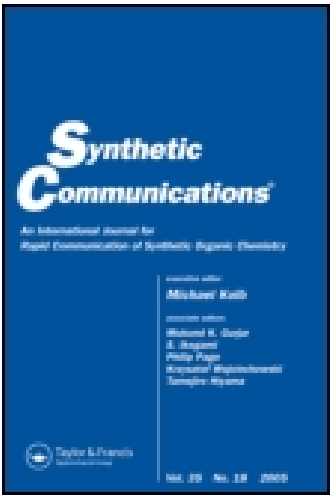


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Total Synthesis of (±)-Infuscol A and (±)-Cuprenenol

A. Srikrishna [a] & G. Satyanarayana [a]
[a] Department of Organic Chemistry , Indian Institute of Science , Bangalore, 560 012, India
Published online: 10 Jan 2011.

To cite this article: A. Srikrishna & G. Satyanarayana (2004) Total Synthesis of (±)-Infuscol A and (±)-Cuprenenol, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 34:21, 3847-3864, DOI: 10.1081/SCC-200034755

To link to this article: http://dx.doi.org/10.1081/SCC-200034755

SYNTHETIC COMMUNICATIONS®
Vol. 34, No. 21, pp. 3847–3864, 2004

Total Synthesis of (±)-Infuscol A and (±)-Cuprenenol

A. Srikrishna* and G. Satyanarayana

Department of Organic Chemistry, Indian Institute of Science, Bangalore, India

ABSTRACT

Total synthesis of the nonaromatic cuparenoid sesquiterpenes (±)-infuscol A and cuprenenol, and (±)-infuscol B and neocuprenenol isolated from the Japanese liverwort *Jungermannia infusca* has been accomplished. Two ring-closing metathesis reaction based strategies have been developed for the generation of the key intermediate of the sequence.

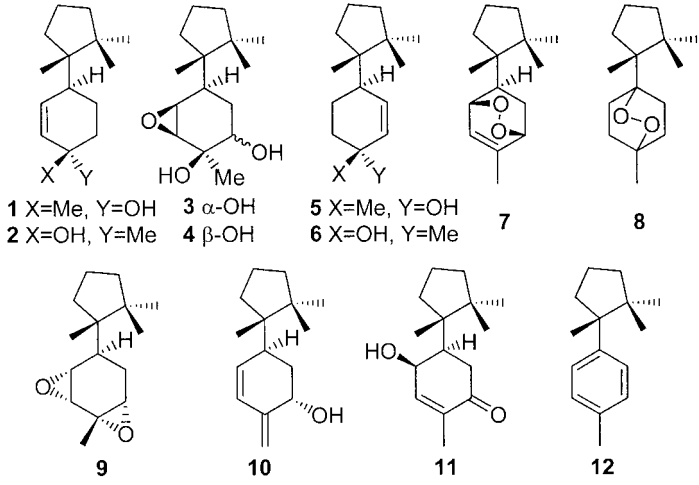
Key Words: Claisen rearrangement; Cuparanes; Ring-closing metathesis reaction; Terpene synthesis.

Liverworts are small plants, and are a rich source of unique, natural products,[1] which are not found in higher plants. The Japanese and

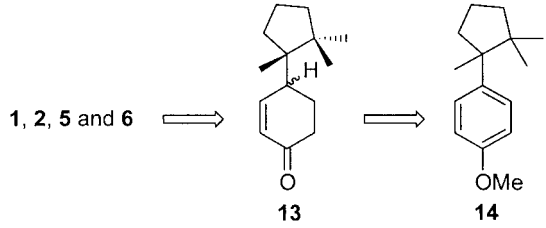
*Correspondence: A. Srikrishna, Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India; Fax: +91-80-23600529; 23600683; E-mail: ask@orgchem.iisc.ernet.in.

DOI: 10.1081/SCC-200034755 0039-7911 (Print); 1532-2432 (Online)

Taiwanese collections of the species *Jungermannia infusca* have yielded diterpenoids, sesquiterpenoids, and aromatic compounds. Recently, Nagashima and coworkers have reported isolation of several nonaromatic cuparenoid sesquiterpenes, infuscols A–D **1–4**, cuprenenol **5**, neocuprenenol **6**, endoperoxides **7** and **8**, diepoxide **9**, δ-cuprenenol **10**, and resulantol **11** along with cuparene **12** from *Jungermannia infusca* collected at Tokushima.[2] Structures of all these nonaromatic cuparenoids have been established based on the spectral studies. Structures of infuscol A **1** and cuprenenol **5** were further confirmed by X-ray crystal structures of the corresponding epoxides.[2a,c] Absolute configuration was established by correlation to (*S*)-cuparene.

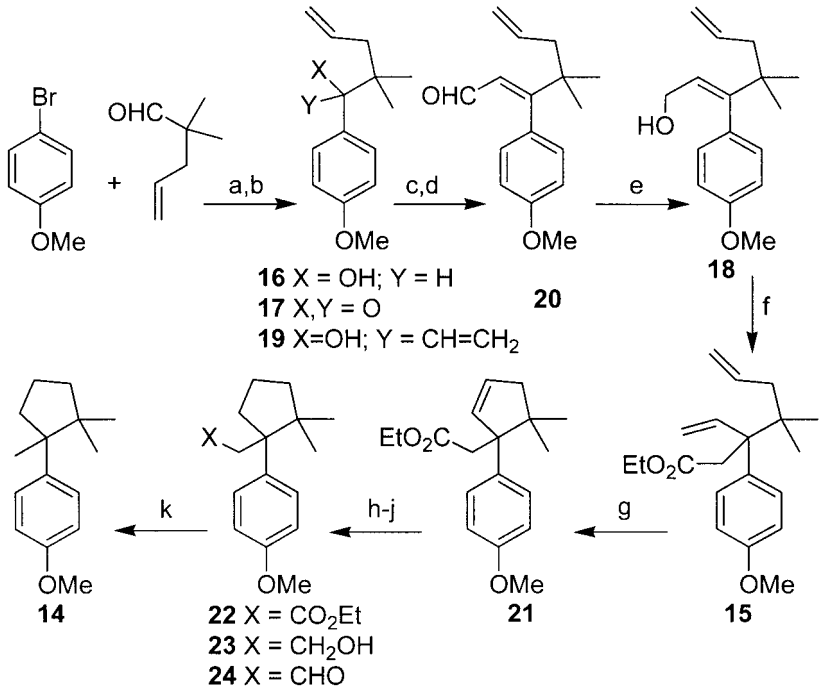


In contrast to the aromatic cuparenes, nonaromatic cuparenes have received very little attention from synthetic chemists.[3] Herein we wish to report the first total synthesis of the nonaromatic cuparenoids (±)-infuscol A **1** and cuprenenol **5** along with infuscol B **2** and neocuprenenol **6**.



Cyclohexenone **13** was readily identified as the appropriate precursor for the synthesis of the infuscols **1**, **2** and cuprenenols **5**, **6**. Based on the

Birch reduction-based protocol, the anisyl group was considered as a masked cyclohexenone, and the norcuparene **14** was contemplated as the key intermediate of the sequence. Two different methodologies, based on Claisen rearrangement and ring-closing metathesis reaction (RCM) as key steps, were developed for the synthesis of the norcuparane **14**. The first methodology, based on the RCM reaction of the diene **15**, is depicted in Sch. 1. Thus, coupling of 4-bromoanisole with 2,2-dimethylpent-4-enal under Barbier conditions followed by oxidation of the resultant benzylic alcohol **16** furnished the aryl ketone **17**. As the conventional Wittig or Horner-Wadsworth-Emmons reactions were not successful due to steric crowding, a three-step strategy was employed for the conversion of the ketone **17** into

