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Enantiospecific approaches to bicyclic vibsanes: a ring-closing metathesis reaction-based strategy to functionalized bicyclo[4.3.1]decanes

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ABSTRACT

An enantiospecific synthesis of functionalized bicyclo[4.3.1]decane, the bicyclic core system present in some bi- and tricyclic vibsane diterpenoids, for example, vibsanin E, via an RCM reaction of 2,6-diallylcarvone derivatives is described. It has been further extended to the synthesis of tricyclo[6.4.1.$0^{1,5}$]tridecanes starting from 2,6,6-triallylcarvones.

1. Introduction

Vibsane diterpenes are rare natural products and they occur exclusively in *Viburnum* species.[1] Representative examples of vibsanes are depicted in Figure 1. This family contains a wide variety of interrelated structural types ranging from mono to tricyclic systems. For example, 11-membered monocyclic vibsanin B **1** is related to cycloheptanoid vibsanin C **2** by a [3,3]-sigmatropic shift[2]

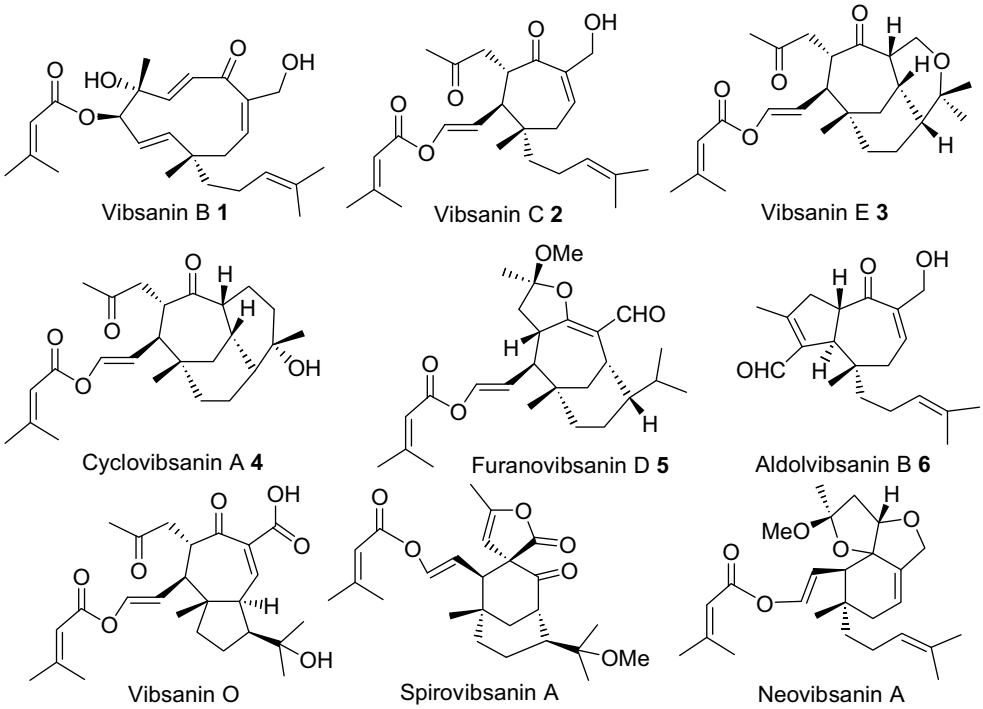

Figure 1.

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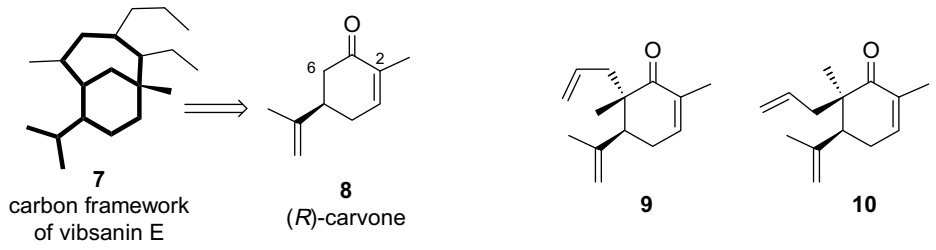
(Cope rearrangement). Similarly, the tricyclic vibsanin E **3**, cyclovibsanins, for example, **4** and furanovibsanins, for example, **5** are related to vibsanin C **2** by an intramolecular ene-reaction followed by either intramolecular etherification,[3] carbocyclization or furan formation of the 1,4-dione moiety. Whereas the hydrolysis of vibsanin C **2**, followed by intramolecular aldol reaction leads to the generation of aldolvibsanin B **6**, some of the vibsanins have shown potential biological activities, such as plant growth inhibition, cytotoxicity, and neurite outgrowth promoting activity.[1–3] Vibsanes are interesting from a synthesis point of view because of the structural diversity present among them coupled with the presence of dense functionality and biological activity. Although there has been no total synthesis reported so far, several efforts have been reported for the construction of the bicyclic core of vibsanin E and its analogues.[4] In continuation of our interest in the enantiospecific construction of polycyclic bridged natural products[5] starting from the readily and abundantly available monoterpene (*R*)-carvone, we have initiated an enantiospecific approach to vibsane diterpenoids. Herein, we report our investigations on the rapid and efficient enantiospecific construction of the bicyclo[4.3.1]decane framework present in some bi- and tricyclic vibsanes employing an RCM-based approach.

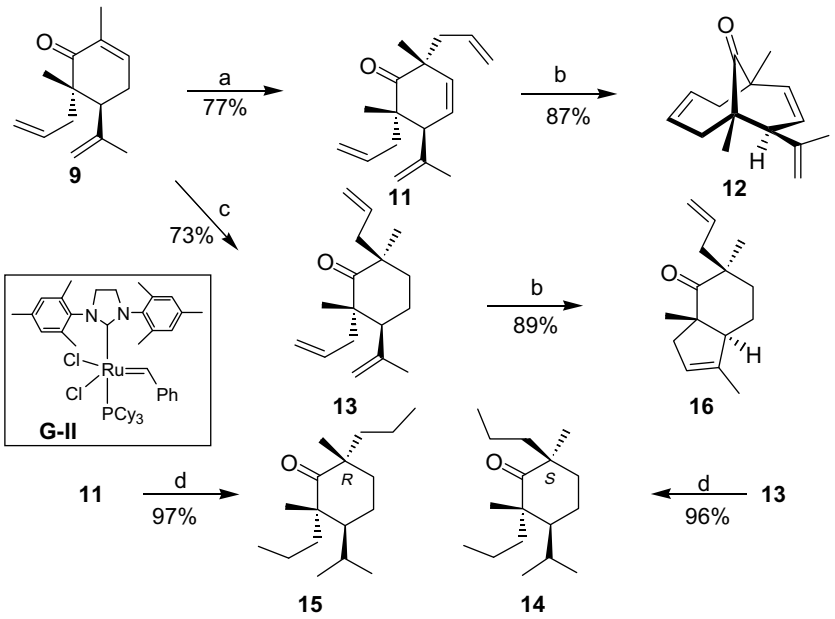
2. Results and discussion

We envisioned the synthesis of the bicyclo[4.3.1]decane ring system **7** present in some bi- and tricyclic vibsanes employing (*R*)-carvone **8** as the chiral starting material (Scheme 1). It was visualized that introduction of two allyl moeities at the C-2 and C-6 carbons of carvone **8** followed by a ring-closing metathesis (RCM) reaction[6] would lead to bicyclo[4.3.1]undecane system.

In order to avoid stereochemical ambiguity, reactions were carried out starting from the stereodefined 6-allyl-6-methylcarvones **9** and **10**, which were obtained[7] by kinetic alkylation of carvone **8** with LDA and methyl iodide, followed by LDA and allyl bromide, or vice versa, respectively. For the allylation at the C-2 carbon of *trans*-methylallylcarvone **9**, two alternate approaches, a base-mediated thermodynamic α-alkylation and a reductive allylation, were explored, which surprisingly produced different stereochemistry at the C-2 position (Scheme 2). Thus, the reaction of enone **9** with sodium hydride and allyl bromide in a mixture of THF and HMPA furnished the α-allylated β-enone **11**, whose structure was established from its spectroscopic data and the stereochemistry was tentatively assigned, and which was confirmed by the RCM reaction. As the reaction was found to be inefficient with first generation catalyst [$Cl_2(PCy_3)_2Ru{=}CHPh$], the RCM reaction was carried out using Grubbs' second generation (G-II) catalyst. Treatment of the diallylated compound **11** with 5 mol % Grubbs' second generation catalyst in methylene chloride led to a clean RCM reaction resulting in the formation of the bicyclo[4.3.1]decanone **12** in 87% yield. The presence of the sodiated molecular ion at *m*/*z* 239.1407 in the high-resolution mass spectrum revealed the loss of an ethylene group supporting the monomeric nature of compound **12**. The presence of four ring olefinic protons in addition



Scheme 1.



