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An enantiospecific synthesis of 2-pupukeanone

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A combination of intermolecular Michael addition followed by intramolecular Michael addition of an enone to methyl acrylate and an intramolecular rhodium carbenoid CH insertion reaction of a diazo ketone have been exploited for the construction of isotwistanes. It has been extended to racemic and enantiospecific synthesis of 2-pupukeanone.

Keywords: Pupukeananes, marine sesquiterpenes, Michael-Michael reaction, rhodium carbenoid, intramolecular CH-insertion

IPC Code: Int. Cl.[8] C07C

In a variety of marine organisms, chemical defense *via* secretion of toxic and/or strong smelling organic compounds from their skin glands is a common phenomenon as part of self defense mechanism to protect themselves from higher animals. The nudibranch *Phyllidia varicosa* Lamarck, 1801 secretes from its skin glands a strong and unusually smelling, heat stable, volatile substance, which is lethal to fish and crustaceans to protect the delicate, shellless, brightly colored opisthobranch mollusk from its predators. Based on this observation research group of Scheuer had investigated on the chemical constituents of the skin extracts of *P. varicosa* and also its prey *Hymeniacidon sp.* (later reclassified as *Ciocalypta sp.*), a sponge, which led to the isolation[1] of two novel sesquiterpenes 9-isocyanopupukeanane **1** and 2-isocyanopupukeanane **2** from both the mollusk and the sponge, containing an unprecedented isotwistane **3** carbon framework.

Presence of an interesting tricyclo[4.3.1.$0^{3,7}$]decane (isotwistane) **3** carbon framework incorporating two quaternary carbon atoms and an isonitrile group made pupukeananes attractive and challenging synthetic targets. As a consequence several methods were developed for the synthesis of 9- and 2-isocyanopupukeananes **1** and **2**, and the corresponding ketones, 9- and 2-pupukeanones **4** and **5** (ref. 2) (**Figure 1**). Herein is described the details of the approach to 2-pupukeanone **5** based on an intramolecular rhodium carbenoid CH insertion reaction[3].

For the synthesis of pupukeananes, the primary task was to generate a suitably functionalized 1,3-dimethyltricyclo[4.3.1.$0^{3,7}$]decane system, such as the dione **6**, a known precursor of 2-pupukeanone **5**. It was contemplated that rhodium catalyzed[4] reaction of the diazo ketone **7**, derived from the bicyclo[2.2.2]-octanecarboxylic acid **8**, would generate the isotwistanedione **6** in a regioselective manner *via* the insertion of the intermediate rhodium carbenoid into the only accessible γ-CH bond (the remaining four γ-CH bonds are non-approachable due to geometric reasons, **Scheme I**). Generation of the bicyclo[2.2.2]octanecarboxylic acid **8** containing two methyl groups at the C-4 and C-6 positions, as required for pupukeananes, could be obtained by an intermolecular Michael-intramolecular Michael reaction sequence[5] of 2,6-dimethylcyclohexenone to methyl acrylate.

Initially, a formal total synthesis of racemic 2-pupukeanone **5** was investigated (**Scheme II**). Generation of the kinetic dienolate of 2,6-dimethyl-cyclohexenone with lithium hexamethyl-disilazide (LHMDS) in hexane at –10°C followed by reaction of the resultant kinetic dienolate with one equivalent of methyl acrylate furnished the bicyclic ketoester **9** *via* intermolecular Michael-intramolecular Michael reaction in 70% yield, in a highly stereoselective manner. Stereochemistry of the ester group in the ketoester **9** was assigned on the basis of the expected interaction of the lithium cation with the enolate and the enone moieties in the intermediate ester enolate during the intramolecular Michael reaction. Stereochemistry of the secondary methyl group was assigned on the basis of thermodynamic reasoning. Next, construction of the third ring *via* rhodium

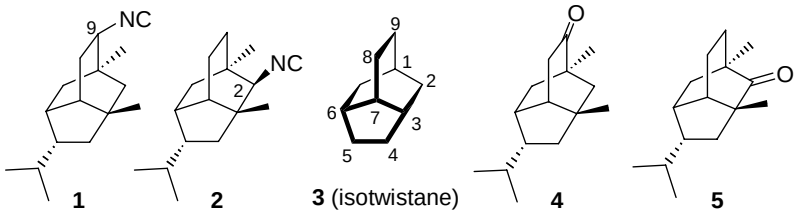
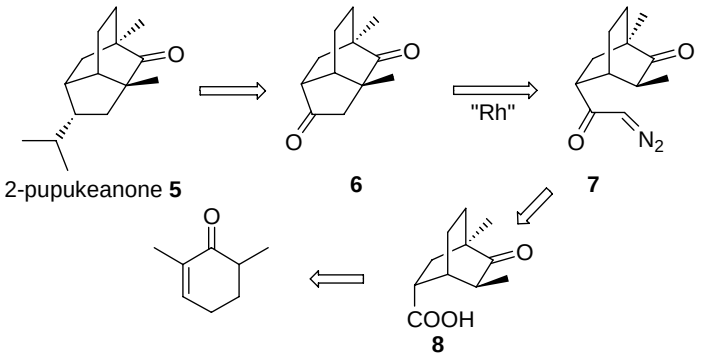
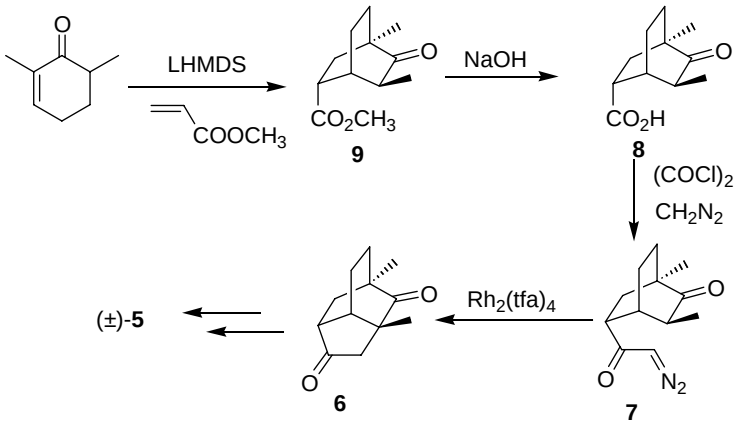


