, the structure of which was established from its spectral data. Reaction of the cyclopentanone **37** with ethanedithiol and a catalytic amount of iodine[12] in dichloromethane at room temperature for one hour, produced the thioketal **38** in 79% yield, which, on desulfurisation with Raney nickel in refluxing ethanol for three hours, quantitatively furnished the deoxygenation product, γ-herbertenol methyl ether **39**, the structure of which was established from its NMR spectral data.

An alternative strategy was also investigated for the synthesis of γ-herbertenol methyl ether **39** starting from the γ,δ-unsaturated ester **33** (Scheme 5). It was thought that γ-herbertenol methyl ether **39** could be prepared via an RCM reaction of the diene ester **40**. Thus, generation of the lithium enolate of the ester **33** with LDA in THF at –70 °C, followed by alkylation with allyl bromide, generated a 9:4 diastereomeric mixture of the ester **40** in 83% yield. Reaction of the diene ester **40** with 5 mol% of Grubbs' first-generation catalyst in anhydrous dichloromethane at room temperature for five hours furnished the ester **41** in near quantitative yield. Generation of the lithium enolate of the ester **41** with LDA in THF and hexamethylphosphoramide (HMPA) at –30 °C, followed by treatment with methyl iodide, furnished a 4:1 diastereomeric mixture of the alkylated product **42** in 68% yield. Catalytic hydrogenation using 10% Pd/C transformed the ester **42** in to the saturated ester **43** in 99% yield. Reduction of the ester **43** with LAH in ether at 0 °C, furnished a 4:1 mixture of the primary alcohol **44**, which on oxidation with PCC and silica gel furnished the aldehyde **45**. Treatment of the aldehyde **45** with hydrazine hydrate in digol for three hours in a sealed tube at 125 °C, followed by treatment of the hydrazone with potassium hydroxide in digol for 12 hours at 190 °C, furnished the deoxygenated compound **39**, which exhibited TLC and spectral data identical to the sample obtained earlier.

Finally, demethylation of the methyl ether **39** with boron tribromide in anhydrous dichloromethane for one hour, furnished γ-herbertenol (**18**) in 89% yield. The structure of this target compound was established from ^1H and ^{13}C NMR spectral data, which were found to be identical to those of the natural product.[5]



Scheme 5 *Reagents and conditions*: (a) LDA, THF, CH_2=$CHCH_2Br$; (b) $PhCH=Ru(PCy_3)_2Cl_2$, CH_2Cl_2; (c) LDA, THF, HMPA, MeI; (d) H_2, 10% Pd/C, EtOH; (e) LAH, Et_2O; (f) PCC, silica gel, CH_2Cl_2; (g) $NH_2NH_2{\cdot}H_2O$, KOH, digol; (h) BBr_3, CH_2Cl_2.

In conclusion, we have accomplished the first total synthesis of (±)-γ-herbertenol (**18**), the first herbertane to be isolated from a non-herbertus source, thus confirming the structure of the natural product. In the present synthesis, a combination of Claisen rearrangement, RCM and alkylation reactions were employed for the efficient generation of the requisite cyclopentane containing two vicinal quaternary carbon atoms.

IR spectra were recorded on a Jasco FTIR 410 spectrophotometer. ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on a JNM λ-300 spectrometer. The chemical shifts (δ ppm) and coupling constants (Hz) are reported in the standard fashion with reference to either internal TMS (for ^1H) or the central line (77.0 ppm) of $CDCl_3$ (for ^{13}C). In the ^{13}C NMR spectra, the nature of the carbons (C, CH, CH_2 or CH_3) was determined by recording DEPT-135 spectra, and is given in parentheses. Low-resolution mass spectra were recorded using a Shimadzu QP-5050A GCMS instrument using a direct-inlet mode. Relative intensities are given in parentheses. High-resolution mass spectra were recorded on a Micromass Q-TOF micro mass spectrometer using electrospray-ionization mode. Hydrogenation reactions at atmospheric pressure were carried out using a balloon filled with hydrogen. Acme silica gel (100–200 mesh) was used for column chromatography (approximately 15–20 g per 1 g of the crude product). All small-scale dry reactions were carried out using standard syringe-septum technique.

3-Methoxy-5-methylbenzyl Bromide (25)
To a magnetically stirred solution of the anisole **24** (500 mg, 3.68 mmol) in CCl_4 (40 mL) was added NBS (622 mg, 3.5 mmol) and benzoyl peroxide (10 mg). The reaction mixture was refluxed for 1 h then the succinimide was filtered off and the filtrate was successively washed with 15 mL each of aq HCl (3 N), sat. aq $NaHCO_3$, H_2O and brine. The organic layer was dried (Na_2SO_4) and the solvent was evaporated to give a residue that was purified on a silica gel column (CH_2Cl_2–hexane, 3:7) to furnish the bromide **25**.

Yield: 657 mg (83%); oil.

IR (neat): 1597, 1327, 1299, 1214, 1194, 1168, 1154, 1066, 931, 839, 696 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.76 (1 H, s), 6.69 (1 H, s), 6.61 (1 H, s), 4.39 (2 H, s), 3.79 (3 H, s), 2.35 (3 H, s).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 159.8 (C), 139.4 (C), 138.7 (C), 122.2 (CH), 115.0 (CH), 111.4 (CH), 54.9 (CH_3), 33.2 (CH_2), 21.5 (CH_3).

MS: *m/z* (%) = 216 (11) $[M + 2]^+$, 215 (17), 214 (11) $[M^+]$, 213 (16), 135 (100), 105 (7), 91 (26).

HRMS: *m/z* [M – Br] calcd for $C_9H_{11}O$: 135.0810; found: 135.0805.

3-Methoxy-5-methylbenzyl Alcohol (26)
To a stirred solution of the bromide **25** (657 mg, 3.06 mmol) in acetone (15 mL) was added $NaHCO_3$ (321 mg, 3.84 mmol) and H_2O (25 mL). The reaction mixture was refluxed for 5 h then cooled to r.t. and extracted with EtOAc (3 × 10 mL). The combined organic layer was washed with brine (15 mL) and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column (EtOAc–hexane, 1:9→3:7) furnished the alcohol **26**.

Yield: 495 mg (80%); oil.

IR (neat): 3379, 1598, 1464, 1325, 1296, 1194, 1152, 1068, 1039, 946, 913, 837 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.70 (1 H, s), 6.66 (1 H, s), 6.58 (1 H, s), 4.56 (2 H, s), 3.77 (3 H, s), 2.31 (3 H, s), 1.73 (1 H, br s).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 160.0 (C), 142.4 (C), 139.4 (C), 120.1 (CH), 114.2 (CH), 109.3 (CH), 65.3 (CH_2), 55.0 (CH_3), 21.7 (CH_3).

MS: *m/z* (%) = 152 (100) $[M^+]$, 137 (30), 123 (61), 109 (28), 108 (30), 91 (38).

HRMS: *m/z* [M – OH] calcd for $C_9H_{11}O$: 135.0810; found: 135.0804.

3-Methoxy-5-methylbenzaldehyde (27)
To a stirred suspension of PCC (691 mg, 4.82 mmol) and silica gel (690 mg) in anhydrous CH_2Cl_2 (2 mL) was added a solution of the alcohol **26** (495 mg, 3.21 mmol) in CH_2Cl_2 (1 mL). The reaction mixture was stirred at r.t. for 15 min then filtered through a small silica gel column. The column was eluted with excess CH_2Cl_2 and the solvent was evaporated to furnished the benzaldehyde **27**.

Yield: 460 mg (94%); oil.

IR (neat): 3005, 2729, 1700, 1596, 1386, 1333, 1297, 1195, 1158, 1066, 849 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 9.90 (1 H, s), 7.23 (1 H, s), 7.16 (1 H, s), 6.95 (1 H, s), 3.84 (3 H, s), 2.41 (3 H, s).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 191.4 (CH), 160.2 (C), 140.0 (C), 138.0 (C), 124.4 (CH), 122.2 (CH), 109.3 (CH), 55.3 (CH_3), 21.3 (CH_3).

