An Enantiospecific Approach to Tricyclic Sesquiterpenes Mayurone and Thujopsenes[1]

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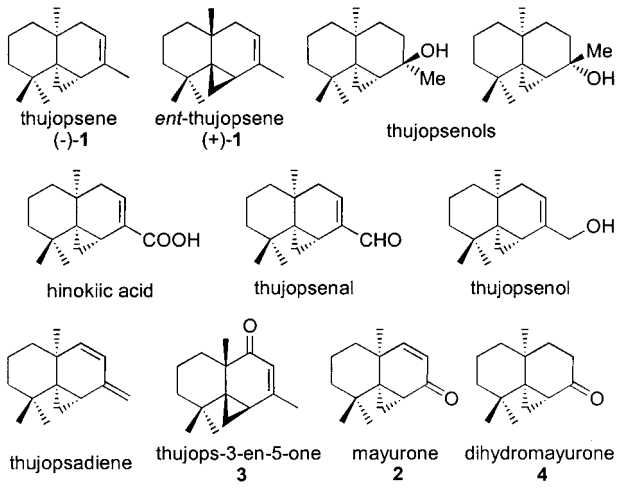
An enantiospecific approach to mayurone and thujopsenes, sesquiterpenes containing three contiguous quaternary carbon atoms, starting from (*R*)-carvone (**8**), is described. (*S*)-3,4,4-Trimethylcarvone (**7**), obtained from (*R*)-carvone, was transformed into the bicyclo[2.2.2]octanone **13** via regioselective intramolecular alkylation of the allyl bromide **11**. Regioselective ozonolysis and Criegee fragmentation of the bicyclic ketone **13** furnished the keto ester **14**. Reductive deoxygenation followed by one-carbon homologation transformed the keto ester **19** into the ester **6**. Intramolecular cyclopropanation of the diazo ketone **25**, derived from the acid **5**, furnished (−)-dihydromayurone (**4**), thus constituting a formal enantiospecific synthesis of mayurone and thujopsenes.

The tricyclic sesquiterpene thujopsene [(−)-**1**] was originally isolated from the wood oil of the Japanese Hiba tree[2] and has since been found to occur widely in genera of natural order *Cupressaceae*. The stereostructure of thujopsene **1** was established by Norin and co-workers,[3] which was soon confirmed by the total synthesis by Dauben and Ashcraft.[4a] In 1965, the research groups of Sukh Dev and Ito reported the isolation of the norketone mayurone (**2**) from *Mayur pankhi* and *Thujopsis dolabrata*, respectively.[5] Subsequently, isolation of various oxidized forms of thujopsenes (Chart 1) has been reported in the literature.[6] In 1985, Matsuo and co-workers reported the isolation of *ent*-thujopsene [(+)-**1**] from the liverwort *Marchantia polymorpha* along with thujopsenone **3**.[7] The presence of a tricyclo[5.4.0.0^{1,3}]undecane framework incorporating a cyclopropane ring and, in particular, the presence of three contiguous quaternary carbon atoms made mayurone and thujopsenes interesting and challenging synthetic targets. In addition to five approaches to racemic thujopsene reported earlier,[4] two

Chart 1



enantioselective approaches[8] to thujopsene via dihydromayurone **4** have been reported by the research groups of Johnson and Lee. Johnson and Barbachyn[8a] have employed a β-hydroxysulfoximine-directed Simmons−Smith reaction for the generation of both the enantiomers of thujopsenes, whereas Lee et al.[8b] employed the Sharpless epoxidation in their enantioselective synthesis of thujopsene. In continuation of our interest in the synthesis of sesquiterpenoids containing multiple contiguous quaternary carbon atoms, both in racemic manner and in enantiospecific manner,[9,10] we have developed an enantiospecific methodology for these terpenoids. Since thujopsene was converted[3,7,11] into mayurone and various oxidized forms of thujopsenes (such as thujopsenal, hinokiic acid, thujops-3-en-5-one, etc.), and mayurone was

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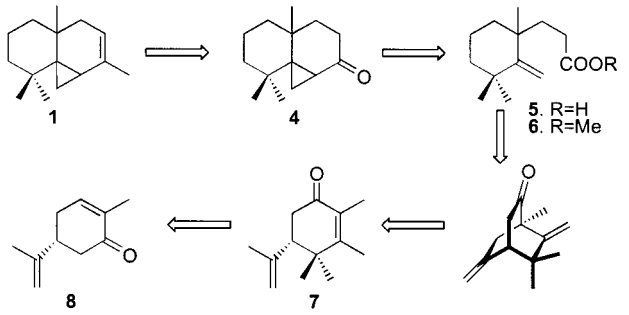
Scheme 1

