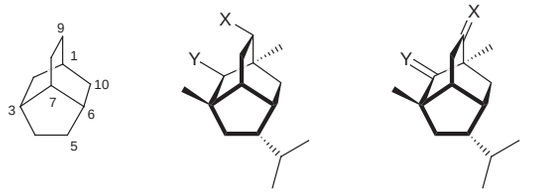
Chiral synthons from carvone. Part 31.† Enantiospecific total synthesis of (+)-2-pupukeanone and 5-*epi*-2-pupukeanone

Adusunilli Srikrishna * and T. Jagadeeswar Reddy

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560012, India

The first enantiospecific total synthesis of (+)-2-pupukeanone and 5-*epi*-2-pupukeanone has been achieved starting from (*R*)-carvone, employing a radical cyclisation reaction based approach. (*R*)-Carvone has been transformed into the bicyclo[2.2.2]octenone 12 *via* kinetic alkylation, bromination of the isopropenyl moiety and intramolecular alkylation, which on further alkylation with prenyl bromide leads to bicyclo[2.2.2]octenone 16. The 5-*exo-trig* radical cyclisation of the bromohydrin 17, obtained from 16, furnishes an epimeric mixture of the isotwistanes 19 and 20 along with a minor amount of the rearranged product 21. Ozonolytic cleavage of the exomethylene moiety, dehydration of the tertiary alcohol and regioselective Wolff–Kishner reduction transforms the isotwistanes 19 and 20 into the enone 24. Alternatively, kinetic alkylation of the bicyclo[2.2.2]octenone 12 with 1,4-dibromo-2-methylbut-2-ene followed by 5-*exo-trig* allyl radical cyclisation of 35 and selective functional group transformations generates the isotwistane 23 and a minor amount of the rearranged product 29. Finally, catalytic hydrogenation transforms the enone 24 into (+)-2-pupukeanone 5 and its C-5 epimer 6.

In a number of marine organisms, chemical defence *via* secretion of toxic and/or strong smelling organic compounds from their skin glands is a common phenomenon to protect themselves from the higher animals. It was observed[1] that 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 shell-less, brightly coloured opisthobranch mollusc from its predators. Scheuer and co-workers reported[2] the isolation of this material from *Phyllidia varicosa* and also from its prey, a sponge *Hymeniacidon sp*., and found it to be a mixture of two metabolites. The structures of these metabolites, incorporating the novel isotwistane (**1**) carbon framework, were established as 9-isocyano- and 2-isocyano-1,3-dimethyl-5-*endo*-isopropyltricyclo[4.3.1.0^{3,7}]decanes (**2** and **3**) *via* a combination of chemical degradation and single crystal X-ray diffraction studies. The presence of a novel tricyclo[4.3.1.0^{3,7}]decane (isotwistane) carbon framework (**1**), isocyanide moiety, two



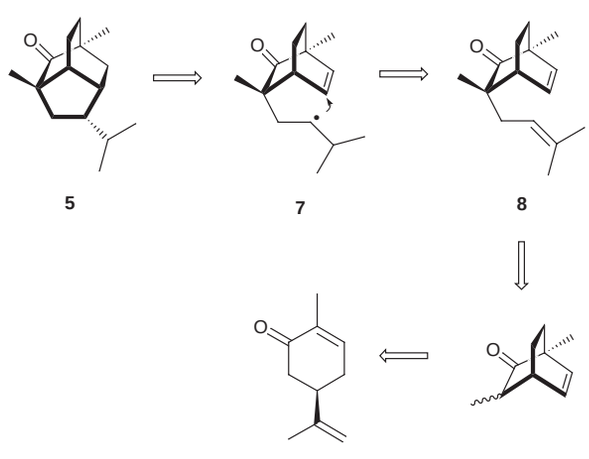
1

2 X = NC; Y = H
3 X = H; Y = NC

4 X = O; Y = H_2
5 X = H_2; Y = O; (5*S*)
6 X = H_2; Y = O; (5*R*)

quaternary carbons, six chiral centres and the unfavourable *endo* orientation of the isopropyl group made pupukeananes attractive and challenging synthetic targets. As a consequence, several methods were developed for the synthesis of racemic pupukeanones (±)-**2** and (±)-**3** and the corresponding ketones, 9- and 2-pupukeanones (±)-**4** and (±)-**5**.[3,4] In addition to the two earlier approaches by Corey and Frater,[4] recently Chang and Chang reported[5a] an intramolecular alkylation based approach to (±)-2-pupukeanone. At the same time, synthesis of 2-pupukeanone employing an allyl radical cyclisation by Subba Rao and Kaliappan,[5b] and a formal total synthesis of (±)-2-pupukeanone based on a vinyl radical cyclisation reaction from our laboratory[5c] were reported. Since there is no report on the synthesis of chiral 2-pupukeanone, we have embarked on the enantiospecific total synthesis of chiral 2-pupukeanone and 5-*epi*-2-pupukeanones **5** and **6** starting from (*R*)-carvone, and herein we describe the details[6] of these investigations.

For the synthesis of chiral 2-pupukeanone, as depicted in retrosynthetic Scheme 1, a 5-*exo-trig* radical cyclisation reac-



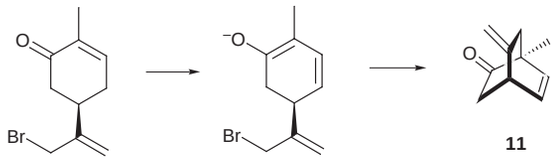
5 **7** **8**

10 **9**

Scheme 1

tion[7] based approach has been envisaged. It was anticipated that the pupukeanone framework can be assembled *via* a 5-*exo-trig* cyclisation of the radical **7**. An appropriate precursor **8** for the generation of the radical **7** can be obtained by kinetic alkylation of the enolate derived from a bicyclo[2.2.2]octenone, *e.g.* **9**, from the *endo* face of the molecule which has enough precedence in the literature.[8] For the construction of a bicyclo[2.2.2]oct-5-en-2-one,[9] (*R*)-carvone **10** was chosen as the chiral starting material. To begin with, attention was focused on the synthesis of a chiral isotwistane derivative from carvone, (see Scheme 3). It was established[9] that the presence of a good leaving group at the C-9 position of carvone and generation of

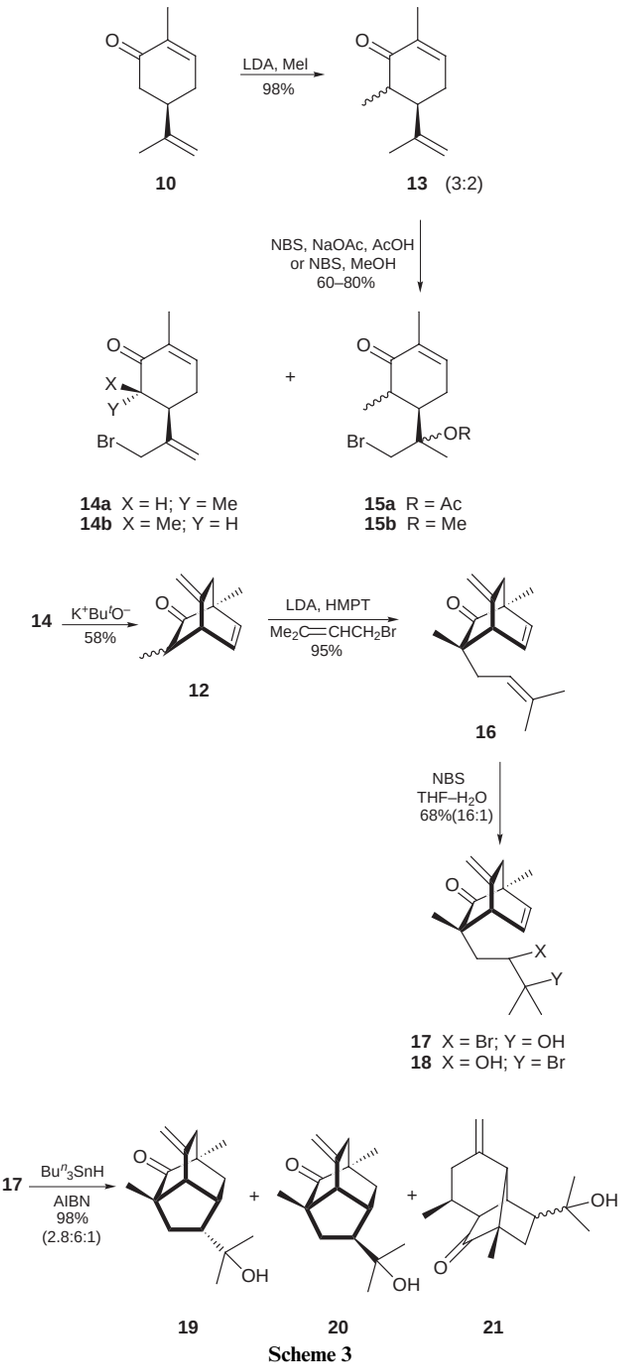
† For part 30, see reference 15.