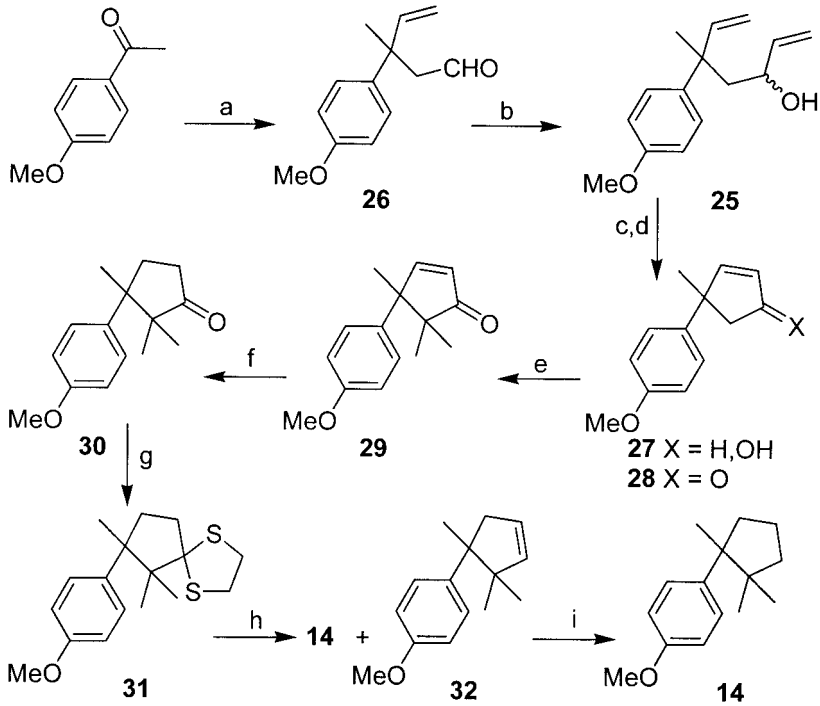


Scheme 1. Reagents, conditions, and yields: (a) Li, THF, 1 h, 85%. (b) PCC, silica gel, CH_2Cl_2, rt, 3 h, 97%. (c) CH_2=CHMgBr, THF, 0°C → rt, 4 h, 70%. (d) PCC, silica gel, CH_2Cl_2, rt, 30 h, 83%. (e) $NaBH_4$, MeOH, 0°C → rt, 2 h, 70%. (f) $CH_3C(OEt)_3$, $EtCO_2H$, sealed tube, 180°C, 48 h, 47%. (g) PhCH=$RhCl_2(PCy_3)_2$, CH_2Cl_2, rt, 8 h, 96%. (h) H_2, 5% Pd/C, EtOH, 1 atm., 3 h, 100%. (i) LAH, Et_2O, 0°C → rt, 1 h, 94%. (j) PCC, silica gel, CH_2Cl_2, rt, 0.5 h, 85%. (k) $(PPh_3)_3RhCl$, C_6H_6, sealed tube, 120°C, 24 h, 82%.

the allyl alcohol **18**. Thus, addition of vinylmagnesium bromide to the ketone **17** followed by oxidation of the resultant allylic tertiary alcohol **19** with pyridinium chlorochromate (PCC) and silica gel furnished the cinnamaldehyde **20** in a highly stereoselective manner, which on regioselective reduction with sodium borohydride furnished the allyl alcohol **18**. Since both *E* and *Z* isomers of the alcohol **18** leads to the same ester **15** after Claisen rearrangement, no attempt was made to establish the stereochemistry in the compounds **20** and **18**, and was tentatively assigned as *Z* based on the steric reasons. Johnson's orthoester Claisen rearrangement[4] of the allyl alcohol **18** with triethyl orthoacetate and a catalytic amount of propionic acid created the second quaternary carbon atom and furnished the key intermediate 1,6-diene **15**. Treatment of the diene **15** with 5 mol% of Grubbs' first generation catalyst induced the RCM reaction[5] to generate the cyclopentene **21** in near quantitative yield. Catalytic hydrogenation of the cyclopentene moiety transformed the ester **21** into the ester **22**. Reduction of the ester moiety in **22** with LAH followed by oxidation of the resultant primary alcohol **23** with PCC and silica gel transformed the ester **22** into the aldehyde **24**. Wilkinson catalyst-mediated decarbonylation transformed the aldehyde **24** into the norcuparane **14**.

The second methodology is based on the RCM reaction of the diene **25** starting from the readily available[6] aldehyde **26**, Sch. 2. Thus, the aldehyde **26** was prepared from 4-methoxyacetophenone employing the Claisen rearrangement as the key step.[6] Addition of vinylmagnesium bromide to the aldehyde **26** generated the RCM precursor, the diene **25** as a mixture of diastereomers. RCM reaction of the diene **25** with first generation Grubbs' catalyst furnished cyclopentenol **27** in near quantitative yield, which on oxidation with PCC and silica gel generated the cyclopentenone **28**. One step dimethylation of the enone **28** with sodium hydride and iodomethane created the second quaternary carbon atom and generated the cyclopentenone **29**. Catalytic hydrogenation transformed the enone **29** into the cyclopentanone **30**. Thioketalization of the cyclopentanone **30** with ethanedithiol and boron trifluoride etherate gave the thioketal **31**. Desulfurization of the thioketal **31** with Raney nickel generated a mixture of the norcuparane **14** along with varying amounts of the cyclopentene **32**. Catalytic hydrogenation of a mixture of **14** and **32** furnished the norcuparane **14**.

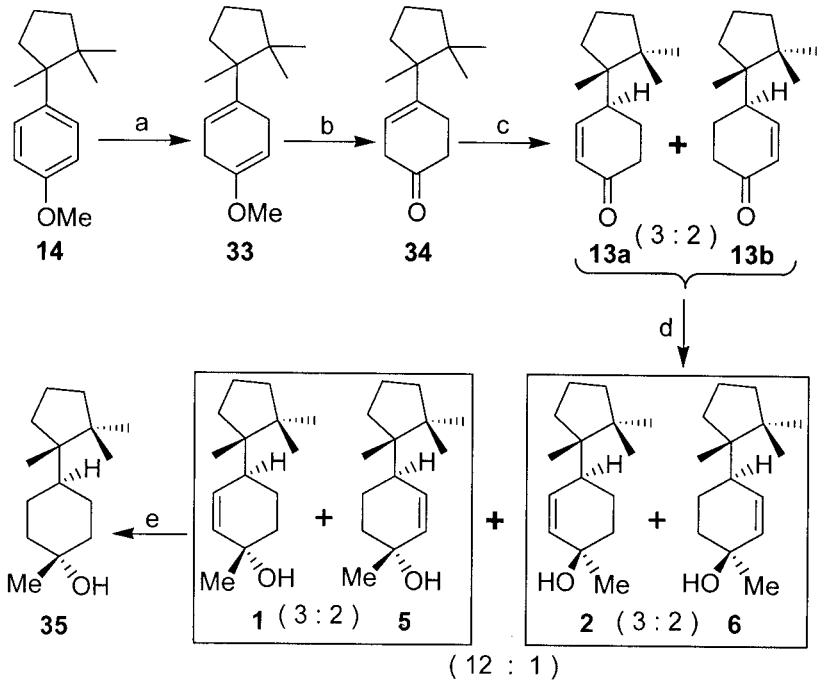
After gaining access to the norcuparane **14**, attention was turned towards its conversion to nonaromatic cuparenoids **1**, **2**, **5**, and **6**, which is depicted in Sch. 3. Thus, Birch reduction of the anisole moiety in **14** with lithium in liquid ammonia and ethanol furnished the diene **33**. Hydrolysis of the enol ether in **33** with aqueous sulphuric acid furnished the enone **34**, which was found to be very sensitive to standard isomerization techniques. After exploring various conditions, rhodium chloride trihydrate[7] was found to be



Scheme 2. Reagents, conditions, and yields: (a) reference 6. (b) CH_2=CHMgBr, THF, 0°C → rt, 4 h, 77%. (c) PhCH=$RuCl_2(PCy_3)_2$, CH_2Cl_2, 6 h, 97%. (d) PCC, silica gel, CH_2Cl_2, 3 h, 96%. (e) NaH, CH_3I, THF, DMF, RT, 12 h, 80%. (f) H_2, 5% Pd/C, EtOH, 5 h, 99%. (g) $(CH_2SH)_2$, $BF_3 . Et_2O$, 0°C → rt, 12 h, 93%. (h) Raney Ni, EtOH, reflux, 2 h. (i) H_2, 5% Pd/C, EtOH, 3 h; 80% from **31**.

ideal for the isomerization of the olefin in **34** to furnish a 3 : 2 diastereomeric mixture of the enone **13**. Finally, addition of methylmagnesium iodide to the diastereomeric mixture of the enone **13** followed by purification on a silica gel column furnished infuscol A **1** and cuprenenol **5** as major products (80%), and infuscol B **2** and neocuprenenol **6** as minor products (7%). The synthetic compounds **1**, **2**, **5**, and **6** exhibited the ^1H and ^{13}C NMR spectral data identical to those of the natural compounds. To unambiguously establish their identity, the mixture of infuscol A **1** and cuprenenol **5** was hydrogenated with 5% palladium over carbon as the catalyst in ethanol to furnish a single isomer of the dihydro derivative **35**.

