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A radical cyclisation based cyclopentenone annulation of allyl alcohols

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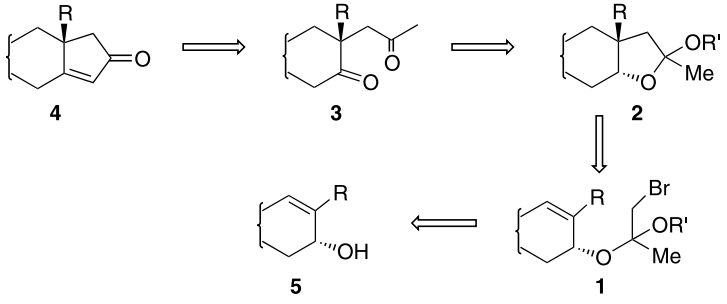
Abstract—A four-step cyclopentenone annulation reaction of allylic alcohols employing a 5-*exo*-trig radical cyclisation reaction of mixed allyl methyl ketals of bromoacetone as the key step is described. The annulated product **12b** obtained from 2,3-dimethylcyclohexenol has been further elaborated into (±)-epibakkenolides employing a 5-*exo*-dig radical cylisation reaction based α-spiro-β-methylene-γ-butyrolactone annulation methodology.

1. Introduction

Although cyclopentanes have been known for over a century and are ubiquitous in nature, interest in their synthesis and reactions remained low until mid-seventies. This can be traced to the fact that until 1960, relatively few cyclopentanoid natural products of reasonable complexity were known that could constitute challenging targets.[1] However, discoveries and developments in the chemistry of natural and unnatural products rekindled interest in the synthetic design of cyclopentanoids and a flurry of activity has been initiated in this area. The methodology of annulating a functionalised cyclopentane ring onto an existing ring residue, a cyclopentannulation, would have the potential to be useful if one could control the chemo-, regio- and stereoselectivity of the reactions involved.[2] The use of radicals in organic chemistry has increased dramatically over the last two decades. At the beginning of the eighties, the place of radical reactions in organic synthesis was limited to a few important functional group transformations. However, during the past two decades, radical carbon–carbon bond forming reactions, particularly, the intramolecular version leading to cyclic compounds, i.e. radical cyclisation reactions, have grown in importance to the present status where they are now routinely considered at the strategy level planning of complex target molecules.[3] For the cyclopentenone annulation of allyl alcohols, we envisaged a four step, radical cyclisation based methodology, which is depicted in Scheme 1 in a retrosynthetic mannner.[4] The 5-*exo*-*trig* radical cyclisation reaction of the bromo ketal **1** generates the cyclic ketal **2**. A one step hydrolysis and oxidation sequence converts the cyclic ketal **2** into a 1,4-diketone **3** which on intramolecular aldol condensation completes the annu-



Scheme 1.

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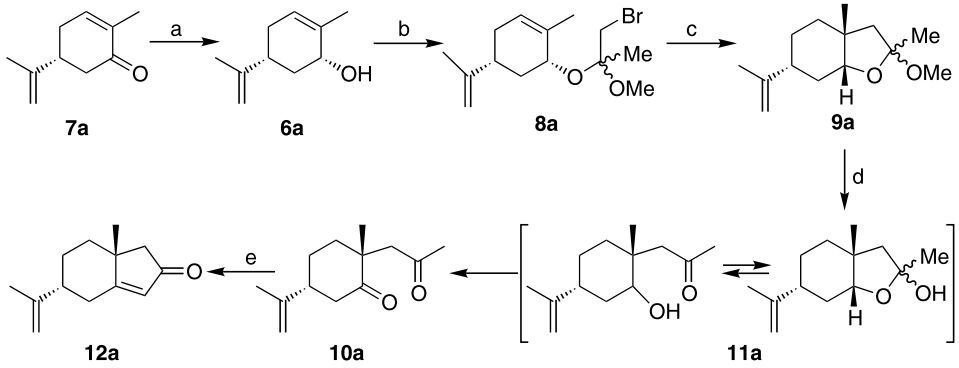
lation of the cyclopentenone moiety to the C_1–C_2 bond of the allyl alcohol to generate the enone **4**. The requisite radical precursor, bromo ketal **1**, can be obtained by a bromoketalisation reaction of the allyl alcohol **5**.