Scheme 2

the thermodynamic dienolate leads to bicyclo[2.2.2]oct-5-en-2-one **11** *via* an intramolecular alkylation reaction (Scheme 2). Comparison of the enones **11** and **9**, readily reveals the presence of an extra methylene group at the C-8 carbon in **11** which needs to be degraded, whereas the C-3 methyl group is missing in **11** which can be obtained by appropriate choice of starting material. The same strategy was opted for in the preparation of an analogue of **9**, the enone **12**, starting from α′-methylcarvone **13** with an option to degrade the C-8 exomethylene group at a later stage.

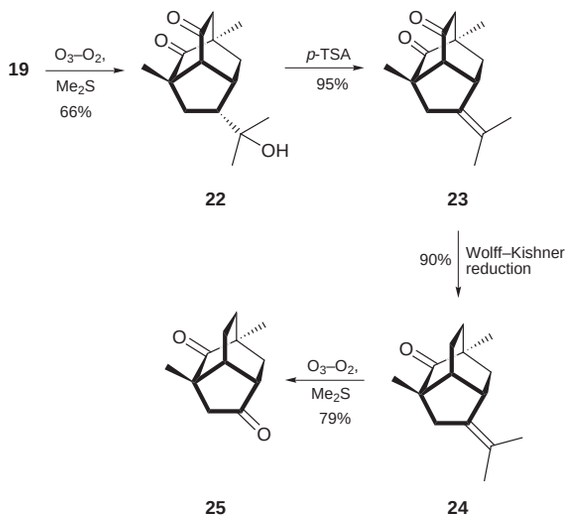
The requisite starting material, α′-methylcarvone **13**, was obtained by alkylation of carvone.[10] Thus, generation of the kinetic enolate of (*R*)-carvone with LDA followed by alkylating with methyl iodide furnished a 3:2 mixture of methylcarvone **13** in 98% yield (Scheme 3).[10] Even though partial crystallisation of the mixture from hexane furnished the *trans* α′-methylcarvone **13a**, the sequence was carried out with the mixture of isomers of **13**, and converged into a single compound at a later stage. Bromination[11] of a 3:2 mixture of methylcarvone **13** using NBS and sodium acetate in 10:1 acetic acid–dichloromethane furnished a 4:1 epimeric mixture of the allyl bromide **14** in 65% yield along with 15% of a mixture of addition products **15a**. Interestingly, reaction of methylcarvone **13** with NBS in 2:3 methanol–dichloromethane furnished stereochemically pure allyl bromide **14a** in 43% yield, in addition to 17% of a mixture of the addition products **15b**. The regioselectivity of the reaction was further established by performing the reaction with a sample enriched with *trans* isomer **13a**. Reaction of a 5:1 mixture of the *trans*- and *cis*-isomers of **13** with NBS in methanol–dichloromethane furnished predominantly the allyl bromide **14a**, in 68% yield. Formation of the allyl bromide **14a** has been observed in the corresponding dimethylated derivatives.[12] Intramolecular alkylation[9] of the allyl bromide **14** using a 1 M solution of potassium *tert*-butoxide in 2-methylpropan-2-ol and THF generated a 3:2 epimeric mixture of the bicyclic compound **12** in 58% yield, whose structure and epimeric nature was established from its spectral data. It is worth mentioning that the intramolecular alkylation reaction of the stereochemically pure allyl bromide **14a** also furnished an epimeric mixture of the bicyclic enones **12**, obviously due to the equilibration of the product after cyclisation under the reaction conditions. Prenyl bromide was selected as the five carbon unit for alkylation, anticipating that the trisubstituted olefin moiety could be exploited to generate a suitable radical precursor. Thus, kinetic alkylation of the enolate generated from the enone **12** using LDA with prenyl bromide in the presence of HMPT at low temperature (−90 °C) stereoselectivity furnished the alkylated product **16** in 95% yield, whose structure was delineated from its spectral data. The stereochemistry of the alkylation was assigned based on precedence in the literature[8] and was confirmed from subsequent transformations. Even though there are three olefinic groups present in **16**, it was anticipated that the electron rich trisubstituted olefin in the side chain could be brominated[11] in a regioselective manner. A bromohydrin was chosen as the radical precursor in anticipation that the *tert*-hydroxy group could be utilised at a later stage for controlling the stereochemistry of the isopropyl group. Thus, slow addition of 1.0 equiv. of NBS to the triene **16** in a 1:1 mixture of water and THF furnished a mixture of the bromohydrin **17** and the regioisomeric bromohydrin **18** in 64 and 4% yield, respectively, which were separated by column chromatography on silica gel. Refluxing a 0.02 M benzene solu-



Scheme 3

tion of the bromohydrin **17** using 1.1 equiv. of tri-*n*-butyltin hydride in the presence of a catalytic amount of AIBN furnished a 2.8:6:1 mixture of the isotwistanes **19**, **20** and the rearranged compound **21** in near quantitative yield. Chromatographic purification on a silica gel column furnished the isotwistane **19** and an inseparable mixture of the isotwistane **20** and the rearranged compound **21**. The individual isomers **20** and **21** were resolved at a later stage of the sequence.

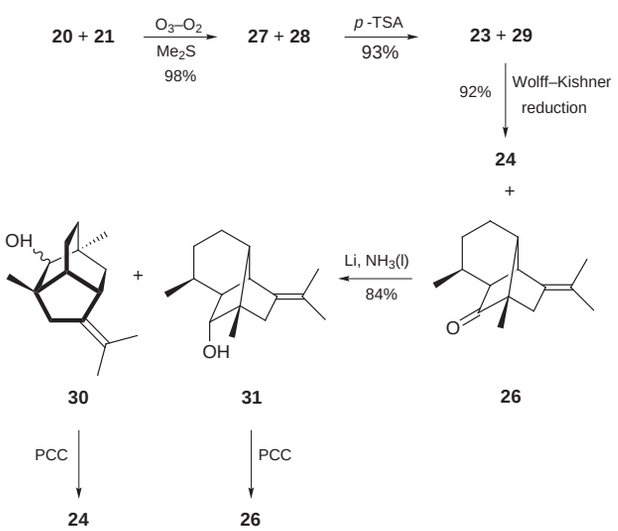
Since dehydration would lead to a diene, resulting in regiochemical problems in the oxidation step, the *exo* methylene moiety in the isotwistanes **19** and **20** was oxidatively cleaved prior to the dehydration of the tertiary alcohol. The sequence was carried out first with the isotwistane **19**, Scheme 4. Thus, ozonation of the isotwistane **19** in methanol and dichloromethane followed by reductive work-up with dimethyl sulfide furnished the diketo alcohol **22**, in 67% yield, which on dehydration with a catalytic amount of *p*-toluenesulfonic acid in refluxing benzene furnished the enedione **23** in 95% yield. Huang–Minlon modified Wolf–Kishner reduction of the enedione **23** furnished the enone **24** in 90% yield *via* regioselective



Scheme 4

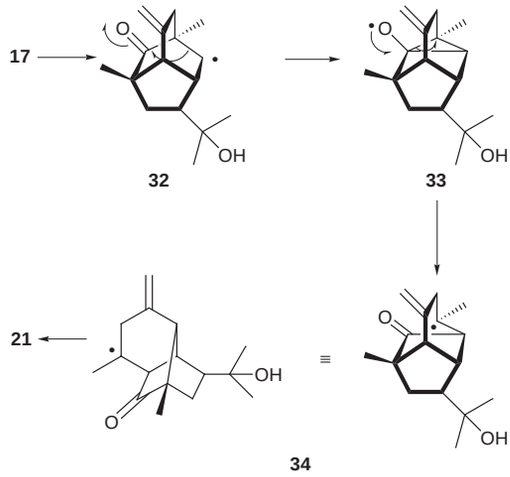
reduction of the C-8 ketone leaving the sterically crowded C-2 ketone intact. The structure of the enone **24** was established from its spectral data and further confirmed by chemical degradation to the dione **25**. Ozonolysis of the enone **24** furnished the dione **25**, in 79% yield, whose structure was established by comparison of its spectral data (IR, ^{1}H and ^{13}C NMR) with that of an authentic[5a,c] racemic sample. Chang and Chang[5a] have stereoselectively transformed the racemic dione **25** into (±)-2-pupukeanone **5** in three steps.