MS: *m/z* (%) = 150 (100) $[M^+]$, 149 (93), 121 (51), 91 (33), 77 (25).

HRMS: *m/z* [M + Na] calcd for $C_9H_{10}O_2Na$: 173.0578; found: 173.0584.

1-(3-Methoxy-5-methylphenyl)ethanol (28)
To a freshly prepared, magnetically stirred, cold (0 °C) suspension of MeMgI [prepared from Mg (288 mg, 12.0 mmol) and MeI (0.9 mL, 14.4 mmol) in anhyd Et_2O (3 mL)] was added a solution of the aldehyde **27** (360 mg, 2.4 mmol) in anhyd Et_2O (2 mL) over a period of 10 min. The reaction mixture was stirred at r.t. for 15 min then poured into ice-cold sat. aq NH_4Cl (10 mL) and extracted with Et_2O (3 × 5 mL). The organic extract was washed with brine (7 mL) and dried (Na_2SO_4). Evaporation of the solvent furnished the alcohol **28**.

Yield: 362 mg (91%); oil.

IR (neat): 3397, 1598, 1465, 1326, 1293, 1194, 1156, 1153, 1101, 1026, 949, 925 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.70 (1 H, s), 6.66 (1 H, s), 6.60 (1 H, s), 4.75 (1 H, q, *J* = 6.3 Hz), 3.76 (3 H, s, OCH_3), 2.31 (3 H, s, $ArCH_3$), 1.95 (1 H, br s, OH), 1.43 (3 H, d, *J* = 6.3 Hz, *sec*-CH_3).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 159.9 (C), 147.5 (C), 139.3 (C), 118.5 (CH), 113.8 (CH), 107.9 (CH), 70.4 (CH), 55.0 (CH_3), 25.3 (CH_3), 21.6 (CH_3).

MS: *m*/*z* (%) = 166 (41) [M$^+$], 151 (28), 123 (100), 108 (25), 91 (22).

HRMS: *m*/*z* [M – OH] calcd for $C_{10}H_{13}O$: 149.0966; found: 149.0966.

3-Methoxy-5-methylacetophenone (22)

Oxidation of the alcohol **28** (300 mg, 1.81 mmol) with PCC (777 mg, 3.6 mmol) and silica gel (780 mg) in dry CH_2Cl_2 (4 mL) for 1 h at r.t., as described above, followed by purification on a silica gel column (EtOAc–hexane, 1:10) furnished the ketone **22**.

Yield: 275 mg (93%); oil.

IR (neat): 3001, 1684, 1594, 1457, 1427, 1358, 1330, 1301, 1218, 1189, 1156, 1064, 973, 930 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 7.30 (1 H, s), 7.23 (1 H, s), 6.87 (1 H, s), 3.80 (3 H, s), 2.50 (3 H, s), 2.40 (3 H, s).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 197.0 (C), 159.9 (C), 139.4 (C), 138.5 (C), 122.0 (CH), 120.3 (CH), 109.5 (CH), 55.2 (CH_3), 26.6 (CH_3), 21.5 (CH_3).

MS: *m*/*z* (%) = 164 (50) [M$^+$], 149 (100), 121 (47).

HRMS: *m*/*z* [M + Na] calcd for $C_{10}H_{12}O_2Na$: 187.0735; found: 187.0728.

Ethyl 3-(3-Methoxy-5-methylphenyl)but-2-enoate (29)

A suspension of NaH (256 mg, 60% dispersion in oil, 6.4 mmol) in hexanes under nitrogen atmosphere was magnetically stirred for 10 min and the solvent was removed by syringe. The oil free NaH was then suspended in dry THF (3 mL) and cooled in an ice bath. Triethyl phosphonoacetate (1.33 mL, 6.7 mmol) was added dropwise and the reaction mixture was stirred at r.t. for 30 min. A solution of the acetophenone **22** (275 mg, 1.68 mmol) in dry THF (2 mL) was added drop wise to the reaction mixture and stirred at r.t. for 8 h. The reaction was then quenched by careful addition of sat. aq NH_4Cl (5 mL) and extracted with Et_2O (3 × 4 mL). The combined organic extract was washed with brine (7 mL) and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column (EtOAc–hexane, 1:20) furnished a 12:1 *E*/*Z* mixture of the cinnamate **29** (352 mg, 90%). Small samples of *E*- and *Z*-isomers were separated by careful column chromatography on silica gel and characterized.

E-isomer:

IR (neat): 1715, 1634, 1627, 1591, 1463, 1339, 1222, 1161, 1045, 847, 687 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.83 (1 H, s), 6.74 (1 H, s), 6.66 (1 H, s), 6.06 (1 H, br s), 4.18 (2 H, q, *J* = 6.9 Hz), 3.79 (3 H, s), 2.56 (3 H, d, *J* = 0.9 Hz), 2.34 (3 H, s), 1.30 (3 H, t, *J* = 6.9 Hz).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 166.3 (C), 159.6 (C), 155.5 (C), 143.6 (C), 139.1 (C), 119.5 (CH), 117.1 (CH), 115.1 (CH), 109.1 (CH), 59.5 (CH_2), 54.9 (CH_3), 21.6 (CH_3), 18.0 (CH_3), 14.4 (CH_3).

MS: *m*/*z* (%) = 234 (58) [M$^+$], 189 (60), 188 (100), 160 (28), 145 (20), 131 (12), 115 (20).

HRMS: *m*/*z* [M + Na] calcd for $C_{14}H_{18}O_3Na$: 257.1154; found: 257.1165.

For *Z*-isomer:

IR (neat): 1715, 1591, 1461, 1367, 1285, 1221, 1155, 1043, 850, 690 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.61 (1 H, s), 6.55 (1 H, s), 6.50 (1 H, s), 5.82 (1 H, br s), 3.98 (2 H, q, *J* = 6.9 Hz), 3.75 (3 H, s), 2.31 (3 H, s), 2.13 (3 H, d, *J* = 1.2 Hz), 1.09 (3 H, t, *J* = 6.9 Hz).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 165.6 (C), 159.2 (C), 154.8 (C), 142.0 (C), 138.7 (C), 120.0 (CH), 117.8 (CH), 114.0 (CH), 109.8 (CH), 59.6 (CH_2), 55.0 (CH_3), 27.2 (CH_3), 21.7 (CH_3), 14.1 (CH_3).

MS: *m*/*z* (%) = 234 (61) [M$^+$], 220 (7), 205 (10), 189 (57), 188 (100), 175 (16), 160 (28), 145 (19), 115 (21).

HRMS: *m*/*z* [M + Na] calcd for $C_{14}H_{18}O_3Na$: 257.1154; found: 257.1148.

3-(3-Methoxy-5-methylphenyl)but-2-en-1-ol (23)

To a cold (–50 °C) magnetically stirred solution of a 12:1 mixture of the cinnamate **29** (352 mg, 1.5 mmol) in dry Et_2O (5 mL) was added LAH (57 mg, 1.50 mmol) and the mixture was stirred for 1 h. EtOAc (0.5 mL) was added to consume the excess LAH, then the reaction was quenched with H_2O (10 mL) and extracted with Et_2O (3 × 5 mL). The combined organic extract was washed with brine (10 mL) and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column (EtOAc–hexane, 1:3) furnished an *E*/*Z* mixture of the alcohol **23** (280 mg, 84%).

E-alcohol:

IR (neat): 3363 (OH), 2920, 2838, 1591, 1453, 1334, 1294, 1205, 1166, 1154, 1064, 997, 847, 696 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.75, 6.67, 6.57 (3 × 1 H, 3 × s, ArH), 5.90 (1 H, td, *J* = 6.6 Hz, 1.5 Hz, H-2), 4.29 (2 H, d, *J* = 6.6 Hz, H-1), 3.77 (3 H, s, OCH_3), 2.31 (3 H, s, $ArCH_3$), 2.03 (3 H, s, H-4), 1.70 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 159.6 (C, C-3′), 144.3 (C), 138.8 (C), 137.8 (C), 126.7 (CH), 119.3 (CH), 113.5 (CH), 108.9 (CH), 59.8 (CH_2, C-1), 55.0 (CH_3, OCH_3), 21.8 (CH_3, $ArCH_3$), 16.2 (CH_3, C-4).