Figure 1



Scheme I

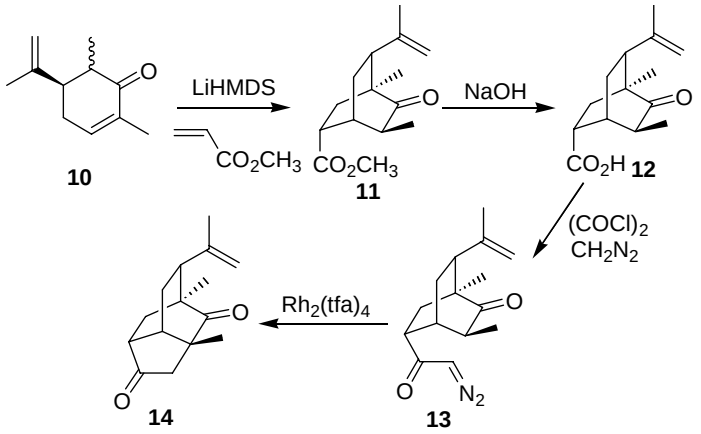


Scheme II

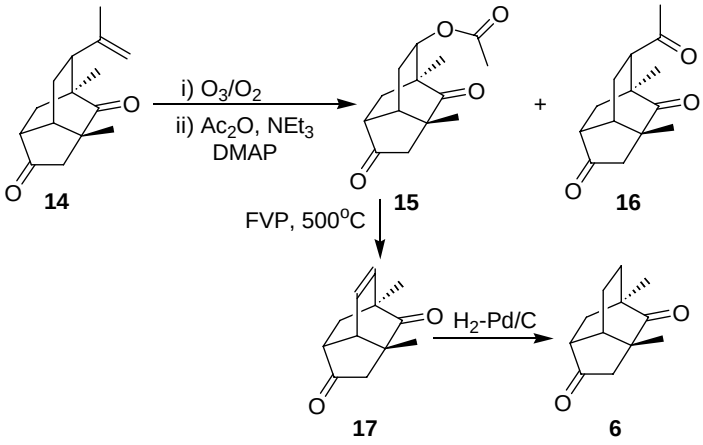
carbenoid C-H insertion was addressed. Accordingly, refluxing a solution of the keto ester **9** and sodium hydroxide in 1:1 methanol and water led to the hydrolysis of the ester moiety to furnish the acid **8** in 96% yield. Reaction of the acid **8** with oxalyl chloride in benzene at RT followed by treatment of the resultant acid chloride with an excess of ethereal diazomethane at 0°C furnished the diazo ketone **7**. Treatment of the diazo ketone **7** with a catalytic amount of rhodium trifluoroacetate in refluxing methylene chloride for 4 hr resulted in the isotwistane dione **6**, in 50% yield (from the acid **8**) *via* regiospecific C-H insertion of the intermediate rhodium carbenoid, which was found to be identical (TLC, MS, IR, ^{1}H and ^{13}C NMR) with the authentic sample. The dione **6** has already been transformed into racemic 2-pupukeanone **5** by Chang and Chang[2h].

After successfully completing the formal total synthesis of racemic 2-pupukeanone **5**, attention was focused on the enantiospecific synthesis. It was obvious that 2,6-dimethylcyclohexenone generates an achiral kinetic dienolate on treatment with a strong base and was not suitable for enantioselective generation of the bicyclo[2.2.2]octanecarboxylic acid **8**. Consequently, 6-methylcarvone **10** was chosen as the chiral equivalent of 2-methylcyclohexenone, identifying the isopropenyl group as a disposable chiral director.

The synthetic sequence was initiated (**Scheme III**) with 6-methylcarvone **10**, which was obtained by



Scheme III



Scheme IV

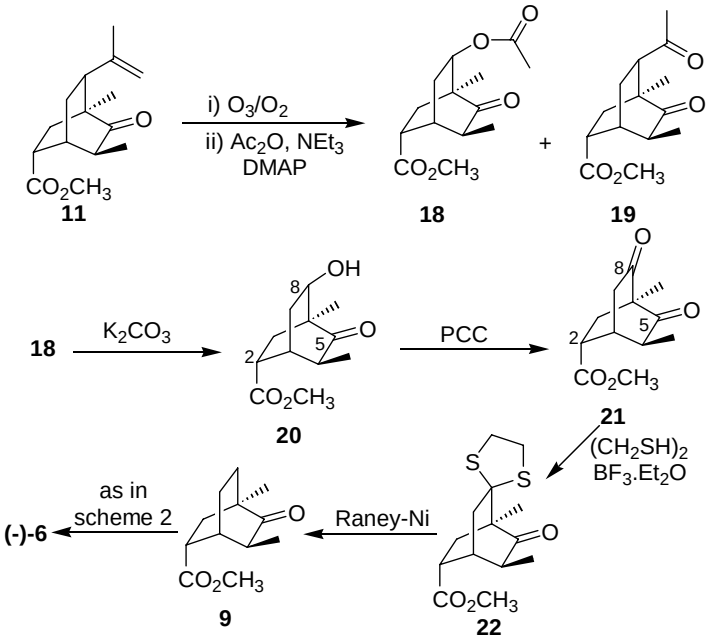
kinetic alkylation of (*R*)-carvone[6]. Reaction of 6-methylcarvone **10** with LHMDS in hexane at –10°C followed by reaction of the resultant kinetic dienolate with one equivalent of methyl acrylate furnished the bicyclic ketoester **11** *via* intermolecular Michael-intramolecular Michael reaction in 70% yield, in a highly regio- and stereoselective manner. Refluxing a solution of the ketoester **11** and sodium hydroxide in 1:1 methanol and water led to the hydrolysis of the ester moiety to furnish the acid **12** in 93% yield, which was transformed into the diazo ketone **13**. Treatment of the diazo ketone **13** with a catalytic amount of rhodium trifluoroacetate in refluxing methylene chloride furnished the isotwistane dione **14**, *via* regiospecific C-H insertion of the intermediate rhodium carbenoid. For further elaboration of the tricyclic dione **14** into 2-pupukeanone **5**, first degradation of the isopropenyl group was addressed. It was anticipated that the isopropenyl group could be converted into an acetoxy group employing a one pot ozonation followed by Criegee rearrangement[7] sequence. Accordingly, ozonolysis of the tricyclic dione **14** in a mixture of methanol-methylene chloride followed by treatment of the resultant methoxyhydroperoxide with a mixture of acetic anhydride, triethylamine and a catalytic amount of 4-*N*,*N*-dimethylaminopyridine (DMAP) in refluxing benzene furnished the diketoacetate **15**, *via* Criegee rearrangement along with varying amounts of the normal ozonolysis product, the trione **16**.

For the reductive degradation of the acetate in **15**, thermal elimination of the acetate followed by hydrogenation of the resultant olefin was explored (**Scheme IV**). Accordingly, sublimation of the acetate **15** through a quartz column packed with quartz chips, maintained at 500°C and connected to vacuum (0.05 mm) resulted in the elimination of acetic acid to furnish the olefin **17**, in 18% yield. Attempts to improve the yield of the reaction were unsuccessful, *e.g.* higher temperature or lower temperature, either resulted in the generation of complex mixture with much lower yield or in the recovery of significant

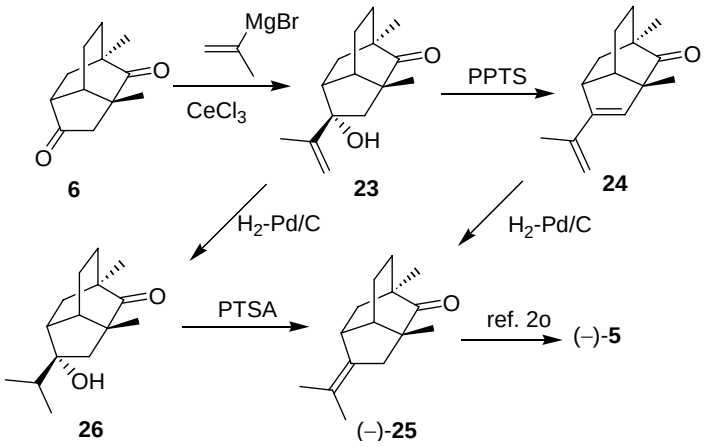
amount of starting material. One of the reasons for the low yield in the pyrolysis might be the presence of a built-in cyclohexene in the product **17**, which might have triggered the decomposition *via* retro Diels-Alder reaction followed by further disintegration. Hydrogenation of the olefin in **17** in ethanol using 10% Pd-C as the catalyst generated the dione **6**, in 90% yield, intermediate in the synthesis of racemic 2-pupukeanone by Chang and Chang[2h].