After successfully transforming the isotwistane **19** into the enone **24**, the mixture of isotwistane **20** and rearranged product **21** was transformed into a mixture of the enones **24** and **26** following the same sequence, *i.e.* ozonolysis (⟶ **27** + **28**), dehydration (⟶ **23** + **29**) and deoxygenation, which was resolved chemically (Scheme 5). Reduction of the carbonyl



Scheme 5

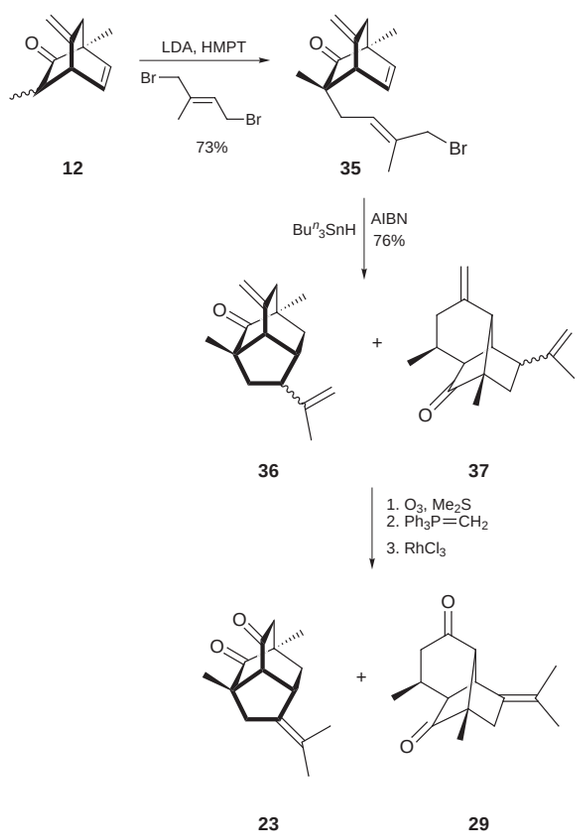
group using lithium in liquid ammonia transformed the mixture of the enones **24** and **26** into a 4.3 : 1 mixture of the alcohols **30** and **31** in 84% yield, which were separated by silica gel column chromatography. The two alcohols **30** and **31** were individually oxidised by PCC to the enones **24** and **26**. A plausible mechanism *via* a homoallyl–homoallyl radical rearrangement for the formation of the rearranged compound **21** from the bromohydrin **17** is depicted in Scheme 6. Addition of the radical **32**, obtained by the initial 5-*exo*-*trig* radical cyclisation of the bromohydrin **17**, to the carbonyl group *via* a 3-*exo*-*trig* cyclisation generates a cyclopropoxy radical **33**. Opening of the



Scheme 6

cyclopropane ring *via* the cleavage of the C-5–C-6 bond leads to the formation of a stable tertiary radical **34** which abstracts hydrogen from tri-*n*-butyltin hydride from the *exo* face resulting in the formation of the product **21**.[13]

An alternative methodology, similar to that used by Kaliappan and Subba Rao,[5b] for the synthesis of enedione **23** *via* a 5-*exo*-*trig* allyl radical cyclisation reaction[14] was also conceived (see Scheme 7). Consequently, regio- and stereo-

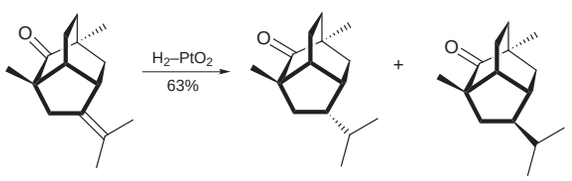


Scheme 7

selective alkylation of the enolate generated from the enone **12** using LDA in the presence of HMPT with 1,4-dibromo-2-methylbut-2-ene at −90 °C furnished the bromo compound **35** in 73% yield. The regioselectivity in the alkylation was established from the absence of a coupling between the bromomethylene and the olefinic proton of the side chain in **35**. The 5-*exo*-*trig* allyl radical cyclisation[14] of the allyl bromide **35** in 0.005 M refluxing benzene solution by slow addition of a solution of tri-*n*-butyltin hydride and AIBN furnished a mixture of iso-

twistane **36** and a minor amount of the rearranged product **37** (Scheme 7). Attention was then turned towards the degradation of the C-8 methylene and isomerisation of the isopropenyl group to an isopropylidene moiety in the isotwistane **36**. Ozonolysis of the mixture of **36** and **37** furnished a mixture of triketones which on regioselective Wittig reaction with methylenetriphenylphosphorane followed by isomerisation of the resultant isopropenyl moiety with $RhCl_3$ furnished a mixture of the enediones **23** and **29**, whose spectral data (IR and ^{1}H NMR) were found to be identical with that of the sample obtained earlier.

Finally, hydrogenation of the enone **24** in ethanol, using platinum oxide as the catalyst, furnished a 2.5:1 mixture of (±)-2-pupukeanone **5** and 5-*epi*-2-pupukeanone **6** in 62% yield (Scheme 8). In an attempt to improve the stereoselectivity,



24 **5** (2.5:1) **6**

Scheme 8

hydrogenation was also carried out on the enedione **23** prior to the deoxygenation but no improvement was noticed in stereoselectivity. The 2-pupukeanone and 5-*epi*-2-pupukeanones (±)-**5** and **6** obtained in this study exhibited spectral data (^{1}H and ^{13}C NMR and mass) identical to that reported for the racemic compounds by Frater and Wenger.[4b]

In conclusion, we have achieved the first enantiospecific total synthesis of (+)-2-pupukeanone and 5-*epi*-2-pupukeanones starting from (*R*)-carvone in 10 steps. Even though the present strategy provided the optical antipodes of the natural series, the ready availability of both (*R*)- and (*S*)-enantiomers of carvone makes the strategy suitable for either of the enantiomeric series.

Experimental

Melting points were recorded using a Tempo melting point apparatus in capillary tubes and are uncorrected. IR Spectra as thin films were recorded on a Perkin-Elmer 781 spectrophotometer. ^{1}H (90, 200 and 400 MHz) and ^{13}C NMR (22.5 and 50 MHz) spectra were recorded on JEOL FX-90Q, Bruker ACF-200 and AMX-400 spectrometers. The chemical shifts (δ ppm) and the coupling constants *J* (Hz) are reported in the standard fashion with reference to either internal tetramethylsilane (for ^{1}H) or the central line (77.1 ppm) of $CDCl_3$ (for ^{13}C). In the ^{13}C NMR spectra, off-resonance multiplicities, when recorded, are given in parentheses. Low and high resolution mass measurements were carried out using a JEOL JMS-DX 303 GC–MS instrument using a direct inlet mode. Relative intensities of the ions are given in parentheses. 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 a Penwalt Wallace and Tierman ozonator. Hydrogenation reactions at atmospheric pressure were carried out using a balloon. Acme's silica gel (100–200 mesh) was used for column chromatography. All small scale dry reactions were carried out using standard syringe–septum techniques. Anhydrous solvents were obtained by standard procedures. AIBN was recrystallised from methanol and stored in the dark. All the commercial reagents, obtained from Fluka or Merck, were used without further purification.