2. Results and discussion

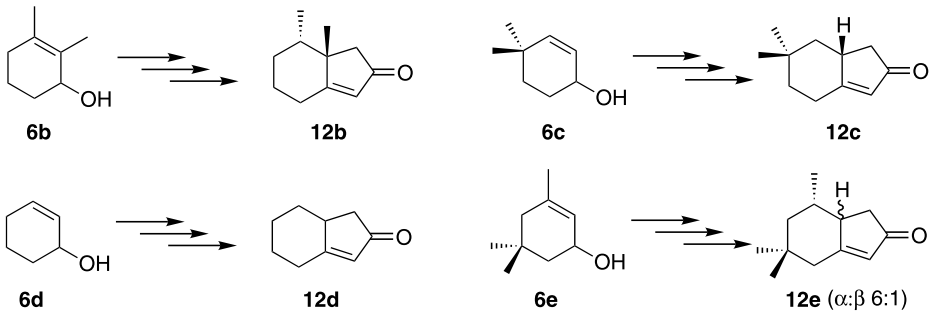
To begin with, the sequence was carried out with carveol **6a**, which was obtained by regio- and stereoselective reduction of (*R*)-carvone **7a** (Scheme 2).[5] Bromination of an enol ether in the presence of an alcohol generates a bromo acetal via the nucleophilic addition of the alcohol to the intermediate bromonium ion, and generally referred as a bromoacetalisation reaction.[6] In the present investigations for the conversion of allyl alcohols to allyl methyl mixed ketals of bromoacetone, *N*-bromosuccinimide (NBS) was chosen as the source of bromonium ion and 2-methoxypropene as the enol ether component. Thus, reaction of 2-methoxypropene with NBS in the presence of carveol **6a** in methylene chloride at −50°C furnished the radical precursor, the bromo ketal **8a**, as a mixture of epimers in 66% yield, whose structure was established from its ^{1}H and ^{13}C NMR spectra. The 5-*exo*-*trig* radical cyclisation reaction was achieved by refluxing a 0.02 M benzene solution of the bromo ketal **8a** with 1.1 equivalents of tri-*n*-butyltin hydride in the presence of a catalytic amount of AIBN to furnish an epimeric mixture (at the ketal carbon) of the cyclic ketal **9a** in 72% yield in a highly regio- and stereoselective manner. In the ^{1}H NMR spectrum, the absence of resonances due to the ring olefinic proton and bromomethylene moiety and the presence of signals, a multiplet at δ 3.40–3.90 due to the ring junction O-CH, two singlets at 3.32 and 3.26 due to O-CH_3, a singlet at 1.76 due to olefinic methyl, two singlets at 1.52 and 1.44 due to CH_3-C-OCH_3, two singlets at 1.22 and 1.12 ppm due to bridgehead methyl group, for the two epimers confirmed the structure of the cyclic ketal **9a**. The *cis* ring junction was a consequence of the addition of the radical to the double bond from the preferred *syn* face of the olefin, which also fixes the β-stereochemistry of the bridgehead methyl group. No attempt was made to separate the methoxy epimers as they will converge into a single diketone in the next step. The conversion of the cyclic ketal **9a** into the diketone **10a** was achieved employing a sonochemically accelerated reaction with Jones reagent[7] via a one pot hydrolysis and oxidation of the resulting hydroxy ketone **11a** (or hemi ketal). Thus, sonochemical irradiation of a solution of the cyclic ketal **9a** and a freshly prepared 1.6 M Jones reagent in acetone furnished, cleanly, the diketone **10a** in 72% yield. The IR spectrum showed absorption bands at 1700 and 890 cm^{-1} due to the C=O and RR′C=CH_2 groups, respectively, and in the mass spectrum the molecular ion appeared at *m*/*z* 208 establishing the structure of the diketone **10a**. In the ^{1}H NMR spectrum, the presence of the resonances, broad singlets at δ 4.79 and 4.71 due to C=CH_2, an AB quartet at 2.83 and 2.65 due to CH_2-CO-CH_3, a singlet at 2.13 due to the acetyl methyl, a singlet at 1.72 due to the olefinic methyl and a singlet at 1.12 due to the *tert*-methyl group; and in the ^{13}C NMR spectrum resonances at 213.4 and 206.8 due to two keto carbons, 147.2 and 110.4 due to two olefinic carbons, 50.6 due to CH_2-CO-CH_3, 47.0 due to the quaternary carbon, 45.6 due to the allylic CH, 42.9 due to the ring CH_2-C=O, 37.1 and 25.6 due to two ring methylenes, 31.6, 22.9 and 20.9 ppm due to three methyl carbons confirmed the structure of the diketone **10a**. Finally, intramolecular aldol condensation of the diketone **10a** using 10% aqueous potassium hydroxide in methanol in a Carius tube at 100–110°C furnished the cyclopentenone **12a** in 79% yield. The presence of the molecular ion at *m*/*z* 190 in the mass spectrum and the presence of absorption bands at 1700, 1630, 1615 and 890 cm^{-1} due to the cyclopentenone and C=CH_2 moieties, respectively, in the IR spectrum established the structure of the enone **12a**. The ^{1}H NMR spectrum of the enone **12a** revealed the presence of a singlet at δ 5.82 due to the ring olefinic proton, three singlets at 4.87, 4.74 and 1.72 due to the isopropenyl moiety, an AB quartet at 2.30 and 2.19 due to CH_2C=O and a singlet at 1.28 ppm due to *tert*-methyl group, which was further confirmed by the 13 lines ^{13}C NMR spectrum.

After successful cyclopentenone ring annulation at the C_1–C_2 carbons of carveol **6a**, to test the generality of the methodology, the sequence was carried out with the allyl alcohols **6b–e** and the results are summarised in Table 1. The allyl alcohols **6b–e** were obtained by a



Scheme 2. *Reagents and conditions*: (a) $LiAlH_4$, Et_2O; (b) NBS, CH_2=C(CH_3)OCH_3, CH_2Cl_2; (c) $^nBu_3SnH$, AIBN, C_6H_6; (d) Jones reagent, acetone,))); (e) KOH, MeOH, THF.

Table 1. Cyclopentenone annulation of allyl alcohols



Entry	Allyl alcohol (% yield)	Bromo ketal (% yield)	Cyclic ketal (% yield)	Diketone (% yield)	Enone (% yield)
A	**6a** (95)	**8a** (66)	**9a** (72)	**10a** (72)	**12a** (79)
B	**6b** (92)	**8b** (59)	**9b** (74)	**10b** (72)	**12b** (94)
C	**6c** (89)	**8c** (83)	**9c** (75)	**10c** (73)	**12c** (92)
D	**6d** (94)	**8d** (79)	**9d** (72)	**10d** (89)	**12d** (68)
E	**6e** (91)	**8e** (83)	**9e** (73)	**10e** (80)	**12e** (85)

regioselective reduction of the corresponding enones **7b–e** in ether with LAH at −70°C. Low temperature bromination of 2-methoxypropene with NBS in the presence of the allyl alcohols **6b–e** in methylene chloride furnished the bromo ketals **8b–e**, respectively, as a mixture of epimers. The key radical cyclisation reaction was carried out by refluxing a 0.02 M benzene solution of the bromo ketals **8b–e** with 1.1 equivalents of tri-*n*-butyltin hydride and a catalytic amount of AIBN to furnish the cyclic ketals **9b–e** as a mixture of methoxy epimers in a stereoselective manner. The stereochemistry of the newly formed *sec*-methyl group in the ketals **9b** and **9e** during the radical cyclisation reaction was assigned as *endo* based on the preferred approach of the hydrogen from the less hindered side of the molecule, by analogy with earlier reports.[8] Sonochemically accelerated reaction with Jones reagent in acetone transformed the cyclic ketals **9b–e** into the corresponding 1,4-diketones **10b–e**. Finally, intramolecular aldol condensation of the diketones **10b–e** in methanol using 10% aqueous potassium hydroxide at 100–110°C in a Carius tube furnished the cyclopentenone annulated products **12b–e**,[9] whose structures rest secured from their spectral data. The stereochemical integrity of the enone **12b** was found to be very good (>95%), obviously due to the very good stereoselectivity in the radical cyclisation reaction **8b→9b**.

The sequence with 2-substituted allyl alcohol **6b** (Table 1, entry B), similar to carveol **6a** generated the annulated product in a highly regio- and stereoselective manner. However, when there is no substituent at the 2-position of the starting allyl alcohol (Table 1, entries E), even though the radical cyclisation reaction proceeded in a stereoselective manner, the annulated product was found to be a mixture of ring junction epimers, because of the equilibration of the diketone **10e** prior to the intramolecular aldol condensation in the last step of the sequence, which was further established by equilibrating the diketone **10e**. The dione **10e** on equilibration with potassium carbonate in methanol furnished a ≈10:1 epimeric mixture of the diketone **10e**, which on intramolecular aldol condensation generated a 6:1 mixture of the enone **12e**. After successfully establishing the generality of the four step, regiospecific cyclopentenone annulation methodology, using a 5-*exo*-*trig* radical cyclisation reaction as the key step, as an application, the cyclopentenone **12b** has been further elaborated to 4-epibakkenolide-A and its spiro epimer.