Since the flash vacuum pyrolysis reaction was found to be inefficient for the generation of the dione **6** from the acetate **15**, an alternate methodology was investigated for the degradation of the isopropenyl group (**Scheme V**). To avoid the regiochemical problems, it was decided to carry out the degradation of the isopropenyl group prior to the formation of the third ring. Accordingly, ozonolysis of the ketoester **11** in a mixture of methanol-methylene chloride followed by treatment of the resultant methoxyhydroperoxide with a mixture of acetic anhydride, triethylamine and a catalytic amount of DMAP in refluxing benzene furnished the bicyclic acetate **18** in 55% yield *via* Criegee rearrangement, along with varying amounts of normal ozonolysis product the diketo ester **19**. Hydrolysis of the bicyclic acetate **18** with potassium carbonate in methanol at RT for 3 hr gave the alcohol **20** in 88% yield. Oxidation of the alcohol **20** with pyridinium chlorochromate (PCC) and silica gel in methylene chloride for 3 hr at RT furnished the diketoester **21** in 90% yield. The C-8 ketone is relatively sterically less crowded than the C-5 ketone, which has been exploited for the regioselective deoxygenation of the C-8 ketone in the diketoester **21** employing a two-step methodology *via* the thioketal **22**. Reaction of the diketoester **21** with one equivalent of ethanedithiol and a catalytic amount of boron trifluoride etherate in benzene at 0°C to RT for 4 hr regioselectively generated the thioketal **22** in 82% yield. Reaction of the thioketal **22** with freshly prepared Raney nickel in refluxing ethanol for 5 hr led to desulfurisation furnishing the ketoester **9** in 79% yield.

After successfully degrading the isopropenyl group, the keto ester **9** was transformed into the dione (–)-**6** following the methodology used in the synthesis of racemic dione **6** *cf.* **Scheme II**. In the next phase of the synthesis, conversion of the dione (–)-**6** into 2-pupukeanone, employing the three-step methodology developed by Chang and Chang[2h] in their synthesis of racemic 2-pupukeanone (±)-**6**, was attended (**Scheme VI)**. Thus, anhydrous cerium chloride catalyzed addition[8] of isopropenylmagnesium bromide to the dione (–)-**6** at 0°C generated regio- and stereoselectively the tertiary alcohol **23**, in 81% yield. Pyridinium *p*-toluenesulfonate (PPTS) catalyzed dehydration of the tertiary alcohol **23** in refluxing dichloroethane furnished the dienone **24** in 71% yield. Hydrogenation of the dienone **24** using 10% Pd-C as the catalyst in ethanol for 8 hr at one atmosphere pressure generated the olefin (–)-**25**, $[\alpha]_D^{24}$ –108.7° (*c*



Scheme V



Scheme VI

1.5, $CHCl_3$) {lit.[2k] for (+)-**25** $[\alpha]_D^{25}$ +102.0° (*c* 2.3, $CHCl_3$)}. The enone **25** exhibited the spectral data identical with those of its optical antipode prepared[2k] earlier.

Alternatively, first hydrogenation of the double bond followed by dehydration of the alcohol was also explored for the conversion of the tertiary alcohol **23** into the enone (–)-**25**. Accordingly, hydrogenation of the tertiary alcohol **23** in ethanol with 10% Pd-C as the catalyst at one atmosphere of hydrogen furnished the alcohol **26** in 90% yield. Reaction of the tertiary alcohol **26** with a catalytic amount of *p*-toluene-sulfonic acid (PTSA) in refluxing benzene for 5 hr resulted in the elimination of alcohol to furnish the enone (–)-**25**. Since the enone (+)-**25** has already been converted into (+)-2-pupukeanone (eq. I.1), present sequence constitutes the formal synthesis of (–)-2-pupukeanone (–)-**5**.

Experimental Section

Melting points were recorded using Tempo and Mettler FP1 melting point apparatus in capillary tubes and are uncorrected. IR spectra were recorded on Perkin-Elmer 781 and Jasco FTIR 410 spectrophotometers. ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded on JNM λ-300 spectrometer. 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 the DEPT-135 spectra, and is given in parentheses. Low-resolution mass spectra were recorded using Jeol JMS-DX 303 and Shimadzu QP-5050A GCMS instruments using direct inlet mode. Relative intensities are given in parentheses. High-resolution mass spectra were recorded using Micromass Q-TOF micro mass spectrometer using electrospray ionisation. Elemental analyses were carried out using Carlo Erba 1106 CHN analyzer. Optical rotations were measured using a Jasco DIP-370 digital polarimeter and $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. Ozonolysis experiments were carried out using Fischer 502 ozone generator. The flow rate of oxygen was adjusted and calibrated to provide 1 mmole of ozone per four minutes. Hydrogenation reaction at one atmospheric pressure was carried out using a balloon filled with hydrogen. Analytical thin-layer chromatographies (TLC) were performed on glass plates (7.5×2.5 and 7.5×5.0 cm) coated with Acme's silica gel G containing 13% calcium sulfate as binder and various combinations of ethyl acetate and hexane were used as eluent. Visualization of spots was accomplished by exposure to iodine vapor. Acme's silica gel (100-200 mesh) was used for column chromatography (approximately 15-20 g per 1 g of the crude product). 15% Silver nitrate impregnated silica gel was prepared as per standard procedure. All small-scale dry reactions were carried out using standard syringe-septum technique. Dry THF was obtained by distillation over sodium-benzophenone ketyl. Dry ether was obtained by distillation over sodium and stored over sodium wire. Dry methylene chloride was prepared by distillation over P_2O_5. Dry methanol was prepared by distillation over magnesium and stored over molecular sieves.