In conclusion, we have accomplished the first total synthesis of the nonaromatic cuparenoid sesquiterpenoids infuscols A and B, cuprenenol and



Scheme 3. Reagents, conditions, and yields: (a) Li, liq. NH_3, THF, EtOH, 2.5 h, 85%. (b) 10% aq. H_2SO_4, THF, 50 min., 90%. (c) 8 mol% $RhCl_3 . 3H_2O$, EtOH, reflux, 3 h, 90%. (d) CH_3MgI, Et_2O, 0–5°C, 0.5 h, 86%. (e) 5% Pd/C, H_2, EtOH, 6 h, 95%.

neocuprenenol isolated from the Japanese liverwort *Jungermannia infusca*. Currently, we are investigating the extension of the methodologies for the enantioselective synthesis of these nonaromatic cuparenoid sesquiterpenes.

EXPERIMENTAL SECTION

Melting points were recorded using Tempo and Mettler FP1 melting point apparatus in capillary tubes and were uncorrected. IR spectra were recorded on a Jasco FTIR 410 spectrophotometer. ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on JNM λ-300 spectrometer, using 1 : 1 mixture of $CDCl_3$ and CCl_4 as solvent. The chemical shifts (δ ppm) and coupling constants (Hz) are reported in the standard fashion with reference to either internal tetramethylsilane (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 are given in parentheses. Low-resolution mass spectra were recorded using a Shimadzu QP-5050A GCMS instrument using direct inlet mode. Relative intensities are given in parentheses. High resolution mass spectra were recorded on a Micromass Q-TOF micro mass spectrometer using electron spray ionization mode.

1-(4-Methoxyphenyl)-2,2-dimethylpent-4-en-1-one (17): To a sonochemically irradiated suspension of lithium (375 mg, 53.5 mmol) in dry THF (5 mL) in a round-bottom flask, placed in an ultrasonic cleaning bath, was added a solution of 2,2-dimethylpent-4-enal (1 g, 8.9 mmol) and 4-bromoanisole (3.34 g, 17.8 mmol) in THF (2 mL) at 15–20°C over a period of 10 min, and sonochemically irradiated for 1 h. Then the reaction mixture was decanted from the excess lithium, quenched with saturated aqueous NH_4Cl solution and extracted with ether (3 × 10 mL). The ether extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexane (1 : 20) as eluent furnished the alcohol **16** (1.67 g, 85%) as oil. [IR (neat): ν_{max}/cm^{-1} 3467, 914. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.17 (2 H, d, $J = 8.4$ Hz), 6.75 (2 H, d, $J = 8.4$ Hz), 5.85 (1 H, t of dd, $J = 16.2$, 10.5 and 7.8 Hz), 5.14 (1 H, d, $J = 10.4$ Hz), 5.13 (1 H, d, $J = 16.8$ Hz), 4.36 (1 H, s), 3.77 (3 H, s), 2.14 (1 H, dd, $J = 13.5$ and 7.2 Hz), 1.97 (1 H, dd, $J = 13.5$ and 7.2 Hz), 1.94 (1 H, br s), 0.86 (3 H, s), 0.79 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 158.8 (C); 135.4 (CH), 134.0 (C), 128.7 (2 C, CH), 117.3 (CH_2), 112.9 (2 C, CH), 80.4 (CH), 54.9 (CH_3), 43.5 (CH_2), 38.5 (C), 23.4 (CH_3), 22.3 (CH_3). Mass: m/z 243 (M + Na, 88%), 220 (M^+, 1), 137 (88), 135 (100), 121 (8), 109 (15), 107 (12)]. To a magnetically stirred solution of the secondary alcohol **16** (1.1 g, 5 mmol) in 5 mL of dry CH_2Cl_2 was added a homogeneous mixture of PCC (3.23 g, 15 mmol) and silica gel (3.23 g) and stirred vigorously for 3 h at RT. The reaction mixture was then filtered through a small silica gel column and eluted the column with CH_2Cl_2. Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexane (1 : 40 to 1 : 20) as eluent furnished the ketone **17** (1.06 g, 97%) as oil. IR (neat): ν_{max}/cm^{-1} 1665, 918. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.76 (2 H, d, $J = 8.7$ Hz), 6.83 (2 H, d, $J = 8.7$ Hz), 5.64 (1 H, t of dd, $J = 16.8$, 10.2 and 6.9 Hz), 4.97 (1 H, d, $J = 10.2$ Hz), 4.94 (1 H, d, $J = 16.8$ Hz), 3.81 (3 H, s), 2.47 (2 H, d, $J = 6.9$ Hz), 1.30 (6 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 204.5 (C), 161.9 (C), 134.3 (C, CH), 130.8 (2 C, CH), 130.6 (CH), 118.0 (CH_2), 113.2 (2 C, CH), 55.1 (CH_3), 47.3 (C), 45.5 (CH_2), 26.2 (2 C, CH_3). Mass: m/z 218 (M^+, 4%), 136 (9), 135 (100), 107 (10), 92 (12). HRMS: m/z Calcd. for $C_{14}H_{19}O_2$ (M + 1): 219.1385. Found: 219.1388.

3-(4-Methoxyphenyl)-4,4-dimethylhepta-1,6-dien-3-ol (19): To a magnetically stirred solution of the ketone **17** (1 g, 4.6 mmol) in THF (3 mL) was added a solution of vinylmagnesium bromide [prepared from magnesium (550 mg, 22.9 mmol) and bromoethylene (1.94 mL, 27.5 mmol) in THF (6 mL)] and stirred for 4 h at RT. The reaction was then quenched with aqueous NH_4Cl solution and extracted with ether (4 × 5 mL). The organic layer was washed with water and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexane (1 : 20) as eluent furnished the tertiary alcohol **19** (800 mg, 70%) as oil. IR (neat): ν_{max}/cm^{-1} 3495, 913. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.34 (2 H, d, $J = 8.7$ Hz), 6.78 (2 H, d, $J = 8.7$ Hz), 6.73 (1 H, dd, $J = 17.0$ and 10.8 Hz), 5.77 (1 H, m), 5.31 (1 H, d, $J = 17.0$ Hz), 5.22 (1 H, d, $J = 10.8$ Hz), 5.02–4.80 (2 H, m), 3.77 (3 H, s), 2.10 (1 H, dd, $J = 13.5$ and 6.9 Hz), 2.01 (1 H, dd, $J = 13.5$ and 7.5 Hz), 1.74 (1 H, brs), 0.86 (6 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 158.3 (C), 142.0 (2 C, CH), 136.2 (CH), 128.6 (2 C, CH), 117.3 (CH_2), 113.5 (CH_2), 112.6 (2 C, CH), 80.77 (C), 55.0 (CH_3), 41.7 (CH_2), 41.2 (C), 22.5 (CH_3), 21.9 (CH_3). Mass: m/z 163 ($M^+ - C_6H_{11}$, 100%), 135 (18), 91 (4). HRMS: m/z Calcd. for $C_{16}H_{21}O$ (M–OH): 229.1592. Found: 229.1602.