Bakkanes are an interesting class of tricyclic sesquiterpenes, containing an unusual α-spiro-β-methylene-γ-butyrolactone moiety fused to a hydrindane framework. The simplest member of this class, bakkenolide-A **13** was isolated in 1967 by Kitahara et al. from the buds of *Petasites japonicus* subsp. *gigantus* Maxim., found in the northern parts of Japan, along with three other higher oxygenated analogues, and named them bakkenolides A–D after the local name of the species (*Bakke*). Simultaneously, Hayashi et al. have also reported the isolation of the same set of compounds and named them fukinanes after the Japanese name (*Fuki*) of the plant. Subsequently a few other bakkanes were isolated[10] from various sources and some of the examples are depicted in Chart 1. The presence of an unusual β-methylene-α-spiro-γ-butyrolactone part structure and the associated biological activities made the bakkenolides attractive and challenging synthetic targets.[11]

The bicyclic enone **12b** obtained by cyclopentenone annulation of 2,3-dimethylcyclohexenol **6b**, was readily identified as the key intermediate for the synthesis of 4-epibakkenolide-A **14** (Scheme 3). For the construction of the spiro lactone moiety, a 5-*exo*-*dig* radical cyclisation reaction based spiroannulation methodology[12] was employed. Thus, catalytic hydrogenation of the enone **12b** using 10%Pd/C in methanol at one atmosphere pressure of hydrogen (balloon) furnished the saturated bicyclic ketone **15**. Wittig reaction of the ketone **15** with methoxymethylenetriphenylphosphorane furnished the enol ether **16**. The regiospecific

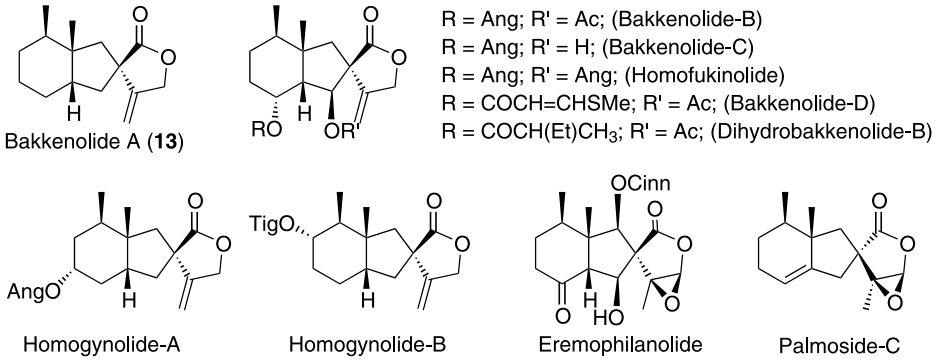
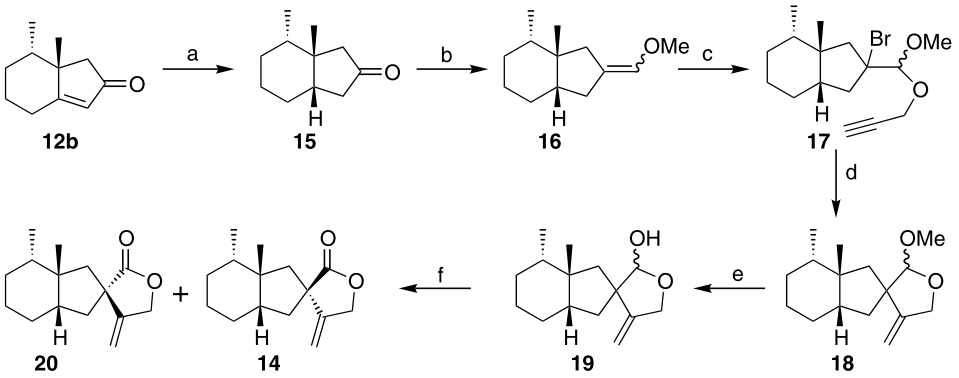


Chart 1.



Scheme 3. *Reagents and conditions*: (a) H_2, 10%Pd/C; MeOH; (b) $Ph_3P{=}CHOMe$, C_6H_6; (c) NBS, $HC{\equiv}CCH_2OH$, CH_2Cl_2; (d) $^nBu_3SnCl$, $NaCNBH_3$, AIBN, *t*-BuOH; (e) Aq. HCl, THF; (f) PCC, silica gel, CH_2Cl_2.

bromoalkoxylation of the enol ether **16** was achieved by treatment with NBS in methylene chloride in the presence of an excess of propargyl alcohol, to furnish the bromo acetal **17** as a mixture of epimers. The key radical cyclisation reaction was achieved by using an in situ generated catalytic tri-*n*-butyltin hydride.[13] Thus, refluxing a 0.1 M *tert*-butanol solution of the bromo acetal **17** with 0.15 equivalents of tri-*n*-butyltin chloride and 1.7 equivalents of sodium cyanoborohydride in the presence of a catalytic amount of AIBN for 1.5 h furnished the 5-*exo*-*dig* radical cyclised product, the spiro acetal **18** as a mixture of spiro and methoxy epimers. Treatment of the spiro acetal **18** with 2.2N aqueous HCl in THF under sonic irradiation for 4 h furnished the lactol **19**. Oxidation of the lactol **19** using PCC and silica gel furnished a 1:1 mixture of 4-epibakkenolide-A **14** and its spiroepimer **20**, whose structures were assigned from the spectroscopic data.

In conclusion, we have developed a four-step methodology for cyclopentenone annulation of allyl alcohols employing a 5-*exo*-trig radical cyclisation reaction as the key step. As an application of the methodology, one of the products has been further elaborated into 4-epi and 4,7-*diepi*-bakkenolides employing a 5-*exo*-dig radical cyclisation based α-spiro-β-methylene-γ-butyrolactone annulation strategy.

3. Experimental

3.1. (1*R*,4*R*)-4-Isopropenyl-1-methylbicyclo[4.3.0]non-6-en-8-one 12a

To a cold (−50°C), magnetically stirred solution of carveol **6a** (500 mg, 3.2 mmol) and 2-methoxypropene (0.62 ml, 6.4 mmol) in CH_2Cl_2 (10 ml) was added a solution of NBS (570 mg, 3.2 mmol) in CH_2Cl_2 (20 ml) over a period of 15 min. The reaction mixture was allowed to warm up to room temperature over a period of 1.5 h, and then diluted with CH_2Cl_2 (15 ml), washed with 2% aq. NaOH, water and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a neutral alumina column using ethyl acetate–hexane (1:40) as eluent furnished the bromo ketal **8a** (660 mg, 66%) as a colourless oil. IR (neat): ν_{max} 1635, 885 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$, 1:1 mixture of epimers): δ 5.55 (1H, br s, C=CH), 4.72 (2H, s, $C{=}CH_2$), 4.38 (1H, br s, O-CH), 3.57 and 3.39 (AB q, J=6.3 Hz) and 3.47 (s) [2H, CH_2-Br], 3.36 and 3.32 (3H, s, O-CH_3), 1.80–2.45 (5H, m), 1.74 (6H, s, 2×olefinic CH_3), 1.54 and 1.58 (3H, s, *tert*-CH_3). ^{13}C NMR (22.5 MHz, $CDCl_3$, 1:1 mixture of epimers): δ 148.7 (s, $C{=}CH_2$), 135.0 (s, $C{=}CH$), 125.3 and 125.0 (d, C=CH), 109.0 (t, C=CH$_2$), 100.7 (s, O-C-O), 72.2 and 71.8 (d, O-CH), 50.0 and 49.0 (q, O-CH_3), 40.7 (d,