(–)-Methyl (1*R*,2*R*,4*S*,6*S*,8*S*)-8-isopropenyl-4,6-dimethyl-5-oxobicyclo[2.2.2]octane - 2 - carboxylate 11. To a cold (–70°C) magnetically stirred solution of hexamethyldisilazane (3.87 mL, 18.3 mmoles) in dry hexane (36 mL) was slowly added a solution of ^{n}BuLi

(2.5 *M* in hexane, 7.3 mL, 18.3 mmoles) and the reaction mixture was stirred for 15 min. To LHMDS thus formed was added dropwise, a solution of 6-methylcarvone[6] **10** (3.0 g, 18.3 mmoles) in dry hexane (30 mL) and the reaction mixture was stirred for 45 min at the same temperature. Methyl acrylate (1.64 mL, 18.3 mmoles) was added to the reaction mixture and stirred for 3 hr at RT. It was then filtered through a small silica gel column using ethyl acetate-hexane (1:3) as eluent. Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexane (1:20) as eluent furnished the bicyclic adduct **11** (3.5 g, 70%) as oil. $[\alpha]_D^{23}$ –56.7° (*c* 7.3, MeOH); IR (neat): 1737, 1719, 1642, 896 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 4.67 (1 H, s), 4.60 (1 H, s), 3.65 (3 H, s), 2.81 (1 H, t, *J* = 9.3 Hz), 2.50-2.35 (2 H, m), 2.21 (1 H, br s), 1.95 (1 H, dd, *J* = 14.3 and 8.1 Hz), 1.85-1.60 (3 H, m), 1.44 (3 H, s), 1.11 (3 H, d, *J* = 6.9 Hz), 0.84 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 217.6 (C), 174.7 (C), 145.8 (C), 114.2 (CH_2), 51.9 (CH_3), 51.5 (CH), 45.6 (C), 42.6 (CH), 41.3 (CH), 37.0 (CH), 35.2 (CH_2), 27.9 (CH_2), 19.4 (CH_3), 17.6 (CH_3), 12.6 (CH_3); MS: *m/z* (%) 250 (M^+, 11), 182 (90), 133 (24), 123 (100), 107 (31), 93 (32). Anal.: Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86; Found: C, 71.53; H, 8.95%.

(–)-(1*R*,2*R*,4*S*,6*S*,8*S*)-8-Isopropenyl-4,6-dimethyl-5-oxobicyclo[2.2.2]octane-2-carboxylic acid 12. A magnetically stirred solution of the keto ester **58** (1.0 g, 4 mmoles) in methanol (5 mL) and 10% aqueous NaOH (5 mL) was refluxed for 8 hr. The reaction mixture was cooled to RT and washed with CH_2Cl_2 (10 mL). Then, the aqueous layer was acidified with 3 *N* HCl and extracted with CH_2Cl_2 (3×15 mL). The CH_2Cl_2 extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent furnished the acid **12** (878 mg, 93%) as a light yellow solid, which was purified by recrystallisation from a mixture of hexane and CH_2Cl_2. m.p. 102-03°C; $[\alpha]_D^{23}$ –77.6° (*c* 1.65, $CHCl_3$); IR (neat): 3100, 1712, 1644, 897 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 4.73 (1 H, s), 4.66 (1 H, s), 2.92 (1 H, ddd, *J* = 10.1, 8.2 and 1.4 Hz), 2.55-2.40 (2 H, m), 2.38-2.30 (1 H, m), 2.02 (1 H, dd, *J* = 14.2 and 8.2 Hz), 1.95-1.65 (4 H, m), 1.50 (3 H, s), 1.19 (3 H, d, *J* = 7.1 Hz), 0.91 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 217.6 (C), 180.9 (C), 145.7 (C), 114.4 (CH_2), 51.6 (CH), 45.7 (C), 42.8 (CH), 41.4 (CH), 37.0 (CH), 35.0 (CH_2), 27.9 (CH_2), 19.5 (CH_3), 17.7 (CH_3), 12.7 (CH_3); MS: *m/z* (%) 236 (M^+, 18), 168 (100), 133 (36), 123 (85), 107 (42), 95 (40), 93 (49). Anal.: Calcd. for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 70.87; H, 8.56%.

(–)-(1*S*,3*R*,6*R*,7*S*,9*S*)-9-Isopropenyl-1,3-dimethyltricyclo[4.3.1.0^{3,7}]decane-2,5-dione 14. To a magnetically stirred solution of the acid **12** (250 mg, 1.06 mmoles) in dry benzene (0.5 mL) was added oxalyl chloride (0.46 mL, 5.3 mmoles) and stirred for 2 hr at RT. Evaporation of the solvent and excess oxalyl chloride under reduced pressure afforded the acid chloride, which was taken in dry ether (3 mL) and added drop wise to a cold (0°C), magnetically stirred ethereal solution of diazomethane (excess, prepared from 2 g of *N*-nitroso-*N*-methylurea and 30 mL of 60% aqueous KOH solution and 25 mL of ether). The reaction mixture was stirred at RT for 2 hr. Careful evaporation of the excess diazomethane and the solvent on water bath and rapid purification of the residue over a neutral alumina column using ethyl acetate-hexane (1:10) as eluent furnished the diazo ketone **13** (248 mg, 90%) as yellow oil, ν_{max} 2103, 1712, 1643, 896 cm^{-1}. To a magnetically stirred, refluxing solution of rhodium trifluoroacetate (13 mg, 2 mole%) in dry CH_2Cl_2 (20 mL) was added dropwise, a solution of the diazo ketone **13** (248 mg, 0.96 mmole) in CH_2Cl_2 (5 mL), and the reaction mixture was refluxed for 4 hr. Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexane (1:10) as eluent furnished the dione **14** (124 mg, 50%) as a white solid which was purified by recrystallisation from a mixture of ethyl acetate and hexane. m.p. 89-90°C;. $[\alpha]_D^{24}$ –63.5° (*c* 1.15, $CHCl_3$); IR (neat): 1745, 1719, 1637, 908 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 4.75 (1 H, s), 4.65 (1 H, s), 2.67 (1 H, d, *J* = 11.0 Hz), 2.55-2.40 (1 H, m), 2.44 and 2.10 (2 H, 2×d, *J* = 19.2 Hz), 2.30-2.15 (2 H, m), 2.02 (1 H, dd, *J* = 14.7 and 11.4 Hz), 1.95-1.80 (1 H, m), 1.58 (3 H, s), 1.35-1.20 (1 H, m), 1.34 (3 H, s), 0.94 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 219.4 (C), 215.0 (C), 146.0 (C), 113.9 (CH_2), 53.3 (CH), 52.5 (C), 48.9 (CH_2), 47.9 (CH), 45.3 (C), 42.5 (CH), 35.9 (CH_2), 23.4 (CH_2), 20.3 (CH_3), 19.0 (CH_3), 18.2 (CH_3); MS: *m/z* (%) 232 (M^+, 36%), 217 (17), 189 (14), 161 (30), 124 (80), 119 (43), 110 (72), 109 (45), 105 (38), 96 (100), 95 (48), 93 (48). Anal.: Calcd. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68; Found: C, 78.08; H, 8.85%; HRMS: *m/z* Calcd. for $C_{15}H_{21}O_2Na$ (M+Na+1): 256.1439; Found: 256.1424.