MS: *m*/*z* (%) = 192 (100) [M$^+$], 177 (27), 163 (84), 159 (25), 149 (32), 135 (35), 123 (39), 115 (24), 105 (16), 91 (32).

HRMS: *m*/*z* [M – OH] calcd for $C_{12}H_{15}O$: 175.1123; found: 175.1124.

3-(3-Methoxy-5-methylphenyl)-3-methylpent-4-enal (21) and 4-(3-Methoxy-5-methylphenyl)-3-methylpent-4-enal (30)

A solution of an *E*/*Z* mixture of the allyl alcohol **23** (54 mg, 0.28 mmol), ethyl vinyl ether (0.27 mL, 2.8 mmol) and mercuric acetate (10 mg) was heated at 100 °C in a Carius tube under N_2 atmosphere for 8 h. The excess pressure was then carefully released and the reaction mixture heated to 175 °C for 16 h. After cooling, the mixture was diluted with Et_2O (5 mL), washed with sat. aq $NaHCO_3$ (3 mL) brine (3 mL), and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column (EtOAc–hexane, 1:20) furnished a 4:1 mixture of the aldehydes **21** and **30** (42 mg, 64%) as an oil.

IR (neat): 2732, 1718, 1675, 1584, 1372, 1282, 1224, 1179, 1051, 1025, 917, 877, 805, 734, 612 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ (signals due to **30**) = 9.71 (1 H, t, *J* = 2.4 Hz, CHO), 6.70, 6.33, 6.61 (3 × 1 H, 3 × s, ArH), 5.19, 5.00 (2 × 1 H, s, H-5), 3.19–3.31 (1 H, m, H-3), 2.70–2.55, 2.45–2.30 (2 × 1 H, 2 × m, H-2), 2.31 (3 H, s, $ArCH_3$), 1.17 (3 H, d, *J* = 6.9 Hz, *sec*-CH_3).

Ethyl 3-(3-Methoxy-5-methylphenyl)-3-methylpent-4-enoate (33)

A solution of the allyl alcohol **23** (240 mg, 1.25 mmol), triethyl orthoacetate (0.91 mL, 5.0 mmol) and propionic acid (10 μl) was placed in a sealed tube and heated to 180 °C for 48 h in an oil bath. The reaction mixture was cooled, diluted with Et_2O (5 mL), washed with HCl (3 M, 5 mL), sat. aq $NaHCO_3$ (5 mL), brine (5 mL) and then dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column (EtOAc–hexane, 1:20) furnished the pentenoate **33**.

Yield: 266 mg (81%); oil.

IR (neat): 1735, 1595, 1463, 1367, 1326, 1294, 1215, 1169, 1155, 1063, 1034, 917, 843, 706 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.65, 6.60, 6.49 (3 × 1 H, 3 × s, ArH], 6.11 (1 H, dd, *J* = 17.4 Hz, 10.8 Hz, H-4), 5.11 (1 H, d, *J* = 10.8 Hz, H-5), 5.05 (1 H, d, *J* = 17.4 Hz, H-5), 3.98 (2 H, q, *J* = 7.2 Hz, OCH_2CH_3), 3.75 (3 H, s, OCH_3), 2.70, 2.68 (2 H, 2 × d, *J* = 14.1 Hz, H-2), 2.32 (3 H, s, $ArCH_3$), 1.51 (3 H, s, *tert*-CH_3), 1.14 (3 H, t, *J* = 7.2 Hz, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 170.7 (C, OC=O), 159.6 (C, C-3′), 147.6 (C, C-1′), 145.6 (CH, C-4), 138.6 (C, C-5′), 119.6 (CH, C-2), 112.3 (CH_2, C-5), 112.1 (CH, C-4), 109.9 (CH), 59.8 (CH_2, OCH_2CH_3), 54.9 (CH_3, OCH_3), 45.7 (CH_2, C-2), 43.5 (C, C-3), 25.7 (CH_3, *tert*-CH_3), 22.0 (CH_3, $ArCH_3$), 14.3 (CH_3, OCH_2CH_3).

MS: *m*/*z* (%) = 262 (10) [M^+], 175 (100), 174 (67), 159 (22), 149 (9), 128 (7), 115 (9), 105 (10).

HRMS: *m*/*z* [M + Na] calcd for $C_{16}H_{22}O_3Na$: 285.1467; found: 285.1471.

3-(3-Methoxy-5-methylphenyl)-3-methylpent-4-en-1-ol (34)

As described above, reduction of the pentenoate **33** (280 mg, 1.07 mmol) with LAH (40 mg, 1.07 mmol) in dry Et_2O (2 mL) at 0 °C for 30 min, followed by purification on a silica gel column (EtOAc–hexane, 1:4→3:7), furnished the alcohol **34**.

Yield: 228 mg (98%); oil.

IR (neat): 3364, 2943, 1594, 1455, 1327, 1291, 1193, 1166, 1154, 1063, 915, 836, 708 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.65, 6.60, 6.54 (3 × 1 H, 3 × s, ArH), 5.99 (1 H, dd, *J* = 17.1 Hz, 10.8 Hz, H-4), 5.09 (1 H, dd, *J* = 10.8, 1.2 Hz, H-5) and 5.06 (1 H, dd, *J* = 17.1 Hz, 1.2 Hz, H-5), 3.75 (3 H, s, OCH_3), 3.62–3.42 (2 H, m, CH_2OH), 2.30 (3 H, s, $ArCH_3$), 2.10–1.90 (2 H, m, H-2), 1.37 (3 H, s, *tert*-CH_3), 1.12 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 159.7 (C, C-3′), 148.3 (C, C-1′), 146.8 (CH, C-4), 138.8 (C, C-5′), 119.7 (CH, C-6′), 111.9 (CH_2, C-5), 111.9 (CH), 110.1 (CH), 59.9 (CH_2, C-1), 54.9 (CH_3, OCH_3), 43.5 (CH_2), 43.3 (C, C-3), 25.6 (CH_3, *tert*-CH_3), 22.0 (CH_3, $ArCH_3$).

MS: *m*/*z* (%) = 220 (21) [M^+], 174 (70), 175 (100), 161 (45), 160 (27), 145, (30), 115 (12), 105 (18).

HRMS: *m*/*z* [M + Na] calcd for $C_{14}H_{20}O_2Na$: 243.1361; found: 243.1351.

3-(3-Methoxy-5-methylphenyl)-3-methylpent-4-enal (21)

As described above, oxidation of the alcohol **34** (190 mg, 0.86 mmol) with PCC (557 mg, 2.60 mmol) and silica gel (560 mg) in CH_2Cl_2 (3 mL), followed by purification on a silica gel column (EtOAc–hexane, 1:20), furnished the aldehyde **21**.

Yield: 145 mg (77%); oil.

IR (neat): 2739, 1720, 1595, 1454, 1330, 1296, 1156, 1064, 916, 838, 700 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 9.52 (1 H, t, *J* = 3.0 Hz, CHO), 6.66, 6.61, 6.51 (3 × 1 H, 3 × s, ArH], 6.06 (1 H, dd, *J* = 17.4 Hz, 10.8 Hz, H-4), 5.18 (1 H, d, *J* = 10.8 Hz, H-5) and 5.10 (1 H, d, *J* 17.1 Hz, H-5), 3.75 (3 H, s, OCH_3), 2.75 and 2.66 (2 H, 2 × dd, *J* = 15.0 Hz, 3.0 Hz, H-2), 2.32 (3 H, s, $ArCH_3$), 1.49 (3 H, s, *tert*-CH_3).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 201.3 (CH, CHO), 159.9 (C, C-3′), 146.8 (C, C-1′), 145.3 (CH, C-4), 139.2 (C, C-5′), 119.5 (CH, C-6′), 113.0 (CH_2, C-5), 112.3 (CH), 110.1 (CH), 55.0 (CH_3, OCH_3), 53.2 (CH_2, C-2), 42.9 (C, C-3), 26.3 (CH_3, *tert*-CH_3), 22.0 (CH_3, $ArCH_3$).