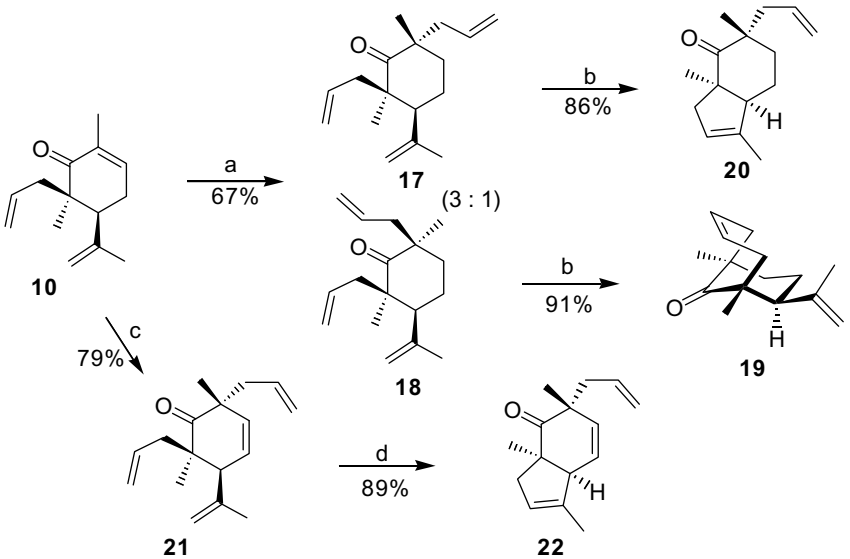
Scheme 2. Reagents and conditions: (a) NaH, THF, HMPA, $BrCH_2CH{=}CH_2$; (b) G-II catalyst (5 mol %), CH_2Cl_2; (c) Li, liq. NH_3, THF, $BrCH_2CH{=}CH_2$; (d) H_2 (1 atm), 10% Pd/C, MeOH.

to two olefinic protons of the isopropenyl group in the ^{1}H NMR spectrum and the presence of six olefinic carbons (one quaternary at 144.6, four methines at 134.5, 130.5, 128.9 and 128.0, and a methylene at 114.4) in the ^{13}C NMR spectrum established the structure of bicyclic ketone **12**.

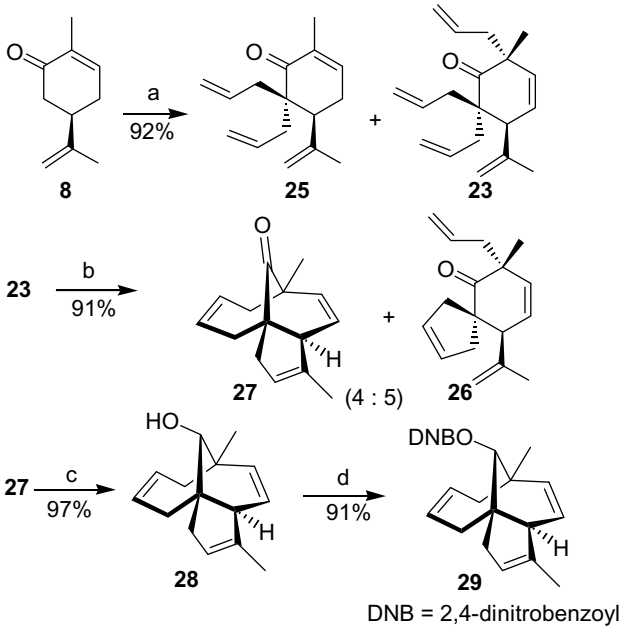
In another direction, reductive allylation of *trans*-allylmethylcarvone **9** with lithium in liquid ammonia and allyl bromide furnished the diallyl compound **13**. The stereochemistry at the newly created quaternary carbon atom in **13** was found, on the basis of the RCM reaction, to be opposite to that of the diallyl compound **11**. This was further confirmed by hydrogenation experiments. Hydrogenation of the diallyl compound **13** with 10% palladium over carbon as the catalyst furnished the saturated compound **14**, which was found to be different from product **15** obtained by hydrogenation of the diallyl compound **11**, thus confirming the epimeric relationship at the newly created quaternary carbon atom of the diallyl compounds **11** and **13**. Treatment of diallylated compound **13** with 5 mol % Grubbs' second generation catalyst in methylene chloride led to a clean RCM reaction resulting in the formation of the bicyclo[4.3.0]nonanone **16**. The structure of the bicyclic ketone **16** was established from its spectroscopic data, in particular the presence of signals due to a typical allyl and cyclopentene olefinic groups in the ^{1}H and ^{13}C NMR spectra.

Next, the sequence was carried out with *cis*-6-allyl-6-methylcarvone **10**, Scheme 3. Accordingly, reductive allylation of the *cis*-allylmethylcarvone **10** with lithium in liquid ammonia and allyl bromide furnished a 3:1 epimeric mixture of the diallyl compounds **17** and **18**, which were separated by column chromatography on a silver nitrate impregnated silica gel column. The formation of two isomers in the reductive allylation reaction is probably the consequence of the opposite influence of the two bulky groups at the C-5 and C-6 carbons of the cyclohexenone. The stereochemistry in the diallyl compounds **17** and **18** were assigned tentatively, and were confirmed on the basis of the RCM reactions. The RCM reactions were found to be efficient with first generation Grubbs' catalyst $Cl_2(PCy_3)_2Ru{=}CHPh$. Thus, treatment of the minor diallylated compound **18** with 10 mol % Grubbs' first generation catalyst in methylene chloride resulted in RCM reaction leading to the formation of the bicyclo[4.3.1]decanone **19**. Similarly, treatment of the major diallylated compound **17** with 10 mol % Grubbs' first generation catalyst in methylene chloride furnished the bicyclo[4.3.0]nonanone **20**. The structures of the bicyclic ketones **19** and **20** were established from their spectroscopic data. Alkylation of *cis*-allylmethylcarvone **10** with sodium hydride and allyl bromide in THF and HMPA exclusively furnished the diallyl compound **21** in 79% yield, which upon RCM reaction with 5 mol % Grubbs' second generation catalyst in methylene chloride furnished the bicyclo[4.3.0]nonanone **22** in 89% yield, whose structure was established from its spectroscopic data.

It was conceived that the presence of two allyl groups at the C-6 position of carvone would effectively lead to bicyclo-[4.3.1]decanes, irrespective of the stereochemistry at the C-2 position, and also could lead to tricyclic compounds by two RCM reactions. Accordingly, the sequence was investigated with the triallyl compounds **23** and **24**. Exhaustive alkylation of carvone **8** with sodium hydride and allyl bromide in THF and HMPA furnished a 2:3 mixture of 6,6-bisallylcarvone **25** and 2,6,6-trisallylcarvone **23**, which were separated by column chromatography on silica gel (Scheme 4). RCM reaction of trisallylcarvone **23** with Grubbs' first generation catalyst in methylene chloride furnished a 5:4 mixture of the spiro compound **26** via mono RCM and tricyclic product **27** via two RCM reactions, in 93% yield, which were separated by column chromatography on silver nitrate impregnated silica gel. The structures of the spiro and tricyclic compounds **26** and **27** were established from their spectroscopic data. Although spectroscopic data clearly established the structure of the tricyclic ketone **27**, in order to completely rule out the possibility of dimeric and oligomeric structure for the product **27** (a serious competing side reaction encountered during RCM mediated construction of medium sized rings and bridged compounds)[8] and to confirm the stereochemistry at the two bridgehead quaternary carbon atoms, single crystal X-ray diffraction analysis of a crystalline derivative of **27** was carried out. Thus, reduction of tricyclic ketone **27** with lithium aluminum hydride (LAH) furnished the secondary alcohol **28** in a highly stereoselective manner. Coupling of the alcohol **28** with 3,5-dinitrobenzoic acid in the presence of dicyclohexylcarbodiimide (DCC) and 4-*N*,*N*-dimethylaminopyridine (DMAP) furnished ester **29**, mp 201–203 °C. Single crystal X-ray diffraction analysis of ester **29** (an ORTEP diagram is depicted in Fig. 2) unambiguously established the stereochemistry in compounds **23**, **26** and **27**.