(–)-(1*S*,3*R*,6*R*,7*S*,9*R*)-9-Acetoxy-1,3-dimethyltricyclo[4.3.1.0^{3,7}]decane-2,5-dione 15. A mixture of ozone in oxygen gas was passed through a cold

(–70°C) solution of the diketone **14** (260 mg, 1.12 mmoles) and $NaHCO_3$ (pinch) in 1:5 MeOH-CH_2Cl_2 (3 mL) till (*ca* 4 min) pale blue color appeared. Excess ozone was flushed off with oxygen. The solvent was evaporated *in vacuo* and the residue was dissolved in dry benzene (2 mL). Triethylamine (0.78 mL, 5.6 mmoles), acetic anhydride (1.06 mL, 11.2 mmoles) and a catalytic amount of DMAP (5 mg) were added to the reaction mixture. It was stirred at RT for 45 min and subsequently refluxed for 6 hr. It was then cooled, diluted with 5 mL of water and extracted with ether (3×6 mL). The ether extract was washed with 3 *N* aqueous HCl, water and brine, and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure and purification of the residue over a silica gel column using ethyl acetate-hexane (1:6) as eluent furnished the diketoacetate **15** (135 mg, 48%), which was purified by recrystallisation from a mixture of ethyl acetate and hexane. m.p. 185-86°C; $[\alpha]_D^{25}$ –31.6° (*c* 0.95, $CHCl_3$); IR (neat): 1745, 1726 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 4.92 (1 H, d, *J* = 9.3 Hz), 2.59 (1 H, dd, *J* = 10.3 and 5.1 Hz), 2.50-2.30 (2 H, m), 2.38 and 2.12 (2 H, 2×d, *J* = 18.7 Hz), 2.10-1.95 (1 H, m), 2.03 (3 H, s), 1.87 (1 H, m of d, *J* = 15.9 Hz), 1.41 (1 H, d, *J* = 14.7 Hz), 1.32 (3 H, s), 0.98 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 215.4 (C), 215.1 (C), 169.8 (C), 76.0 (CH), 52.4 (C), 49.3 (CH_2), 47.9 (CH), 46.5 (C), 42.6 (CH), 30.7 (CH_2), 26.6 (CH_2), 20.9 (CH_3), 18.2 (CH_3), 16.8 (CH_3); MS: *m/z* (%) 250 (M^+, 4), 208 (10), 190 (20), 162 (12), 161 (10), 147 (12), 119 (15), 98 (12), 145 (11), 94 (35), 93 (30), 92 (25), 43 (100). Anal.: Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25; Found: C, 67.09; H, 7.35%. Further elution of the column with ethyl acetate-hexane (1:3) furnished normal ozonolysis product, the trione **16** (38 mg, 15%). $[\alpha]_D^{25}$ –22.2° (*c* 1.85, $CHCl_3$); IR (neat): 1745, 1722 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 2.90 (1 H, dd, *J* = 11.4 and 4.8 Hz), 2.60 (1 H, dd, *J* = 10.5 and 4.5 Hz), 2.41 (1 H, d, *J* = 18.9 Hz), 2.30-1.90 (5 H, m), 2.18 (3 H, s), 1.36 (3 H, s), 1.34 (1 H, d, *J* = 14.1 Hz), 0.97 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 215.2 (C), 215.1 (C), 209.4 (C), 56.3 (CH), 52.7 (C), 49.5 (CH_2), 48.1 (CH), 44.1 (C), 42.3 (CH), 33.8 (CH_2), 31.6 (CH_3), 21.0 (CH_2), 18.9 (CH_3), 18.8 (CH_3); MS: *m/z* (%) 234 (M^+, 11), 190 (20), 163 (20), 147 (15), 131 (20), 123 (20), 121 (25), 119 (38), 109 (38), 96 (35), 95 (33), 93 (38), 43 (100).

(–)-(1*S*,3*R*,6*R*,7*S*)-4,6-Dimethyltricyclo[4.3.1.0^{3,7}]-dec-8-ene-2,5-dione 17. Flash vacuum pyrolysis of the tricyclic acetate **15** was carried out in a quartz column (30 cm×1.5 cm) packed with quartz chips, connected to a vacuum line, a collection flask and a trap cooled in liquid nitrogen. The quartz column was heated with a nicrome coil wound around it and insulated by asbestos padding. The column temperature was controlled by a variac and measured by a thermocouple (chromel alumel) using a Keithley digital multimeter. The column was preheated and equilibrated to 500°C. The acetate **15** (100 mg, 0.40 mmole) was slowly sublimed (80-150°C/1-7 mm) through the quartz tube. The condensate which was deposited in the receiving flask was collected, and purified on a silica gel column using ethyl acetate-hexane (1:10) as eluent to furnish the olefin **17** (14 mg, 18%) as a colorless oil. $[\alpha]_D^{23}$ –147.1° (*c* 0.7, $CHCl_3$); IR (neat): 1748, 1720 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 6.35 (1 H, dd, *J* = 7.8 and 6.3 Hz), 6.05 (1 H, d, *J* = 8.1 Hz), 3.04 (1 H, dd, *J* = 6.6 and 4.5 Hz), 2.57 (1 H, dd, *J* = 11.1 and 4.5 Hz), 2.37 and 2.09 (2 H, 2×d, *J* = 19.0 Hz), 1.77 (1 H, dd, *J* = 13.5 and 11.4 Hz), 1.49 (1 H, d, *J* = 13.5 Hz), 1.24 (3 H, s), 1.22 (3 H, s) [2 × *tert*-CH_3]; MS: *m/z* (%) 165 (M-C_3H_5, 25), 134 (7), 86 (45), 84 (80), 71 (15), 69 (15), 51 (30), 49 (100).

(–)-(1*R*,3*R*,6*R*,7*S*)-1,3-Dimethyltricyclo[4.3.1.0^{3,7}]-decane-2,5-dione 6. To a magnetically stirred solution of the olefin **17** (14 mg, 0.07 mmole) in ethanol (1 mL) was added 10% Pd-C (10 mg) and the reaction mixture was stirred at RT in hydrogen atmosphere, created by evacuative displacement of air (balloon), for 2 hr. 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 (1:10) as eluent furnished the dione **6** (12.5 mg, 90%) as oil. $[\alpha]_D^{23}$ –28.1° (*c* 3.6, $CHCl_3$) {Lit.[2k] for (+)-**6** $[\alpha]_D^{25}$ +27.0° (*c* 2.0, $CHCl_3$)}; IR (neat): 1745, 1718 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 2.69 (1 H, dd, *J* = 10.4 and 5.0 Hz), 2.37 and 2.12 (2 H, 2×d, *J* = 18.7 Hz), 2.30-2.20 (1 H, m), 2.05-1.80 (3 H, m), 1.75-1.60 (2 H, m), 1.43 (1 H, d, *J* = 14.0 Hz), 1.31 (3 H, s), 0.96 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 218.5 (C), 216.5 (C), 52.4 (C), 48.8 (CH), 48.6 (CH_2), 43.3 (CH), 42.3 (C), 32.6 (2 C, CH_2), 20.3 (CH_3), 18.8 (CH_3), 16.3 (CH_2); MS: *m/z* (%) 192 (M^+, 45), 164 (10), 149 (25), 138 (20), 121 (26), 107 (25), 94 (45), 93 (60), 84 (55), 49 (100).