3-(4-Methoxyphenyl)-4,4-dimethylhepta-2,6-dienal (20): To a magnetically stirred suspension of PCC (8.2 g, 38.0 mmol) and silica gel (8.2 g) in dry CH_2Cl_2 (7 mL) was added a solution of the tertiary alcohol **19** (780 mg, 3.17 mmol) in CH_2Cl_2 (2 mL) and stirred vigorously for 30 h at RT. The reaction mixture was then filtered through a small silica gel column, and the column eluted with more CH_2Cl_2. Evaporation of the solvent and purification of residue on a silica gel column using ethyl acetate-hexane (1 : 20) as eluent furnished the aldehyde **20** (643 mg, 83%) as oil. IR (neat): ν_{max}/cm^{-1} 2747, 1675, 1638, 917. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 9.10 (1 H, d, $J = 7.5$ Hz), 7.04 (2 H, d, $J = 8.4$ Hz), 6.87 (2 H, d, $J = 8.4$ Hz), 6.09 (1 H, d, $J = 7.5$ Hz), 5.73 (1 H, t of dd, $J = 17.4$, 10.2 and 6.9 Hz), 5.08 (1 H, d, $J = 10.2$ Hz), 5.03 (1 H, d, $J = 17.4$ Hz), 3.82 (3 H, s), 2.17 (2 H, d, $J = 6.9$ Hz), 1.12 (6 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 193.7 (CH), 171.7 (C), 159.2 (C), 134.2 (CH), 130.2 (2 C, CH), 128.8 (CH), 128.4 (C), 118.2 (CH_2), 113.2 (2 C, CH), 55.0 (CH_3), 44.8 (CH_2), 40.5 (C), 26.7 (2 C, CH_3). Mass: m/z 244 (M^+, 15%), 203 (100), 201 (40), 188 (96), 187 (34), 175 (35), 173 (35), 161 (22), 160 (22), 159 (25), 135 (75), 133 (25), 121 (50), 115 (20). HRMS: m/z Calcd. for $C_{16}H_{20}O_2Na$ (M + Na): 267.1361. Found: 267.1380.

3-(4-Methoxyphenyl)-4,4-dimethylhepta-2,6-dien-1-ol (18): To an ice cold, magnetically stirred solution of the aldehyde **20** (630 mg, 2.58 mmol) in dry methanol (3 mL) was added $NaBH_4$ (98 mg, 2.58 mmol) and stirred for 2 h at the same temperature. The reaction was then quenched with water

(5 mL) followed by 3 N aqueous HCl (5 mL) and extracted with CH_2Cl_2 (5 × 6 mL). The combined CH_2Cl_2 extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexane (1 : 30 to 1 : 10) as eluent furnished the primary alcohol **18** (450 mg, 70%) as oil. IR (neat): ν_{max}/cm^{-1} 3353, 913. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 6.87 (2 H, d, $J = 9.0$ Hz), 6.78 (2 H, d, $J = 9.0$ Hz), 5.76 (1 H, t of dd, $J = 16.8$, 10.2 and 7.5 Hz), 5.67 (1 H, t, $J = 6.6$ Hz), 5.01 (1 H, d, $J = 10.2$ Hz), 4.96 (1 H, $J = 16.8$ Hz), 3.77 (3 H, s), 3.70 (2 H, d, $J = 6.6$ Hz), 2.04 (2 H, d, $J = 7.5$ Hz), 1.23 (1 H, br s), 1.02 (6 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 158.3 (C), 150.8 (C), 135.6 (CH), 131.2 (C), 130.3 (2 C, CH), 125.8 (CH), 117.1 (CH_2), 113.2 (2 C, CH), 60.7 (CH_2), 54.9 (CH_3), 45.0 (CH_2), 39.0 (C), 27.2 (2 C, CH_3). Mass: m/z 246 (M^+, 25%), 203 (30), 187 (75), 172 (50), 161 (90), 149 (35), 135 (37), 121 (75), 91 (100). HRMS: m/z Calcd. for $C_{16}H_{22}O_2Na$ (M + Na): 269.1517. Found: 269.1519.

Ethyl 3-(4-Methoxyphenyl)-4,4-dimethyl-3-vinylhept-6-enoate (15): A solution of the allyl alcohol **18** (410 mg, 1.66 mmol), triethyl orthoacetate (2.12 mL, 11.66 mmol), and a catalytic amount of propionic acid was placed in a sealed tube and heated to 180°C for 2 days in an oil bath. The reaction mixture was then cooled, diluted with ether (5 mL), washed with 3 N aqueous HCl (5 mL) followed by saturated $NaHCO_3$ solution (5 mL) and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexane (1 : 40) as eluent furnished the ester **15** (250 mg, 47%) as oil. IR (neat): ν_{max}/cm^{-1} 1749, 1717, 913. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.23 (2 H, d, $J = 9.3$ Hz), 6.76 (2 H, d, $J = 9.3$ Hz), 6.52 (1 H, dd, $J = 17.7$ and 11.4 Hz), 5.66 (1 H, t of dd, $J = 17.4$, 9.9 and 7.2 Hz), 5.32 (1 H, d, $J = 11.4$ Hz), 5.10 (1 H, d, $J = 17.4$ Hz), 4.95 (1 H, d, $J = 10.2$ Hz), 4.90 (1 H, d, $J = 17.4$ Hz), 3.89 (2 H, q, $J = 6.9$ Hz), 3.77 (3 H, s), 3.19 and 2.88 (2 H, AB q, $J = 16.5$ Hz), 1.99 and 1.87 (2 H, 2 × dd, $J = 13.2$ and 7.8 Hz), 1.06 (3 H, t, $J = 6.9$ Hz), 0.82 (3 H, s), 0.79 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 170.9 (C), 157.6 (C), 139.4 (CH), 135.7 (CH), 133.0 (C), 130.1 (2 C, CH), 117.5 (CH_2), 116.0 (CH_2), 112.3 (2 C, CH), 59.6 (CH_2), 54.8 (CH_3), 52.2 (C), 42.0 (CH_2), 40.4 (C), 36.7 (CH_2), 22.5 (2 C, CH_3), 14.2 (CH_3). Mass: m/z 234 ($M^+ - 82$, 16%), 233 (43), 187 (7), 160 (24), 159 (100), 145 (34), 115 (8). HRMS: m/z Calcd. for $C_{20}H_{28}O_3Na$ (M + Na): 339.1936. Found: 339.1928.

Ethyl 2-[1-(4-methoxyphenyl)-5,5-dimethylcyclopent-3-en-1-yl]acetate (21): To a magnetically stirred solution of the dieneester **15** (150 mg, 0.7 mmol) in anhydrous CH_2Cl_2 (18 mL) was added a solution of Grubbs' first generation catalyst (28 mg, 5 mol%) in anhydrous CH_2Cl_2 (15 mL) and the reaction mixture was stirred at room temperature for 4 h. Evaporation of

the solvent under reduced pressure and purification of the residue on a silica gel column using ethyl acetate-hexane (1 : 30) as eluent furnished the cyclized compound **21** (134 mg, 98%) as oil. IR (neat): ν_{max}/cm^{-1} 1734. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.13 (2 H, d, $J = 9.0$ Hz), 6.76 (2 H, d, $J = 9.0$ Hz), 6.26 (1 H, d, $J = 6.0$ Hz), 5.85 (1 H, t of d, $J = 6.0$ and 2.4 Hz), 3.87 (2 H, q, $J = 7.2$ Hz), 3.76 (3 H, s), 3.03 and 2.47 (2 H, 2 × d, $J = 15$ Hz), 2.31 (1 H, m of d, $J = 15.6$ Hz), 2.14 (1 H, m of d, $J = 15.6$ and 3.0 Hz), 1.13 (3 H, s), 1.02 (3 H, t, $J = 7.2$ Hz), 0.44 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 171.5 (C), 157.9 (C), 138.5 (CH), 134.4 (C), 129.4 (CH), 127.6 (2 C, CH), 113.2 (2 C, CH), 59.7 (CH_2), 57.7 (C), 54.9 (CH_3), 47.2 (CH_2), 45.8 (C), 41.4 (CH_2), 27.9 (CH_3), 23.6 (CH_3), 14.2 (CH_3). Mass: m/z 288 (M^+, 27%), 207 (24), 201 (100), 199 (28), 185 (19), 171 (51), 159 (23), 149 (23), 128 (12), 121 (23), 115 (17). HRMS: m/z Calcd. for $C_{18}H_{24}O_3Na$ (M + Na): 311.1623. Found: 311.1615.