C-5), 36.9 and 36.7 (t, CH_2-Br), 35.9 and 35.7 (t, C-6), 30.7 (t, C-4), 22.4 and 21.9 (q), 20.3 (q) and 19.9 (q). Mass: m/z 223 (M-Br, 1%), 191 (40), 153 (100), 155 (100), 135 (100), 119 (60), 107 (100), 93 (100). HRMS: m/z for $C_{13}H_{19}O$ (M-Br,CH_3OH), calcd: 191.1436. Found: 191.1424. A magnetically stirred solution of the bromo ketal **8a** (304 mg, 1.0 mmol), $^nBu_3SnH$ (0.3 ml, 1.1 mmol) and catalytic amount of AIBN in benzene (56 ml) was refluxed for 2.5 h. The reaction mixture was cooled, washed with 1% aqueous ammonia and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a neutral alumina column using ethyl acetate–hexane (1:40) as eluent furnished an epimeric mixture of the cyclic ketal **9a** (163 mg, 72%) as an oil. IR (neat): ν_{max} 1640, 885 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$, ≈1:1 mixture of methoxy epimers): δ 4.72 (2H, s, C=CH_2), 3.40–3.90 (1H, m, O-CH), 3.32 and 3.26 (3H, s, O-CH_3), 1.30–2.50 (9H, m), 1.76 (3H, s, olefinic CH_3), 1.52 and 1.44 (3H, s, CH_3-C-OCH_3) 1.22 and 1.12 (3H, s, *tert*-CH_3). To a solution of the cyclic ketal **9a** (50 mg, 0.22 mmol) in acetone (0.3 ml) was added freshly prepared Jones reagent (1.6 M, 0.3 ml, 0.48 mmol) and the reaction mixture was sonicated for 5 min in an ultrasonic cleaning bath. Isopropyl alcohol (0.2 ml) was added to consume the excess reagent and the solvent was evaporated under reduced pressure. The residue was taken in ether and washed with saturated aq. $NaHCO_3$ and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished the diketone **10a** (33 mg, 72%) as an oil. IR (neat): ν_{max} 1700, 1630, 890 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 4.79 (1H, br s) and 4.71 (1H, br s) [C=CH_2], 2.83 and 2.65 (2H, AB q, J=16.2 Hz, CH_2COCH_3), 2.30–2.60 (2H, m), 2.13 (3H, s, CH_3-C=O), 1.98 (1H, t of d, J=13.3 and 4.0 Hz), 1.60–1.90 (3H, m), 1.72 (3H, s, olefinic CH_3), 1.52 (1H, t of t, J=9.8 and 4.3 Hz), 1.12 (3H, s, *tert*-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, SEFT): δ 213.4 (C, ring C=O), 206.8 (C, CH_3-C=O), 147.2 (C, C=CH_2), 110.4 (CH_2, C=CH_2), 50.6 (CH_2, CH_2COCH_3), 47.0 (C, C-2), 45.6 (CH, C-5), 42.9 (CH_2, C-6), 37.1 (CH_2, C-3), 31.6 (CH_3, CH_3-C=O), 25.6 (CH_2, C-4), 22.9 (CH_3, olefinic CH_3), 20.9 (CH_3, *tert*-CH_3). Mass: m/z 208 (M^+, 16%), 151 (36), 152 (44), 123 (16), 111 (20), 110 (24), 109 (34), 95 (42), 43 (100). To a solution of the diketone **10a** (25 mg, 0.12 mmol) in methanol (0.3 ml), placed in a Carius tube, was added 10% aq. KOH (0.1 ml, 0.15 mmol) and heated the reaction mixture at 100–110°C for 2.5 h. The reaction mixture was cooled, diluted with ether (5 ml), washed with 0.5N aq. HCl and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished the enone **12a** (18 mg, 79%) as an oil. $[\alpha]_D^{26}$: +23.5 (*c* 2, $CHCl_3$). IR (neat): ν_{max} 1700, 1630, 1615, 890 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 5.82 (1H, s, olefinic H), 4.87 (1H, s) and 4.74 (1H, s) [C=CH_2], 2.94 (1H, d, J=11.2 Hz), 2.60–2.75 (2H, m), 2.30 and 2.19 (2H, AB q, J=18.3 Hz, CH_2-C=O), 1.40–2.00 (4H, m), 1.72 (3H, s, olefinic CH_3), 1.28 (3H, s, *tert*-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.9 (C-8), 186.7 (C-6), 145.8 (C=CH_2), 128.0 (C-7), 112.4 (C=CH_2), 52.5 (C-9), 51.7 (C-1), 43.3, 40.9, 34.8, 30.6, 25.1, 23.7, 22.8. Mass: m/z 190 (M^+, 62%), 148 (30), 147 (50), 133 (40), 125 (35), 119 (40), 109 (30), 107 (40), 105 (42). HRMS: m/z for $C_{13}H_{18}O$, calcd: 190.1358. Found: 190.1341.