(−)-(5*R*,6*S*)-5-(3-Bromoprop-1-en-2-yl)-2,6-dimethylcyclohex-2-enone 14a

To a cold (−10 °C) magnetically stirred solution of a 5:1 mixture of methylcarvone **13** (121 mg, 0.74 mmol) in a 3:2 mixture of CH_2Cl_2 and MeOH (2.5 ml) was slowly added NBS (144 mg, 0.81 mmol) over a period of 20 min. The reaction mixture was slowly warmed up to RT and stirred for 16 h at RT. It was then diluted with water (3 ml) and extracted with CH_2Cl_2 (3 × 5 ml). The combined organic layer was washed with 5% aq. NaOH (2 ml) followed by brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate–hexane (1:40 to 1:10) as eluent furnished the allyl bromide **14a** (121 mg, 68%), mp 52–53 °C (hexanes); $[\alpha]_D^{26}$ −37.9 (*c* 2.7, $CHCl_3$); ν_{max}/cm^{-1} 1670, 900; δ_H(400 MHz, $CDCl_3$) 6.68 (1 H, br s, CH=C−C=O), 5.39 (1 H, s) and 5.11 (1 H, s) (C=CH_2), 3.99 and 3.97 (2 H, AB q, *J* 10.3, CH_2Br), 2.4–2.7 (4 H, m), 1.78 (3 H, s, olefinic CH_3), 1.13 (3 H, d, *J* 6.7, *sec*-CH_3); δ_C(22.5 MHz, $CDCl_3$) 199.6 (s, C=O), 146.0 (s, *C*=CH_2), 142.1 (d, *C*H=C−C=O), 134.0 (s, CH=*C*−C=O), 116.5 (t, C=*C*H_2), 45.7 (d) and 44.9 (d) (C-5 and -6), 35.3 (t, *C*H_2Br), 32.1 (t, C-4), 15.5 (q) and 12.3 (q) (2 × CH_3); *m*/*z* 244 (M^+ + 2, 0.8%), 242 (M^+, 0.8), 163 (21), 82 (100). Further elution of the column furnished a diastereomeric mixture of the addition product **15b** (40 mg, 20%).

(−)-(1*S*,3*R*,4*R*)- and (1*S*,3*S*,4*R*)-1,3-Dimethyl-8-methylenebicyclo[2.2.2]oct-5-en-2-one 12

To a cold (−5 °C) magnetically stirred solution of potassium *tert*-butoxide [35.9 mmol, prepared from potassium (1.4 g, 35.9 mmol) and Bu^{t}OH (40 ml)] in THF (56 ml) under a nitrogen atmosphere was added the bromoenone **14** (4.5 g, 18.5 mmol) in THF (85 ml). The reaction mixture was slowly warmed up to RT and stirred for 3 h. It was then quenched with water and extracted with diethyl ether (3 × 50 ml). The 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 using ethyl acetate–hexane (1:99 to 1:50) as eluent furnished a 3:2 epimeric mixture of the bicyclic compound **12** (1.75 g, 58%) as an oil; $[\alpha]_D^{26}$ −525 (*c* 3.4, $CHCl_3$); ν_{max}/cm^{-1} 1715, 1650, 880; δ_H(90 MHz, $CDCl_3$, 3:2 diastereomeric mixture) 6.56 and 6.43 (1 H, dd, *J* 7.7 and 6.4, H-5), 5.89 and 5.84 (1 H, dd, *J* 7.7 and 1.5, H-6), 4.94 (s) and 4.84 (q, *J* 1.0) and 4.73 (q, *J* 1.0) [2 H, C(8)=CH_2], 3.0–3.25 (1 H, m, H-4), 1.9–2.5 (3 H, m), 1.23 (3 H, s, *tert*-CH_3), 1.11 and 1.02 (3 H, d, *J* 7.0, *sec*-CH_3); δ_C(22.5 MHz, $CDCl_3$, 3:2 mixture) 213.8 and 212.9 (s, C=O), 146.6 and 143.3 (s, *C*=CH_2), 135.8 and 134.1 (d) and 133.6 and 132.5 (d) (*C*H=*C*H), 105.7 and 107.7 (t, C=*C*H_2), 49.9 and 49.5 (s, C-1), 49.1 and 48.8 (d, C-3), 41.7 and 43.6 (d, C-4), 38.0 and 37.5 (t, C-7), 16.7 (q) and 14.9 (q) (2 × CH_3); *m*/*z* 162 (M^+, 10%), 133 (25), 106 (100), 91 (92); HRMS: *m*/*z* for $C_{11}H_{14}O$, Calc.: 162.1048. Found: 162.1049.

(−)-(1*S*,3*S*,4*S*)-1,3-Dimethyl-3-(3-methylbut-2-en-1-yl)-8-methylenebicyclo[2.2.2]oct-5-en-2-one 16

To a cold (−90 °C) magnetically stirred solution of LDA [prepared from diisopropylamine (452 mg, 0.63 ml, 4.47 mmol) and Bu^{n}Li (4.43 mmol, 2.05 ml of a 2.16 M solution in hexane)] in 3 ml of dry THF was added a solution of the dienone **12** (244 mg, 1.5 mmol) in 3 ml of dry THF over a period of 10 min. The reaction mixture was stirred for 40 min at the same temperature and then HMPT (714 mg, 0.7 ml, 3.98 mmol) was added. The reaction mixture was stirred for 10 min and treated with prenyl bromide (882 mg, 0.69 ml, 5.92 mmol), slowly warmed up to RT and stirred for 8 h. It was then diluted with water (2 ml) and extracted with diethyl ether (3 × 15 ml). The combined organic extracts were washed with 3 M HCl (2 ml), saturated aqueous $NaHCO_3$ 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 1:20) as eluent furnished the alkylated compound **16** (328 mg, 95%) as an oil; $[\alpha]_D^{24}$ −304 (*c* 1.71, $CHCl_3$); ν_{max}/cm^{-1} 1715, 1645, 880;

δ_H(200 MHz, $CDCl_3$) 6.45 (1 H, dd, *J* 7.9 and 6.4, H-5), 5.82 (1 H, dd, *J* 7.9 and 1.5, H-6), 5.13 (1 H, t, with further couplings, *J* 8.1, H-2′), 4.91 (1 H, br s) and 4.78 (1 H, br s) [C(8)=CH_2], 3.03 (1 H, dd, *J* 6.4 and 1.5, H-4), 2.33 and 2.19 (2 H, t of AB q, *J* 16.9 and 2.1, H-7), 2.19 and 2.02 (2 H, d of AB q, *J* 17.4 and 8.1, H-1′), 1.75 (3 H, s) and 1.59 (3 H, s) [CH=C(CH_3)$_2$], 1.23 [3 H, s, C(1)–CH_3], 0.99 [3 H, s, C(3)–CH_3]; δ_C(22.5 MHz, $CDCl_3$) 216.0 (s, C=O), 145.1 (s, C-8), 135.7 (d) and 132.4 (d) (C-5 and -6), 134.3 (s, C-3′), 119.1 (d, C-3′), 108.2 [t, C(8)=CH_2], 51.8 (d, C-4), 50.1 (s) and 46.7 (s) (C-1 and -3), 38.5 (t) and 35.9 (t) (C-7 and -1′), 26.0 (q), 21.6 (q), 18.0 (q) and 17.4 (q) (4 × CH_3); *m*/*z* 230 (M^+, 8%), 125 (15), 106 (100), 91 (75); HRMS: *m*/*z* for $C_{16}H_{22}O$, Calc.: 230.1671. Found: 230.1656.