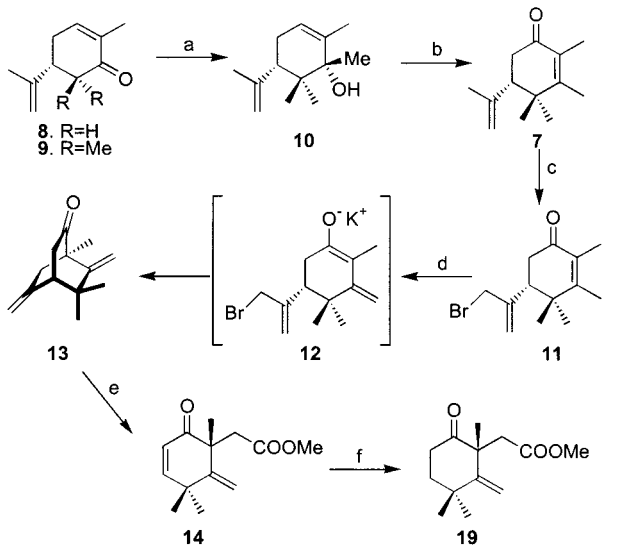


converted into thujopsadiene, attention was focused on the enantiospecific synthesis of thujopsene **1** via dihydromayurone **4.**

The retrosynthetic analysis of thujopsene is depicted in Scheme 1. Since Lee and co-workers have already reported the synthesis of dihydromayurone **4** via the intramolecular cyclopropanation of the diazoketone derived from the acid **5** in their enantioselective synthesis of thujopsene,[8b] the optically active ester **6** was considered as the target molecule. It was anticipated that alkylation with an equivalent of a propionic acid side chain at the α-position, followed by reductive deoxygenation of the ketone moiety and degradation of the isopropenyl group, would convert the cyclohexenone **7** into the ester **6**. The readily available monoterpene (*R*)-carvone (**8**) was considered as a suitable starting material for the generation of the cyclohexenone **7**.

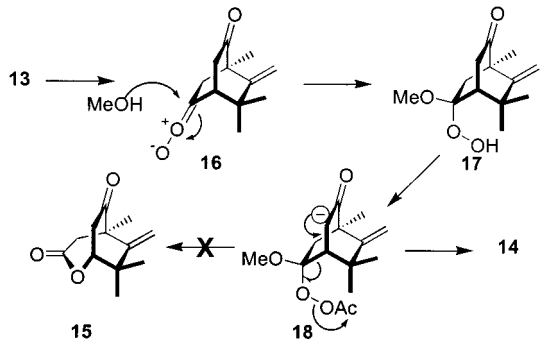
The synthetic sequence starting from (*S*)-6,6-dimethylcarvone (**9**), obtained from **8** by sequential kinetic alkylation using LDA and methyl iodide,[12] is depicted in Scheme 2. For the conversion of dimethylcarvone **9** into (*S*)-3,4,4-trimethylcarvone (**7**), an alkylative 1,3-enone transposition methodology was employed.[13] Thus, regioselective 1,2-addition of methyllithium to dimethylcarvone **9** followed by oxidation of the resulting allylic tertiary alcohol **10** with a mixture of pyridinium chlorochromate (PCC) and silica gel in methylene chloride generated the trimethylcarvone **7**, in 70% yield. Instead of the degradation of the isopropenyl group and introduction of a side chain at C-2 position, stereospecific translocation of the isopropenyl group from C-5 to the C-2 position as the acetate side chain was envisaged. An intramolecular alkylation strategy[14] was adopted for joining the isopropenyl carbon and the C-2 carbon of trimethylcarvone **7**. Thus, reaction of the trimethylcarvone **7** with *N*-bromosuccinimide (NBS) in methanol−methylene chloride medium furnished the allyl bromide **11**, in 90% yield, in a highly regioselective manner.[15]

Scheme 2[a]



[a] Reagents: (a) MeLi; (b) PCC, silica gel; (c) NBS; (d) K^+ $^tBuO^-$; (e) O_3; Ac_2O, NEt_3, DMAP; (f) H_2, 5% Pd/C.