Ethyl 2-[1-(4-methoxyphenyl)-2,2-dimethylcyclopentyl]acetate (22): To freshly activated 5% Pd-C (7 mg) was added a solution of the ester **21** (108 mg, 0.57 mmol) in ethanol (3 mL). The reaction mixture was stirred for 3 h at RT in an atmosphere of hydrogen, created by evacuative replacement of air (balloon), and then the catalyst was filtered off. Evaporation of the solvent furnished the hydrogenated compound **22** (109 mg, 100%) as oil. IR (neat): ν_{max}/cm^{-1} 1731. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.15 (2 H, d, $J = 8.7$ Hz), 6.74 (2 H, d, $J = 8.7$ Hz), 3.82 (2 H, q, $J = 7.2$ Hz), 3.75 (3 H, s), 2.94 and 2.41 (2 H, 2 × d, $J = 14.1$ Hz), 2.62–2.45 (1 H, m), 2.26–2.12 (1 H, m), 1.90–1.75 (2 H, m), 1.60–1.45 (2 H, m), 1.05 (3 H, s), 0.95 (3 H, t, $J = 7.2$ Hz), 0.58 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 171.7 (C), 157.5 (C), 135.7 (C), 128.2 (2 C, CH), 112.6 (2 C, CH), 59.4 (CH_2), 54.7 (CH_3), 52.5 (C), 45.5 (C), 40.7 (CH_2), 39.1 (CH_2), 34.2 (CH_2), 25.9 (CH_3), 24.4 (CH_3), 20.1 (CH_2), 14.0 (CH_3). Mass: m/z 291 ($M^+ + 1$, 13%), 290 (57), 220 (77), 207 (32), 203 (100), 165 (43), 159 (50), 149 (47), 148 (67), 147 (95), 121 (81). HRMS: m/z Calcd. for $C_{18}H_{26}O_3Na$ (M + Na): 313.1780. Found: 313.1772.

2-[1-(4-Methoxyphenyl)-2,2-dimethylcyclopentyl]ethanol (23): To a cold (0°C), magnetically stirred solution of the ester **22** (104 mg, 0.55 mmol) in 10 mL of dry ether was added $LiAlH_4$ (21 mg, 0.55 mmol) and stirred for 45 min. The reaction mixture was then diluted with ether (5 mL) and carefully quenched with water (2 mL). The organic layer was separated and the aqueous phase was extracted with ether (10 mL). The combined organic phase was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexane (1 : 10 to 1 : 5) as eluent furnished the primary alcohol **23** (84 mg, 94%). IR (neat): ν_{max}/cm^{-1} 3355. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.14 (2 H, d, $J = 8.7$ Hz), 6.75 (2 H, d, $J = 8.7$ Hz), 3.76 (3 H, s),

3.36 (1 H, d of t, $J = 9.9$ and 5.4 Hz), 3.23 (1 H, d of t, $J = 9.9$ and 5.4 Hz), 2.35–2.10 (2 H, m), 1.90–1.65 (5 H, m), 1.60–1.40 (2 H, m), 1.07 (3 H, s), 0.54 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 157.4 (C), 136.3 (C), 128.3 (2 C, CH), 113.0 (2 C, CH), 60.7 (CH_2), 54.9 (CH_3), 52.0 (C), 45.2 (C), 39.3 (CH_2), 37.6 (CH_2), 33.3 (CH_2), 26.2 (CH_3), 24.5 (CH_3), 20.1 (CH_2). Mass: m/z 249 ($M^+ + 1$, 6%), 248 (47), 203 (61), 178 (60), 173 (34), 165 (37), 147 (100), 135 (86), 121 (99), 115 (18), 91 (36). HRMS: m/z Calcd. for $C_{16}H_{24}O_2Na$ (M + Na): 271.1674. Found: 271.1671.

4-(1,2,2-Trimethylcyclopentyl)anisole (14): To a magnetically stirred suspension of PCC (139 mg, 0.65 mmol) and silica gel (139 mg) in dry CH_2Cl_2 (0.5 mL) was added a solution of the primary alcohol **23** (32 mg, 0.13 mmol) in CH_2Cl_2 (0.5 mL) and stirred vigorously for 30 min at RT. The reaction mixture was then filtered through a small silica gel column, and the column eluted with more CH_2Cl_2. Evaporation of the solvent furnished the aldehyde **24** (27 mg, 85%) as oil. [IR (neat): ν_{max}/cm^{-1} 2733, 1719. ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 9.24 (1 H, t, $J = 3.0$ Hz), 7.20 (2 H, d, $J = 8.7$ Hz), 6.80 (2 H, d, $J = 8.7$ Hz), 3.77 (3 H, s), 2.99 (1 H, d, $J = 15.0$ Hz), 2.70–2.45 (1 H, m), 2.36 (1H, dd, $J = 15.0$ and 3.0 Hz), 2.00–1.88 (3 H, m), 1.70–1.50 (2 H, m), 1.06 (3 H, s), 0.57 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 203.0 (CH), 157.8 (C), 134.9 (C), 128.4 (2 C, CH), 113.3 (2 C, CH), 54.8 (CH_3), 51.4 (C), 48.8 (CH_2), 45.3 (C), 39.0 (CH_2), 33.9 (CH_2), 25.8 (CH_3), 24.2 (CH_3), 19.9 (CH_2)]. Wilkinson catalyst (28 mg, 0.03 mmol) was added to a solution of the aldehyde **24** (27 mg), obtained above, in dry benzene and heated at 120–130°C for 2 days in a sealed tube. Evaporation of the solvent under reduced pressure followed by purification on a silica gel column using ethyl acetate-hexane (1 : 30) as eluent furnished the decarbonylated compound **14** (14 mg, 82% based on the recovered aldehyde **24**) as oil. IR (neat): ν_{max}/cm^{-1} 1514. ^{1}H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.20 (2 H; d, $J = 8.4$ Hz), 6.75 (2 H, d, $J = 8.4$ Hz), 3.76 (3 H, s), 2.55–2.35 (1 H, m), 1.80–1.45 (5 H, m), 1.24 (3 H, s), 1.04 (3 H, s), 0.55 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 157.3 (C), 139.3 (C), 127.7 (2 C, CH), 112.7 (2 C, CH), 54.8 (CH_3), 49.9 (C), 44.3 (C), 39.7 (CH_2), 36.9 (CH_2), 26.5 (CH_3), 24.4 (CH_3), 24.3 (CH_3), 19.8 (CH_2). Mass: m/z 218 (M^+, 24%), 161 (50), 149 (30), 148 (100), 147 (28), 135 (65), 91 (23). HRMS: m/z Calcd. for $C_{16}H_{24}O_2Na$ (M + 1): 219.1749. Found: 217.1742. Further elution of the column with CH_2Cl_2 furnished the unreacted aldehyde **24** (8 mg).