(–)-Methyl (1*R*,2*R*,4*S*,6*S*,8*R*)-8-acetoxy-4,6-dimethyl-5-oxobicyclo[2.2.2]octane-2-carboxylate 18. Ozone in oxygen gas was passed through a cold

(–70°C) solution of the ketoester **11** (500 mg, 2.0 mmole) and $NaHCO_3$ (pinch) in 1:5 MeOH-CH_2Cl_2 (5 mL) till (*ca* 8 min) pale blue color appeared. Excess ozone from the reaction mixture was flushed off with oxygen. Solvent was evaporated *in vacuo* (at RT) and the residue was dissolved in dry benzene (5 mL). Triethylamine (1.4 mL, 10.0 mmoles), acetic anhydride (1.89 mL, 20.0 mmoles) and a catalytic amount of DMAP (5 mg) were added to the reaction mixture and stirred at RT for 45 min, and subsequently it was refluxed for 6 hr. It was then cooled, diluted with 5 mL of water and extracted with ether (3×6 mL). The ether extract was washed with 3 *N* aqueous HCl and brine, and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure and purification of the residue over a silica gel column using ethyl acetate-hexane (1:6) as eluent furnished the acetate **18** (295 mg, 55%) as colorless solid, which was purified by recrystallisation from a mixture of CH_2Cl_2 and hexane. m.p. 102-03°C; $[\alpha]_D^{23}$ –32.7° (*c* 3.0, $CHCl_3$); IR (neat): 1731 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 4.89 (1 H, dd, *J* = 9.3 and 3.6 Hz), 3.68 (3 H, s), 2.74 (1 H, ddd, *J* = 11.1, 6.0 and 2.1 Hz), 2.40-2.15 (3 H, m), 2.13 (1 H, dd, *J* = 14.7 and 6.3 Hz), 1.98 (3 H, s), 1.80 (1 H, dd, *J* = 14.7 and 11.1 Hz), 1.71 (1 H, t of d, *J* = 14.7 and 3.0 Hz), 1.12 (3 H, d, *J* = 7.5 Hz), 0.94 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 213.3 (C), 173.8 (C), 169.8 (C), 75.1 (CH), 52.1 (CH_3), 46.4 (C), 42.4 (CH), 41.6 (CH), 36.8 (CH), 31.1 (CH_2), 30.3 (CH_2), 20.8 (CH_3), 16.3 (CH_3), 13.1 (CH_3); MS: *m/z* (%) 268 (M^+, 15), 208 (38), 152 (80), 149 (32), 140 (30), 123 (70), 122 (40), 121 (65), 93 (100), 88 (85). Anal.: Calcd. for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51; Found: C, 62.53; H, 7.62%. Further elution of the column with ethyl acetate-hexane (1:6) furnished normal ozonolysis product **19** (70 mg, 14%). $[\alpha]_D^{23}$ –51.4° (*c* 3.5, $CHCl_3$); IR (neat): 1724, 1650 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 3.70 (3 H, s), 2.91 (1 H, dd, *J* = 10.3 and 7.4 Hz), 2.77 (1 H, ddd, *J* = 10.6, 7.3 and 1.8 Hz), 2.50-2.20 (2 H, m), 2.12 (3 H, s), 2.04 (1 H, dd, *J* = 14.0 and 7.2 Hz), 2.00-1.75 (3 H, m), 1.21 (3 H, d, *J* = 7.4 Hz), 0.97 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 213.7 (C), 209.3 (C), 174.0 (C), 54.5 (CH_3), 51.9 (CH), 44.3 (C), 42.4 (CH), 41.6 (CH), 36.4 (CH), 33.6 (CH_2), 31.2 (CH_3), 25.6 (CH_2), 18.0 (CH_3) 13.0 (CH_3); MS: *m/z* (%) 252 (M^+, 22), 182 (18), 181 (10), 149 (12), 124 (20), 123 (100), 122 (20), 121 (40), 93 (55). Anal.: Calcd. for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99; Found: C, 66.10; H, 8.13%.

(–)-Methyl (1*R*,2*R*,4*S*,6*S*,8*R*)-8-hydroxy-4,6-dimethyl-5-oxobicyclo[2.2.2]octane-2-carboxylate 20. To a magnetically stirred solution of the acetate **18** (294 mg, 1.1 mmoles) in methanol (4 mL) was added K_2CO_3 (456 mg, 3.3 mmoles) and stirred at RT for 3 hr. The reaction mixture was diluted with ether (10 mL) and 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 (1:2) as eluent furnished the hydroxyketoester **20** (218 mg, 88%) as colorless oil. $[\alpha]_D^{24}$ –43.3° (*c* 2.4, $CHCl_3$); IR (neat): 3494, 1723 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 3.82 (1 H, dd, *J* = 9.2 and 3.7 Hz), 3.70 (3 H, s), 2.72 (1 H, ddd, *J* = 11.0, 6.2 and 1.8 Hz), 2.40-2.20 (2 H, m), 2.20-2.00 (3 H, m), 1.85-1.60 (1 H, m), 1.71 (1 H, dd, *J* = 14.7 and 11.0 Hz), 1.14 (3 H, d, *J* = 6.9 Hz), 1.04 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 215.1 (C), 174.3 (C), 74.3 (CH), 52.1 (CH_3), 48.8 (C), 42.7 (CH), 41.9 (CH), 37.1 (CH), 32.9 (CH_2), 30.2 (CH_2), 16.3 (CH_3) 13.0 (CH_3); MS: *m/z* (%) 209 (M-OH, 20), 187 (25), 145 (30), 132 (55), 105 (100), 93 (30); HRMS: *m/z* Calcd. for $C_{12}H_{18}O_4Na$ (M+Na): 249.1103; Found: 249.1104.

(–)-Methyl (1*R*,2*R*,4*S*,6*S*)-4,6-dimethyl-5,8-dioxobicyclo[2.2.2]octane-2-carboxylate 21. To a magnetically stirred solution of the alcohol **20** (218 mg, 0.96 mmole) in 2 mL of dry CH_2Cl_2 was added a homogeneous mixture of PCC (413 mg, 1.93 mmoles) and silica gel (413 mg) and stirred vigorously for 3 hr 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 (1:10 to 1:3) as eluent furnished the diketoester **21** (194 mg, 90%) as oil. $[\alpha]_D^{24}$ –5.5° (*c* 6.2, $CHCl_3$); IR (neat): 1738, 1710 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 3.75 (3 H, s), 2.93 (1 H, ddd, *J* = 11.1, 6.9 and 2.1 Hz), 2.70-2.55 (2 H, m), 2.54 (1 H, dd, *J* = 18.9 and 2.5 Hz), 2.45-2.35 (2 H, m), 1.99 (1 H, dd, *J* = 14.4 and 11.1 Hz), 1.17 (3 H, d, *J* = 7.5 Hz), 1.10 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 208.1 (C), 205.9 (C), 173.2 (C), 62.0 (C), 52.4 (CH_3), 42.0 (CH), 41.9 (CH), 39.6 (CH_2), 36.5 (CH), 31.5 (CH_2), 13.9 (CH_3), 12.1 (CH_3); MS: *m/z* (%) 224 (M^+, 15), 182 (40), 137 (15), 123 (50), 122 (25), 109 (32), 95 (22), 69 (100). Anal.: Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19; Found: C, 64.44; H, 7.19%.