HRMS: *m*/*z* [M + Na] calcd for $C_{14}H_{18}O_2Na$: 241.1204; found: 241.1208.

5-(3-Methoxy-5-methylphenyl)-5-methylhepta-1,6-dien-3-ol (20)

To a cold (–20 °C) magnetically stirred solution of the aldehyde **21** (145 mg, 0.66 mmol) in THF (3 mL) was added, dropwise, a solution of vinylmagnesium bromide [prepared from Mg (89 mg, 3.33 mmol) and vinyl bromide (0.28 mL, 3.99 mmol) in THF (5 mL)]. The reaction was stirred at –20 °C for 5 min then quenched with cold sat. aq NH_4Cl (10 mL) and extracted with Et_2O (2 × 4 mL). The organic layer was washed with H_2O (5 mL) and brine (5 mL), and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column (EtOAc–hexane, 1:9), furnished a ~1:1 diastereomeric mixture of the alcohol **20**.

Yield: 134 mg (82%); oil.

IR (neat): 3437, 1594, 1456, 1427, 1323, 1291, 1193, 1167, 1154, 1062, 994, 918, 845 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ (mixture of diastereomers) = 6.67, 6.62, 6.48 (3 × 1 H, 3 × s, ArH), 6.10 and 6.04 (1 H, dd, *J* = 17.1 Hz, 10.5 Hz, H-6), 5.85–5.69 (1 H, m, H-2), 5.15–4.90 (4 H, m, H-1 and H-7), 4.17–4.00 (1 H, m, H-3), 3.74 (3 H, s, OCH_3), 2.31 (3 H, s, $ArCH_3$), 2.05–1.82 (2 H, m, H-4), 1.45 and 1.42 (3 H, s, *tert*-CH_3), 1.30 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ (mixture of diastereomers) = 159.7 and 159.6 (C, C-3′), 148.4 and 148.3 (C, C-1′), 147.4 and 146.8 (CH, C-6), 142.2 and 142.1 (CH, C-2), 138.8 and 138.7 (C, C-5′), 119.9 and 119.8 (CH, C-6′), 113.4 (CH_2, C-7), 112.1 and 111.8 (CH_2, C-1), 112.0 and 111.9 (CH), 110.3 and 110.2 (CH), 70.3 and 70.2 (CH, C-3), 54.8 (CH_3, OCH_3), 48.2 (CH_2, C-4), 43.9 and 43.8 (C, C-5), 25.8 and 25.6 (CH_3, *tert*-CH_3), 22.0 (CH_3).

MS: *m*/*z* (%) = 176 (100) [M^+], 175 (30), 161 (83), 149 (21), 145 (46), 135 (15), 115 (14), 105 (14), 91 (21).

HRMS: *m*/*z* [M + Na] calcd for $C_{16}H_{22}O_2Na$: 269.1517; found: 269.1519.

4-(3-Methoxy-5-methylphenyl)-4-methylcyclopent-2-en-1-ol (35)

To a magnetically stirred solution of a 1:1 diastereomeric mixture of the hydroxydiene **20** (133 mg, 0.54 mmol) in anhydrous CH_2Cl_2 (20 mL) was added a solution of PhCH=Ru(PCy_3)Cl_2 (Grubbs catalyst; 22 mg, 5 mol%) in anhydrous CH_2Cl_2 (34 mL) and the reaction mixture was stirred at r.t. for 1 h. Evaporation of the solvent under reduced pressure and purification of the residue on a silica gel column (EtOAc–hexane, 1:10→1:5), furnished a 1:1 diastereomeric mixture of the cyclopentenol **35**.

Yield: 105 mg (90%); oil.

IR (neat): 3361, 1606, 1593, 1454, 1324, 1165, 1154, 1061, 1044, 843, 778, 702 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ (mixture of diastereomers) = 6.66 and 6.11 (1 H, s, ArH), 6.58 and 6.53 (1 H, s, ArH) and 6.47 (1 H, s, ArH), 5.98 (1 H, d, *J* = 5.4 Hz, H-3), 5.83 (1 H, dd, *J* = 5.4

Hz, 1.8 Hz, H-2), 4.92–4.80 (1 H, m, H-1), 3.75 and 3.74 (3 H, s, OCH_3), 2.44 (dd, *J* = 13.5 Hz, 7.5 Hz) and 2.39 (dd, *J* = 13.5 Hz, 6.9 Hz) [1 H, H-5A], 2.30 and 2.29 (3 H, s, $ArCH_3$), 1.89 (dd, *J* = 13.5 Hz, 4.8 Hz) and 1.81 (dd, *J* = 13.5 Hz, 4.2 Hz) [1 H, H-5B], 1.88–1.78 (1 H, br s, OH), 1.51 and 1.38 (3 H, s, *tert*-CH_3).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ (mixture of diastereomers) = 159.7 and 159.6 (C, C-3′), 150.8 and 150.2 (C, C-1′), 143.1 and 142.6 (CH, C-3), 138.9 and 138.8 (C, C-5′), 132.5 and 132.4 (CH, C-2), 119.0 (CH, C-6′), 111.8 and 111.6 (CH), 109.3 (CH), 77.2 (CH, C-1), 54.9 (CH_3, OCH_3), 52.3 and 51.5 (C, C-4), 51.4 and 50.9 (CH_2, C-5), 30.1 and 28.6 (CH_3, *tert*-CH_3), 21.9 (CH_3, $ArCH_3$).

MS: *m*/*z* (%) = 218 (100) [M$^+$], 203 (85), 200 (39), 185 (37), 175 (93), 163 (35), 135 (59), 115 (33).

HRMS: *m*/*z* [M + Na] calcd for $C_{14}H_{18}O_2Na$: 241.1204; found: 241.1197.

4-(3-Methoxy-5-methylphenyl)-4-methylcyclopent-2-enone (36)

To a magnetically stirred suspension of PCC (198 mg, 0.92 mmol) and anhydrous AcONa (191 mg, 2.3 mmol) in anhydrous CH_2Cl_2 (3 mL) was added a solution of the allyl alcohol **35** (100 mg, 0.46 mmol) in CH_2Cl_2 (1 mL). The mixture was stirred at r.t. for 6 h then filtered through a small silica gel column. The column was eluted with excess CH_2Cl_2 and the eluent was evaporated to furnish the cyclopentenone **36**.

Yield: 90 mg (91%); oil.

IR (neat): 1716, 1594, 1460, 1328, 1297, 1153, 1053, 835, 799, 701 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 7.59 (1 H, d, *J* = 5.4 Hz, H-3), 6.58 (1 H, s) and 6.50 (2 H, br s) [3 × ArH], 6.16 (1 H, d, *J* = 5.4 Hz, H-2), 3.76 (3 H, s, OCH_3), 2.60 and 2.46 (2 H, 2 × d, *J* = 18.6 Hz, H-5), 2.31 (3 H, s, $ArCH_3$), 1.60 (3 H, s, *tert*-CH_3).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 208.3 (C, C-1), 170.5 (CH, C-3), 160.0 (C, C-3′), 146.8 (C, C-1′), 139.5 (C, C-5′), 131.7 (CH, C-2), 118.9 (CH, C-6′), 112.4 (CH), 109.4 (CH), 55.0 (CH_3, OCH_3), 51.8 (CH_2, C-5), 48.1 (C, C-4), 27.4 (CH_3, *tert*-CH_3), 21.9 (CH_3, $ArCH_3$).

MS: *m*/*z* (%) = 216 (81) [M$^+$], 201 (100), 185 (9), 173 (30), 158 (23), 141 (8), 128 (15), 115 (18).

HRMS: *m*/*z* [M + Na] calcd for $C_{14}H_{16}O_2Na$: 239.1048; found: 239.1045.

4-(3-Methoxy-5-methylphenyl)-4,5,5-trimethylcyclopent-4-enone (19)

A suspension of NaH (96 mg, 60% dispersion in oil, 2.4 mmol) in hexanes (1 mL) under nitrogen atmosphere was magnetically stirred for 10 min and the solvent was removed by syringe. The oil free NaH was then suspended in dry THF (1 mL) and anhydrous DMF (0.3 mL), MeI (0.2 mL. 3.18 mmol) and the enone **36** (86 mg, 0.4 mmol) were added sequentially. The reaction mixture was stirred at r.t. for 12 h then quenched with H_2O (3 mL) and extracted with Et_2O (3 × 3 mL). The combined organic extract was washed with brine (5 mL) and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column (EtOAc–hexane, 1:9), furnished the enone **19**.