(−)-(1*S*,3*S*,4*S*)-3-(2-Bromo-3-hydroxy-3-methylbutyl)-1,3-dimethyl-8-methylenebicyclo[2.2.2]oct-5-en-2-one 17 and (−)-(1*S*,3*S*,4*S*)-3-(3-bromo-2-hydroxy-3-methylbutyl)-1,3-dimethyl-8-methylenebicyclo[2.2.2]oct-5-en-2-one 18

To a cold (−10 °C) magnetically stirred solution of the triene **16** (1.18 g, 5.13 mmol) in THF (19.5 ml) and water (4.9 ml) was slowly added NBS (869 mg, 4.88 mmol) over a period of 45 min. The reaction mixture was slowly warmed up to RT and stirred for 24 h. It was then diluted with water (10 ml) and extracted with CH_2Cl_2 (3 × 25 ml). The organic extracts were 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 : 50 to 1 : 7) as eluent furnished first the unreacted starting material (320 mg, 27%). Further elution of the column furnished the regioisomeric bromohydrins **18** (70 mg, 4%) and **17** (783 mg, 64% based on consumed starting material) as oils. *For the bromohydrin* **17**: $[\alpha]_D^{25}$ −255 (*c* 1.22, $CHCl_3$); ν_{max}/cm^{-1} 3460, 1710, 1650, 885; δ_H(200 MHz, $CDCl_3$) 6.58 (1 H, dd, *J* 7.9 and 6.4, H-5), 5.81 (1 H, dd, *J* 7.9 and 1.5, H-6), 4.99 (1 H, s) and 4.83 (1 H, s) [C(8)=CH_2], 4.22 (1 H, dd, *J* 8.5 and 1.3, CHBr), 3.52 (1 H, dd, *J* 6.4 and 1.4, H-4), 2.0–2.4 (3 H, m), 1.92 (1 H, dd, *J* 16.2 and 8.5, H-1′a), 1.32 (3 H, s) and 1.27 (3 H, s) [HOC(CH_3)$_2$], 1.22 [3 H, s, C(1)–CH_3], 1.07 [3 H, s, C(3)–CH_3]; δ_C(22.5 MHz, $CDCl_3$) 216.1 (s, C=O), 144.4 (s, *C*=CH_2), 136.5 (d) and 131.8 (d) (*C*H=*C*H), 108.9 (t, C=*C*H_2), 72.9 (s, *C*OH), 63.3 (d, *C*HBr), 51.9 (d, C-4), 50.0 (s) and 45.6 (s) (C-1 and -3), 41.9 (t), 38.2 (t), 26.1 (q) and 25.5 (q) [OC(*C*H_3)$_2$], 21.5 (q) and 17.4 (q) [2 × *tert*-CH_3]; *m*/*z* 327 (M^+ + 1, 1.2%), 329 (M^+ + 3, 1), 311 (24), 247 (12), 229 (15), 201 (30), 141 (20), 107 (100); HRMS: *m*/*z* for $C_{16}H_{23}O_2$ (M − Br), Calc.: 247.1698. Found: 247.1681. *For the minor bromohydrin* **18**: ν_{max}/cm^{-1} 3500, 1720, 1650, 875; δ_H(90 MHz, $CDCl_3$) 6.19 (1 H, dd, *J* 8.4 and 6.5, H-5), 5.87 (1 H, dd, *J* 8.4 and 1.5, H-6), 4.81 (1 H, q, *J* 1.9) and 4.7 (1 H, q, *J* 1.9) (C=CH_2), 4.09 (1 H, dd, *J* 9.6 and 6.4, C*H*OH), 3.55 (1 H, d, *J* 3.0), 2.8 (1 H, dd, *J* 6.4 and 1.9), 1.6–2.5 (4 H, m), 1.69 (3 H, s) and 1.64 (3 H, s) [(CH_3)$_2$CBr], 1.2 [3 H, s, C(1)–CH_3], 1.11 [3 H, s, C(3)–CH_3]; *m*/*z* 329 (M^+ + 2, 6%), 327 (M^+, 6), 311 (4), 247 (6), 220 (44), 222 (44), 159 (11), 134 (85), 132 (85), 106 (100), 95 (60), 91 (100).

(+)-(1*R*,3*S*,5*R*,6*S*,7*S*)- and (+)-(1*R*,3*S*,5*S*,6*S*,7*S*)-5-(2-Hydroxypropan-2-yl)-1,3-dimethyl-8-methylenetricyclo-[4.3.1.0^{3,7}]decan-2-one 19 and 20

To a refluxing solution of the bromohydrin **17** (700 mg, 2.14 mmol) and Bu$^n_3$SnH (649 mg, 0.59 ml, 2.23 mmol) in dry benzene (200 ml) was added AIBN (catalytic) and refluxed for 4 h. The solvent was evaporated under reduced pressure, diluted with water and extracted with diethyl ether (2 × 20 ml). The combined organic extracts were washed with 1% aq. ammonia 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 : 20 to 1 : 5) furnished first the isotwistane **19** (150 mg, 28%), mp 80–82 °C; $[\alpha]_D^{25}$ +18.0 (*c* 1.67, $CHCl_3$); ν_{max}/cm^{-1} 3500, 1710, 1650, 885; δ_H(90 MHz, $CDCl_3$) 4.91 (1 H, q, *J* 1.9) and 4.78 (1 H, q, *J* 1.9) (C=CH_2), 1.35–2.65 (9 H, m), 1.25 (3 H, s) and 1.12 (3 H, s) [HOC(CH_3)$_2$], 1.09 (3 H, s, *tert*-CH_3), 0.93 (3 H, s, *tert*-CH_3); δ_C(22.5 MHz, $CDCl_3$) 221.9 (C=O), 143.8 (*C*=CH_2), 110.1 (C=*C*H_2), 71.4 (*C*OH), 57.6, 54.7, 50.6, 43.0, 41.0, 40.4, 36.2, 31.7, 30.4, 28.7, 23.3 and 19.5; *m*/*z* 248 (M^+, 15%), 190 (30), 159 (20), 136 (100); HRMS: *m*/*z* for $C_{16}H_{24}O_2$, Calc.: 248.1776. Found: 248.1782. Further elution of the column furnished a ~1 : 6 mixture of the rearranged product **21** and the isotwistane **20** (370 mg, 70%), mp 106–108 °C; $[\alpha]_D^{27}$ +49.0 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} 3480, 1715, 885; δ_H(200 MHz, $CDCl_3$, peaks due to the isotwistane **20**) 4.97 (1 H, br s) and 4.87 (1 H, br s) (C=CH_2), 2.25–2.5 (2 H, m), 2.27 (2 H, br s, allylic CH_2), 1.85–2.05 (2 H, m), 1.25–1.6 (3 H, m), 1.20 (3 H, s) and 1.16 (3 H, s) [HOC(CH_3)$_2$], 1.09 (3 H, s, *tert*-CH_3), 0.98 (3 H, s, *tert*-CH_3); δ_C(22.5 MHz, $CDCl_3$, peaks due to the isotwistane **20**) 221.3 (s, C=O), 143.1 (s, *C*=CH_2), 110.6 (t, C=*C*H_2), 72.0 (s, *C*OH), 57.9 (d), 55.2 (2 C, s and t), 43.6 (s), 42.2 (d), 40.3, 39.6, 39.1, 28.1 (q), 26.6 (q), 19.5 (q) and 18.8 (q) (4 × CH_3); *m*/*z* 248 (M^+, 20%), 190 (35), 187 (20), 159 (30), 147 (20), 136 (70), 59 (100); HRMS: *m*/*z* for $C_{16}H_{24}O_2$, Calc.: 248.1776. Found: 248.1760.

(+)-(1*R*,3*S*,5*R*,6*R*,7*R*)-5-(2-Hydroxypropan-2-yl)-1,3-dimethyltricyclo[4.3.1.0^{3,7}]decane-2,8-dione 22

A pre-cooled (−90 °C) mixture of ozone in oxygen was passed through a solution of the isotwistane **19** (60 mg, 0.24 mmol) and $NaHCO_3$ (catalytic) in MeOH (0.1 ml) and CH_2Cl_2 (4 ml) until the blue colour persisted. The excess ozone was removed by flushing the solution with oxygen. Dimethyl sulfide (169 mg, 0.2 ml, 2.7 mmol) was added to the reaction mixture, which was slowly warmed up to RT and stirred for 8 h. Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate–hexane (1 : 5 to 1 : 2.5) as eluent furnished the diketo alcohol **22** (40 mg, 67%), which was recrystallised from a 1 : 10 mixture of ethyl acetate and hexane, mp 106–108 °C; $[\alpha]_D^{25}$ +26.6 (*c* 1.28, $CHCl_3$); ν_{max}/cm^{-1} 3490, 1720, 1700; δ_H(200 MHz, $CDCl_3$) 2.81 (1 H, dd, *J* 10.8 and 5.6, H-6), 2.72 (1 H, d, *J* 12.7, H-10a), 2.49 (1 H, d, *J* 4.4, H-7), 2.22 (2 H, s, H-9), 2.1–2.25 (1 H, m, H-5), 2.0 (1 H, dd, *J* 13.3 and 7.6, H-4$_{endo}$), 1.75 (1 H, dd, *J* 13.3 and 11.3, H-4$_{exo}$), 1.59 (1 H, dd, *J* 14.4 and 9.9, H-10$_{exo}$), 1.30 (3 H, s) and 1.20 (3 H, s) [HOC(CH_3)$_2$], 1.18 (3 H, s) and 1.07 (3 H, s) (2 × *tert*-CH_3); *m*/*z* 250 (M^+, 8%), 232 (35), 192 (28), 161 (22), 138 (45), 109 (18), 59 (100); HRMS: *m*/*z* for $C_{15}H_{22}O_3$, Calc.: 250.1569. Found: 250.1570.