(–)-Methyl (1*R*,2*R*,4*R*,6*S*)-4,6-dimethyl-5-oxo-bicyclo[2.2.2]octanespiro - [8.2'] - 1,3-dithiolane - 2 - carboxylate 22. To an ice cold, magnetically stirred solution of the diketoester **21** (194 mg, 0.87 mmole) and ethanedithiol (0.08 mL, 0.96 mmole) in dry benzene (3 mL) was added a catalytic amount of $BF_3.OEt_2$ (0.01 mL) and stirred at RT for 4 hr. After the completion of the reaction it was diluted with ether (10 mL), washed successively 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 (1:10) as eluent, furnished the thioketal **22** (213 mg, 82%) as colorless oil. $[\alpha]_D^{24}$ –81.0° (*c* 4.2, $CHCl_3$); IR (neat): 1725 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 3.70 (3 H, s), 3.50-3.10 (4 H, m), 2.95 (1 H, m of t, *J* = 10.5 Hz), 2.80-2.55 (2 H, m), 2.50-2.35 (1 H, m), 2.27 (1 H, br s), 2.20 (1 H, dd, *J* = 15.0 and 10.5 Hz), 2.07 (1 H, dd, *J* = 15.0 and 7.8 Hz), 1.16 (3 H, s), 1.15 (3 H, d, *J* = 7.5 Hz); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 213. 0 (C), 174.1 (C), 70.8 (C), 52.6 (C), 51.9 (CH_3), 46.4 (CH_2), 41.7 (CH), 41.5 (CH_2), 41.0 (CH), 40.5 (CH_2), 37.5 (CH), 31.4 (CH_2), 16.2 (CH_3), 13.3 (CH_3); MS: *m/z* (%) 300 (M^+, 60), 272 (17), 215 (100), 185 (30), 145 (32), 119 (50), 118 (100), 105 (60), 91 (50). Anal.: Calcd. for $C_{14}H_{20}O_3S_2$: C, 55.97; H, 6.71; Found: C, 55.82; H, 6.83%.

(–)-Methyl (1*R*,2*R*,4*R*,6*S*)-4,6-dimethyl-5-oxo-bicyclo[2.2.2]octane-2-carboxylate 9. To a magnetically stirred solution of the thioketal **22** (213 mg, 0.71 mmole) in dry ethanol (5 mL) was added an excess of Raney nickel (210 mg) and refluxed for 8 hr. 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 (1:20 to 1:10) as eluent, furnished the ester **9** (118 mg, 79%) as colorless oil. $[\alpha]_D^{24}$ - 48.2° (*c* 5.0, $CHCl_3$); IR (neat): 1730, 1723 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 3.66 (3 H, s), 2.78 (1 H, ddd, *J* = 11.0, 7.0 and 1.8 Hz), 2.32 (1 H, q, *J* = 7.3 Hz), 2.20 (1 H, br s), 2.04 (1 H, ddd, *J* = 14.3, 7.3 and 2.9 Hz), 1.90-1.45 (5 H, m), 1.07 (3 H, d, *J* = 7.3 Hz), 0.92 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 217.3 (C), 174.7 (C), 51.9 (CH_3), 42.6 (CH), 42.5 (C), 41.9 (CH), 37.5 (CH), 32.7 (CH_2), 31.5 (CH_2), 21.6 (CH_2), 20.1 (CH_3) 13.0 (CH_3); MS: *m/z* (%) 210 (M^+, 15%), 149 (15), 124 (100), 123 (30), 109 (20), 95 (40), 93 (70). Anal.: Calcd. for $C_{12}H_{18}O_3$: C, 68.55; H, 8.61; Found: C, 68.16; H, 8.66%.

(–)-(1*R*,3*R*,6*R*,7*S*)-1,3-Dimethyltricyclo[4.3.1.0^{3,7}]-decan-2,5-dione 6. A magnetically stirred solution of the keto ester **9** (118 mg, 0.56 mmole) in methanol (2 mL) and 10% aqueous NaOH (2 mL) was refluxed for 8 hr. The reaction mixture was cooled to RT and washed with CH_2Cl_2 (5 mL). Then the aqueous layer was acidified with 3 *N* HCl and extracted with CH_2Cl_2 (3×5 mL). The CH_2Cl_2 extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent furnished the acid **8** (105 mg, 96%) as colorless oil. To a magnetically stirred solution of the acid **8** (105 mg, 0.54 mmole) in dry benzene (0.5 mL) was added oxalyl chloride (0.23 mL, 2.68 mmoles) and stirred for 2 hr at RT. Evaporation of the solvent and excess oxalyl chloride under reduced pressure afforded the acid chloride, which was taken in dry ether (2 mL) and added dropwise to a cold, magnetically stirred ethereal solution of diazomethane (excess, prepared from 1 g of *N*-nitroso-*N*-methylurea and 20 mL of 60% aqueous KOH solution and 20 mL of ether) and the reaction mixture was stirred at RT for 2 hr. Careful evaporation of the solvent and excess diazomethane on water bath and purification of the residue over a silica gel column using ethyl acetate-hexane (1:10) as eluent furnished the diazo ketone **7** (107 mg, 95%) as yellow oil. To a magnetically stirred, refluxing solution of rhodium trifluoroacetate (7 mg, 2 mole%) in dry CH_2Cl_2 (10 mL) was added dropwise, a solution of the diazo ketone **7** (107 mg, 0.51 mmole) in CH_2Cl_2 (3 mL), and the reaction mixture was refluxed for 4 hr. Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexane (1:10) as eluent furnished the dione **6** (49 mg, 53%) as oil, which was identified by comparison of the TLC, IR and ^1H NMR spectral data with that obtained earlier.

(–)-(1*R*,3*R*,5*S*,6*R*,7*S*)-5-Hydroxy - 5- isopropenyl-1,3-dimethyltricyclo[4.3.1.0^{3,7}]decan-2-one 23. Cerium chloride heptahydrate (149 mg, 0.4 mmole) was dried at 150°C and 0.2 mm for 4 hr and blanketed with nitrogen while being cooled. Dry THF was introduced and the slurry was stirred at RT for 10 min. A solution of the dione **6** (49 mg, 0.26 mmole) in THF was added to the reaction mixture and stirred for 0.5 hr at 0°C. A solution of isopropenylmagnesium bromide [prepared from 2-bromopropene (0.035 mL, 0.4 mmole) and magnesium (12.5 mg, 0.52 mmole)] in THF was transferred *via* syringe into the reaction mixture and stirred for 10 hr. The reaction was quenched with saturated aqueous NH_4Cl solution and extracted with