5-Methyl-5-(4-methoxyphenyl)hepta-1,6-dien-3-ol (25): To a magnetically stirred solution of the aldehyde **26** (360 mg, 1.764 mmol) in THF (3 mL) was added vinylmagnesium bromide [prepared from magnesium (210 mg, 8.82 mmol) and bromoethylene (0.746 mL, 10.6 mmol) in THF (5 mL)] and

stirred for 4 h at room temperature. The reaction was then quenched with aqueous NH_4Cl solution and extracted with ether (5 × 6 mL). The organic layer was washed with water and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate-hexane (1 : 10) as eluent furnished a 1 : 1 diastereomeric mixture of the dienol **25** (315 mg, 77%) as oil. IR (neat): ν_{max}/cm^{-1} 3435, 917. ^1H NMR (300 MHz, $CDCl_3$+ CCl_4, 1 : 1 diastereomeric mixture): δ 7.21 and 7.20 (2 H, d, $J = 8.7$ Hz), 6.79 and 6.78 (2 H, d, $J = 8.7$ Hz), 6.10 (dd, $J = 17.1$ and 10.8 Hz) and 6.05 (dd, $J = 17.4$ and 10.8 Hz) [1 H], 5.85–5.60 (1 H, m), 5.15–4.90 (4 H, m), 4.20–4.00 (1 H, m), 3.75 (3 H, s), 2.04–1.87 (2 H, m), 1.46 & 1.43 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$, 1 : 1 diastereomeric mixture): δ 157.8 (C), 147.7 and 147.1 (CH), 142.1 and 142.0 (CH), 138.7 (C), 127.7 and 127.6 (2 C, CH), 113.6 and 113.5 (2 C, CH), 113.5 and 113.4 (CH_2), 111.9 and 111.7 (CH_2), 70.3 (CH), 55.0 (CH_3), 48.3 (CH_2), 43.2 (C), 25.9 and 25.7 (CH_3). Mass: m/z 232 (M^+, 20%), 162 (14), 161 (100), 146 (10), 121 (10), 91 (17). HRMS: m/z Calcd. for $C_{15}H_{20}O_2Na$ (M + Na): 255.1361. Found 255.1374.

4-Methyl-4-(4-methoxyphenyl)cyclopent-2-en-1-ol (27): To a magnetically stirred solution of the dienol **25** (221 mg, 0.952 mmol) in anhydrous CH_2Cl_2 (25 mL) was added a solution of Grubbs' first generation catalyst (39 mg, 5 mol%) in anhydrous CH_2Cl_2 (20 mL) and the reaction mixture was stirred at room temperature for 6 h. Evaporation of the solvent under reduced pressure and purification of the residue over a silica gel column using ethyl acetate-hexane (1 : 5) as eluent furnished the cyclized compound **27** (189 mg, 97%) as oil. IR (neat): ν_{max}/cm^{-1} 3362. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$, 1 : 1 diastereomeric mixture): δ 7.19 and 7.11 (2 H, d, $J = 8.7$ Hz), 6.78 and 6.50 (2 H, d, $J = 8.7$ Hz), 6.00–5.93 (1 H, m), 5.84–5.78 (1 H, m), 4.95–4.80 (1 H, m), 3.75 (3 H, s), 2.46–2.30 (1 H, m), 2.15 (1 H, s), 1.90–1.75 (1 H, m), 1.51 and 1.38 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 157.6 (C), 143.2 and 142.8 (CH), 141.4 and 140.8 (C), 132.1 (CH), 126.7 and 126.5 (2 C, CH), 113.6 and 113.5 (2 C, CH), 77.2 and 77.1 (CH), 55.0 (CH_3), 51.5 and 51.0 (CH_2), 51.6 and 50.9 (C), 30.0 and 28.4 (CH_3). Mass: m/z 204 (M^+, 22%), 190 (13), 189 (100), 174 (19), 161 (27), 121 (17), 115 (15), 91 (15). HRMS: m/z Calcd. for $C_{13}H_{16}O_2Na$ (M + Na): 227.1048. Found: 227.1052.

4-Methyl-4-(4-methoxyphenyl)cyclopent-2-enone (28): To a magnetically stirred solution of the secondary alcohol **27** (186 mg, 0.911 mmol) in 3 mL of dry CH_2Cl_2 was added a homogeneous mixture of PCC (589 mg, 2.735 mmol) and silica gel (589 mg) and stirred vigorously for 3 h at RT. The reaction mixture was then filtered through a small silica gel column and eluted the column with an excess of CH_2Cl_2. Evaporation of the solvent and purification of the residue over a silica gel column using ethyl

acetate-hexane (1 : 40 to 1 : 20) as eluent furnished the cyclopentenone **28** (177 mg, 96%) as oil. IR (neat): ν_{max}/cm^{-1} 1714. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.58 (1 H, d, $J = 5.4$ Hz), 7.13 (2 H, d, $J = 8.7$ Hz), 6.80 (2 H, d, $J = 8.7$ Hz), 6.14 (1 H, d, $J = 5.4$ Hz), 3.76 (3 H, s), 2.52 (2 H, AB q, $J = 18.6$ Hz), 1.60 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 208.7 (C), 170.9 (CH), 158.2 (C), 137.1 (C), 131.3 (CH), 126.6 (2 C, CH), 114.0 (2 C, CH), 55.0 (CH_3), 51.8 (CH_2), 47.4 (C), 27.2 (CH_3). Mass: m/z 202 (M^+, 30%), 188 (10), 187 (100), 159 (10), 144 (14), 128 (7), 115 (12). HRMS: m/z Calcd. for $C_{13}H_{15}O_2$ (M + 1): 203.1072. Found 203.1071.

4-(4-Methoxyphenyl)-4,5,5-trimethylcyclopent-2-enone (29): To a magnetically stirred suspension of NaH (149 mg, 60% dispersion in oil, 3.71 mmol, washed with dry hexane) in THF (1 mL) was added a solution of ketone **28** (150 mg, 0.74 mmol) in THF (1.5 mL) and DMF (0.5 mL), and stirred for 40 min at RT. To the reaction mixture was then added iodomethane (0.23 mL, 3.712 mmol) and stirred for 12 h at RT. It was then quenched with water (3 mL) and extracted with ether (4 × 5 mL). The combined ether extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column by using ethyl acetate-hexane (1 : 20) as eluent furnished the dimethylated ketone **29** (136 mg, 80%) as oil. M.p. 64–66°C. IR (neat): ν_{max}/cm^{-1} 1709. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.67 (1 H, d, $J = 6.0$ Hz), 7.04 (2 H, d, $J = 8.4$ Hz), 6.80 (2 H, d, $J = 8.4$ Hz), 6.17 (1 H, d, $J = 6.0$ Hz), 3.77 (3 H, s), 1.43 (3 H, s), 1.15 (3 H, s), 0.50 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 213.6 (C), 168.1 (CH), 158.3 (C), 135.3 (C), 129.3 (CH), 127.7 (2 C, CH), 113.6 (2 C, CH), 55.0 (CH_3), 54.1 (C), 51.6 (C), 26.3 (CH_3), 25.9 (CH_3), 20.1 (CH_3). Mass: m/z 230 (M^+, 30%), 216 (10), 215 (100), 172 (19), 115 (8), 91 (4). HRMS: m/z Calcd. for $C_{15}H_{19}O_2$ (M + 1): 231.1385. Found: 231.1397.

3-(4-Methoxyphenyl)-2,2,3-trimethylcyclopentanone (30): To activated 5% Pd-C (25 mg) was added a solution the enone **29** (95 mg, 0.413 mmol) in ethanol (3 mL). The reaction mixture was stirred for 3 h at RT in an atmosphere of hydrogen, created by evacuative replacement of air (balloon) and then the catalyst was filtered off. Evaporation of the solvent furnished the saturated ketone **30** (95 mg, 99%). M.p. 67–69°C. IR (neat): ν_{max}/cm^{-1} 1737. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.25 (2 H, d, $J = 8.7$ Hz), 6.82 (2 H, d, $J = 8.7$ Hz), 3.78 (3 H, s), 2.70–2.30 (3 H, m), 1.88 (1 H, ddd, $J = 12.3$, 9.0 and 2.0 Hz), 1.23 (3 H, s), 1.13 (3 H, s), 0.59 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 221.2 (C), 158.0 (C), 136.9 (C), 127.4 (2 C, CH), 113.5 (2 C, CH), 54.9 (CH_3), 53.2 (C), 48.0 (C), 33.6 (CH_2), 29.9 (CH_2), 25.5 (CH_3), 22.2 (CH_3), 18.5 (CH_3). Mass: m/z 233 ($M^+ + 1$, 5%), 232 (36), 217 (12), 161 (100), 148 (42),

91 (18). HRMS: m/z Calcd. for $C_{15}H_{20}O_2Na$ (M + Na): 255.1361. Found 255.1377.