Scheme 3



Generation of the thermodynamic dienolate **12** of the allyl bromide **11** with potassium *tert*-butoxide in *tert*-butyl alcohol and THF induced the regioselective intramolecular alkylation to furnish the bicyclo[2.2.2]octanone **13**, thus forming the second quaternary carbon atom. The steric hindrance of the C-6 *exo*-methylene group was exploited for the regioselective cleavage of the C-8 *exo*-methylene group in the bicyclo[2.2.2]octanone **13**. For the selective oxidative cleavage of the C-4−C-8 bond in the bicyclic ketone **13**, a Criegee rearrangement[16] was explored. Thus, controlled ozonolysis of the bicyclic ketone **13** in a mixture of methanol−methylene chloride followed by treatment of the intermediate methoxy hydroperoxide with a mixture of acetic anhydride, triethylamine, and a catalytic amount of 4-*N*,*N*-(dimethylamino)pyridine (DMAP) in refluxing benzene furnished the ketoester **14**, via the Criegee fragmentation, instead of the expected lactone **15**. The structure of the enone **14** was established from its spectral data. Facile formation of the ester **14** can be rationalized as depicted in Scheme 3. Stereoselective addition of methanol to the carbonyl oxide **16**, formed in the ozonolysis reaction, from the less hindered face of the molecule furnishes the methoxy hydroperoxide **17**, which on acetylation generates the acetate **18**. The

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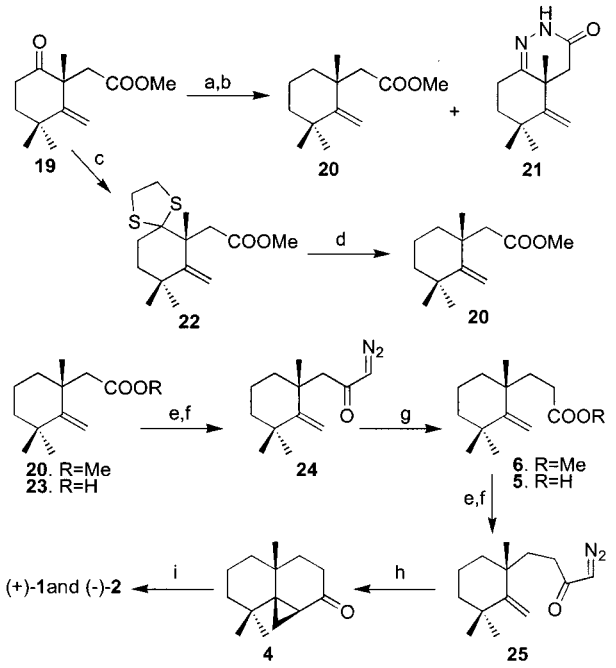
Scheme 4[a]



[a] Reagents: (a) NH_2NH_2, $(CH_2OH)_2$, digol; (b) CH_2N_2; (c) $(CH_2SH)_2$, $BF_3{\cdot}Et_2O$; (d) Raney Ni; (e) NaOH; (f) $(COCl)_2$, CH_2N_2; (g) *hν*, MeOH; (h) Cu, $CuSO_4$; or $Rh_2(OAc)_4$; (i) refs 8 and 7.

orientation of the acetate group in the methoxy acetate **18** was ideally suited for the facile elimination reaction under the basic conditions of the reaction to furnish the ester **14** via the cleavage of the C-4−C-8 bond, instead of generating **15** via the Criegee rearrangement.