(+)-(1*R*,3*S*,6*S*,7*R*)-5-Isopropylidene-1,3-dimethyltricyclo-[4.3.1.0^{3,7}]decane-2,8-dione 23

A magnetically stirred solution of the diketo alcohol **22** (40 mg, 0.16 mmol) and PTSA (catalytic) in dry benzene (4 ml) was refluxed for 6 h. The solvent was evaporated under reduced pressure. The reaction mixture was then diluted with diethyl ether (10 ml), washed with saturated aq. $NaHCO_3$ 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 to 1 : 5) as eluent furnished the enedione **23** (35 mg, 95%); $[\alpha]_D^{26}$ +82.4 (*c* 3.12, $CHCl_3$); ν_{max}/cm^{-1} 1730, 1710; δ_H(200 MHz, $CDCl_3$) 3.26 (1 H, dd, *J* 9.0 and 5.3, H-6), 2.56 (1 H, d, *J* 5.3, H-7), 2.51 (1 H, d, *J* 16.0, H-9a), 2.26 (2 H, close AB q, H-4), 2.12 (1 H, d, *J* 16.0, H-9b), 2.03 (1 H, dd, *J* 13.3 and 9.1, H-10$_{exo}$), 1.63 (3 H, s) and 1.57 (3 H, s) (2 × olefinic CH_3), 1.42 (1 H, dd, *J* 13.2, H-10$_{endo}$), 1.19 (3 H, s) and 1.07 (3 H, s) (2 × *tert*-CH_3); δ_C(22.5 MHz, $CDCl_3$) 217.6 (s, C=O), 211.7 (s, C=O), 136.1 (s) and 124.6 (s) (*C*=*C*), 62.2 (d, C-7), 54.9 (s) and 44.9 (s) (C-1 and -3), 47.9 (t), 42.2 (t), 40.1 (d), 39.1 (t), 21.0 (q), 20.6 (q), 19.4 (q) and 19.2 (q) (4 × CH_3); *m*/*z* 232 (M^+, 72%), 217 (10), 189 (12), 161 (15), 149 (27), 121 (100); HRMS: *m*/*z* for $C_{15}H_{20}O_2$, Calc: 232.1463. Found: 232.1471.

(+)-(1*S*,3*S*,6*S*,7*R*)-5-Isopropylidene-1,3-dimethyltricyclo-[4.3.1.0^{3,7}]decane-2-one 24

A solution of the dione **23** (31 mg, 0.134 mmol) and hydrazine monohydrate (93 mg, 0.09 ml, 1.86 mmol, 99%) in diethylene glycol (digol, 0.9 ml) and ethylene glycol (0.25 ml) were placed in a Carius tube, and heated to 180 °C for 2 h. The Carius tube was cooled to 70 °C and a solution of sodium (37 mg, 1.61 mmol) in digol (0.75 ml) was added. The reaction mixture was further heated at 180 °C for 4 h. It was then cooled to RT, poured into water (5 ml) and extracted with CH_2Cl_2 (3 × 5 ml). The organic extracts were 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 (1:40) as eluent furnished the enone **24** (26 mg, 90%); $[a]_D^{26}$ +101.8 (*c* 2.26, $CHCl_3$); ν_{max}/cm^{-1} 1725 and 1710; δ_H(200 MHz, $CDCl_3$) 2.92 (1 H, dd, *J* 8.7 and 3.8, H-6), 2.34 (1 H, d, *J* 16.7), 1.5–2.1 (8 H, m), 1.63 (3 H, s) and 1.53 (3 H, s) (2 × olefinic CH_3), 1.19 (3 H, s) and 0.90 (3 H, s) (2 × *tert*-CH_3); δ_C(22.5 MHz, $CDCl_3$) 222.5 (s, C=O), 137.5 (s) and 122.7 (s) (*C*=*C*), 53.8 and 42.3 (s, C-1 and -3), 45.5 (d, C-6), 42.6 (t, C-4), 40.7 (d, C-7), 38.4 (t), 32.8 (t), 20.8 (2 C, q and t), 20.5 (q), 18.7 (q), 17.1 (q); *m*/*z* 218 (M^+, 100%), 203 (11), 175 (42), 165 (52), 147 (28), 134 (84); HRMS: *m*/*z* for $C_{15}H_{22}O$, Calc.: 218.1671. Found: 218.1670.

(+)-(1*S*,3*S*,6*S*,7*R*)-1,3-Dimethyltricyclo[4.3.1.0^{3,7}]decane-2,5-dione 25

Ozonolytic cleavage of the isopropylidene moiety in compound **24** (35 mg, 0.16 mmol) in 0.1 ml MeOH and CH_2Cl_2 (3 ml) followed by reductive work-up with dimethyl sulfide (0.2 ml), as described for compound **22**, followed by purification on a silica gel column using ethyl acetate–hexane (1:5 to 1:2.5) as eluent furnished the dione **25** (24.3 mg, 79%), which was identified by comparison [5a,c] of its spectral data (IR, ^{1}H and ^{13}C NMR) with that of the authentic racemic sample; $[a]_D^{25}$ +27.0 (*c* 2.0, $CHCl_3$); ν_{max}/cm^{-1} 1740, 1710; δ_H(400 MHz, $CDCl_3$) 2.68 (1 H, dd, *J* 10.8 and 5.1, H-6), 2.35 (1 H, d, *J* 18.6, H-4a), 2.25 (1 H, m), 2.11 (1 H, d, *J* 18.6 and 1.4, H-4b), 2.02 (1 H, dd, *J* 14.8 and 10.8, H-10$_{exo}$), 1.85–2.1 (2 H, m), 1.6–1.75 (2 H, m), 1.4 (1 H, d, *J* 14.8, H-10$_{endo}$), 1.31 (3 H, s) and 0.96 (3 H, s) (2 × *tert*-CH_3); δ_C(50 MHz, $CDCl_3$) 219.2 (C=O), 217.1 (C=O), 52.4 (quat. C), 48.9, 48.7, 43.3, 42.4 (quat. C), 32.6 (2 C), 20.1, 18.6 and 16.2; *m*/*z* 192 (M^+, 100%), 164 (21), 149 (31), 138 (29), 121 (33), 107 (25), 94 (73).

(+)-(1*S*,3*S*,6*S*,7*R*)-5-Isopropylidene-1,3-dimethyltricyclo-[4.3.1.0^{3,7}]decan-2-one 24 and (+)-(1*R*,2*R*,5*S*,6*S*,8*S*)-10-isopropylidene-5,8-dimethyltricyclo[4.4.0.0^{2,8}]decan-7-one 26