7-(4-Methoxyphenyl)-6,6,7-trimethyl-1,4-dithiaspiro[4.4]nonane (31): A solution of the ketone **30** (77 mg, 0.331 mmol), ethanedithiol (0.195 mL, 2.323 mmol), and $BF_3 . OEt_2$ (0.09 mL, 0.774 mmol) in dry benzene (1 mL) was magnetically stirred at 0°C to RT for 12 h. The reaction was then quenched with aqueous $NaHCO_3$ solution and extracted with ether. The ether extract was washed with 5% aqueous NaOH solution and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate-hexane (1 : 50) as eluent furnished the thioketal **31** (95 mg, 93%) as oil. IR (neat): ν_{max}/cm^{-1} 1608, 1578, 1512. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 7.21 (2 H, d, $J = 8.7$ Hz), 6.76 (2 H, d, $J = 8.7$ Hz), 3.78 (3 H, s), 3.35–3.20 (4 H, m), 2.70–2.45 (3 H, m), 1.80–1.70 (1 H, m), 1.48 (3 H, s), 1.19 (3 H, s), 0.67 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 157.5 (C), 139.8 (C), 127.8 (2 C, CH), 113.0 (2 C, CH), 82.0 (C), 55.0 (CH_3), 52.0 (C), 49.9 (C), 45.6 (CH_2), 40.1 (CH_2), 38.0 (CH_2), 36.9 (CH_2), 28.2 (CH_3), 28.1 (CH_3), 21.3 (CH_3). Mass: m/z 308 (M^+, 2%), 233 (2), 199 (3), 190 (7), 177 (9), 175 (8), 149 (11), 148 (100), 133 (10), 121 (6). HRMS: m/z Calcd. for $C_{17}H_{24}OS_2Na$ (M + Na): 331.1166. Found 331.1176.

4-(1,1,2-Trimethylcyclopentyl)anisole (14): To a magnetically stirred solution of the thioketal **31** (55 mg, 0.178 mmol) in dry ethanol (3 mL) was added an excess of Raney nickel and refluxed for 2 h. The reaction mixture was cooled and filtered through a short silica gel column to remove the catalyst. Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate-hexane (1 : 50) as eluent furnished a mixture of the cyclopentene and cyclopentane (31 mg). To activated 5% Pd-C (15 mg) was added a solution of the mixture of **14** and **32** (31 mg) in ethanol (3 mL). The reaction mixture was stirred for 3 h at RT in an atmosphere of hydrogen, created by evacuative replacement of air (balloon), and then the catalyst was filtered off. Evaporation of the solvent furnished the saturated compound **14** (31 mg, 80%) as oil, which was identified by comparison of the spectral data with that of the sample obtained earlier.

4-(1,2,2-Trimethylcyclopentyl)cyclohex-3-enone (34): Lithium (350 mg, 50 mmol) was slowly added to a magnetically stirred solution of the norcuparane **14** (179 mg, 0.82 mmol) in dry THF (6 mL) and freshly distilled (over sodamide) liquid ammonia (100 mL) and absolute ethanol (6 mL). The dark colored solution was stirred for 2.5 h and then quenched with solid NH_4Cl. Ammonia was slowly evaporated and the residue was taken in water and extracted with ether (3 × 10 mL). The organic layer was washed with saturated aq. NaCl solution and dried (Na_2SO_4). Evaporation

of the solvent furnished the diene **33** (175 mg), which was taken in THF (3 mL) and 10% aq. H_2SO_4 (3 mL) was added. The mixture was stirred for 50 min at RT. It was then taken in ether (20 mL), washed with saturated aq. $NaHCO_3$ solution and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate-hexane (1 : 9) as eluent furnished the enone **34** (147 mg, 90% from **14**) as oil. IR (neat): ν_{max}/cm^{-1} 1723. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 5.50 (1 H, t, $J = 3.6$ Hz), 2.82 (2 H, d, $J = 3.6$ Hz), 2.57–2.20 (4 H, m), 2.25–2.00 (1 H, m), 1.70–1.35 (5 H, m), 1.00 (6 H, s), 0.78 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 209.7 (C), 145.3 (C), 117.8 (CH), 51.5 (C), 43.7 (C), 40.5 (CH_2), 39.9 (CH_2), 38.8 (CH_2), 36.9 (CH_2), 26.8 (CH_3), 26.4 (CH_2), 25.2 (CH_3), 22.2 (CH_3), 19.4 (CH_2). Mass: m/z 206 (M^+, 18%), 136 (45), 123 (30), 109 (28), 107 (32), 93 (85), 91 (43), 69 (100). HRMS: m/z Calcd. for $C_{14}H_{22}ONa$ (M + Na): 229.1568. Found 229.1565.

4-(1,2,2-Trimethylcyclopentyl)cyclohex-2-enone (13): $RhCl_3 . 3H_2O$ (5 mg, 0.019 mmol) was added to a solution of the enone **34** (50 mg, 0.24 mmol) in absolute ethanol (1.6 mL) and heated at 100–110°C in a sealed tube for 3 h. Evaporation of the solvent under reduced pressure and purification of the residue on a silica gel column using ethyl acetate-hexane (1 : 30) as eluent furnished a 3 : 2 diastereomeric mixture of the enone **13** (45 mg, 90%) as oil. IR (neat): ν_{max}/cm^{-1} 1685. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$, 3 : 2 diastereomeric mixture): δ 6.82 (d, $J = 10.2$ Hz) and 7.07 (d, $J = 10.5$ Hz) [1 H], 6.00–5.90 (1 H, m), 2.62–2.10 (4 H, m), 1.90–1.35 (7 H, m), 1.01 and 1.12 (3 H, s), 1.01 and 0.99 (3 H, s), 0.80 and 0.83 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$, 3 : 2 diastereomeric mixture): δ 198.6 and 198.4 (C), 154.8 and 152.8 (CH), 130.2 and 130.1 (CH), 47.8 and 47.5 (C), 45.2 and 43.1 (CH), 43.9 and 44.1 (C), 42.3 and 41.9 (CH_2), 39.7 and 38.7 (CH_2), 38.4 and 37.6 (CH_2), 26.4 and 25.3 (CH_2), 25.9 and 25.8 (CH_3), 25.2 and 24.6 (CH_3), 19.1 and 18.9 (CH_2), 18.4 and 18.3 (CH_3). Mass: m/z 207 ($M^+ + 1$, 1%), 136 (4), 123 (17), 122 (15), 111 (63), 96 (68). HRMS: m/z Calcd. for $C_{14}H_{22}ONa$ (M + Na): 229.1581. Found: 229.1568.

Infuscol-A (1) and (+)-Cuprenenol (5): To a cold (0°C), magnetically stirred solution of methylmagnesium iodide (3.398 mmol), prepared from magnesium (82 mg, 3.4 mmol) and iodomethane (0.21 mL, 3.4 mmol) and a catalytic amount of iodine in 3 mL of dry ether, was added a solution of the diastereomeric mixture of the enone **13** (70 mg, 0.34 mmol) in dry ether (2 mL). The reaction mixture was slowly warmed up to RT and stirred for 0.5 h. It was then poured into saturated aq. NH_4Cl solution and extracted with ether (3 × 3 mL). The ether extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a