Yield: 72 mg (78%); oil.

IR (neat): 1712, 1594, 1456, 1385, 1324, 1298, 1193, 1170, 1156, 1118, 1061, 707, 623 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 7.65 (1 H, d, *J* = 5.7 Hz, H-3), 6.49, 6.48, 6.43 (3 × 1 H, 3 × s, ArH), 6.13 (1 H, d, *J* = 5.7 Hz, H-2), 3.72 (3 H, s, OCH_3), 2.29 (3 H, s, $ArCH_3$), 1.39, 1.13, 0.52 (3 × 3 H, 3 × s, *tert*-CH_3].

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 213.0 (C, C=O), 167.7 (CH, C-3), 159.7 (C, C-3′), 144.7 (C, C-1′), 138.9 (C, C-5′), 129.3 (CH, C-2), 120.0 (CH, C-6′), 112.1 (CH), 110.7 (CH), 54.8 (C, C-4), 54.6 (C, C-5), 51.3 (CH_3, OCH_3), 26.3, 26.0, 20.0 (3 × CH_3, *tert*-CH_3], 22.0 (CH_3, $ArCH_3$).

MS: *m*/*z* (%) = 244 (37) [M$^+$], 229 (100), 215 (5), 201 (8), 186 (13), 159 (7), 128 (7), 115 (9).

HRMS: *m*/*z* [M + Na] calcd for $C_{16}H_{20}O_2Na$: 267.1361; found: 267.1362.

3-(3-Methoxy-5-methylphenyl)-2,2,3-trimethylcyclopentanone (37)

To activated 10% Pd/C (10 mg) was added a solution of the enone **19** (71 mg, 0.29 mmol) in EtOH (1 mL) and the reaction mixture was stirred at r.t. for 2 h in an atmosphere of hydrogen created by evacuative replacement of air (balloon). The catalyst was then filtered off using a small silica gel column. Evaporation of the solvent furnished the cyclopentanone **37**.

Yield: 71 mg (99%); oil.

IR (neat): 1738, 1607, 1595, 1460, 1376, 1322, 1297, 1155, 1101, 1058, 843, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.75, 6.70, 6.57 (3 × 1 H, 3 × s, ArH), 3.79 (3 H, s, OCH_3), 2.70–2.30 (3 H, m), 2.35 (3 H, s, $ArCH_3$), 1.86 (1 H, ddd, *J* = 12.3 Hz, 8.4 Hz 1.8 Hz), 1.24, 1.19, 0.63 (3 × 3 H, 3 × s, *tert*-CH_3].

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 221.4 (C, C=O), 159.5 (C, C-3′), 146.5 (C, C-1′), 138.7 (C, C-5′), 119.7 (CH, C-6′), 111.5 (CH), 110.5 (CH), 54.9 (CH_3, OCH_3), 53.1 (C, C-2), 48.6 (C, C-3), 33.6 (CH_2), 29.8 (CH_2), 25.5, 22.1, 18.6 (3 × CH_3, *tert*-CH_3], 22.0 (CH_3, $ArCH_3$).

MS: *m*/*z* (%) = 246 (56) [M$^+$], 231 (7), 213 (9), 203 (8), 189 (6), 175 (100), 162 (32), 145 (8), 115 (8), 105 (7).

HRMS: *m*/*z* [M + Na] calcd for $C_{16}H_{22}O_2Na$: 269.1517; found: 269.1522.

7-(3-Methoxy-5-methylphenyl)-6,6,7-trimethyl-1,4-dithiaspiro[4.4]nonane (38)

To a magnetically stirred solution of the ketone **37** (63 mg, 0.26 mmol) in dry CH_2Cl_2 (0.22 mL) was added 1,2-ethanedithiol (0.22 mL, 2.56 mmol) and iodine (7 mg, 10 mol%). The mixture was stirred at r.t. for 1 h, then aq $Na_2S_2O_3$ (1 M, 1 mL), followed by aq NaOH (10%, 5 mL) were added and the reaction was stirred for 5 min. The product was extracted with CH_2Cl_2 (2 × 3 mL) and the organic extract was washed with brine (4 mL) and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column (CH_2Cl_2–hexane, 1:9), furnished the thioketal **38**.

Yield: 65 mg (79%); oil.

IR (neat): 1606, 1593, 1376, 1362, 1320, 1292, 1228, 1191, 1167, 1154, 1094, 1062, 952, 922, 833, 707 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.69, 6.65, 6.48 (3 × 1 H, 3 × s, ArH), 3.76 (3 H, s, OCH_3), 3.33–3.10 (4 H, m, SCH_2CH_2S), 2.70–2.40 (3 H, m), 2.32 (3 H, s, $ArCH_3$), 1.80–1.66 (1 H, m), 1.47, 1.21, 0.70 (3 × 3 H, 3 × s, *tert*-CH_3).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 159.3 (C, C-3′), 149.4 (C, C-1′), 138.0 (C, C-5′), 120.3 (CH, C-6′), 111.0 (2 × C, CH), 82.2 (C, C-5), 54.9 (CH_3, OCH_3), 51.8 (C), 50.5 (C), 45.5 (CH_2), 40.2 (CH_2), 37.9 (CH_2), 36.8 (CH_2), 28.2, 28.1, 22.2 (3 × CH_3, *tert*-CH_3), 21.3 (CH_3, $ArCH_3$).

MS: *m*/*z* (%) = 322 (10) [M$^+$], 308 (6), 262 (4), 191 (20), 189 (23), 175 (8), 162 (100), 131 (56).

HRMS: *m*/*z* [M + Na] calcd for $C_{18}H_{26}OS_2Na$: 345.1323; found: 345.1331.

5-Methyl-3-(1,2,2-trimethylcyclopentyl)anisole (γ-Herbertenol Methyl Ether) (39)

To a magnetically stirred solution of the thioketal **38** (65 mg, 0.2 mmol) in dry EtOH (3 mL) was added Raney nickel (100 mg, excess). The mixture was refluxed for 3 h then cooled and filtered through a short silica gel column using excess CH_2Cl_2. Evaporation of the solvent furnished γ-herbertenol methyl ether **39**.

Yiled: 47 mg (100%); oil.

IR (neat): 3067, 1607, 1594, 1461, 1427, 1374, 1320, 1295, 1193, 1167, 1154, 1062, 831, 704 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.71, 6.68, 6.49 (3 × 1 H, 3 × s, ArH), 3.76 (3 H, s, OCH_3), 2.55–2.35 (1 H, m), 2.32 (3 H, s, $ArCH_3$), 1.85–1.45 (5 H, m), 1.23, 1.07, 0.57 (3 × 3 H, 3 × s, *tert*-CH_3).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 159.1 (C, C-1), 149.1 (C, C-3), 137.8 (C, C-5), 120.5 (CH, C-6), 111.0 (CH), 110.9 (CH), 54.9 (CH_3, OCH_3), 50.7 (C, C-1′), 44.3 (C, C-2′), 39.9 (CH_2), 36.9 (CH_2), 26.7, 24.6, 24.4 (3 × CH_3, *tert*-CH_3], 22.0 (CH_3, $ArCH_3$), 19.6 (CH_2, C-4′).

MS: *m*/*z* (%) = 232 (25) [M^+], 175 (2), 163 (34), 162 (32), 150 (100), 135 (20), 115 (8), 105 (6), 91 (14).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{25}O$: 233.1905; found: 233.1909.