Ozonolysis of a 6:1 mixture of the isotwistane **20** and the rearranged product **21** (154 mg, 0.62 mmol) in 8 ml of CH_2Cl_2 containing 0.2 ml of MeOH and a catalytic amount of $NaHCO_3$ and reductive work-up with dimethyl sulfide (424 mg, 6.82 mmol, 0.5 ml), as described for compound **22**, followed by purification of the product on a silica gel column using ethyl acetate–hexane (1:5 to 1:2) as eluent furnished a 6:1 mixture of the diketo alcohols **27** and **28** (152 mg, 98%); $[a]_D^{26}$ +56.8 (*c* 5.35, $CHCl_3$); ν_{max}/cm^{-1} 3440, 1710; δ_H(200 MHz, $CDCl_3$) peaks due to the isotwistane **27**: 2.6–2.75 (1 H, m, H-6), 2.55 (1 H, d, *J* 5.5, H-7), 2.24 (2 H, close AB q, H-9), 2.07 (1 H, ddd, *J* 13.2, 8.9 and 4.5, H-5), 1.6–1.75 (2 H, m), 1.45 (1 H, dd, *J* 12.4 and 8.4, H-4), 1.37 (1 H, d, *J* 14.0), 1.22 (3 H, s) and 1.15 (3 H, s) [(C*H*$_3$)$_2$COH], 1.17 (3 H, s) and 1.1 (3 H, s) (2 × *tert*-CH_3); δ_C(22.5 MHz, $CDCl_3$) peaks due to the isotwistane **27**: 217.8 (s, C-2), 212.7 (s, C-8), 71.6 (s, *C*OH), 61.3 (d, C-7), 58.9 (d), 55.8 (s) and 44.8 (s) (C-1 and -3), 47.4 (t, C-9), 41.7 (t), 39.4 (t), 38.1 (d), 28.3 (q) and 26.5 (q) [OC(*C*H$_3$)$_2$], 19.1 (q) and 18.8 (q) (2 × *tert*-CH_3). Peaks due to compound **28**: 212.7 (s, C-2), 211.1 (s, C-8), 71.0 (s, *C*OH), 63.9 (d, C-7), 59.5, 57.0, 50.7, 47.4, 43.7, 36.0, 33.0, 28.5 (q) and 27.2 (q) [OC(*C*H$_3$)$_2$], 18.8 (q) and 11.1 (q) (2 × CH_3); *m*/*z* 250 (M^+, 16%), 232 (18), 192 (45), 138 (25), 59 (100); HRMS: *m*/*z* for $C_{15}H_{22}O_3$, Calc.: 250.1569. Found: 250.1568.

Dehydration of a mixture of the diketo alcohols **27** and **28** (130 mg, 0.52 mmol), obtained above, using *p*-toluenesulfonic acid (10 mg) in benzene (13 ml) at 100 °C for 12 h furnished a mixture of the diones **23** and **29** (112 mg, 93%). Huang–Minlon modified Wolff–Kishner reduction of a 6:1 mixture of the diones **23** and **29** (125 mg, 0.538 mmol) using hydrazine monohydrate (371 mg, 0.36 ml, 7.41 mmol, 99%) in digol (3.6 ml) and ethylene glycol (0.9 ml), and sodium (148 mg, 6.43 mmol) in digol (3 ml) at 180 °C for 4 h as described earlier, furnished a mixture of the enediones **24** and **26** (108 mg, 92% yield).

Reduction of the mixture of enones 24 and 26

To a blue coloured magnetically stirred solution of lithium (15 mg, 2.15 mmol) in freshly distilled ammonia (35 ml) was slowly added a mixture of the enones **24** and **26** (38 mg, 0.174 mmol) in 1 ml of dry THF. The reaction mixture was stirred for 1 h and quenched with solid ammonium chloride. The excess ammonia was evaporated, the residue was taken up in water (5 ml) and extracted with diethyl ether (2 × 10 ml). The combined organic extracts were 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 (1:50 to 1:20) as eluent afforded an epimeric mixture of the alcohol **30** (26 mg, 68%) and the alcohol **31** (6.1 mg, 16%) as oils.

Oxidation of compound 31

To a magnetically stirred solution of the alcohol **31** (6 mg, 0.027 mmol) in CH_2Cl_2 (0.2 ml) was added a mixture of PCC (6 mg, 0.28 mmol) and silica gel (6 mg), which was stirred for 1 h at RT. The reaction mixture was then charged to a silica gel column and eluted with ethyl acetate–hexane (1:40) to furnish the enone **26** (5.2 mg, 88%); $[a]_D^{28}$ +115.0 (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} 1735; δ_H(200 MHz, $CDCl_3$) 2.7 (1 H, s, C*H*-C=O), 1.4–2.25 (9 H, m), 1.67 (3 H, s) and 1.51 (3 H, s) (2 × olefinic CH_3), 1.01 (3 H, s, *tert*-CH_3), 1.0 (3 H, d, *J* 6.7, *sec*-CH_3); δ_C(50 MHz, $CDCl_3$) 57.5, 52.3, 50.9, 49.1, 41.4, 34.3, 27.6, 22.7, 22.3, 20.7, 19.8, 11.8.

Oxidation of compound 30

Oxidation of an epimeric mixture of the alcohol **30** (35 mg, 0.159 mmol) with PCC (50 mg, 0.232 mmol) and silica gel (50 mg) for 1 h furnished the tricyclic ketone **24** (32 mg, 92%), which was identified by comparison of TLC and spectral data (IR and ^{1}H NMR) with the sample derived from the isotwistane **19**.

(−)-(1*S*,3*S*,4*S*)-3-(4-Bromo-3-methylbut-2-en-1-yl)-1,3-dimethyl-8-methylenebicyclo[2.2.2]oct-5-en-2-one 35

Alkylation of the bicyclic enone **12** (732 mg, 4.52 mmol) in THF (9 ml) using LDA [generated from diisopropylamine (1.343 g, 1.86 ml, 13.2 mmol) and Bu^{n}Li (13.1 mmol, 6.7 ml of a 1.96 M solution in hexane) in THF (10 ml)] in the presence of HMPT (1.54 g, 1.5 ml, 9.44 mmol) with 1,4-dibromo-2-methylbut-2-ene (3.5 ml) as described for compound **16**, followed by purification of the product over a silica gel column using ethyl acetate–hexane (0:1 to 1:20) as eluent furnished the bromo compound **35** (1.022 g, 73%); $[a]_D^{28}$ −273.7 (*c* 2.62, $CHCl_3$); ν_{max}/cm^{-1} 1715, 1650; δ_H(200 MHz, $CDCl_3$) 6.46 (1 H, dd, *J* 7.9 and 6.5, H-5), 5.83 (1 H, dd, *J* 7.9 and 1.6, H-6), 5.62 (1 H, t, *J* 7.7, H-2′), 4.93 (1 H, s) and 4.80 (1 H, s) [C(8)=C*H*$_2$], 4.0 (2 H, s, C*H*$_2$Br), 3.0 (1 H, dd, *J* 6.5 and 1.6, H-4), 2.0–2.4 (4 H, m, H-7 and -1′), 1.89 (3 H, s, olefinic CH_3), 1.23 [3 H, s, C(1)–CH_3], 1.01 [3 H, s, C(3)–CH_3]; δ_C(22.5 MHz, $CDCl_3$) 215.4 (s, C=O), 144.6 (s, C-8), 135.6 (d) and 132.6 (d) (C-5 and -6), 134.6 (s, C-3′), 126.3 (d, C-2′), 108.6 [t, C(8)=*C*H$_2$], 52.0 (d, C-4), 50.2 (s) and 46.5 (s) (C-1 and -3), 41.2 (t), 38.2 (t) and 36.3 (t) (C-7, -1′

and -4′), 21.8 (q), 17.3 (q) and 14.9 (q) (3 × CH_3); *m*/*z* 229 (M^+ − Br, 40%), 106 (100), 91 (100); HRMS: *m*/*z* for $C_{16}H_{21}O$ (M − Br), Calc.: 229.1593. Found: 229.1588.

(1*R*,3*S*,6*R*,7*S*)-5-Isopropenyl-1,3-dimethyl-8-methylenetricyclo-[4.3.1.0^{3,7}]decan-2-one 36 and (1*R*,2*R*,5*S*,6*S*,8*S*)-10-isopropenyl-5,8-dimethyl-3-methylenetricyclo[4.4.0.0^{2,8}]decan-7-one 37

A solution of Bu^n_3SnH (303 mg, 0.28 ml, 1.04 mmol) and AIBN (20 mg) in 170 ml of benzene was prepared, 30 ml of which was added to a refluxing solution of the bromide **35** (300 mg, 0.97 mmol) in benzene (29 ml). The remaining solution of the Bu^n_3-SnH and AIBN was added dropwise to the reaction mixture over a period of 2 h and refluxed for a further 8 h. The solvent was evaporated under reduced pressure. The reaction mixture was diluted with water (5 ml) and extracted with diethyl ether (3 × 25 ml). The extract was washed with 1% aq. ammonia 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 (0 : 1 to 1 : 40) as eluent furnished an epimeric mixture of the isotwistanes **36** and minor amounts of the rearranged product **37** (170 mg, 76%) as an oil; ν_{max}/cm^{-1} 3080, 1720, 1640, 890; δ_H(200 MHz, $CDCl_3$) 4.94 (1 H, q, *J* 2.0) and 4.87 (1 H, q, *J* 2.0) [C(8)=CH_2], 4.8 (1 H, m) and 4.71 (1 H, s) (CH_3-C=CH_2), 1.9–2.45 (6 H, m), 1.74 (3 H, d, *J* 1.0, olefinic CH_3), 1.65–1.8 (1 H, m), 1.47 (1 H, dd, *J* 11.6 and 5.3), 1.2–1.25 (1 H, m), 1.10 (3 H, s) and 0.99 (3 H, s) (2 × *tert*-CH_3); *m*/*z* 230 (M^+, 100%), 215 (20), 187 (40), 159 (45), 145 (50), 133 (70), 119 (50), 107 (52), 105 (52), 91 (60); HRMS: *m*/*z* for $C_{16}H_{22}O$, Calc.: 230.1671. Found: 230.1656.