Controlled hydrogenation of the enone **14** using 5% Pd/C as the catalyst furnished the ketoester **19**. It was readily identified that deoxygenation of the ketoester **19** followed by homologation of the ester generates the requisite precursor **6** for thujopsenes and mayurones. Accordingly, Wolff−Kishner reduction of the ketoester **19** was explored first. However, Wolff−Kishner reduction of the ketoester **19** using Huang−Minlon modified conditions followed by esterification with diazomethane furnished the deoxygenated ester **20**, in 25% yield, along with a substantial amount (>40%) of the hexahydrocinnolinone **21**, obviously formed via initial conversion of the ester to acid hydrazide followed by intramolecular condensation with the ketone moiety (Scheme 4). Hence, a two-step methodology via the corresponding thioketal was employed. Thus, reaction of the ketoester **19** with ethanedithiol and boron trifluoride etherate in benzene furnished the thioketal **22**, which on desulfurization with Raney nickel in refluxing ethanol furnished the ester **20**. For the homologation of the ester **20**, a photochemical Wolff rearrangement was employed, as in the racemic synthesis by Smith et al.[4e] Thus, hydrolysis of the ester group in **20** furnished the acid **23**. Reaction of the acid **23** with oxalyl chloride followed by treatment of the resultant acid chloride with an excess of ethereal diazomethane furnished the diazo ketone **24**. Irradiation of the diazo ketone **24** in methanol with a medium-pressure mercury vapor lamp in a Pyrex vessel furnished the homologated ester **6**. Hydrolysis of the ester group in **6** furnished the acid **5**, which was converted into the diazo ketone **25** via the corresponding acid chloride. Reaction of the diazo ketone **25** either with copper and anhydrous copper sulfate in refluxing cyclohexane or with rhodium acetate in benzene at room temperature furnished (−)-dihydromayurone (**4**). Mp: 105−106 °C (lit.[5] mp: 106−108 °C), which exhibited IR and ^{1}H and ^{13}C NMR spectral data identical to those reported by Lee et al.[8b] Since dihydromayurone **4** has been converted into thujopsene and mayurone, which were converted into other thujopsenes, the present sequence constitutes an enantiospecific formal synthesis of mayurone and thujopsenes.

In conclusion, we have developed an enantiospecific approach to mayurone and thujopsenes, the tricyclic sesquiterpenes containing three contiguous quaternary carbon atoms, starting from the readily available monoterpene (*R*)-carvone via (*R*)-6,6-dimethylcarvone and (*S*)-3,4,4-trimethylcarvones. An intramolecular alkylation reaction followed by a facile Criegee fragmentation reaction sequence was exploited for the generation of the key chiral center in the molecule. An intramolecular cyclopropanation of a diazo ketone generated the requisite cyclopropane moiety as well as the third quaternary carbon atom.

Experimental Section

All the IR spectra were recorded as thin films, and the ^{1}H (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in a 1:1 mixture of $CDCl_3$ and CCl_4. In the ^{13}C NMR spectra, the nature of the carbons (C, CH, CH_2, or CH_3) was determined on the basis of the DEPT-135 experiment, and is given in parentheses. $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. Silica gel (100−200 mesh) was used for column chromatography. All the solvent extracts were washed with brine, dried over anhydrous Na_2SO_4, and concentrated on a rotavap under reduced pressure.

(+)-(5*S*)-5-Isopropenyl-2,3,4,4-tetramethylcyclohex-2-enone (7). To a cold (0 °C), magnetically stirred solution of 6,6-dimethylcarvone[12] **9** (1 g, 5.62 mmol) in ether (2 mL) was slowly added a solution of methyllithium (1.1 M in ether, 6.1 mL, 6.7 mmol) over a period of 20 min. The reaction mixture was slowly warmed to rt and stirred for 1 h. It was then poured into a cold saturated aqueous NH_4Cl solution and extracted with ether. Evaporation of the solvent furnished the tertiary alcohol **10**, which was taken in 5 mL of CH_2Cl_2, and PCC (1.8 g, 8.4 mmol) and silica gel (1.8 g) were added. The reaction mixture was stirred for 12 h, filtered through a small silica gel column, and eluted from the column with more CH_2Cl_2. Evaporation of the solvent and purification of the product on a silica gel column using ethyl acetate−hexane (1:50) as eluent furnished trimethylcarvone **7** (750 mg, 70%) as an oil. $[\alpha]_D^{24}$: +88 (*c* 4.3, $CHCl_3$). IR: ν_{max} (cm^{-1}) 1665, 1615, 895. ^{1}H NMR: δ 4.93 (1 H, br s), 4.75 (1 H, br s), 2.65−2.40 (3 H, m), 1.89 (3 H, s), 1.77 (3 H, s), 1.71 (3 H, s), 1.18 (3 H, s), 1.07 (3 H, s). ^{13}C NMR: δ 197.3 (C), 160.4 (C), 145.4 (C), 130.4 (C), 115.2 (CH_2), 51.7 (CH), 39.5 (2 C, C and CH_2), 26.9 (CH_3), 23.1 (CH_3), 21.8 (CH_3), 16.4 (CH_3), 11.6 (CH_3). MS: *m*/*z* 192 (M^+, 19), 177 (62), 150 (23), 135 (58), 124 (55), 109 (100). HRMS: *m*/*z* for $C_{13}H_{20}O$, calcd 192.1514, found 192.1523.