Scheme 3. Reagents and conditions: (a) Li, liq. NH_3, THF, $BrCH_2CH{=}CH_2$, **17**:**18** 3:1; (b) $Cl_2(PCy_3)_2Ru{=}CHPh$ (10 mol %), CH_2Cl_2; (c) NaH, THF, HMPA, $BrCH_2CH{=}CH_2$; (d) G-II catalyst (5 mol %), CH_2Cl_2.



Scheme 4. Reagents and conditions: (a) NaH, THF, HMPA, $BrCH_2CH{=}CH_2$; (b) $Cl_2(PCy_3)_2Ru{=}CHPh$ (10 mol %), CH_2Cl_2; (c) LAH, Et_2O; (d) DCC, DMAP, 3,5-dinitrobenzoic acid, CH_2Cl_2.

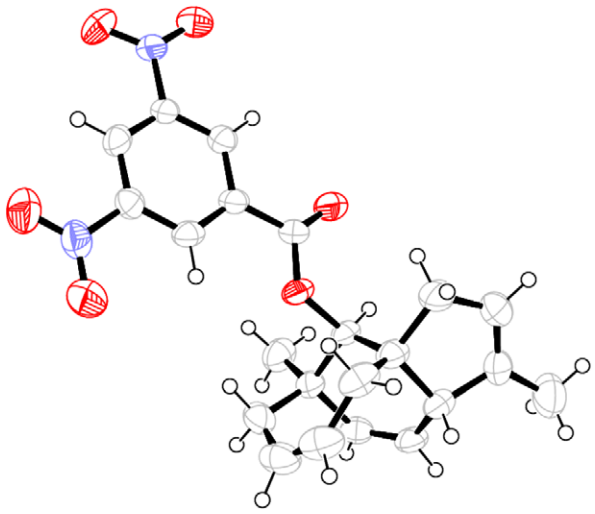


Figure 2. ORTEP diagram of **29**.

Reductive alkylation of 6,6-diallylcarvone **25** with lithium in liquid ammonia and allyl bromide furnished the second trisallylcarvone **24** in a highly stereoselective manner (Scheme 5). RCM reaction of the trisallylcarvone **24** with Grubbs' first generation catalyst furnished a 1:1 mixture of the spiro compound **30** and the bicyclo[4.3.1]decanone **31**, which were separated on a silver nitrate impregnated silica gel column, and the structures were established from their spectroscopic data. The *trans*-disposition of the allyl and isopropenyl groups in the bicyclic compound **31** and the low reactivity of the first generation Grubbs' catalyst might be responsible for the reaction to stop after the first RCM reaction. Treatment of the bicyclic compound **31** with Grubbs' second generation catalyst yielded the tricyclic system **32** in 92% yield, whose structure was established from its spectroscopic data.

3. Conclusion

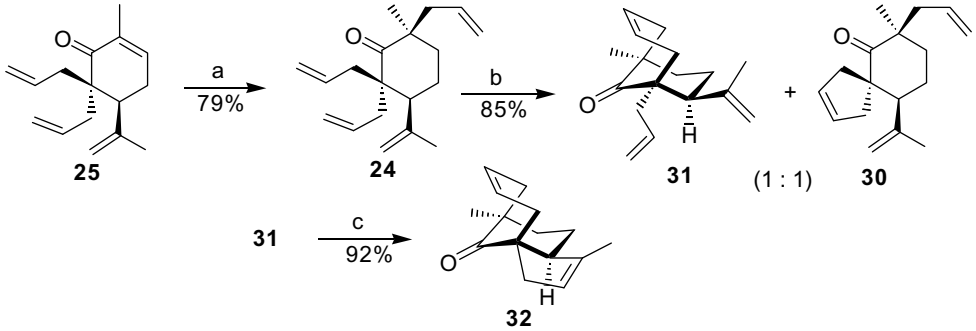
In conclusion, we have developed a rapid and efficient enantiospecific synthesis of the bicyclo[4.3.1]decane ring system of vibsanins, containing functionality in all the three bridges. It has been further extended to the enantiospecific synthesis of tricyclo-[6.4.1]tridecanes via two RCM reactions. A novel reversal of the stereoselectivity in the C-2 alkylation of carvones under base-mediated α-alkylation and reductive allylation was also discovered, which should be quite useful in stereoselective synthesis.

4. Experimental

IR spectra were recorded on a Jasco FTIR 410 spectrophotometer. ^1H (300 and 400 MHz) and ^{13}C (75 and 100 MHz) NMR spectra were recorded on JEOL JNM λ-300 and Brucker Avance 400 spectrometers. 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, the nature of carbons (C, CH, CH_2 and CH_3) was determined by recording the DEPT-135 spectra, and is given in parentheses. High-resolution mass spectra were recorded using Micromass Q-TOF micro mass spectrometer using electronspray ionization mode. 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}. All small-scale dry reactions were carried out using standard syringe-septum technique. Reactions were monitored by TLC on silica gel using a combination of hexane and ethyl acetate as eluents. Acme's silica gel (100–200 mesh) was used for column chromatography (approximately 20 g per one g of crude material).

4.1. (2*R*,5*S*,6*S*)-2,6-Bisallyl-5-isopropenyl-2,6-dimethylcyclohex- 3-enone 11

To a magnetically stirred suspension of NaH (116 mg, 60% dispersion in oil, 2.9 mmol, washed with dry hexanes) in THF (1 mL) and HMPA (1 mL) was added a solution of enone **9** (60 mg, 0.29 mmol) in THF (1 mL), followed by allyl bromide (0.25 mL,



Scheme 5. Reagents and conditions: (a) Li, liq. NH_3, THF, $BrCH_2CH{=}CH_2$; (b) $Cl_2(PCy_3)_2Ru{=}CHPh$ (10 mol %), CH_2Cl_2; (c) G-II catalyst (5 mol %), CH_2Cl_2.

2.9 mmol), and reaction mixture was stirred for 10 h at rt. It was then quenched with water (3 mL) and extracted with ether (3 mL × 3). The combined ether extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using CH_2Cl_2–hexane (1:9) as eluent furnished the ketone **11** (55 mg, 77%). $[\alpha]_D^{23} = -289$ (*c* 2.4, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3077, 3018, 2979, 2933, 1702, 1640, 1457, 1438, 1378, 1290, 995, 916, 760, 732; ^1H NMR (400 MHz, $CDCl_3$): δ 5.65–5.55 (4H, m), 5.03 (2H, d, *J* 10.5 Hz), 4.99 (2H, d, *J* 16.9 Hz), 4.78 (1H, s), 4.71 (1 H, s), 3.04 (1H, d, *J* 4.6 Hz), 2.40–2.30 (2H, m), 2.26 (1H, dd, *J* 13.6 and 7.8 Hz), 2.18 (1H, dd, *J* 13.6 and 6.9 Hz), 1.51 (3H, s, olefinic-CH_3) 1.12 (3H, s) and 0.91 (3H, s) [2 × *tert*-CH_3]; ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.9 (C, C=O), 144.0 (C, *C*=CH_2), 133.7 (CH), 133.4 (CH), 133.1 (CH), 126.7 (CH), 118.6 (CH_2), 118.5 (CH_2), 115.3 (CH_2), 54.8 (CH), 49.9 (C), 46.7 (C), 44.3 (CH_2), 42.9 (CH_2), 24.8 (CH_3), 20.8 (CH_3), 19.6 (CH_3); HRMS: *m*/*z* calcd for $C_{17}H_{24}ONa$ (M+Na): 267.1725; found: 267.1712.