Ethyl 2-Allyl-3-(3-methoxy-5-methylphenyl)-3-methylpent-4-enoate (40)

To a cold (–70 °C), magnetically stirred solution of diisopropylamine (0.27 mL, 1.93 mmol) in dry THF (4 mL) was added a solution of *n*-BuLi (2.2 M in hexane, 0.8 mL, 1.76 mmol). The solution was stirred for 10 min, then a solution of the ester **33** (230 mg, 0.88 mmol) in dry THF (3 mL) was added dropwise. The reaction mixture was stirred for 40 min then allyl bromide (0.15 mL, 1.76 mmol) was added and stirring was continued at r.t. for 3 h. The reaction mixture was then diluted with H_2O (5 mL) and extracted with Et_2O (3 × 4 mL). The combined organic extract was washed with aq HCl (3 M, 5 mL), sat. aq $NaHCO_3$ (5 mL) brine (5 mL) and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column (EtOAc–hexane, 1:20), furnished a 9:4 diastereomeric mixture of the diene ester **40**.

Yield: 203 mg (83%); oil.

IR (neat): 1720, 1641, 1595, 1371, 1344, 1323, 1292, 1228, 1184, 1166, 1156, 1063, 995, 918, 845, 702 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ (mixture of diastereomers) = 6.72 and 6.70 (1 H, s), 6.66 and 6.67 (1 H, s) and 6.51 (1 H, s) [3 × ArH], 6.35 and 6.14 (1 H, dd, *J* = 17.4 Hz, 10.7 Hz, H-4), 5.75–5.55 (1 H, m, H-2′), 5.25–4.90 (4 H, m, H-5 and H-3′), 3.97 and 3.87 (2 H, q, *J* = 6.9 Hz, OCH_2CH_3), 3.75 (3 H, s, OCH_3), 2.92 (dd, *J* = 11.7 Hz, 3.0 Hz) and 2.89 (dd, *J* = 10.5 Hz, 2.4 Hz) [1 H, H-1′A], 2.46–2.24 (1 H, m, H-1′B), 2.31 and 2.30 (3 H, s, $ArCH_3$), 2.05–1.92 and 2.18–2.11 (1 H, m), 1.47 and 1.46 (3 H, s, *tert*-CH_3), 1.10 and 0.99 (3 H, t, *J* = 6.9 Hz, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ (mixture of diastereomers) = 173.3 and 173.2 (C, OC=O), 159.5 (C, C-3′), 147.2 and 147.1 (C, C-1′), 144.0 and 143.4 (CH, C-4), 138.6 (C, C-5′), 135.9 (CH, C-2′), 119.9 and 120.0 (CH, C-6′), 116.4 and 116.3 (CH_2, C-3′), 113.7 and 113.8 (CH_2, C-5), 112.0 and 112.1 (CH), 110.2 (CH), 59.7 (CH_2, OCH_2CH_3), 54.8 and 54.9 (CH, C-1), 54.7 (CH_3, OCH_3), 46.3 (C, C-3), 32.8 and 32.7 (CH_2, C-1′), 21.9 (CH_3, $ArCH_3$), 20.9 and 21.5 (CH_3, *tert*-CH_3), 14.3 and 14.1 (CH_3, OCH_2CH_3).

MS: *m*/*z* (%) = 302 (3) [M^+], 187 (4), 176 (50), 175 (100), 161 (18), 161 (16), 145 (17), 115 (10), 105 (12).

HRMS: *m*/*z* [M + Na] calcd for $C_{19}H_{26}O_3Na$: 325.1780; found: 325.1766.

Ethyl 2-(3-Methoxy-5-methylphenyl)-2-methylcyclopent-3-ene-1-carboxylate (41)

To a magnetically stirred solution of a 9:4 diastereomeric mixture of the diene **40** (203 mg, 0.67 mmol) in anhydrous CH_2Cl_2 (40 mL) was added a solution of Grubbs' I catalyst (25 mg, 5 mol%) in anhydrous CH_2Cl_2 (10 mL). The reaction mixture was stirred at r.t. for 5 h then the solvent was evaporated under reduced pressure and the residue was purified on a silica gel column (EtOAc–hexane, 1:30), to furnish a 9:4 diastereomeric mixture of the cyclopentenecarboxylate **41**.

Yield: 177 mg (96%); oil.

IR (neat): 1733, 1594, 1455, 1370, 1324, 1296, 1192, 1166, 1057, 845, 701 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ (mixture of diastereomers) = 6.67 and 6.73 (1 H, s), 6.50 and 6.70 (1 H, s) and 6.49 and 6.53 (1 H, s) [3 × ArH], 5.86 and 5.78 (1 H, dt, *J* = 5.8 Hz, 2.4 Hz, H-3), 5.56 and 5.61 (1 H, dt, *J* = 5.8 Hz, 2.1 Hz, H-4), 3.74–3.55 and 4.30–3.96 (2 H, m, OCH_2CH_3), 3.71 and 3.76 (3 H, s, OCH_3), 3.03 and 3.14 (1 H, t, *J* = 8.4 Hz, H-1), 3.05–2.85 (1 H, m) and 2.58–2.45 (1 H, m) [H-5], 2.28 and 2.32 (3 H, s, $ArCH_3$), 1.68 and 1.32 (3 H, s, *tert*-CH_3), 0.93 (t, *J* = 6.9 Hz) and 1.26 (t, *J* = 7.2 Hz) [3 H, OCH_2CH_3].

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ (mixture of diastereomers) = 172.5 and 173.2 (C, OC=O), 159.2 and 159.7 (C, C-3′), 144.2 and 150.0 (C, C-1′), 138.7 and 138.6 (C, C-5′), 138.1 and 138.6 (CH, C-3), 128.4 and 127.9 (CH, C-4), 120.3 and 119.5 (CH, C-6′), 112.4 and 112.0 (CH), 110.4 and 109.7 (CH), 59.8 and 60.0 (CH_2, OCH_2CH_3), 55.9 and 55.5 (CH_3, OCH_3), 55.9 and 55.0 (C, C-2), 54.9 (CH, C-1), 34.6 and 34.5 (CH_2, C-5), 27.9 (CH_3, *tert*-CH_3), 21.8 (CH_3, $ArCH_3$), 13.8 and 14.4 (CH_3, OCH_2CH_3).

MS: *m*/*z* (%) = 274 (76) [M^+], 259 (9), 246 (7), 228 (15), 213 (71), 201 (74), 200 (78), 186 (84), 185 (100), 174 (59), 159 (34), 141 (20), 128 (35), 115 (35).

HRMS: *m*/*z* [M + Na] calcd for $C_{17}H_{22}O_3Na$: 297.1457; found: 297.1467.

Ethyl 2-(3-Methoxy-5-methylphenyl)-1,2-dimethylcyclopent-3-en-1-carboxylate (42)

To a cold (–30 °C) magnetically stirred solution of LDA [prepared from diisopropylamine (0.12 mL, 0.84 mmol) and a solution of *n*-BuLi (2.5 M in hexane, 0.29 mL, 0.73 mmol) in anhydrous THF (2 mL)] was added, dropwise, a solution of the ester **41** (100 mg, 0.36 mmol) in a mixture of anhydrous THF (1 mL) and anhydrous HMPA (1 mL). The reaction was stirred for 40 min at the same temperature then MeI (0.05 mL, 0.73 mmol) was added and stirred at r.t. for 7 h. The mixture was diluted with H_2O (5 mL) and extracted with Et_2O (3 × 4 mL). The combined organic layer was washed with aq HCl (3 M, 5 mL), sat. aq $NaHCO_3$ (5 mL), brine (7 mL) and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column (EtOAc–hexane, 1:20), furnished a 4:1 diastereomeric mixture of the ester **42**.

Yileld: 71 mg (68%); oil.