(+)-(5*R*)-5-(3-Bromopropen-2-yl)-2,3,4,4-tetramethylcyclohex-2-enone (11). To an ice cold, magnetically stirred solution of the enone **7** (1 g, 5.2 mmol) in a 3:2 mixture of CH_2Cl_2 and methanol (5 mL) was slowly added NBS (1.1 g, 6.2 mmol) over a period of 20 min. The reaction mixture was stirred for 6 h, diluted with water, and extracted with CH_2Cl_2. The combined CH_2Cl_2 extract was washed with 5% aqueous NaOH. Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate−hexane (1:50 to 1:20) as eluent furnished the allyl bromide **11** (1.27 g, 90%) as an oil. $[\alpha]_D^{25}$: +14.8 (*c* 6.4, $CHCl_3$). IR: ν_{max} (cm^{-1}) 1662, 1612, 920. ^{1}H NMR: δ 5.43 (1 H, s), 5.02 (1 H, s), 3.95 and 3.90 (2 H, AB q, J = 10.0 Hz), 2.74 (1 H, dd, J = 9.4 and 6.9 Hz), 2.60−2.45 (2 H, m), 1.88 (3 H, s), 1.74 (3 H, s), 1.14 (3 H, s), 1.08 (3 H, s). ^{13}C NMR: δ 196.7 (C), 160.1 (C),

145.9 (C), 130.6 (C), 118.9 (CH_2), 47.5 (CH), 40.6 (CH_2), 39.8 (C), 38.6 (CH_2), 26.7 (CH_3), 21.5 (CH_3), 16.5 (CH_3), 11.7 (CH_3). HRMS: *m/z* for $C_{13}H_{19}O$ (M − Br), calcd 191.1436, found 191.1433.

(−)-(1*R*,4*S*)-1,5,5-Trimethyl-6,8-bis(methylene)bicyclo-[2.2.2]octan-2-one (13). To a cold (−5 °C), magnetically stirred 1 M solution of potassium *tert*-butoxide (2.2 mmol) [prepared from potassium (87 mg, 2.2 mmol) and *tert*-butyl alcohol (2.2 mL)] in 2.5 mL of THF was added a solution of the bromo enone **11** (280 mg, 1.04 mmol) in 2.5 mL of THF. The reaction mixture was slowly warmed to rt and stirred for 12 h. It was then quenched with water and extracted with ether. Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate−hexane (1:50) as eluent furnished the bicyclic compound **13** (150 mg, 76%) as an oil. $[\alpha]_D^{24}$: −5.4 (*c* 7.9, $CHCl_3$). IR: ν_{max} (cm^{-1}) 1727, 1652, 1636, 894. ^{1}H NMR: δ 4.95 (2 H, s), 4.88 (1 H, br s), 4.74 (1 H, br s), 2.61 (1 H, dd, J = 18.9 and 2.6 Hz), 2.45−2.30 (2 H, m), 2.30−2.20 (1 H, m), 2.20 (1 H, dd, J = 18.9 and 2.6 Hz), 1.14 (3 H, s), 1.12 (3 H, s), 1.09 (3 H, s). ^{13}C NMR: δ 210.8 (C), 156.5 (C), 145.7 (C), 108.9 (CH_2), 108.7 (CH_2), 52.7 (C), 50.6 (CH), 40.8 (CH_2), 38.6 (CH_2), 37.8 (C), 31.4 (CH_3), 28.6 (CH_3), 16.5 (CH_3). MS: *m/z* 190 (M^+, 37), 175 (23), 161 (20), 149 (25), 147 (62), 133 (100), 119 (48), 105 (70). HRMS: *m/z* for $C_{13}H_{18}O$, calcd 190.1358, found 190.1358.