silica gel column using ethyl acetate-hexane (1 : 10) as eluent furnished first a mixture of infuscol B (**2**) and neocuprenenol (**6**) (5 mg, 7%). IR (neat): ν_{max}/cm^{-1} 3371. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ Peaks due to infuscol B (**2**): 5.62 (2 H, m), 2.10 (1 H, m), 1.83–1.30 (11 H, m), 1.23 (3 H, s), 1.01 (3 H, s), 0.96 (3 H, s), 0.78 (3 H, s). Peaks due to neocuprenenol (**6**): 5.87 (1 H, m of d, $J = 10.2$ Hz), 5.62 (1 H, m), 2.13 (1 H, m), 1.83–1.30 (11 H, m), 1.24 (3 H, s), 1.08 (3 H, s), 0.95 (3 H, s), 0.80 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ Peaks due to infuscol B (**2**): 134.2 (CH), 134.0 (CH), 66.4 (C), 47.6 (C), 44.4 (CH), 44.1 (C), 42.4 (CH_2), 39.6 (CH_2), 37.4 (CH_2), 29.5 (CH_3), 25.8 (CH_3), 24.6 (CH_3), 21.1 (CH_2), 19.3 (CH_2), 17.9 (CH_3). Peaks due to neocuprenenol (**6**): 134.1 (CH), 132.5 (CH), 66.8 (C), 47.3 (C), 44.0 (C), 42.6 (CH), 42.2 (CH_2), 38.8 (CH_2), 38.0 (CH_2), 29.9 (CH_3), 26.2 (CH_3), 25.3 (CH_3), 22.0 (CH_2), 19.2 (CH_2), 17.7 (CH_3). Further elution of the column with the same solvent furnished a mixture of infuscol A (**1**) and cuprenenol (**5**) (60 mg, 80%) as oil. IR (neat): ν_{max}/cm^{-1} 3364. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ Peaks due to infuscol A (**1**): 5.63–5.53 (2 H, m), 2.32–2.18 (1 H, m), 1.87–1.31 (11 H, m), 1.23 (3 H, s), 0.98 (3 H, s), 0.95 (3 H, s), 0.75 (3 H, s). Peaks due to cuprenenol (**5**): 5.70 (1 H, t of d, $J = 10.5$ and 1.2 Hz), 5.56 (1 H, t of d, $J = 10.5$ and 2.4 Hz), 2.32–2.18 (1 H, m), 1.87–1.31 (11 H, m), 1.23 (3 H, s), 1.05 (3 H, s), 0.95 (3 H, s), 0.76 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ Peaks due to infuscol A (**1**): 135.8 (CH), 131.2 (CH), 69.5 (C), 47.7 (C), 44.1 (C), 44.0 (CH), 42.2 (CH_2), 39.6 (CH_2), 38.7 (CH_2), 28.2 (CH_2), 25.2 (CH_3), 24.6 (CH_3), 23.8 (CH_2), 19.3 (CH_3), 17.6 (CH_3). Peaks due to cuprenenol (**5**): 135.8 (CH), 129.7 (CH), 69.5 (C), 47.6 (C), 44.1 (C), 42.3 (2 C, CH_2 and CH), 39.4 (CH_2), 39.0 (CH_2), 28.4 (CH_3), 26.1 (CH_3), 25.8 (CH_3), 24.6 (CH_2), 19.2 (CH_2), 17.8 (CH_3). Mass: m/z 207 ($M^+ - 16$, 3%), 137 (5), 123 (5), 119 (7), 111 (57), 94 (34), 69 (100).

***trans*-1-Methyl-4-(1,2,2-trimethylcyclopentyl)cyclohexanol (35):** To activated 5% Pd-C (10 mg) was added a solution of a mixture of infuscol A (**1**) and cuprenenol (**5**) (6 mg, 0.027 mmol) in ethanol (3 mL). The reaction mixture was stirred for 6 h at RT in an atmosphere of hydrogen, created by evacuative replacement of air (balloon) and then the catalyst was filtered off. Evaporation of the solvent furnished the saturated compound **35** (6 mg, 99%) as oil, which was solidified on standing. M.p. 83–85°C. IR (neat): ν_{max}/cm^{-1} 3370. ^1H NMR (300 MHz, $CDCl_3 + CCl_4$): δ 1.85–1.10 (16 H, m), 1.18 (3 H, s), 0.99 (3 H, s), 0.92 (3 H, s), 0.79 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3 + CCl_4$): δ 70.4 (C), 47.3 (C), 44.9 (CH), 44.0 (C), 42.3 (CH_2), 41.2 (CH_2), 40.7 (CH_2), 40.0 (CH_2), 26.8 (CH_2), 25.6 (CH_3), 25.4 (2 C, CH_2 and CH_3), 24.8 (CH_3), 19.0 (CH_2), 16.9 (CH_3). Mass: m/z 206 ($M^+ - H_2O$, 25%), 163 (13), 149 (14), 148 (13), 135 (31), 122 (30), 121 (75), 109 (28), 108 (100), 107 (31), 95 (66), 93 (43).

ACKNOWLEDGMENTS

We thank Professors Y. Asakawa and F. Nagashima for providing the copies of the NMR spectra of natural infuscols A and B, cuprenenol, and neocuprenenol; and C.S.I.R., New Delhi for the award of a research fellowship to G.S.

REFERENCES

1. Asakawa, Y. *Progress in the Chemistry of Organic Natural Products*; Herz, W., Kirby, G.W., Moore, R.E., Steglich, W., Tamm, Ch., Eds.; Springer-Verlag: Wien, New York, 1995; Vol. 65.
2. (a) Nagashima, F.; Suzuki, M.; Takaoka, S.; Asakawa, Y. Sesqui- and diterpenoids from the Japanese liverwort *Jungermannia infusca*. J. Nat. Prod. **2001**, *64*, 1309–1317. For the first report on the isolation of cuprenenol from *Jungermannia Rosulans*, see: (b) Matsuo, A.; Terada, I.; Nakayama, M.; Hayashi, S. Cuprenenol and rosulantol, new cuparane class sesquiterpene alcohols from the liverwort *Jungermannia rosulans*. Tetrahedron Lett. **1977**, 3821–3824. For the isolation of cuprenenol and neocuprenenols from *Jungermannia infusca* collected at different locations, see: (c) Nagashima, F.; Tanaka, H.; Takaoka, S.; Asakawa, Y. Sesqui- and diterpenoids from the Japanese liverwort *Jungermannia hattoriana*. Phytochemistry **1997**, *45*, 353–363; (d) Nagashima, F.; Suzuki, M.; Takaoka, S.; Asakawa, Y. New sesqui- and diterpenoids from the Japanese liverwort *Jungermannia infusca* (Mitt) Steph. Chem. Pharm. Bull. **1998**, *46*, 1184–1185; (e) Nagashima, F.; Suzuki, M.; Takaoka, S.; Asakawa, Y. New acorane- and cuparane type sesqui and new Labdane and secolabdane type diterpenoids from the Japanese liverwort *Jungermannia infusca* (Mitt.) Steph. Tetrahedron **1999**, *55*, 9117–9132.
3. To the best of our knowledge, there is no report in the literature on the synthesis of these nonaromatic cuparenoids infuscols A-D, cuprenenol, and neocuprenenol.
4. Johnson, W.S.; Werthemann, L.; Bartlett, W.R.; Brocksom, T.J.; Li, T.-t.; Faulkner, D.J.; Petersen, M.R. A simple stereoselective version of the Claisen rearrangement leading to trans trisubstituted olefinic bonds. Synthesis of squalene. J. Am. Chem. Soc. **1970**, *92*, 741–743.
5. (a) Grubbs, R.H.; Chang, S. Recent advances in olefin metathesis and its applications in organic synthesis. Tetrahedron **1998**, *54*, 4413–4450; (b) Fürstner, A. Olefin metathesis and beyond. Angew. Chem., Int. Ed. **2000**, *39*, 3013–3043; (c) Trnka, T.M.; Grubbs, R.H. The development

of L2X2Ru=CHR olefin metathesis catalysts: An organometallic success story. Acc. Chem. Res. **2001**, *34*, 18–29.
6. Srikrishna, A.; Reddy, T.J.; Kumar, P.P.; Vijaykumar, D. A methodology for spirocyclopentannulation. Stereoselective total synthesis of tochuinyl acetate and dihydrotochuinyl acetate. Synlett **1996**, 67–68.
7. Grieco, P.A.; Nishizawa, M.; Marinovic, N.; Ehmann, W.J. Remote double bond migration via rhodium catalysis: A novel enone transposition. J. Am. Chem. Soc. **1976**, *98*, 7102–7104.

Received in India June 14, 2004