3.2. (1β,2α)-1,2-Dimethylbicyclo[4.3.0]non-6-en-8-one 12b

To a cold (−78°C), magnetically stirred solution of the enone **7b** (980 mg, 8.9 mmol) in ether (20 ml) was added $LiAlH_4$ (167 mg, 4.5 mmol) and the reaction mixture was stirred for 1.5 h. Ethyl acetate (0.5 ml) was added to the reaction mixture to consume the excess reagent. The reaction was then quenched with water and extracted with ether (2×10 ml). Evaporation of the solvent and purification of the product on a silica gel column with CH_2Cl_2 as eluent furnished the allyl alcohol **6b** (920 mg, 92%) as an oil. IR (neat): ν_{max} 3330 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$): δ 3.95 (1H, br s, O-CH), 1.40–2.10 (7H, m), 1.76 (3H, s) and 1.65 (3H, s) [2×olefinic CH_3]. The bromoacetalisation reaction of the allyl alcohol **6b** (500 mg, 3.97 mmol) at −50°C with 2-methoxypropene (0.7 ml, 7.94 mmol) and NBS (1.41 g, 7.94 mmol) in CH_2Cl_2 (30 ml) for 1.5 h as described for the bromo ketal **8a**, and purification of the product on a neutral alumina column with ethyl acetate–hexane (1:40) as eluent furnished the bromo ketal **8b** (638 mg, 59%) as a colourless oil. IR (neat): ν_{max} 1110 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$, 3:2 mixture of epimers): δ 4.13 (1H, br s), 3.46 (2H, AB q, J=5.4 Hz), 3.32 and 3.36 (3H, s), 1.40–2.20 (6H, m), 1.69 (3H, s), 1.61 (3H, s), 1.59 and 1.57 (3H, s, *tert*-CH_3). ^{13}C NMR (22.5 MHz, $CDCl_3$, 3:2 mixture of epimers): δ 132.5 and 132.3, 126.1, 100.5, 71.6 and 70.9, 49.6 and 48.8, 36.3, 31.9, 30.6 and 30.1, 22.3 and 22.0, 19.7, 18.7 and 18.2, 17.2 and 16.6. Mass: m/z 276 and 278 (M^+ and M^++2, 0.2%), 165 (21), 151 (100), 153 (100), 125 (20), 109 (100). The 5-*exo*-*trig* radical cyclisation reaction of the bromo ketal **8b** (138 mg, 0.5 mmol) in benzene (28 ml) with $^nBu_3SnH$ (0.15 ml, 0.55 mmol) and a catalytic amount of AIBN for 2.5 h as described for the cyclic ketal **9a**, and purification of the product on a neutral alumina column using ethyl acetate–hexane (1:40) as eluent furnished the cyclic ketal **9b** (72 mg, 74%) as an oil. IR (neat): ν_{max} 1375, 1065 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$, ≈1:1 mixture of methoxy epimers): δ 3.10–3.56 (1H, m), 3.32 and 3.25 (3H, s), 1.10–2.20 (8H, m), 1.46 (3H, s) 1.20 and 1.18 (3H, s, *tert*-CH_3), 0.88 and 0.84 (3H, overlapping d, *sec*-CH_3). Sonochemically accelerated reaction of the cyclic ketal **9b** (60 mg, 0.3 mmol) in acetone (0.5 ml) with Jones reagent (1.6 M, 0.2 ml, 0.32 mmol) for 5 min as described for the diketone **10a** and purification of the product on a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished the diketone[9] **10b** (40 mg, 72%) as an oil. IR (neat): ν_{max} 1710 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$): δ 2.93 and 2.68 (2H, AB q, J=17 Hz, CH_2-CO-CH_3), 2.42 (2H, m), 2.14 (3H, s, CH_3-C=O), 1.35–2.10 (6H, m), 1.22 (3H, s, *tert*-CH_3), 0.91 (3H, d, J=7.2 Hz, *sec*-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 214.4 (ring C=O), 207.1 (CH_3-C=O), 51.1, 46.2, 43.2, 38.1, 31.7, 29.0, 26.0, 20.9, 16.1. Mass: m/z 182 (M^+, 5%), 139

(20), 125 (100). HRMS: m/z for $C_{11}H_{18}O_2$, calcd: 182.1307. Found: 182.1295. The intramolecular aldol condensation of the diketone **10b** (40 mg, 0.22 mmol) in methanol (0.5 ml) with 10% aq. KOH (0.15 ml, 0.26 mmol) at 100–110°C for 2.5 h as described for the enone **12a**, and purification of the product on a silica gel (0.5 g) column using ethyl acetate–hexane (1:10) as eluent furnished the enone **12b**[9] (34 mg, 94%) as an oil. IR (neat): ν_{max} 1700, 1615 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 5.85 (1H, d, $J=1.3$ Hz, olefinic H), 0.9–2.70 (7H, m), 2.52 and 2.02 (2H, AB q, $J=18.1$ Hz, CH_2-C=O), 1.38 (3H, s, *tert*-CH_3) and 0.86 (3H, d, $J=7.2$ Hz, *sec*-CH_3). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 209.6 (C-9), 187.1 (C-6), 128.6 (C-7), 48.7 (C-9), 48.4 (C-1), 39.2, 29.1, 28.3, 27.4, 22.3 (*tert*-CH_3), 15.5 (*sec*-CH_3). Mass: m/z 164 (M^+, 65%), 149 (20), 136 (70), 122 (35), 121 (100), 108 (40), 107 (65), 93 (50). HRMS: m/z for $C_{11}H_{16}O$, Calcd.: 164.1201. Found: 164.1190.

3.3. 3,3-Dimethylbicyclo[4.3.0]non-6-en-8-one 12c

The regioselective reduction of the enone **7c** (500 mg, 4.03 mmol) in ether (15 ml) at −78°C with $LiAlH_4$ (90 mg, 2.4 mmol) for 1.5 h as described for the allyl alcohol **6b**, and purification of the product on a silica gel column with CH_2Cl_2 as eluent furnished the allyl alcohol **6c** (450 mg, 89%) as an oil. IR (neat): ν_{max} 3330 cm^{-1}. ^{1}H NMR (90 MHz, $CDCl_3$): δ 5.54 (2H, m), 4.13 (1H, br s), 1.30–2.10 (5H, m), 1.02 (3H, s), 0.98 (3H, s). The bromoacetalisation reaction of the allyl alcohol **6c** (385 mg, 3.06 mmol) at −50°C with 2-methoxypropene (0.58 ml, 6.1 mmol) and NBS (1.09 g, 6.1 mmol) in CH_2Cl_2 (30 ml) for 1.5 h as described for the bromo ketal **8a**, and purification of the product on a neutral alumina column using ethyl acetate–hexane (1:40) as eluent furnished the bromo ketal **8c** (700 mg, 83%) as a colourless oil. IR (neat): ν_{max} 1215, 1115, 1080, 1035 cm^{-1}. ^{1}H NMR (90 MHz, $CDCl_3$, ≈1:1 mixture of epimers): δ 5.56 and 5.48 (2H, s), 4.25 (1H, m), 3.50 and 3.34 (2H, AB q, $J=11$ Hz, CH_2-Br), 3.28 and 3.26 (3H, s, O-CH_3), 1.16–2.00 (4H, m), 1.50 and 1.38 (3H, s), 1.01 (3H, s), 0.97 (3H, s). ^{13}C NMR (50 MHz, $CHCl_3$+$CDCl_3$): δ 140.5 and 140.4, 126.6 and 126.3, 100.4, 66.3 and 66.2, 49.0, 35.6, 34.3 and 34.1, 31.5, 29.5 and 29.3, 28.5, 27.6, 22.1. Mass: m/z 261 (M−CH_3, 0.5%), 165 (50), 153 (100), 151 (100), 140 (20), 125 (80), 110 (60), 109 (100), 93 (20). The 5-*exo*-*trig* radical cyclisation reaction of the bromo ketal **8c** (138 mg, 0.5 mmol) in benzene (28 ml) with ^{n}Bu_3SnH (0.15 ml, 0.55 mmol) and a catalytic amount of AIBN for 2.5 h as described for the cyclic ketal **9a**, and purification of the product on a neutral alumina column using ethyl acetate–hexane (1:40) as eluent furnished the cyclic ketal **9c** (73.3 mg, 75%) as an oil. IR (neat): ν_{max} 1105, 1025 cm^{-1}. ^{1}H NMR (90 MHz, $CDCl_3$, ≈1:1 mixture of methoxy epimers): δ 3.90–4.20 (1H, m), 3.25 and 3.20 (3H, s), 1.00–2.20 (9H, m), 1.42 and 1.36 (3H, s), 0.88 (3H, s), 0.84 (3H, s). Sonochemically accelerated reaction of the cyclic ketal **9c** (62 mg, 0.32 mmol) in acetone (0.5 ml) with Jones reagent (1.6 M, 0.45 ml, 0.7 mmol) for 5 min as described for the diketone **10a**, and purification of the product on a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished the diketone **10c** (42 mg, 73%) as an oil. IR (neat): ν_{max} 1710 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 3.00–3.20 (1H, m), 2.92 (1H, dd, $J=17.3$ and 7.7 Hz) and 2.08 (1H, dd, $J=17.4$ and 4.7 Hz) [CH_2COCH_3], 2.40–2.60 (1H, m) and 2.20–2.30 (1H, m), 2.20 (3H, s, CH_3-C=O), 1.00–1.80 (4H, m), 1.25 (3H, s), 0.99 (3H, s). ^{13}C NMR (50 MHz, $CHCl_3$+$CDCl_3$): δ 211.9 (ring C=O), 207.2 (CH_3-*C*=O), 46.2, 42.9, 42.0, 39.8, 37.7, 31.1, 30.3, 27.5, 24.1. The intramolecular aldol condensation of the diketone **10c** (120 mg, 0.66 mmol) in methanol (0.5 ml) with 10% aq. KOH (0.55 ml, 0.99 mmol) at 100–110°C for 2.5 h as described for the enone **12a**, and purification of the product on a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished the enone **12c** (100 mg, 92%) as an oil. IR (neat): ν_{max} 1705, 1620 cm^{-1}. ^{1}H NMR (90 MHz, $CDCl_3$): δ 5.85 (1H, s, olefinic H), 2.40–2.80 (3H, m), 1.90–2.30 (3H, m), 1.40–1.80 (3H, m), 1.09 (3H, s) and 0.83 (3H, s) [2×*tert*-CH_3]. Mass: m/z 164 (M^+, 100), 149 (25), 119 (25), 109 (27), 108 (53), 107 (25), 97 (28), 96 (30), 95 (25), 91 (25). HRMS: m/z for $C_{11}H_{16}O$, calcd: 164.1201. Found: 164.1217.