4.2. (1*S*,6*R*,9*S*)-9-Isopropenyl-1,6-dimethylbicyclo[4.3.1]deca-3,7-dien-10-one 12

To a magnetically stirred solution of the diallylcarvone **11** (24 mg, 0.98 mmol) in anhydrous CH_2Cl_2 (10 mL, 0.01 M) was added Grubbs' second generation catalyst (5 mg, 5 mol %). The reaction mixture was stirred magnetically for 8 h at rt and the catalyst was filtered off through a short silica gel column. Evaporation of the solvent, followed by purification on a silica gel column using CH_2Cl_2–hexane (1:9) as eluent furnished bicyclic ketone **12** (18 mg, 86%) as an oil. $[\alpha]_D^{23} = -265$ (*c* 1.1, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3073, 3019, 2970, 2869, 1702, 1641, 1456, 1374, 1213, 1164, 1014, 997, 894, 810, 760, 672. ^1H NMR (400 MHz, $CDCl_3$): δ 5.85–5.75 (1H, m), 5.65–5.55 (1H, m), 5.51 (1H, dd, *J* 9.8 and 4.9 Hz), 5.38 (1H, d, *J* 9.8 Hz), 4.70 (1H, s), 4.67 (1H, s), 2.98 (1H, d, *J* 4.9 Hz), 2.34 (1H, dd *J* 15.0 and 7.6 Hz), 2.12 (1H, dd, *J* 15.7 and 6.6 Hz), 2.09 (1H, dd, *J* 15.7 and 4.5 Hz), 1.90 (1H, dd, *J* 15.0 and 4.8 Hz), 1.39 (3H, s, olefinic–CH_3), 1.23 (3H, s) and 0.97 (3H, s) [2 × *tert*-CH_3]; ^{13}C NMR (100 MHz, $CDCl_3$): δ 214.5 (C, C=O), 144.6 (C, *C*=CH_2), 134.5 (CH), 130.5 (CH), 128.9 (CH), 128.0 (CH), 114.4 (CH_2), 60.3 (CH), 50.9 (C), 48.2 (C), 41.8 (CH_2), 40.2 (CH_2), 25.2 (CH_3), 22.5 (CH_3), 19.1 (CH_3); HRMS: *m*/*z* calcd for $C_{15}H_{20}ONa$ (M+Na): 239.1412; found: 239.1407.

4.3. (2*S*,3*S*,6*R*)-2,6-Bisallyl-5-isopropenyl-2,6-dimethylcyclohexanone 13

To freshly distilled liquid ammonia (50 mL) was added Li metal (14 mg, 2 mmol). To the resultant blue coloured solution was added a solution of the enone **9** (50 mg, 0.24 mmol) in dry THF (4 mL) for over a period of 10 min. After 15 min the reaction mixture was quenched with a solution of allyl bromide (0.18 mL, 2 mmol) in dry THF (1 mL) and the reaction was slowly allowed to attain rt. Water (5 mL) was added to the reaction mixture after 3 h and extracted with ether (3 mL × 3). The combined organic extract was washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using CH_2Cl_2–hexane (1:9) as eluent furnished ketone **13** (44 mg, 73%) as an oil. $[\alpha]_D^{23} = +56.9$ (*c* 11.3, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3077, 2978, 2932, 2871, 1694, 1638, 1457, 1434, 1376, 998, 914; ^1H NMR (300 MHz, $CDCl_3$): δ 5.80–5.45 (2H, m), 5.15–4.95 (4H, m), 4.91 (1H, br s), 4.70 (1H, br s), 2.70–2.55 (2H, m), 2.35–2.05 (3H, m), 2.00–1.80 (2H, m), 1.78 (3H, s, olefinic-CH_3), 1.70–1.40 (2H, m), 1.04 (3H, s) and 1.02 (3H, s) [2 × *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$): δ 217.7 (C, C=O), 145.2 (C, *C*=CH_2), 135.6 (CH), 133.7 (CH), 118.3 (CH_2), 118.1 (CH_2), 114.7 (CH_2), 52.4 (C), 48.7 (CH), 47.2 (C), 43.4 (CH_2), 42.3 (CH_2), 34.9 (CH_2), 24.8 (CH_3), 23.4 (CH_3), 23.2 (CH_3), 22.9 (CH_2); HRMS: *m*/*z* calcd for $C_{17}H_{26}ONa$ (M+Na): 269.1881; found: 269.1878.

4.4. (2*S*,3*S*,6*S*)-3-Isopropyl-2,6-dimethyl-2,6-dipropylcyclohexanone 14

To a solution of the ketone **13** (28 mg, 0.11 mmol) in methanol (1 mL) was added activated 10% Pd–C (10 mg). The reaction mixture was stirred for 1 h at rt in an atmosphere of hydrogen, created by evacuative replacement of air (balloon), and then the catalyst was filtered off. Evaporation of the solvent furnished saturated ketone **14** (29 mg, 97%) as an oil. $[\alpha]_D^{24} = +51.7$ (*c* 3.0, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 2958, 2933, 2873, 1692 (C=O), 1467, 1374, 1104, 1065, 1039, 993, 978; ^1H NMR (400 MHz, $CDCl_3$): δ 1.95–1.75 (3H, m), 1.70–1.30 (6H, m), 1.30–1.10 (5H, m), 0.98 (3H, s) and 0.95 (3H, s) [2 × *tert*-CH_3], 0.90–0.80 (12H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 218.2 (C, C=O), 53.6 (C), 47.5 (C), 46.0 (CH), 41.8 (CH_2), 39.3 (CH_2), 37.4 (CH_2), 26.2 (CH), 25.1 (CH_3), 24.7 (CH_3), 22.8 (CH_3), 19.2 (CH_3), 18.6 (CH_2), 17.4 (CH_2), 17.2 (CH_2), 14.9 (CH_3), 14.7 (CH_3). HRMS: *m*/*z* calcd for $C_{17}H_{32}ONa$ (M+Na): 275.2351; found: 275.2351.

4.5. (2*S*,3*S*,6*R*)-3-Isopropyl-2,6-dimethyl-2,6-dipropylcyclohexanone 15

To a solution of ketone **11** (40 mg, 0.16 mmol) in methanol (1 mL) was added activated 10% Pd–C (10 mg). The reaction mixture was stirred for 1 h at rt in an atmosphere of hydrogen, created by evacuative replacement of air (ballon), and then the catalyst was filtered off. Evaporation of the solvent furnished the saturated ketone **15** (39 mg, 97%) as an oil. $[\alpha]_D^{24} = +19.4$ (*c* 3.7, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 2959, 2934, 2872, 1694, 1464, 1375, 1105, 1054, 1019, 994, 734; ^1H NMR (400 MHz, $CDCl_3$): δ 2.00–1.88 (1H, m), 1.80 (1H, quintet, *J* 6.9 Hz), 1.68–1.50 (6H, m), 1.25–1.05 (5H, m), 1.02 (3H, s) and 0.98 (3H, s) [2 × *tert*-CH_3], 0.93 (3 H, d *J* 7.0 Hz), 0.90–0.80 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 219.9 (C, C=O), 53.6 (C), 47.4 (C), 45.5 (CH), 43.0 (CH_2), 39.5 (CH_2), 35.1 (CH_2), 27.3 (CH_3), 26.1 (CH), 24.7 (CH_3), 24.1 (CH_3), 19.1 (CH_3), 18.4 (CH_2), 17.5 (CH_2), 17.4 (CH_2), 14.9 (2 C, CH_3); HRMS: *m*/*z* calcd for $C_{17}H_{32}ONa$ (M+Na): 275.2351; found: 275.2351.

4.6. (1*S*,3*R*,6*S*)-3-Allyl-1,3,7-trimethylbicyclo[4.3.0]non-7-en-2-one 16

RCM reaction of ketone **13** (46 mg, 0.19 mmol) in anhydrous CH_2Cl_2 (19 mL, 0.01 M) using Grubbs' second generation catalyst (8 mg, 5 mol %) for 8 h at rt, followed by purification on a silica gel column using CH_2Cl_2–hexane (1:9) as eluent furnished the bicyclic ketone **16** (36 mg, 89%) as an oil. $[\alpha]_D^{23} = +101$ (*c* 2.8, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3077, 3043, 2964, 2936, 2875, 1712, 1640, 1452, 1376, 1243, 1005, 915, 830, 795; ^1H NMR (300 MHz, $CDCl_3$): δ 5.61 (1H, ddt, *J* 14.7, 8.1 and 6.3 Hz), 5.31 (1H, br s), 5.10–4.95 (2H, m), 2.85–2.75 (1H, m), 2.50–2.30 (2H, m), 2.25–1.85 (4H, m), 1.80–1.50 (2H, m), 1.67 (3H, s, olefinic-CH_3), 1.18 (3H, s) and 1.04 (3H, s) [2 × *tert*-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$): δ 217.9 (C, C=O), 138.8 (C, *C*=CH_2), 134.6 (CH), 123.3 (CH), 118.2 (CH_2), 56.8 (C), 48.8 (CH), 47.2 (C), 45.4 (CH_2), 39.2 (CH_2), 31.7 (CH_2), 28.6 (CH_3), 17.3 (CH_2), 16.7 (CH_3), 14.6 (CH_3); HRMS: *m*/*z* calcd for $C_{15}H_{22}ONa$ (M+Na): 241.1568; found: 241.1557.