IR (neat): 3052, 1725, 1594, 1378, 1322, 1291, 1263, 1200, 1167, 1154, 1112, 1055, 1027, 845, 702 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ (mixture of diastereomers) = 6.64 and 6.75 (1 H, s), 6.60 and 6.73 (1 H, s), 6.48 and 6.54 (1 H, s) [3 × ArH], 5.92–5.89 and 5.77–5.73 (1 H, m, H-3), 5.68–5.65 and 5.54–5.51 (1 H, m, H-4), 3.70–3.43 and 4.26–4.13 (2 H, m, OCH_2CH_3), 3.73 and 3.77 (3 H, s, OCH_3), 3.19 (dt, *J* = 16.5 Hz, 2.4 Hz) and 3.33 (br d, *J* = 16.8 Hz) [1 H, H-5A], 2.28 and 2.32 (3 H, s, $ArCH_3$), 2.11 (ddd, *J* = 16.5 Hz, 2.4 Hz, 1.2 Hz) and 2.14 (ddd, *J* = 16.8 Hz, 2.7 Hz, 1.2 Hz) [1 H, H-5B], 1.50 (3 H, s, C2-CH_3), 1.34 and 0.79 (3 H, s, C1-CH_3), 0.91 and 1.33 (3 H, t, *J* = 7.2 Hz, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ (mixture of diastereomers) = 175.0 and 175.9 (C, OC=O), 159.2 and 159.1 (C, C-3′), 145.2 and 145.1 (C, C-1′), 137.7 and 138.1 (CH, C-3′), 138.0 (C, C-5′), 128.6 and 127.3 (CH, C-4), 120.4 and 121.4 (CH), 112.3 and 111.7 (CH), 110.6 and 111.7 (CH), 59.9 and 60.2 (CH_2, OCH_2CH_3), 57.1 and 57.4 (C), 56.9 and 55.8 (C), 54.9 (CH_3, OCH_3), 43.2 and 42.9 (CH_2, C-5), 22.5 and 24.7 (CH_3) and 21.8 and 24.1 (CH_3) [2 × *tert*-CH_3], 21.8 and 21.9 (CH_3, $ArCH_3$), 14.4 and 13.7 (CH_3, OCH_2CH_3).

MS: *m*/*z* (%) = 288 (10) [M$^+$], 215 (10), 199 (9), 186 (40), 174 (100), 159 (20), 141 (8), 128 (9), 115 (18).

HRMS: *m*/*z* [M + Na] calcd for $C_{18}H_{24}O_3Na$: 311.1623; found: 311.1617.

Ethyl 2-(3-Methoxy-5-methylphenyl)-1,2-dimethylcyclopentanecarboxylate (43)

Catalytic hydrogenation of a diastereomeric mixture of the unsaturated ester **42** (71 mg, 0.25 mmol) with activated 10% Pd/C (15 mg) in EtOH (1.5 mL) for 2 h at 1 atm hydrogen furnished the ester **43**.

Yield: 71 mg (99%); oil.

IR (neat): 1718, 1606, 1595, 1381, 1323, 1296, 1192, 1167, 1156, 1142, 1113, 1061, 1026, 833, 704 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ (mixture of diastereomers) = 6.66 (1 H, s), 6.63 (1 H, s) and 6.48 and 6.50 (1 H, s) [3 × ArH], 3.85–3.60 (m) and 4.15 (q, *J* = 7.2 Hz) [2 H, OCH_2CH_3], 3.74 and 3.75 (3 H, s OCH_3), 2.65–2.30 (2 H, m), 2.29 and 2.31 (3 H, s, $ArCH_3$), 2.10–1.50 (4 H, m), 1.36 and 0.85 (3 H, s, *tert*-CH_3), 1.32 (3 H, s, *tert*-CH_3), 0.90 and 1.31 (3 H, t, *J* = 7.2 Hz, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ (mixture of diastereomers) = 176.2 and 176.5 (C, OC=O), 159.1 (C, C-3′), 148.0 and 147.4 (C, C-1′), 137.8 and 137.7 (C, C-5′), 119.9 and 120.8 (CH, C-6′), 111.6 and 111.5 (CH), 110.3 and 111.3 (CH), 59.7 and 60.1 (CH_2, OCH_2CH_3), 56.4 and 55.4 (C), 54.9 (CH_3, OCH_3), 51.8 and 52.6 (C), 38.2 and 38.1 (CH_2), 36.3 and 36.8 (CH_2), 24.7 and 26.5 (CH_3) and, 20.7 and 22.8 (CH_3) [2 × *tert*-CH_3], 22.0 and 21.9 (CH_3, $ArCH_3$), 21.3 (CH_2, C-4), 13.7 and 14.3 (CH_3, OCH_2CH_3).

MS: *m*/*z* (%) = 290 (52) [M$^+$], 216 (47), 189 (42), 188 (24), 176 (100), 175 (22), 173 (22), 162 (40), 161 (84), 145 (39), 135 (36), 115 (79), 105 (14).

HRMS: *m*/*z* [M + Na] calcd for $C_{18}H_{26}O_3Na$: 313.1780; found: 313.1780.

2-(3-Methoxy-5-methylphenyl)-1,2-dimethylcyclopentylmethanol (44)

Reduction of the ester **43** (40 mg, 0.14 mmol) with LAH (26 mg, 0.69 mmol) in Et_2O (1 mL) at 0 °C, followed by purification on a silica gel column using (EtOAc–hexane, 1:9), furnished a diastereomeric mixture of the alcohol **44** (29 mg, 85%) as an oil. Small samples of *cis* and *trans* isomers of **44** were separated by column chromatography on silica gel (EtOAc–hexane, 1:12) and characterized.

cis-**44**:

IR (neat): 3410, 1606, 1593, 1460, 1377, 1319, 1294, 1194, 1153, 1059, 1028, 949, 922, 833, 706 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.75, 6.71, 6.52 (3 × 1 H, 3 × s, ArH), 3.76 (3 H, s, OCH_3), 3.10 and 3.03 (2 H, 2 × d, *J* = 10.8 Hz, CH_2OH), 2.55–2.40 (1 H, m), 2.32 (3 H, s, $ArCH_3$), 1.90–1.50 (5 H, m), 1.28, 1.12 (2 × 3 H, 2 × s, *tert*-CH_3], 0.64 (1 H, br s, OH).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 159.5 (C, C-3′), 148.0 (C, C-1′), 138.6 (C, C-5′), 120.0 (CH, C-6′), 111.5 (CH), 110.8 (CH), 69.4 (CH_2, CH_2OH), 54.9 (CH_3, OCH_3), 49.8 (C), 49.4 (C), 37.6 (CH_2), 35.1 (CH_2), 25.3, 22.1 (2 × *tert*-CH_3), 20.3 (CH_2, C-4), 19.6 (CH_3, $ArCH_3$).

trans-**44**:

IR (neat): 3398, 1606, 1594, 1463, 1375, 1320, 1295, 1192, 1160, 1155, 1062, 1019, 832, 705 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ = 6.70, 6.68, 6.58 (3 × 1 H, 3 × s, ArH], 3.76 (3 H, s, OCH_3), 3.70 and 3.64 (2 H, 2 × d, *J* = 10.5 Hz, CH_2OH), 2.60–2.46 (1 H, m), 2.32 (3 H, s, $ArCH_3$), 1.90–1.40 (5 H, m), 1.28 (3 H, s, *tert*-CH_3), 1.30 (1 H, br s, OH), 0.65 (3 H, s, *tert*-CH_3).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ = 159.2 (C, C-3′), 148.5 (C, C-1′), 138.0 (C, C-5′), 120.8 (CH, C-6′), 111.5 (CH), 111.2 (CH), 68.9 (CH_2, CH_2OH), 54.9 (CH_3, OCH_3), 51.0 (C), 48.9 (C), 38.0 (CH_2), 35.2 (CH_2), 23.8 (CH_3) and 22.2 (CH_3) [2 × *tert*-CH_3], 21.6 (CH_3, $ArCH_3$), 20.0 (CH_2, C-4).

MS: *m*/*z* (%) = 248 (24) [M$^+$], 220 (11), 175 (22), (16), 163 (52), 163 (39), 152 (28), 151 (15) 150 (100), 149 (38), 135 (34), 123 (21), 115 (15), 105 (12).

HRMS: *m*/*z* [M + Na] calcd for $C_{16}H_{24}O_2Na$: 271.1674; found: 271.1679.

2-(3-Methoxy-5-methylphenyl)-1,2-dimethylcyclopentane-1-carboxaldehyde (45)

Oxidation of a diastereomeric mixture of the alcohol **44** (27 mg, 1.09 mmol) with PCC (117 mg, 0.54 mmol) and silica gel (117 mg) in CH_2Cl_2 (1 mL) at r.t. for 30 min, followed by purification on a silica gel column (EtOAc–hexane, 1:20), furnished a diastereomeric mixture of the aldehyde **45**.