3.4. Bicyclo[4.3.0]non-6-en-8-one 12d

The bromoacetalisation reaction of cyclohexenol **6d** (400 mg, 4.54 mmol) at −50°C with 2-methoxypropene (0.85 ml, 9.1 mmol) and NBS (1.42 g, 8.0 mmol) in CH_2Cl_2 (30 ml) for 1.5 h as described for the bromo ketal **8a**, and purification of the product on a neutral alumina column with ethyl acetate–hexane (1:40) as eluent furnished the bromo ketal **8d** (795 mg, 79%) as a colourless oil. IR (neat): ν_{max} 1650, 1210, 1110, 1075, 1040 cm^{-1}. ^{1}H NMR (90 MHz, $CDCl_3$, ≈1:1 mixture of epimers): δ 5.40–5.90 (2H, m), 4.26 (1H, m), 3.38 and 3.34 (2H, s), 2.68 (3H, s), 1.30–2.10 (6H, m), 1.54 and 1.48 (3H, s). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ 129.8 and 128.8 (d) and 129.1 and 128.6 (d), 100.0 (s), 65.2 and 63.9 (d), 48.5 and 48.2 (q), 35.2 (t), 30.2 (t), 24.9 (t), 24.5 (t), 21.7 and 19.3 (q). Mass: m/z 217 and 219 (M−OCH_3, 1%), 151 (55), 153 (55), 112 (10), 81 (100). The 5-*exo*-*trig* radical cyclisation reaction of the bromo ketal **8d** (375 mg, 1.5 mmol) in benzene (80 ml) with ^{n}Bu_3SnH (0.45 ml, 1.65 mmol) and a catalytic amount of AIBN for 2.5 h as described for the cyclic ketal **9a**, and purification of the product on a neutral alumina column using ethyl acetate–hexane (1:40) as eluent furnished the cyclic ketal **9d** (184 mg, 72%) as an oil. IR (neat): ν_{max} 1210, 1185, 1155, 1115, 1080, 1065, 1040 cm^{-1}. ^{1}H NMR (90 MHz, $CDCl_3$, ≈1:1 mixture of methoxy epimers): δ 3.80–4.35 (1H, m), 3.22 and 3.20 (3H, s), 1.20–2.20 (11H, m), 1.35 and 1.36 (3H, s). Sonochemically accelerated reaction of the cyclic ketal **9d** (184 mg, 1.1 mmol) in acetone (1.5 ml) with Jones reagent (1.6 M, 1.5 ml, 2.4 mmol) for 5 min as described for the diketone **10a**, and purification of the product on a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished the diketone[9] **10d** (150 mg, 89%) as an oil. IR (neat): ν_{max} 1710 cm^{-1}. ^{1}H NMR (90 MHz, $CDCl_3$): δ 2.75–3.20 (3H, m, CH-C=O and CH_2COCH_3), 2.17 (3H, s, CH_3-C=O), 1.10–2.60 (8H, m). The intramolecular aldol condensation of the diketone **10d** (10 mg, 0.07 mmol) in ethanol (0.2 ml) with

10% aq. KOH (0.04 ml, 0.08 mmol) at 100–110°C for 2.5 h as described for the enone **12a**, and purification of the product on a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished the enone[9] **12d** (6 mg, 68%) as an oil. IR (neat): ν_{max} 1705, 1620 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 5.83 (1H, s, olefinic H), 2.82 (1H, d, $J=13.7$ Hz), 2.40–2.70 (2H, m), 1.00–2.40 (8H, m).