(+)-Methyl (1*R*)-1,5,5-Trimethyl-6-methylenecyclohex-3-en-2-one-1-acetate (14). Precooled dry ozone in oxygen gas was passed through a cold (−70 °C) suspension of the bicyclic ketone **13** (200 mg, 1.05 mmol) and $NaHCO_3$ (10 mg) in 1:4 MeOH−CH_2Cl_2 (5 mL) for 5 min. Exess ozone was flushed off with oxygen. The solvent was evaporated in vacuo, and the residue was dissolved in 2 mL of dry benzene. To this mixture were added acetic anhydride (1 mL, 10.5 mmol), triethylamine (0.7 mL, 5.2 mmol), and a catalytic amount of DMAP, and the resulting mixture was stirred at rt for 15 min and then refluxed for 6 h. The reaction mixture was diluted with water and extracted with ether. The ether extract was washed with 3 N aqueous HCl and water. Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate−hexane (1:50) as eluent furnished first the unreacted starting material **13** (80 mg). Further elution of the column with ethyl acetate−hexane (1:20 to 1:10) as eluent furnished the Criegee fragmentation product **14** (93 mg, 67% based on the starting material consumed) as an oil. $[\alpha]_D^{25}$: +38 (*c* 1.08, $CHCl_3$). IR: ν_{max} (cm^{-1}) 1740, 1680, 1622, 902. ^{1}H NMR: δ 6.52 (1 H, d, J = 10.2 Hz), 5.98 (1 H, d, J = 10.2 Hz), 5.15 (1 H, s), 5.10 (1 H, s), 3.55 (3 H, s), 3.33 and 2.75 (2 H, 2 × d, J = 16.7 Hz), 1.38 (3 H, s), 1.34 (3 H, s), 1.29 (3 H, s). ^{13}C NMR: δ 200.0 (C), 171.1 (C), 157.4 (C), 155.6 (CH), 124.0 (CH), 110.4 (CH_2), 51.3 (CH_3), 49.3 (C), 42.8 (CH_2), 37.5 (C), 33.1 (CH_3), 31.3 (CH_3), 30.9 (CH_3). MS: *m/z* 222 (M^+, 16), 191 (51), 175 (64), 163 (33), 147 (74), 135 (31), 121 (100), 105 (55), 96 (40), 91 (44).

(+)-Methyl (1*R*)-1,5,5-Trimethyl-6-methylenecyclohexan-2-one-1-acetate (19). To a magnetically stirred solution of the enone **14** (200 mg, 0.90 mmol) in EtOAc (2 mL) was added 5% Pd−C (30 mg), and the reaction mixture was stirred under hydrogen, created by evacuative displacement of air (balloon) for 30 min. The reaction mixture was passed 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 (1:20 to 1:10) as eluent furnished the ketone **19** (182 mg, 90%) as an oil. $[\alpha]_D^{25}$: +20.8 (*c* 1.2, $CHCl_3$). IR: ν_{max} (cm^{-1}) 1740, 1713, 1627, 899. ^{1}H NMR: δ 5.05 (1 H, s), 4.94 (1 H, s), 3.57 (3 H, s), 3.23 and 2.71 (2 H, 2 × d, J = 16.5 Hz), 2.70−2.45 (2 H, m), 1.90−1.75 (2 H, m), 1.25 (3 H, s), 1.24 (3 H, s), 1.21 (3 H, s). ^{13}C NMR: δ 212.8 (C), 171.4 (C), 159.6 (C), 108.6 (CH_2), 51.4 (CH_3), 51.3 (C), 44.1 (CH_2), 35.7 (C), 35.5 (CH_2), 34.5 (CH_2), 31.4 (CH_3), 30.3 (2 C, CH_3). MS: *m/z* 224 (M^+, 83), 193 (44), 165 (85), 151 (26), 137 (37), 123 (42), 109 (100), 95 (42).