4.7. (2*R*,3*S*,6*S*)- and (2*R*,3*S*,6*R*)-2,6-Bisallyl-3-isopropenyl-2,6-dimethylcyclohexanones 17 and 18

To freshly distilled liquid ammonia (50 mL) was added Li metal (35 mg, 5 mmol). To the resultant blue coloured solution was added a solution of enone **10** (102 mg, 0.5 mmol) in dry THF

(4 mL) for over a period of 10 min. After 15 min the reaction mixture was quenched with a solution of allyl bromide (0.43 mL, 5 mmol) in dry THF (1 mL). Workup as described for the compound **13**, followed by purification over a $AgNO_3$ impregnated silica gel column using CH_2Cl_2–hexane (1:9) as eluent furnished the (2*R*,3*S*,6*S*)-isomer **17** (61 mg, 50%) as an oil. $[\alpha]_D^{22} = +2.7$ (*c* 1.7, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3077, 2976, 2936, 2870, 1694 (C=O), 1639, 1461, 1376, 995, 914, 898; ^1H NMR (400 MHz, $CDCl_3$): δ 5.62 (1H, dddd, *J* 17.0, 10.4, 8.0, and 6.8 Hz), 5.50 (1H, ddt, *J* 17.3, 10.2 and 7.2 Hz), 5.10–4.85 (5H, m), 4.60 (1H, br s), 2.50 (1H, dd, *J* 14.2 and 7.0 Hz), 2.31 (1H, dd, *J* 13.7 and 6.6 Hz), 2.23–2.05 (3H, m), 2.00–1.90 (1H, m), 1.77 (3H, s, olefinic-CH_3), 1.80–1.60 (3H, m), 1.09 (3H, s) and 1.08 (3H, s) [2 × *tert*-CH_3]; ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.9 (C, C=O), 144.8 (C, *C*=CH_2), 134.7 (CH), 134.3 (CH), 117.9 (CH_2), 117.7 (CH_2), 114.5 (CH_2), 53.7 (CH), 51.6 (C), 47.2 (C), 44.8 (CH_2), 39.2 (CH_2), 35.0 (CH_2), 24.7 (CH_3), 24.4 (CH_3), 23.2 (CH_3), 22.8 (CH_2); HRMS: *m*/*z* calcd for $C_{17}H_{26}ONa$ (M+Na): 269.1881. Found: 269.1880.

Further elution of the column with CH_2Cl_2–hexane (1:4) gave (2*R*,3*S*,6*R*)-isomer **18** (21 mg, 17%) as an oil. $[\alpha]_D^{22} = +25.8$ (*c* 1.7, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3077, 2975, 2935, 2872, 1694 (C=O), 1639, 1457, 1375, 995, 914, 894; ^1H NMR (400 MHz, $CDCl_3$): δ 5.69 (1H, ddt, *J* 17.4, 10.2 and 7.4 Hz), 5.54 (1H, ddt, *J* 17.3, 10.2 and 7.3 Hz), 5.10–4.90 (5H, m), 4.51 (1H, s), 2.46 (1H, dd, *J* 14.2 and 7.2 Hz), 2.35–2.15 (4H, m), 1.98 (1H, dt, *J* 14.2 and 6.2 Hz), 1.87–1.80 (2H, m), 1.77 (3H, s, olefinic-CH_3), 1.43 (1H, dt, *J* 14.1 and 6.2 Hz), 1.14 (3H, s) and 1.08 (3H, s) [2 × *tert*-CH_3]; ^{13}C NMR (100 MHz, $CDCl_3$): δ 217.3 (C, C=O), 144.5 (C, *C*=CH_2), 134.3 (CH), 133.9 (CH), 118.4 (CH_2), 117.9 (CH_2), 114.3 (CH_2), 52.8 (CH), 51.1 (C), 47.0 (C), 42.9 (CH_2), 39.2 (CH_2), 33.7 (CH_2), 25.7 (CH_3), 24.5 (CH_3), 24.3 (CH_3), 22.0 (CH_2); HRMS: *m*/*z* calcd for $C_{17}H_{26}ONa$ (M+Na): 269.1881. Found: 269.1882.

4.8. (1*R*,6*R*,7*S*)-7-Isopropenyl-1,6-dimethylbicyclo[4.3.1]dec-3-en-10-one 19

RCM reaction of ketone **18** (16 mg, 0.07 mmol) in anhydrous CH_2Cl_2 (7 mL, 0.01 M) using Grubbs' first generation catalyst (5 mg, 10 mol %) for 8 h at rt, followed by purification on a silica gel column using CH_2Cl_2–hexane (1:19) as eluent furnished the bicyclic ketone **19** (13 mg, 91%) as an oil. $[\alpha]_D^{23} = +13.3$ (*c* 1.1, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3076, 3034, 2970, 2930, 1698 (C=O), 1640, 1451, 1376, 1199, 1012, 995, 894, 855; ^1H NMR (400 MHz, $CDCl_3$): δ 5.85–5.75 (2H, m), 4.89 (1H, s), 4.73 (1H, s), 2.72 (1H, dd, *J* 15.5 and 6.0 Hz), 2.63 (1H, dt, *J* 13.7 and 4.6 Hz), 2.54 (1H, dd, *J* 15.8 and 5.2 Hz), 2.21 (1H, dd, *J* 13.4 and 4.0 Hz), 2.00–1.85 (2H, m), 1.79 (3H, s, olefinic-CH_3), 1.80–1.70 (1H, m), 1.62 (1H, td, *J* 13.7 and 5.1 Hz), 1.45–1.35 (1H, m), 1.08 (3H, s) and 1.06 (3H, s) [2 × *tert*-CH_3]; ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.8 (C, C=O), 145.4 (C, *C*=CH_2), 130.1 (2C, CH), 113.8 (CH_2, C=*C*H_2), 56.0 (CH), 52.3 (C), 48.4 (C), 40.6 (CH_2), 37.8 (CH_2), 33.5 (CH_2), 27.4 (CH_3), 25.4 (CH_2), 24.9 (CH_3), 23.8 (CH_3); HRMS: *m*/*z* calcd for $C_{15}H_{22}ONa$ (M+Na): 241.1568; found: 241.1570.

4.9. (1*R*,3*S*,6*S*)-3-Allyl-1,3,7-trimethylbicyclo[4.3.0]nona-4,7-dien-2-one 20

RCM reaction of ketone **17** (16 mg, 0.07 mmol) in anhydrous CH_2Cl_2 (7 mL, 0.01 M) using Grubbs' first generation catalyst (5 mg, 10 mol %) for 8 h at rt, followed by purification on a silica gel column using CH_2Cl_2–hexane (1:19) as eluent furnished the bicyclic ketone **20** (12 mg, 86%) as an oil. $[\alpha]_D^{23} = -66.6$ (*c* 1.0, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3076, 3041, 2962, 2930, 2864, 1694 (C=O), 1448, 1373, 1015, 996, 915; ^1H NMR (400 MHz, $CDCl_3$): δ 5.65 (1 H, ddt, *J* 17.3, 10.3 and 7.6 Hz), 5.20 (1H, br s, H-8), 5.05 (1H, d, *J* 10.3 Hz), 5.02 (1H, d, *J* 17.3 Hz), 2.63 (1H, dm, *J* 16.5 Hz), 2.40–2.30 (2H, m), 2.20–2.05 (2H, m), 1.92–1.85 (1H, m), 1.80–1.25 (3H, m), 1.68 (3H, s, olefinic-CH_3), 1.17 (3H, s) and 1.06 (3H, s) [2 × *tert*-CH_3]; ^{13}C NMR (100 MHz, $CDCl_3$): δ 220.4 (C, C=O), 141.8 (C), 134.2 (CH), 122.1 (CH), 118.1 (CH_2), 56.5 (CH), 53.3 (C), 46.9 (C), 45.3 (CH_2), 43.7 (CH_2), 32.4 (CH_2), 27.2 (CH_3), 25.5 (CH_3), 22.9 (CH_2), 14.8 (CH_3); HRMS: *m*/*z* calcd for $C_{15}H_{22}ONa$ (M+Na): 241.1568; found: 241.1563.