3.5. (1α and 1β,2α)-2,4,4-Trimethylbicyclo[4.3.0]non-6-en-8-one 12e

Regioselective reduction of isophorone (**7e**, 2.0 g, 14.5 mmol) in ether (30 ml) at −78°C with $LiAlH_4$ (270 mg, 7.25 mmol) for 1.5 h as described for the allyl alcohol **6b**, and purification of the product on a silica gel column with CH_2Cl_2 as eluent furnished the allyl alcohol **6e** (1.85 g, 91%) as an oil. IR (neat): ν_{max} 3300, 1660 cm^{-1}. ^{1}H NMR (90 MHz, $CDCl_3$): δ 5.36 (1H, br s, olefinic H), 3.80–4.14 (1H, m, O-CH), 2.88 (1H, s, OH), 1.00–2.20 (4H, m), 1.66 (3H, s, olefinic CH_3), 1.00 (3H, s) and 0.90 (3H, s) [2×*tert*-CH_3]. The bromoacetalisation reaction of the allyl alcohol **6e** (500 mg, 3.57 mmol) at −50°C with 2-methoxypropene (0.68 ml, 7.14 mmol) and NBS (712 mg, 4.0 mmol) in CH_2Cl_2 (30 ml) for 1.5 h as described for the bromo ketal **8a**, and purification of the product on a neutral alumina column using ethyl acetate–hexane (1:40) as eluent furnished the bromo ketal **8e** (865 mg, 83%) as a colourless oil. IR (neat): ν_{max} 1660, 1210, 1110, 1075, 1050, 1010 cm^{-1}. ^{1}H NMR (90 MHz, $CDCl_3$): δ 5.34 (1H, br s, olefinic H), 4.34 (1H, br s, O-CH), 3.50 and 3.35 (AB q, $J=10$ Hz) and 3.40 (s) [2H, CH_2-Br], 3.30 and 3.26 (3H, s, O-CH_3), 1.30–2.00 (4H, m), 1.68 (3H, s, olefinic CH_3), 1.52 and 1.38 (3H, s), 1.00 (3H, s), 0.91 (3H, s). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ 136.3 and 135.5 (s, *C*=CH), 122.5 and 122.3 (d, C=*C*H), 100.5 (s, O-C-O), 67.1 and 71.8 (d, O-CH), 49.1 and 50.0 (q, O-CH_3), 43.9 and 44.2 (t), 43.7 and 43.5 (s), 42.3 and 35.8 (t), 31.4 (2 C, q and t), 26.3 (q), 23.8 (q), 22.4 (q). Mass: *m*/*z* 179 [(M–CH_3OH,Br), 22%], 151 and 153 (100), 139 (22), 123 (90). HRMS: *m*/*z* for $C_{12}H_{19}O$ (M–CH_3OH,Br), calcd: 179.1436. Found: 179.1427. The 5-*exo*-*trig* radical cyclisation reaction of the bromo ketal **8e** (220 mg, 0.75 mmol) in benzene (40 ml) with ^{n}Bu_3SnH (0.25 ml, 0.92 mmol) and a catalytic amount of AIBN for 2.5 h as described for the cyclic ketal **9a**, and purification of the product on a neutral alumina column using ethyl acetate–hexane (1:40) as eluent furnished the cyclic ketal **9e** (117 mg, 73%) as an oil. IR (neat): ν_{max} 1210, 1100, 1070, 1040, 1015 cm^{-1}. ^{1}H NMR (90 MHz, $CDCl_3$, ≈1:1 mixture of methoxy epimers): δ 4.00–4.40 (1H, m, O-CH), 3.29 and 3.26 (3H, s, O-CH_3), 1.20–2.80 (8H, m), 1.47 and 1.41 (3H, s, *tert*-CH_3), 0.91 (3H, d, $J=7.2$ Hz, *sec*-CH_3), 0.95 (3H, s) and 0.88 (3H, s) [2×*tert*-CH_3]. Sonochemically accelerated reaction of the cyclic ketal **9e** (89 mg, 0.42 mmol) in acetone (0.5 ml) with Jones reagent (1.6 M, 0.5 ml, 0.9 mmol) for 5 min as described for the diketone **10a**, and purification of the product on a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished a ≈3:1 epimeric mixture of the diketone **10e** (69 mg, 84%) as oil. IR (neat): ν_{max} 1705 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$, peaks due to the major isomer): δ 3.01 (1H, m, CH-C=O), 2.70 (1H, dd, $J=16.7$ and 9.0 Hz) and 2.41 (1H, dd, $J=16.8$ and 5.1 Hz) [CH_2COCH_3], 2.10–2.36 (2H, m), 2.19 (3H, s, CH_3-C=O), 1.45–1.70 (3H, m), 1.02 (3H, s) and 0.99 (3H, s) [2×*tert*-CH_3], 0.92 (3H, d, $J=7.2$ Hz, *sec*-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, SEFT, peaks due to the major isomer): δ 212.4 (C, ring C=O), 206.8 (C, CH_3-C=O), 52.6 (CH_2, CH_2COCH_3), 49.4 (CH, CH-C=O), 43.6 (CH_2, ring CH_2-C=O), 40.3 (CH_2, C-4), 36.6 (C, C-5), 33.3 (CH_3, CH_3-C=O), 30.6 (CH, C-5), 29.9 (CH_3), 28.3 (CH_3), 17.8 (CH_3). Mass: *m*/*z* 181 (M$^+$–CH_3, 100), 149 (22), 123 (82), 109 (15), 97 (15), 95 (16). The intramolecular aldol condensation of the diketone **10e** (60 mg, 0.31 mmol) in methanol (0.5 ml) with 10% aq. KOH (0.4 ml, 0.36 mmol) at 100–110°C for 2.5 h as described for the enone **12a**, and purification of the product on a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished a 6:1 epimeric mixture of the enones **12e** (46 mg, 85%) as an oil. IR (neat): ν_{max} 1700, 1615 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, 6:1 mixture of epimers, peaks due to major isomer): δ 5.82 (1H, s, olefinic H), 2.54 (1H, dd, $J=18.5$ and 6.4 Hz) and 2.04 (1H, dd, $J=18.4$ and 1.6 Hz) [H-9], 2.45 (1H, dd, $J=13.2$ and 2.1 Hz) and 2.10 (1H, d, $J=14.3$ Hz) [H-5], 2.10–2.20 (1H, m, H-1), 1.75–1.90 (1H, m, H-2), 1.35–1.55 (2H, m), 1.06 (3H, s) and 0.82 (3H, s) [2×*tert*-CH_3], 0.98 (3H, d, $J=6.3$ Hz, *sec*-CH_3). peaks due to the minor isomer: δ 5.80 (s, olefinic H), 1.14 (d, $J=6.4$ Hz, *sec*-CH_3), 1.09 (s) and 0.94 (s) [2×*tert*-CH_3]. ^{13}C NMR (100 MHz, $CDCl_3$, 6:1 mixture of epimers, peaks due to the major isomer): δ 207.8 (C-8), 182.0 (C-6), 127.2 (C-7), 47.3, 46.1, 42.6, 39.6, 35.1, 31.0, 30.8, 24.1, 19.6. peaks due to the minor isomer: δ 207.8 (C-8), 188.3 (C-6), 123.6 (C-7), 46.5, 46.1, 41.0, 37.0, 33.1, 30.6, 28.4, 23.4, 16.7. Mass: *m*/*z* 178 (M$^+$, 51%), 163 (30), 135 (15), 121 (35), 107 (15), 96 (40), 83 (100). HRMS: *m*/*z* for $C_{12}H_{18}O$, calcd: 178.1358. Found: 178.1345.