Conversion of 36 and 37 into 23 and 29

Ozonolysis of a mixture of **36** and **37** (272 mg, 1.183 mmol) in 0.1 ml MeOH and CH_2Cl_2 (5 ml) at −90 °C and reductive work-up with dimethyl sulfide (847 mg, 1 ml, 13.63 mmol) as described for the diketone **22** followed by purification over a silica gel column using ethyl acetate–hexane (1 : 5 to 1 : 2) as eluent furnished the triketone (162 mg, 59%) as an oil. $[a]_D^{25}$ +70.0 (*c* 3.2, $CHCl_3$); ν_{max}/cm^{-1} 1720, 1700; δ_H(400 MHz, $CDCl_3$) 2.94 (1 H, dd, *J* 9.5 and 5.0, H-5), 2.7–2.9 (2 H, m), 2.54 (1 H, d, *J* 5.0, H-7), 2.26 (2 H, close AB q), 2.19 (3 H, s, CH_3C=O), 2.1–2.2 (1 H, m), 1.86 (1 H, dd, *J* 13.4 and 6.5, H-10$_{exo}$), 1.42 (1 H, d, *J* 14.0, H-4$_{exo}$), 1.2 (3 H, s) and 1.13 (3 H, s) (2 × *tert*-CH_3); δ_C(22.5 MHz, $CDCl_3$, peaks due to major isomer) 216.4 (s, C-2), 210.2 (s, C-8), 206.9 (s, CH_3C=O), 60.3 (d, C-7), 58.8 (d, C-5), 55.5 (s) and 44.5 (s) (C-1 and -3), 46.9 (t), 39.3 (t), 38.5 (t), 38.2 (d, C-6), 28.5 (q, CH_3C=O) and 18.7 (2 C, q, 2 × *tert*-CH_3); *m*/*z* 234 (M^+, 56%), 219 (15), 206 (10), 191 (17), 163 (21), 148 (26), 135 (20), 123 (40), 43 (100); *m*/*z* for $C_{14}H_{18}O_3$, Calc.: 234.1256. Found: 234.1265.

To a cold (0 °C), magnetically stirred suspension of methyltriphenylphosphonium iodide (162 mg, 0.4 mmol) in benzene (4 ml) was added potassium *tert*-amyloxide (0.384 mmol) [prepared from potassium (15 mg, 0.384 mmol) in 0.4 ml *tert*-amyl alcohol] in benzene (0.6 ml) and the resultant yellow reaction mixture was stirred for 20 min at RT. To the methylenetriphenylphosphorane thus formed, was added a solution of the 5-acetylisotwistane-2,8-dione obtained in the previous experiment (76 mg, 0.325 mmol) in benzene (2 ml) and stirred at RT for 7 min. The reaction mixture was then quenched with water (2 ml) and extracted with diethyl ether (3 × 5 ml). The 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 using ethyl acetate–hexane (1 : 20 to 1 : 5) as eluent furnished a mixture of the diketones (40.7 mg, 80% yield, based on the starting material consumed); $[a]_D^{28}$ +60.4 (*c* 1.82, $CHCl_3$); ν_{max}/cm^{-1} 3080, 1720, 1650, 890; δ_H(200 MHz, $CDCl_3$) 4.73 (2 H, br s, C=CH_2), 2.6–2.65 (2 H, m), 2.0–2.4 (5 H, m), 1.73 (3 H, s, olefinic CH_3), 1.53 (1 H, dd, *J* 13.0 and 6.5), 1.42 (1 H, d, *J* 13.8), 1.19 (3 H, s, *tert*-CH_3) and 1.11 (3 H, s, *tert*-CH_3); *m*/*z* 232 (M^+, 93%), 217 (22), 189 (21), 161 (16), 121 (100), 105 (29); HRMS: *m*/*z* for $C_{15}H_{20}O_2$, Calc.: 232.1463. Found: 232.1468.

Isomerisation of the diketones obtained above (40 mg, 0.172 mmol) using rhodium chloride (5 mg) in refluxing ethanol (3 ml) for 18 h followed by evaporation of the solvent under reduced pressure and purification of the residue over a silica gel column using ethyl acetate–hexane (1 : 10 to 1 : 5) as eluent furnished a mixture of the enedione **23** and **29** (35 mg, 88%), which were identified by spectral comparison (IR and ^{1}H NMR) with the mixture obtained earlier.

(+)-(1*S*,3*S*,5*S*,6*R*,7*R*)- and (1*S*,3*S*,5*R*,6*R*,7*R*)-1,3-Dimethyl-5-isopropyltricyclo[4.3.1.0^{3,7}]decan-2-one (2-pupukeanone 5 and 5-*epi*-2-pupukeanone 6)

Platinum oxide (20 mg) was placed in a RB flask and activated with hydrogen (balloon). To the activated PtO_2 was added a solution of the enone **24** (40 mg, 0.183 mmol) in ethanol (4 ml). The reaction mixture was magnetically stirred for 24 h under a hydrogen atmosphere created by evacuative displacement of air. The catalyst was filtered off and the filtrate was added to a fresh sample of preactivated PtO_2 (10 mg). The reaction mixture was further stirred for 24 h 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 : 40 to 1 : 25) as eluent furnished a 2.5 : 1 epimeric mixture of 2-pupukeanone **5** and 5-*epi*-2-pupukeanone **6** (25 mg, 63%) as an oil, which were identified by comparison[4b] of the ^{1}H and ^{13}C NMR and mass spectra with those reported for the racemic compounds in the literature; $[a]_D^{24}$ +26.0 (*c* 1.54, $CHCl_3$); ν_{max}/cm^{-1} 1710; δ_H(400 MHz, $CDCl_3$) peaks due to 2-pupukeanone **5**: 2.32 (1 H, dd, *J* 8.7 and 3.7, H-6), 1.54–1.85 (9 H, m), 1.38–1.45 (1 H, m, H-5), 1.31 (1 H, dd, *J* 13.9 and 7.8), 1.14 (3 H, s) and 0.92 (3 H, s) (2 × *tert*-CH_3), 0.84 (3 H, d, *J* 6.9) and 0.83 (3 H, d, *J* 6.7) [$CH(CH_3)_2$]. Peaks due to 5-*epi*-2-pupukeanone **6**: 2.14 (1 H, dd, *J* 9.0 and 5.2, H-6), 1.96 (1 H, dd, *J* 13.1 and 9.1), 1.12 (3 H, s) and 0.91 (3 H, s) (2 × *tert*-CH_3), 0.89 (3 H, d, *J* 6.9) and 0.81 (3 H, d, *J* 6.7) [$CH(CH_3)_2$]; δ_C(22.5 MHz, $CDCl_3$) peaks due to 2-pupukeanone **5**: 222.7 (C=O), 53.9, 49.4, 47.3, 42.0, 41.5, 38.8, 33.9, 30.0, 29.3, 21.6 (2 C), 20.3, 19.0 and 17.6. Peaks due to 5-*epi*-2-pupukeanone **6**: 54.5, 54.0, 44.2, 42.2, 42.0, 41.5, 40.4, 33.0, 32.7, 21.2, 20.3, 20.1, 19.0, 16.9; *m*/*z* 220 (M^+, 65%), 189 (25), 177 (38), 159 (62), 149 (80), 135 (17), 121 (25), 107 (23), 93 (100).

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