4.10. (2*R*,5*S*,6*R*)-2,6-Bisallyl-5-isopropenyl-2,6-dimethylcyclohex-3-enone 21

To a magnetically stirred suspension of NaH (192 mg, 60% dispersion in oil, 5.0 mmol, washed with dry hexanes) in THF (1 mL) and HMPA (1 mL) was added a solution of enone **10** (102 mg, 0.5 mmol) in THF (1 mL), followed by allyl bromide (0.43 mL, 5.0 mmol), and reaction mixture was stirred for 10 h at rt. It was then quenched with water (3 mL) and extracted with ether (3 mL × 3). The combined ether extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue over a silica gel column using CH_2Cl_2–hexane (1:9) as eluent furnished ketone **21** (94 mg, 77%). $[\alpha]_D^{23} = -254$ (*c* 3.1, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3076, 3018, 2978, 2934, 2876, 1703 (C=O), 1639, 1459, 1439, 1374, 993, 914; ^1H NMR (400 MHz, $CDCl_3$): δ 5.80–5.60 (2H, m), 5.61 (2H, br s), 5.10–4.90 (4H, m), 4.85 (1H, s), 4.75 (1H, s), 2.94 (1H, s), 2.45 (1H, dd, *J* 14.3 and 7.3 Hz), 2.35 (1H, dd, *J* 13.6 and 5.8 Hz), 2.19 (1H, dd, *J* 13.6 and 7.1 Hz), 1.99 (1H, dd, *J* 14.3 and 7.3 Hz), 1.56 (3H, s, olefinic-CH_3), 1.14 (3H, s) and 1.13 (3H, s) [2 × *tert*-CH_3]; ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.9 (C, C=O), 143.8 (C, *C*=CH_2), 134.9 (CH), 133.5 (CH), 133.3 (CH), 127.1 (CH), 118.3 (CH_2), 117.9 (CH_2), 115.5 (CH_2), 56.2 (CH), 49.1 (C), 47.5 (C), 44.5 (CH_2), 38.3 (CH_2), 24.6 (CH_3), 23.3 (CH_3), 21.2 (CH_3); HRMS: calcd for $C_{17}H_{24}ONa$ (M+Na): *m*/*z* 267.1725; found: 267.1726.

4.11. (1*R*,3*R*,6*S*)-3-Allyl-1,3,7-trimethylbicyclo[4.3.0]nona-4,7-dien-2-one 22

RCM reaction of ketone **21** (30 mg, 0.12 mmol) in anhydrous CH_2Cl_2(19 mL, 0.01 M) using Grubbs' second generation catalyst (10 mg, 5 mol %) for 6 h at rt, followed by purification on a silica gel column using CH_2Cl_2–hexane (1:9) as eluent furnished the bicyclic ketone **22** (25 mg, 94%) as an oil. $[\alpha]_D^{22} = -187$ (*c* 2.4, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3077, 3020, 2967, 2930, 2869, 2853, 1700 (C=O), 1640, 1452, 1367, 1105, 1014, 996, 916; ^1H NMR (400 MHz, $CDCl_3$): δ 5.73 (1H, dd, *J* 10.2 and 3.4 Hz), 5.68–5.50 (1H, m), 5.50 (1H, dd, *J* 10.2 and 1.8 Hz), 5.20 (1H, br s), 4.98 (1H, d, *J* 12.3 Hz), 4.97 (1H, d, *J* 15.7 Hz), 2.89 (1H, br s H-6), 2.64 (1H, dd, *J* 16.2 and 2.0 Hz), 2.47 (1H, dd, *J* 13.4 and 7.8 Hz), 2.11 (1H, d, *J* 16.2 Hz), 2.04 (1H, dd, *J* 13.4 and 6.9 Hz), 1.74 (3H, s, olefinic-CH_3), 1.18 (3H, s) and 1.11 (3H, s) [2 × *tert*-CH_3]; ^{13}C NMR (100 MHz, $CDCl_3$): δ 217.9 (C, C=O), 141.1 (C, C-7), 134.0 (CH), 131.9 (CH), 125.0 (CH), 122.2 (CH), 118.0 (CH_2), 56.7 (CH, C-6), 52.4 (C), 47.4 (C), 44.9 (CH_2), 44.2 (CH_2), 26.5 (CH_3), 24.8 (CH_3), 15.1 (CH_3); HRMS: *m*/*z* calcd for $C_{15}H_{20}ONa$ (M+Na): 239.1412; found: 239.1400.

4.12. (2*R*,5*S*)-2,6,6-Trisallyl-5-isopropenyl-2-methylcyclohex-3-enone 23

To a magnetically stirred suspension of NaH (400 mg, 60% dispersion in oil, 10 mmol, washed with dry hexanes) in THF (1 mL) and HMPA (1 mL) was added a solution of carvone **8** (150 mg, 1 mmol) in THF (1 mL), followed by allyl bromide (0.52 mL, 6 mmol), and the reaction mixture was stirred for 10 h at rt. It was then quenched with water (3 mL) and extracted with ether (3 mL × 3). The combined ether extract was washed with brine

and dried over Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using CH_2Cl_2–hexane (1:9) as eluent first furnished trisallyl carvone **23** (148 mg, 55%). $[\alpha]_D^{26} = -221.9$ (*c* 4.7, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3076, 3018, 2978, 2930, 1836, 1700 (C=O), 1639, 1441, 995, 915; ^1H NMR (300 MHz, $CDCl_3$): δ 5.85–5.60 (4H, m), 5.50 (1H, ddt, *J* 16.8, 13.5 and 6.9 Hz), 5.15–4.95 (6H, m), 4.87 (1H, br s), 4.80 (1H, br s), 3.15 (1H, br s), 2.65–2.45 (3H, m), 2.30 and 2.21 (2H, 2 × dd, *J* 13.5 and 8.1 Hz), 1.99 (1 H, dd, 14.4 and 6.9 Hz), 1.75–1.63 (1H, m), 1.60 (3H, s), 1.16 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 215.4 (C, C=O), 143.6 (C, *C*=CH_2), 134.1 (CH), 133.5 (CH), 133.2 (CH), 133.1 (CH), 126.7 (CH), 118.7 (CH_2), 118.6 (CH_2), 118.5 (CH_2), 115.9 (CH_2), 53.7 (CH, C-5), 52.3 (C, C-6), 47.1 (C, C-2), 44.3 (CH_2), 38.6 (CH_2), 35.2 (CH_2), 24.6 (CH_3), 21.1 (CH_3); HRMS: *m*/*z* calcd for $C_{19}H_{26}ONa$ (M+Na): 293.1881; found: 293.1884.

Further elution of the column with CH_2Cl_2–hexane (1:4) gave (5*S*)-6,6-bisallyl-5-isopropenyl-2-methylcyclohex-2-enone **25** (86 mg, 37%). $[\alpha]_D^{23} = -47.5$ (*c* 10, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3076, 2978, 2949, 2920, 1668, 1639, 1439, 1376, 1189, 1074, 997, 912; ^1H NMR (300 MHz, $CDCl_3$): δ 6.48 (1H, br s, H-3), 5.83–5.53 (2H, m, 2 × C*H*=CH_2), 5.10–4.93 (4H, m, 2 × CH=C*H*$_2$), 4.78 (1H, s) and 4.70 (1H, s) [C=CH_2], 2.80–2.00 (7H, m), 1.76 (3H, s) and 1.64 (3H, s) [2 × olefinic-CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$): δ 201.8 (C, C=O), 145.8 (C, *C* = CH_2), 140.0 (CH, C-3), 134.7 (C, C-2), 134.4 (CH), 133.9 (CH), 118.2 (CH_2), 118.0 (CH_2), 114.6 (CH_2), 50.3 (C, C-6), 48.9 (CH, C-5), 38.7 (CH_2), 35.2 (CH_2), 28.9 (CH_2), 22.3 (CH_3), 16.6 (CH_3); HRMS: *m*/*z* calcd for $C_{16}H_{23}O$ (M+H): 231.1749; found: 231.1749.