3.6. (1β,2α)-1,2-Dimethylbicyclo[4.3.0]nonan-8-one 15

To a solution of the enone **12b** (30 mg, 0.18 mmol) in methanol (0.5 ml) was added 10%Pd/C (catalytic, ≈3 mg). The flask was filled with hydrogen via evacuative displacement and the reaction mixture was magnetically stirred under hydrogen (balloon) atmosphere for 5 h. The catalyst was filtered off and the solvent was evaporated under reduced pressure. Purification of the product on a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished the saturated ketone **15** (30 mg, 99%) as oil. IR (neat): ν_{max} 1745 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.62 (1H, dd, $J=18.8$ and 7.4 Hz, H-7_A), 2.29 and 1.86 (2H, AB q, $J=18.3$ Hz, H-9), 1.00–2.00 (9H, m), 1.09 (3H, s, *tert*-CH_3), 0.87 (3H, d, $J=6.6$ Hz, *sec*-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.9, 42.7, 42.5, 42.2, 39.2, 31.4, 30.9, 26.9, 25.2, 17.4 (ketone carbon not seen). Mass: *m*/*z* 166 (M$^+$, 58%), 151 (20), 123 (32), 110 (25), 109 (100), 108 (37), 97 (25), 96 (35), 95 (40). HRMS: *m*/*z* for $C_{11}H_{18}O$, calcd: 166.1358. Found: 166.1351.

3.7. 1,2-Dimethylbicyclo[4.3.0]nonane-8,3′spiro-[4′-methylenedihydrofuran-2′(3′H)-one] [4-epi-bakkenolide-A 14 and 4,7-diepibakkenolide-A 20]

To a magnetically stirred solution of potassium *tert*-amylate [prepared from 51 mg (1.32 mmol) of potassium in *tert*-amyl alcohol (1.5 ml] in dry THF (2 ml) at room temperature was added (methoxymethyl)-triphenylphosphonium chloride (480 mg, 1.4 mmol) and the resulting red coloured solution was stirred at room temperature for 15 min. To the ylide thus formed, was added the ketone **15** (100 mg, 0.6 mmol) and stirred at room temperature for 2 h. The reaction mixture was then diluted with ether (5 ml), washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a neutral alumina column using ethyl acetate–hexane (1:40) as eluent furnished the enol ether **16** (105 mg, 62%) as oil. IR (neat): ν_{max} 1690 cm^{-1}. To a cold (–40°C), magnetically stirred solution of NBS (50 mg, 0.28 mmol) and propargyl alcohol (0.05 ml, 0.86 mmol) in CH_2Cl_2 (4 ml) was added a solution of the enol ether **16** (46 mg, 0.24 mmol) in CH_2Cl_2 (1 ml) over a period of 15 min. The reaction mixture was stirred for 45 min at the same temperature, diluted with CH_2Cl_2 (5 ml), washed with 1% aq. NaOH and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a neutral alumina column using ethyl acetate–hexane (1:40) as eluent furnished the bromo acetal **17** (58 mg, 75%) as oil. IR (neat): ν_{max} 3300 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$, 3:1 mixture of epimers): δ 4.51 and 4.48 (1H, s), 4.46 and 4.41 (2H, s), 3.64 and 3.62 (3H, s), 1.0–2.80 (13H, m), 1.32 and 0.98 (3H, s), 0.82 and 0.80 (3H, d, $J=7.2$ Hz). Mass: m/z 297 and 299 [(M–OCH_3), 1%], 249 (22), 217 (20), 193 (30), 161 (42), 149 (25), 109 (42), 100 (60), 99 (100), 93 (40). A magnetically stirred suspension of the bromo acetal **17** (116 mg, 0.36 mmol), $^nBu_3SnCl$ (0.015 ml, 0.056 mmol), $NaCNBH_3$ (40 mg, 0.64 mmol) and AIBN (catalytic) in *tert*-butanol (3 ml) was refluxed for 1.5 h. The solvent was then evaporated under reduced pressure and the residue taken in water (5 ml) and extracted with ether (3×5 ml). The combined ether extract was washed with 1% aqueous ammonia and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel column using ethyl acetate–hexane (1:40) as eluent furnished the spiro acetal **18** (72 mg, 83%) as colourless oil. IR (neat): ν_{max} 880 cm^{-1}. ^1H NMR (90 MHz, $CDCl_3$, ≈1:1 mixture of spiro epimers): δ 5.05 (1H, br s) and 4.95 and 4.85 (1H, br s) [C=CH_2], 4.7 and 4.65 (1H, s, O-CH-OCH_3), 4.47 and 4.28 (2H, t of AB q, $J=12$ and 2 Hz, O-CH_2), 3.32 and 3.34 (3H, s, O-CH_3), 1.00–2.60 (12H, m), 1.03 and 1.01 (3H, s, *tert*-CH_3), 0.90 and 0.80 (3H, d, $J=7.2$ Hz, sec-CH_3). Mass: m/z 219 (M–OCH_3, 20%), 190 (55), 175 (65), 147 (100), 133 (40), 119 (35), 105 (35), 95 (35), 93 (35). HRMS: m/z for $C_{16}H_{26}O_2$, calcd: 250.1933. Found: 250.1920. To a solution of the spiro acetal **18** (7 mg, 0.028 mmol) in THF (0.5 ml) at room temperature was added 2.2N aq. HCl (1 ml) and sonicated for 4 h in an ultrasonic cleaning bath. The reaction mixture was diluted with ether (5 ml), washed with saturated aq. $NaHCO_3$ and brine, and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel column using ethyl acetate–hexane (1:10) as eluent furnished the hemi acetal **19** (5.6 mg, 76%) as a colourless oil. To a magnetically stirred solution of the hemi acetal **19** (5.6 mg, 0.024 mmol) in CH_2Cl_2 (1 ml) was added PCC (20 mg, 0.093 mmol) and silica gel (20 mg). The reaction mixture was stirred at room temperature for 2 h and filtered through a silica gel column using CH_2Cl_2 as eluent. Evaporation of the solvent and further purification of the product on a silica gel column using ethyl acetate–hexane (1:40) as eluent furnished a 1:1 epimeric mixture of epibakkenolides-A **14** and **20** (5.3 mg, 95%) as a colourless oil. IR (neat): ν_{max} 1775, 1670, 895 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.20 and 5.18 (1H, s) and 5.04 and 5.02 (1H, s) [C=CH_2], 4.75 and 4.68 (2H, AB q, $J=12$ Hz, O-CH_2), 2.65 (0.5H, dd, $J=13.6$ and 6.8 Hz), 2.39 (0.5H, d, $J=13.4$ Hz), 2.27 (0.5H, dd, $J=13.6$ and 6.4 Hz), 1.40–2.00 (10.5H, m), 1.24 and 1.13 (3H, s, *tert*-CH_3), 0.89 and 0.86 (3H, d, $J=6.8$ Hz, sec-CH_3). Mass: m/z 234 (M^+, 36%), 219 (21, M–CH_3), 175 (21), 149 (50), 147 (35), 133 (25), 124 (100), 123 (43), 111 (55), 109 (70). HRMS: m/z for $C_{15}H_{22}O_2$, calcd: 234.1620. Found: 234.1612.

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