Yield: 23 mg (86%); oil.

IR (neat): 2723, 1717, 1594, 1459, 1320, 1296, 1155, 1059, 833, 705 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4): δ (2:1 diastereomeric mixture) = 9.95 and 9.01 (1 H, s, CHO), 6.69 and 6.66 (1 H, s, ArH) and 6.55–6.50 (2 H, m, ArH), 3.77 (3 H, s, OCH_3), 2.55–2.17 (2 H, m), 2.32 (3 H, s, $ArCH_3$), 2.04–1.44 (4 H, m), 1.27 and 1.39 (3 H, s, *tert*-CH_3), 0.79 and 1.31 (3 H, s, *tert*-CH_3).

^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4): δ (2:1 diastereomeric mixture) = 205.4 and 206.1 (CH, CHO), 159.6 (C, C-3′), 145.8 and 147.5 (C, C-1′), 138.9 and 138.7 (C, C-5′), 119.9 and 120.1 (CH, C-6′), 112.0 and 111.8 (CH), 110.5 (CH), 58.5 and 58.1 (C, C-1), 54.9 (CH_3, OCH_3), 50.4 and 54.1 (C, C-2), 37.8 and 37.5 (CH_2), 32.2 and 33.0 (CH_2), 24.7 and 25.6 (CH_3), 22.0 (CH_3, $ArCH_3$), 20.7 and 20.6 (CH_2, C-4), 16.8 and 19.0 (CH_3).

MS: *m*/*z* (%) = 246 (14) [M$^+$], 218 (48), 203 (8), 176 (40), 175 (100), 163 (22), 162 (35), 161 (35), 160 (18), 150 (31), 149 (22), 135 (23), 115 (18), 105 (18).

HRMS: *m*/*z* [M + Na] calcd for $C_{16}H_{22}O_2Na$: 269.1517; found: 269.1503.

5-Methyl-3-(1,2,2-trimethylcyclopentyl)anisole (39)

A solution of the aldehyde **45** (9 mg, 0.037 mmol) and hydrazine hydrate (0.05 mL, 1.1 mmol) in digol (0.5 mL) was heated to 125 °C for 3 h in a sealed tube. After cooling to r.t., KOH (61 mg, 1.1 mmol) was added and the reaction mixture and heated to 190 °C for 12 h. The reaction mixture was then cooled to r.t., acidified with aq HCl (3 M, 5 mL) and extracted with CH_2Cl_2 (3 × 2 mL). The combined organic extract was washed with brine (3 mL) and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column (CH_2Cl_2–hexane, 1:20), furnished γ-herbertenol methyl ether **39** (5 mg, 59%), which exhibited TLC and spectral data identical to those of the sample obtained earlier.

5-Methyl-3-(1,2,2-trimethylcyclopentyl)phenol (γ-Herbertenol) (18)

To a cold (–50 °C) magnetically stirred solution of γ-herbertenol methyl ether **39** (6 mg, 0.026 mmol) in dry CH_2Cl_2 (1 mL), was added drop wise a solution of BBr_3 (1 M in CH_2Cl_2, 0.1 mL, 0.1 mmol). The reaction mixture was allowed to come to r.t. and stirred for 1 h then quenched with sat. aq $NaHCO_3$ (4 mL) and extracted with CH_2Cl_2 (3 × 2 mL). The combined organic extract was washed with brine (4 mL) and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column (EtOAc–hexane, 1: 20), furnished γ-herbertenol **18** (5 mg, 89%) as a colorless solid[5] that was recrystallized (CH_2Cl_2–hexane).

Mp: 64–67 °C.

IR (neat): 3337, 1615, 1595, 1458, 1374, 1298, 1227, 1156, 1012, 967, 842, 704 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.71, 6.61, 6.44 (3 × 1 H, 3 × s, ArH), 4.56 (1 H, s, OH), 2.53–2.40 (1 H, m), 2.30 (3 H, s, $ArCH_3$), 1.85–1.50 (5 H, m), 1.24, 1.08, 0.59 (3 × 3 H, 3 × s, *tert*-CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.9 (C, C-1), 149.5 (C, C-3), 138.2 (C, C-5), 120.6 (CH, C-4), 113.2 (CH) and 111.5 (CH) [C-2 and C-6], 50.6 (C, C-1′), 44.3 (C, C-2′), 39.9 (CH_2), 36.9 (CH_2), 26.7, 24.6, 24.5 (3 × CH_3, *tert*-CH_3], 21.9 (CH_3, $ArCH_3$), 19.8 (CH_2, C-4′).

MS: *m*/*z* (%) = 218 (24) [M^+], 204 (6), 175 (5), 161 (20), 149 (34), 148 (49), 136 (100), 121 (26), 108 (8), 91 (15).

Acknowledgment

We thank Prof. Becker and Dr. Feld for providing the copies of the NMR spectra of natural γ-herbertenol. P.C.R. thanks the CSIR, New Delhi for the award of a research fellowship.

References

(1) (a) Irita, H.; Hashimoto, T.; Fukuyama, Y.; Asakawa, Y. *Phytochemistry* **2000**, *55*, 247. (b) Asakawa, Y. *Phytochemistry* **2001**, *56*, 297.
(2) Enzell, C.; Erdtman, H. *Tetrahedron* **1958**, *4*, 361.
(3) Matsuo, A.; Yuki, S.; Nakayama, M. *J. Chem. Soc., Chem. Commun.* **1981**, 864.
(4) (a) Matsuo, A.; Yuki, S.; Nakayama, M.; Hayashi, S. *Chem. Lett.* **1982**, 463. (b) Matsuo, A.; Nakayama, N.; Nakayama, M. *Phytochemistry* **1985**, *24*, 777. (c) Matsuo, A.; Yuki, S.; Nakayama, M. *J. Chem. Soc., Perkin Trans. 1* **1986**, 701. (d) Asakawa, Y.; Matsuda, R.; Schofield, W. B.; Gradstein, S. R. *Phytochemistry* **1982**, *21*, 2471. (e) Matsuo, A.; Yuki, S.; Nakayama, M. *Chem. Lett.* **1983**, 1041. (f) Buchanan, M. S.; Connolly, J. D.; Rycroft, D. S. *Phytochemistry* **1996**, *43*, 1245.
(5) (a) Feld, H.; Zapp, J.; Becker, H. *Phytochemistry* **2003**, *64*, 1335. (b) It is worth noting that the structures of two sesquiterpenes HM-2 and HM-3, isolated from the phytopathogenic fungus *Helicobasidium mompa*,[13a] were assigned as herbertenoids. However, recently the structures were revised as cuparenoids by total synthesis.[13b,c]
(6) (a) Srikrishna, A.; Satyanarayana, G. *Tetrahedron* **2006**, *47*, 1277. (b) Srikrishna, A.; Rao, M. S. *Synlett* **2002**, 340. (c) Srikrishna, A.; Lakshmi, B. V. *Tetrahedron Lett.* **2005**, *46*, 4879; and references cited therein.
(7) (a) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. (b) Fürstner, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 3013. (c) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18. (d) Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117.
(8) Attempts at converting the bromide **25** into the aldehyde **27** using the Kornblum oxidation gave a mixture of the aldehyde **27** and the alcohol **26**.
(9) Thomas, A. F. *J. Chem. Soc., Chem. Commun.* **1967**, 947.
(10) Srikrishna, A.; Krishnan, K.; Venkateswarlu, S. *J. Chem. Soc., Chem. Commun.* **1993**, 143.
(11) Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T. T.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741.
(12) Firouzabadi, H.; Iranpoor, N.; Hazarkhani, H. *J. Org. Chem.* **2001**, *66*, 7527.
(13) (a) Kajimoto, T.; Yamashita, M.; Imamura, Y.; Takahashi, K.; Nohara, T.; Shibata, M. *Chem. Lett.* **1989**, 527. (b) Srikrishna, A.; Ravikumar, P. C. *Tetrahedron Lett.* **2005**, *46*, 6105. (c) Srikrishna, A.; Ravikumar, P. C. *Tetrahedron* **2006**, *62*, 9393.