4.13. (7*R*,10*S*)-7-Allyl-10-isopropenyl-7-methylspiro[4.5]deca-2,8-dien-6-one 26 and (1*R*,5*S*,8*R*)-4,8-dimethyltricyclo-[6.4.1.0^{1,5}]trideca-3,6,10-trien- 13-one 27

To a magnetically stirred solution of trisallylcarvone **23** (50 mg, 0.18 mmol) in anhydrous CH_2Cl_2 (18 mL, 0.01 M) was added Grubbs' first generation catalyst (15 mg, 10 mol %). The reaction mixture was stirred magnetically for 2 h at rt and the catalyst was filtered off through a short silica gel column. Evaporation of the solvent and purification of the residue on an $AgNO_3$ impregnated silica gel column using ethyl acetate–hexane (1:49) as eluent furnished the spiro ketone **26** (22 mg, 50%) as an oil. $[\alpha]_D^{26} = -366$ (*c* 2.2, $CHCl_3$); IR (neat): ν_{max}/ cm^{-1} 3074, 3018, 2976, 2931, 2854, 1703, 1639, 1456, 1439, 1373, 1338, 1151, 1134, 997, 916, 897, 760, 667; ^1H NMR (300 MHz, $CDCl_3$): δ 5.85–5.60 (4H, m), 5.47–5.40 (1H, m), 5.15–4.97 (2H, m), 4.76 (1H, s), 4.68 (1H, s), 3.30–3.05 (2H, m), 2.64–2.10 (5H, m), 1.48 (3H, s, olefinic-CH_3), 1.18 (3H, s, *tert*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 214.0 (C, C=O), 144.8 (C, *C*=CH_2), 134.6 (CH), 133.2 (CH), 130.0 (CH), 126.7 (CH), 125.6 (CH), 118.4 (CH_2), 114.6 (CH_2), 57.3 (C), 56.4 (CH, C-10), 47.4 (C), 45.5 (CH_2), 44.8 (CH_2), 36.3 (CH_2), 24.5 (CH_3), 19.9 (CH_3); HRMS: *m*/*z* calcd for $C_{17}H_{22}ONa$ (M+Na): 265.1568; found: 265.1569.

Further elution of the column with ethyl acetate–hexane (1:19) gave (1*R*,5*S*,8*R*)-4,8-dimethyltricyclo[6.4.1.0^{1,5}]trideca-3,6,10-trien-13-one **27** (18 mg, 41%) as an oil; $[\alpha]_D^{26} = -101.8$ (*c* 1.7, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3020, 2967, 2929, 2852, 1703 (C=O), 1448, 1370, 1348, 1212, 1161, 1151, 1083, 987, 886, 817, 797, 703, 673; ^1H NMR (300 MHz, $CDCl_3$): δ 5.90 (1H, dd, *J* 10.2 and 3.9 Hz), 5.83 (1H, dt, *J* 8.7 and 3.0 Hz), 5.78–5.65 (1H, m), 5.33 (1H, dd, *J* 10.2 and 2.1 Hz), 5.21 (1H, br s), 3.46 (1H, dq, *J* 10.5 and 2 Hz), 3.25 (1H, br s), 2.37 (1H, dd, *J* 15.0 and 8.4 Hz), 2.15–1.90 (4H, m), 1.63 (3H, s, olefinic-CH_3), 1.19 (3H, s, *tert*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 215.1 (C, C=O), 139.8 (C), 131.9 (CH), 130.0 (CH), 128.7 (CH), 128.5 (CH), 123.2 (CH), 58.6 (C), 58.5 (CH), 47.6 (C), 40.8 (CH_2), 39.7 (CH_2), 39.6 (CH_2), 24.8 (CH_3), 15.1 (CH_3); HRMS: *m*/*z* calcd for $C_{15}H_{18}ONa$ (M+Na): 237.1255; found: 237.1254.

4.14. (1*R*,5*S*,8*R*,13*R*)-1,4-Dimethyltricyclo[6.4.1.0^{1,5}]trideca-3,6,10-trien-13-ol 28

To a cold (0 °C), magnetically stirred solution of the tricyclic ketone **27** (45 mg, 0.22 mmol) in dry ether (2 mL) was added $LiAlH_4$ (25 mg, 0.66 mmol), and reaction mixture was stirred for 1 h at rt. The reaction mixture was then diluted with ether (3 mL) and quenched with a few drops of water. The organic layer was separated and the aqueous phase was extracted with ether (3 × 3 mL). The combined organic layer was washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate–hexane (1:9) as eluent furnished the alcohol **28** (44 mg, 97%) as an oil. $[\alpha]_D^{24} = -62.2$ (*c* 2.6, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3422, 3014, 2960, 2923, 2851, 1454, 1376, 1144, 1098, 1049, 1023, 858, 817, 790, 750, 709, 647; ^1H NMR (400 MHz, $CDCl_3$): δ 5.77 (1H, dd, *J* 10.0 and 4.1 Hz), 5.57 and 5.40 (2H, 2 × ddt, *J* 11.6, 8.4 and 3.2 Hz), 5.27 (1H, dd, *J* 10.0 and 2.2 Hz), 5.14 (1H, br s), 3.45 (1H, s), 2.91 (1H, br s), 2.79 (1H, dq, *J* 15.6 and 2.8 Hz), 2.65–2.50 (2H, m), 2.00 (1H, dm, *J* 15.6 Hz), 1.87 (1H, dd, *J*, 15,8 and 8.6 Hz), 1.78–1.72 (2H, m), 1.66 (3H, s, olefinic-CH_3) and 1.08 (3H, s, *tert*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.6 (C), 133.8 (CH), 129.7 (CH), 128.5 (CH), 127.4 (CH), 121.1 (CH), 78.7 (CH), 56.2 (CH), 47.4 (C), 44.9 (CH_2), 38.7 (C), 34.9 (CH_2), 33.8 (CH_2), 28.6 (CH_3), 15.1 (CH_3); HRMS: *m*/*z* calcd for $C_{15}H_{20}ONa$ (M+Na): 239.1412; found: 239.1401.

4.15. (1*R*,5*S*,8*R*,13*R*)-1,4-Dimethyltricyclo[6.4.1.0^{1,5}]trideca-3,6,10-trienyl 3,5-dinitrobenzoate 29

To a magnetically stirred solution of alcohol **28** (35 mg, 0.16 mmol) in CH_2Cl_2 (2 mL) were added 3,5-dinitrobenzoic acid (170 mg, 0.8 mmol), DCC and a catalytic amount of DMAP (10 mg), and reaction mixture was stirred at rt for 4 h. The reaction mixture was then diluted with water (5 mL) and extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layer was washed with brine (5 mL) and dried over Na_2SO_4. Evaporation of the solvent and purification of the residue over a silica gel column using ethyl acetate–hexane (1:99) as eluent furnished the ester (58 mg, 91%), which was recrystallized from a 1:1 mixture of ethyl acetate and hexane. Mp: 201–203 °C; $[\alpha]_D^{26} = +10.3$ (*c* 4.3, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3113, 3032, 2968, 2920, 2854, 2800, 1724, 1548, 1450, 1342, 1277, 1171, 1090, 1072, 918, 859, 749, 719; ^1H NMR (400 MHz, $CDCl_3$): δ 9.25 (1H, t, *J* 2.0 Hz), 9.20 (2H, d, *J* 2.0 Hz), 5.91 (1H, dd, *J*, 10.0 and 4.1 Hz), 5.76 and 5.58 (2H, 2 × ddt, *J* 11.3, 8.5 and 2.9 Hz), 5.40–5.30 (2H, m), 5.21 (1H, br s), 3.06 (1H, br s), 2.92 (1H, dq, *J*, 15.9 and 2.9 Hz), 2.68 (1H, dd, *J* 15.9 and 2.9 Hz), 2.20–1.85 (4H, m), 1.74 (3H, s, olefinic-CH_3), 1.03 (3H, s, *tert*-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8 (C, C=O), 148.9 (2C, C), 141.6 (C), 134.2 (C), 132.6 (CH), 129.8 (CH), 129.3 (2C, CH), 128.5 (CH), 127.9 (CH), 122.3 (CH), 120.9 (CH), 83.9 (CH, C-13), 56.5 (CH, C-5), 47.1 (C), 44.4 (CH_2), 38.8 (C), 36.0 (CH_2), 35.0 (CH_2), 28.3 (CH_3), 15.0 (CH_3); Anal. Calcd for $C_{22}H_{22}N_2O_6$: C, 64.38; H, 5.40; N, 6.82. Found: C, 64.31; H, 5.71; N, 6.72.