(−)-Methyl (1*R*)-1,3,3-Trimethyl-2-methylenecyclohexane-1-acetate (20). A solution of the ketone **19** (112 mg, 0.5 mmol), ethanedithiol (0.12 mL, 1.5 mmol), and BF_3·OEt_2 (0.06 mL, 0.5 mmol) in dry benzene (0.5 mL) was magnetically stirred at 0−5 °C for 2 h. The reaction was quenched with aqueous $NaHCO_3$ solution and extracted with ether. The ether extract was washed with 5% aqueous NaOH solution. 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 **22** (27 mg, 60% based on the starting material consumed) as an oil. $[\alpha]_D^{26}$: +14.4 (*c* 1.8, $CHCl_3$). IR: ν_{max} (cm^{-1}) 1741, 1623, 908. ^{1}H NMR: δ 5.13 (1 H, s), 5.06 (1 H, s), 3.60 (3 H, s), 3.35−3.15 (4 H, m), 3.07 and 2.72 (2 H, 2 × d, J = 14.6 Hz), 2.48 (1 H, ddd, J = 14.5, 11.0 and 3.7 Hz), 2.17 (1 H, td, J = 13.9 and 4.8 Hz), 1.75 (1 H, ddd, J = 14.2, 11.0, and 4.0 Hz), 1.60 (3 H, s), 1.56 (1 H, td, J = 14.2 and 4.4 Hz), 1.16 (6 H, s). ^{13}C NMR: δ 171.5 (C), 155.7 (C), 112.9 (CH_2), 80.9 (C), 51.0 (CH_3), 49.1 (C), 43.0 (CH_2), 39.9 (CH_2), 39.6 (CH_2), 39.5 (CH_2), 37.8 (CH_2), 35.9 (C), 32.5 (CH_3), 31.1 (CH_3), 23.8 (CH_3). Further elution of the column with ethyl acetate−hexane (1:20 to 1:10) as eluent furnished the unreacted ketoester **19** (78 mg). To a magnetically stirred solution of the thioketal **22** (85 mg, 0.283 mmol) in dry ethanol was added an excess of Raney Ni, and the resulting mixture was refluxed for 30 min. The reaction mixture was 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 the ester **20** (53.5 mg, 90%) as an oil. $[\alpha]_D^{25}$: −3.7 (*c* 3, $CHCl_3$). IR: ν_{max} (cm^{-1}) 1739, 1624, 902. ^{1}H NMR: δ 4.99 (1 H, s), 4.89 (1 H, s), 3.61 (3 H, s), 2.53 and 2.48 (2 H, AB q, J = 13.5 Hz), 1.75−1.30 (6 H, m), 1.25 (3 H, s, CH_3), 1.14 (3 H, s, CH_3), 1.13 (3 H, s, CH_3). ^{13}C NMR: δ 172.1 (C), 160.7 (C), 108.7 (CH_2), 51.0 (CH_3), 46.0 (CH_2), 40.8 (CH_2), 38.91 (CH_2), 38.86 (C), 36.4 (C), 32.5 (CH_3), 31.2 (CH_3), 29.7 (CH_3), 18.6 (CH_2).

(+)-Methyl 3-[(1*R*)-1,3,3-Trimethyl-2-methylenecyclohexyl]propionate (6). To a solution of the ester **20** (25 mg, 0.12 mmol) in 1 mL of methanol was added 10% aqueous NaOH solution (1 mL), and the resulting mixture was refluxed for 12 h. The reaction mixture was cooled, acidified with 3 N aqueous HCl, and then extracted with ether. Evaporation of the solvent furnished the acid[4e] **23** (22 mg, 94%) as an oil. IR: ν_{max} (cm^{-1}) 1706, 903. ^{1}H NMR: δ 5.02 (1 H, s), 4.94 (1 H, s), 2.53 (2 H, s), 1.90−1.30 (6 H, m), 1.29 (3 H, s, CH_3), 1.15 (6 H, s). ^{13}C NMR: δ 178.5 (C), 160.4 (C), 109.0 (CH_2), 46.1 (CH_2), 40.8 (CH_2), 38.9 (CH_2), 38.8 (C), 36.4 (C), 32.6 (CH_3), 31.2 (CH_3), 29.7 (CH_3), 18.6 (CH_2). A solution of the acid **23** (22 mg, 0.11 mmol) and oxalyl chloride (0.1 mL, 1.1 mmol) in dry benzene (1 mL) was stirred for 2 h at rt. Evaporation of benzene and the excess oxalyl chloride under reduced pressure furnished the acid chloride, which was taken in dry ether and added, dropwise, to a cold (0 °C), magnetically stirred ethereal solution of diazomethane (3 mL, excess prepared from *N*-nitroso-*N*-methylurea and 60% aqueous KOH solution), and the resulting mixture was stirred at rt for 2 h. Careful evaporation of the excess diazomethane and ether on a water bath followed by purification on a short silica gel column using ethyl acetate−hexane (1:10) as eluent furnished the diazo ketone **24** (22 mg, 89%) as a yellow oil. IR: ν_{max} (cm^{-1}) 2100, 1633, 901. A solution of the diazo ketone in methanol (20 mL) was placed in a Pyrex photochemical reactor and irradiated with a Hanovia medium-pressure mercury vapor lamp for 1 h. Evaporation of the solvent and purification of the photolyzate on a silica gel column using ethyl acetate−hexane (1:50) as eluent furnished the homologated ester **6**[4e] (17.5 mg, 78%) as an oil. $[\alpha]_D^{26}$: +32.7 (*c* 1.65, $CHCl_3$). IR: ν_{max} (cm^{-1}) 1741, 1622, 901. ^{1}H NMR: δ 5.04 (1 H, s), 4.79 (1 H, s), 3.64 (3 H, s), 2.30−2.00 (3 H, m), 1.85−1.65 (1 H, m), 1.60−1.20 (6 H, m), 1.12 (3 H, s), 1.11 (3 H, s), 1.05 (3 H, s). ^{13}C NMR: δ 174.4 (C), 159.2 (C), 109.5 (CH_2), 51.4 (CH_3), 41.5 (CH_2), 40.5 (CH_2), 39.2 (C), 36.5 (C), 35.0 (CH_2), 32.7 (CH_3), 30.0 (CH_2), 29.7 (CH_3), 29.6 (CH_3), 18.6 (CH_2).