ethyl acetate. The extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate-hexane (1:15 to 1:10) as eluent, furnished the alcohol **23** (46 mg, 81%) as colorless oil. $[\alpha]_D^{23}$ –56.5° (*c* 4.6, $CHCl_3$); IR (neat): 3462, 1710, 1639, 896 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 4.91 (1 H, s), 4.83 (1 H, s) 2.35 (1 H, dd, *J* = 9.3 and 4.8 Hz), 2.11 (1 H, d, *J* = 14.5 Hz), 2.06 (1 H, d, *J* = 14.4 Hz), 2.00-1.93 (1 H, m), 1.84 (3 H, s), 1.80-1.70 (2 H, m), 1.69 (1 H, d, *J* = 14.4 Hz), 1.65-1.45 (3 H, m), 1.40 (1 H, br s), 1.11 (3 H, s), 0.97 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 220.8 (C), 150.5 (C), 109.8 (CH_2), 80.6 (C), 52.9 (C), 49.5 (CH_2), 45.3 (CH), 44.7 (CH), 41.8 (C), 33.4 (CH_2), 29.3 (CH_2), 20.3 (CH_3), 19.3 (CH_3), 18.8 (CH_3), 17.2 (CH_2); HRMS: *m/z* Calcd. for $C_{15}H_{22}O_2Na$ (M+Na): 257.1517; Found: 257.1532.

(–)-(1*R*,3*S*,6*R*,7*S*)-5-Isopropenyl-1,3-dimethyltricyclo[4.3.1.0^{3,7}]dec-4-en-2-one 24. To a solution of the alcohol **23** (25 mg, 0.11 mmole) in dichloroethane (2 mL) was added PPTS (3 mg, 0.011 mmole). The reaction mixture was refluxed for 6 hr. It was then diluted with ether (5 mL), 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 diene **24** (16 mg, 71%) as oil. $[\alpha]_D^{24}$ –527° (*c* 1.2, $CHCl_3$); IR (neat): 1712, 890 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 5.45 (1 H, s), 4.94 (2 H, s), 2.94 (1 H, dd, *J* = 8.4 and 5.4 Hz), 2.42-2.35 (1 H, m), 1.95 (1 H, dd, *J* = 12.6 and 8.4 Hz), 1.95-1.40 (5 H, m), 1.84 (3 H, s), 1.24 (3 H, s), 0.92 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 214.0 (C), 152.7 (C), 137.5 (C), 130.5 (CH), 113.7 (CH_2), 59.5 (C), 50.6 (CH), 44.6 (C), 41.7 (CH), 39.8 (CH_2), 35.6 (CH_2), 21.5 (CH_3), 20.1 (CH_3), 17.3 (CH_2), 15.9 (CH_3); MS: *m/z* (%) 189 (M-C_2H_3, 13), 149 (15), 133 (20), 124 (20), 105 (10), 95 (15), 93 (15), 91 (15), 49 (100); HRMS: *m/z* Calcd. for $C_{15}H_{21}O$ (M+1): 217.1592; Found: 217.1575.

(–)-(1*R*,3*R*,5*R*,6*R*,7*S*)-5-Hydroxy-5-isopropyl-1,3-dimethyltricyclo[4.3.1.0^{3,7}]decan-2-one 26. To a magnetically stirred solution of the alcohol **23** (25 mg, 0.11 mmole) in ethanol (1 mL) was added 10% Pd-C (10 mg) and the reaction mixture was stirred at RT in hydrogen atmosphere, created by evacuative displacement of air (balloon), for 3 hr. 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 (1:10) as eluent, furnished the alcohol **26** (22 mg, 90%) as oil. $[\alpha]_D^{24}$ –61.5° (*c* 2.05, $CHCl_3$); IR (neat): 3511, 1710 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 2.29 (1 H, dd, *J* = 8.8 and 5.2 Hz), 1.98 (1 H, d, *J* = 13.6 Hz), 1.85-1.40 (9 H, m), 1.08 (3 H, s), 0.93 (3 H, s), 0.92 (3 H, d, *J* = 6.3 Hz), 0.91 (3 H, d, *J* = 6.6 Hz); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 220.7 (C), 80.8 (C), 53.3 (C), 50.8 (CH_2), 45.1 (CH), 45.0 (CH), 42.2 (C), 38.0 (CH), 32.9 (CH_2), 29.4 (CH_2), 20.2 (CH_3), 19.3 (CH_3), 17.5 (CH_3), 17.3 (CH_2), 16.9 (CH_3); MS: *m/z* (%) 236 (M^+, 5), 233 (20), 219 (10), 193 (60), 147 (100), 135 (60), 121 (40), 105 (40), 105 (40), 93 (40); HRMS: *m/z* Calcd. for $C_{15}H_{24}O_2Na$ (M+Na): 259.1674; Found: 259.1672.

(–)-(1*R*,3*R*,6*R*,7*S*)-5-Isopropylidene-1,3-dimethyltricyclo[4.3.1.0^{3,7}]decan-2-one 25.

Procedure 1:

To a solution of the alcohol **26** (22 mg, 0.09 mmole) in benzene (2 mL) was added PTSA (6 mg, 0.03 mmole) and the reaction mixture was refluxed for 5 hr. It was then diluted with ether, washed with saturated aqueous $NaHCO_3$ 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 (1:50 to 1:25) as eluent, furnished the olefin **25** (17 mg, 83%) as an oil[2o].

Procedure 2:

To a magnetically stirred solution of the diene **24** (16 mg, 0.075 mmole) in ethanol (1 mL) was added 10% Pd-C (6 mg) and the reaction mixture was stirred at RT in hydrogen atmosphere, created by evacuative displacement of air (balloon), for 8 hr. 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 (1:50) as eluent, furnished the olefin **25** (14 mg, 90%) as oil[2o]. $[\alpha]_D^{24}$ –108.7° (c 1.5, $CHCl_3$) {Lit. for (+)-**25**: $[\alpha]_D^{26}$ +101.8° (*c* 2.26, $CHCl_3$)}; IR (neat): 1714 cm^{-1}; ^1H NMR ($CDCl_3$ + CCl_4): δ 2.90 (1 H, dd, *J* = 8.8 and 4.8 Hz), 2.32 (1 H, d, *J* = 16.2 Hz), 2.01 (1 H, m of d, *J* = 16.2 Hz), 1.93 (1 H, dd, *J* = 12.8 and 9.2 Hz), 1.88-1.74 (3 H, m), 1.62 (3 H, s), 1.65-1.50 (2 H, m), 1.53 (3 H, s), 1.20-1.05 (1 H, m), 1.17 (3 H, s), 0.89 (3 H, s); ^{13}C NMR ($CDCl_3$ + CCl_4): δ 221.5 (C), 137.5 (C), 122.6 (C), 53.7 (C), 45.4 (CH), 42.6 (CH_2), 42.2 (C), 40.8 (CH), 38.5 (CH_2), 32.8 (CH_2), 20.9 (CH_3), 20.7 (CH_3), 20.6 (CH_3), 18.8 (CH_3), 17.2 (CH_2); MS: *m/z* (%) 203 (M-Me, 4), 163 (20), 149 (20), 135 (15), 124 (100), 109

(50). HRMS: *m/z* Calcd. for $C_{15}H_{23}O$ (M+1): 219.1749; Found: 219.1752.

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