Crystal data: X-ray data were collected at 296 K on a SMART CCD-BRUKER diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The structure was solved by direct methods (SIR 92). Refinement was by full-matrix least-squares procedures on F2 using SHELXL-97. The non-hydrogen atoms were refined anisotropically, whereas hydrogen atoms were refined isotropically. Mol. For. $C_{22}H_{22}N_2O_6$; M_W = 410.15; colourless; Crystal system: monoclinic; Space group *P*1211; cell parameters, *a* = 8.716(4) Å, *b* = 6.691(3) Å, *c* = 17.428(8) Å; α = 90.00, β = 97.640(8), γ = 90.00, *V*=1007.3(8) Å^3, *Z* = 2, D_c=1.201 g cm^{-3}, *F*(000) = 384, μ=0.083 mm^{-1}. Total number of l.s. parameters = 273, R_1 = 0.0590 for 2582 $F_0 > 2\sigma(F_0)$ and 0.0915 for all

3733 data. wR_2 = 0.1170, GOF = 1.014, restrained GOF = 1.014 for all data. An ORTEP diagram is depicted in Figure 2. Crystallographic data have been deposited with Cambridge crystallographic data centre (CCDC 693972).

4.16. (3*S*,6*R*)-2,2,6-Trisallyl-3-isopropenyl-6-methylcyclohexanone 24

To freshly distilled liquid ammonia (50 mL) was added Li metal (18 mg, 2.5 mmol). To the resultant blue coloured solution was added a solution of the enone **25** (115 mg, 0.5 mmol) in dry THF (4 mL) for over a period of 10 min. After 15 min, the reaction mixture was quenched with a solution of allyl bromide (0.26 mL, 3 mmol) in dry THF (1 mL). Workup followed by purification over a silica gel column using CH_2Cl_2–hexane (1:19) furnished ketone **24** (108 mg, 79%) as an oil. $[\alpha]_D^{23} = +65.6$ (*c* 1.6, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3078, 2979, 2934, 2873, 1690 (C=O), 1449, 1376, 1177, 1066, 995, 914; ^1H NMR (400 MHz, $CDCl_3$): δ 5.66 (1H, ddt, *J* 17.1, 10.1 and 7.4 Hz), 5.60–5.35 (2H, m), 5.10–4.80 (7H, m), 4.54 (1H, s), 2.59 (1H, dd, *J* 14.5 and 6.4 Hz), 2.55–2.45 (2H, m), 2.23 (1H, dd, *J* 13.7 and 7.4 Hz), 2.20–2.10 (3H, m), 1.95–1.75 (3H, m), 1.76 (3H, s, olefinic-CH_3), 1.45–1.35 (1H, m), 1.03 (3H, s, *tert*-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.4 (C, C=O), 144.4 (C, *C*=CH_2), 134.9 (CH), 134.0 (CH), 133.7 (CH), 118.4 (CH_2), 118.2 (CH_2), 118.1 (CH_2), 114.7 (CH_2), 54.8 (C), 49.0 (CH), 46.9 (C), 42.8 (CH_2), 39.2 (CH_2), 37.6 (CH_2), 33.3 (CH_2), 24.8 (CH_3), 24.2 (CH_3), 21.8 (CH_2); HRMS: *m*/*z* calcd for $C_{19}H_{28}ONa$ (M+Na): 295.2038; found: 295.2038.

4.17. (1*R*,6*R*,7*S*)-6-Allyl-7-isopropenyl-1-methylbicyclo[4.3.1]dec-3-en-10-one 31

RCM reaction of the ketone **24** (50 mg, 0.22 mmol) in anhydrous CH_2Cl_2 (22 mL, 0.01 M) using Grubbs' first generation catalyst (8 mg, 5 mol %) for 8 h at rt, followed by purification over a $AgNO_3$ impregnated silica gel column using ethyl acetate–hexane (1:49) as eluent first furnished bicyclic ketone **31** (16 mg, 36%) as an oil. $[\alpha]_D^{24} = -11.3$ (*c* 1.0, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3074, 3039, 2961, 2928, 2871, 1707 (C=O), 1637, 1472, 1449, 1377, 1191, 1179, 1005, 908, 749, 700; ^1H NMR (400 MHz, $CDCl_3$): δ 5.90–5.60 (3H, m), 4.98 (1H, d, *J* 16.7 Hz), 4.97 (1H, d, *J* 10.6 Hz), 4.87 (1H, s), 4.77 (1H, s), 2.75 (1H, dd, *J* 14.9 and 6.4 Hz), 2.70–2.55 (2H, m), 2.37 (1H, dd, *J* 13.3 and 3.9 Hz), 2.30 (1H, dd, *J* 13.7 and 6.3 Hz), 2.15 (1H, dd, *J* 13.7 and 7.9 Hz), 1.98–1.75 (3H, m), 1.78 (3H, s, olefinic-CH_3), 1.60 (1H, td, *J* 13.6 and 4.8 Hz), 1.50–1.40 (1H, m), 1.07 (3H, s, *tert*-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 214.2 (C, C=O), 145.2 (C, *C*=CH_2), 136.8 (CH), 131.0 (CH), 129.2 (CH), 116.9 (CH_2), 114.5 (CH_2), 56.4 (C), 54.3 (CH), 48.4 (C), 42.3 (CH_2), 40.8 (CH_2), 36.7 (CH_2), 31.9 (CH_2), 27.1 (CH_3), 25.2 (CH_2), 23.1 (CH_3); HRMS: *m*/*z* calcd for $C_{17}H_{24}ONa$ (M+Na): 267.1725; found: 267.1720.

Further elution of the column with ethyl acetate–hexane (3:97) gave (7*R*,10*S*)-7-allyl-10-isopropenyl-7-methylspiro[4.5]dec-2-en-6-one **30** (18 mg, 41%) as an oil. $[\alpha]_D^{24} = -52.5$ (*c* 1.0, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3076, 3058, 2931, 2870, 1694 (C=O), 1639, 1458, 1375, 1120, 1004, 913, 894; ^1H NMR (400 MHz, $CDCl_3$): δ 5.66 (1H, ddt, *J* 17.6, 10.5 and 7.4 Hz), 5.53–5.50 (1H, m), 5.45–5.40 (1H, m), 5.10–4.95 (2H, m), 4.85 (1H, br s), 4.36 (1H, br s), 3.00–2.80 (2H, m), 2.50–2.15 (5H, m), 2.05–1.90 (2H, m), 1.85–1.70 (1H, m), 1.70 (3H, s, olefinic-CH_3), 1.45–1.30 (1H, m), 1.14 (3H, s, *tert*-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.9 (C, C=O), 145.3 (C, *C*=CH_2), 134.3 (CH), 128.9 (CH), 126.7 (CH), 118.1 (CH_2), 113.6 (CH_2), 57.9 (C), 53.1 (CH), 46.9 (C), 44.7 (CH_2), 43.9 (CH_2), 39.9 (CH_2), 32.6 (CH_2), 26.2 (CH_3), 23.3 (CH_3), 21.9 (CH_2); HRMS: *m*/*z* calcd for $C_{17}H_{24}ONa$ (M+Na): 267.1725; found: 267.1713.

4.18. (1*S*,5*S*,8*R*)-4,8-Dimethyltricyclo[6.4.1.0^{1,5}]trideca-3,10-dien-13-one 32

RCM reaction of the bicyclic ketone **31** (10 mg, 0.04 mmol) in anhydrous CH_2Cl_2(4 mL, 0.01 M) using Grubbs' second generation catalyst (1 mg, 5 mol %) for 5 h at rt, followed by purification on a silica gel column using CH_2Cl_2–hexane (1:9) as eluent furnished the tricyclic ketone **32** (8 mg, 90%) as an oil. $[\alpha]_D^{24} = +82.6$ (*c* 1.0, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3040, 3016, 2962, 2928, 2873, 2850, 1705 (C=O), 1666, 1446, 1378, 1220, 1005, 910, 817, 794, 665, 645; ^1H NMR (400 MHz, $CDCl_3$): δ 5.80–5.60 (2H, m), 5.34 (1H, br s), 2.76 (1H, dd, *J* 17.0 and 7.1 Hz), 2.65–2.50 (2H, m), 2.20–1.70 (8H, m), 1.66 (3H, s, olefinic-CH_3), 1.13 (3H, s, *tert*-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.8 (C, C=O), 138.8 (C, C-4), 130.3 (CH), 127.4 (CH), 123.4 (CH), 61.3 (C), 56.4 (CH, C-5), 47.8 (C), 42.6 (CH_2), 41.8 (CH_2), 40.1 (CH_2), 32.3 (CH_2), 28.1 (CH_3), 22.3 (CH_2), 14.9 (CH_3); HRMS: *m*/*z* calcd for $C_{15}H_{20}ONa$ (M+Na): 239.1412; found: 239.1407.

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