(−)-(1*R*,3*S*,7*R*)-7,11,11-Trimethyltricyclo[5.4.0.0^{1,3}]-undecan-4-one (4). Hydrolysis of the ester **6** (20 mg, 0.089 mmol) in 1 mL of methanol using 10% aqueous NaOH solution (1 mL) for 12 h, as described in the previous experiment, furnished the acid[8b] **5** (17 mg, 91%) as an oil. Reaction of the acid **5** (17 mg, 0.08 mmol) with oxalyl chloride (0.07 mL, 0.8 mmol) in dry benzene (1 mL) for 2 h at rt furnished the acid

chloride, which on treatment with an excess of an ethereal solution of diazomethane (3 mL) followed by purification of the product, as described in the previous reaction, furnished the diazo ketone **25** (17 mg, 90%) as a yellow oil. IR (neat): ν_{max} (cm^{-1}) 2102, 1641, 902. The diazo ketone **25** was taken in dry cyclohexane (4 mL) and added dropwise to a magnetically stirred, refluxing (using two 100 W tungsten lamps) suspension of Cu powder (50 mg) and anhydrous $CuSO_4$ (40 mg) in 4 mL of dry cyclohexane, the resulting mixture was refluxed for 4 h. The reaction mixture was then cooled, and the catalyst was filtered off. Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate−hexane (1:20 to 1:10) as eluent furnished dihydromayurone[4e,8] **4** (6 mg, 36% from the acid **5**), which was recrystallized from hexanes.

Alternatively,[8a] a solution of the diazo ketone **25** (9 mg, 0.0385 mmol) and rhodium acetate (1 mg) in benzene (5 mL) was magnetically stirred at room temperature for 12 h. Evaporation of the solvent followed by purification as above furnished dihydromayurone **4** (5 mg, 57% from the acid **5**).

Mp: 105−106 °C (lit.[5] mp: 106−108 °C). $[\alpha]_D^{22}$: −71.0 (*c* 1.0, $CHCl_3$), [lit.[5] for (+)-**4**, $[\alpha]_D$: +75.4]. IR: ν_{max} (cm^{-1}) 1681. ^1H NMR: δ 2.52 (1 H, ddd, J = 18.9, 13.5, and 7.2 Hz), 2.12 (1 H, ddd, J = 18.9, 6.3, and 1.8 Hz), 2.00−1.50 (2 H, m), 1.75−1.45 (4 H, m), 1.22 (3 H, s), 1.40−1.10 (4 H, m), 1.14 (3 H, s), 0.99 (1 H, dd, J = 10.5 and 5.1 Hz), 0.63 (3 H, s). ^{13}C NMR: δ 209.4 (C), 40.2 (CH_2), 38.9 (C), 35.2 (CH_2), 35.0 (CH_2), 33.8 (C), 33.0 (CH_2), 32.9 (C), 32.5 (CH), 28.6 (CH_3), 28.5 (CH_3), 27.3 (CH_3), 18.9 (CH_2), 13.2 (CH_2).

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Supporting Information Available: ^1H and ^{13}C NMR spectra for compounds **4, 6, 7, 11, 13, 14, 19, 20, 22,** and **23**. This material is available free of charge via the Internet at http://pubs.acs.org.

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