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A rapid and efficient enantiospecific synthesis of the functionalized ABC-ring system of tetranortriterpene dumsins and their analogues

Adusumilli Srikrishna *, Vijendra H. Pardeshi, Pinnu Thriveni

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India

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ABSTRACT

A rapid and enantiospecific synthesis of the ABC ring system of tetranortriterpene dumsin and its analogues, starting from the readily available monoterpene (*R*)-carvone employing two RCM reactions as key steps, is described.

1. Introduction

Phytochemicals acting as deterrents to insect feeding are frequently found in pest-resistant plants, which can provide lead compounds to develop environmentally friendly pest control agents. The roots of the widely distributed East African plant Msinduzi, *Croton jatrophoides* Pax. (Euphorbiaceae), has long been used by the native population to alleviate stomachaches and to offset the symptoms of the common cold. In the search for environmentally friendly pest control agents, Kubo et al. have screened extracts of the bitter root bark of *C. jatrophoides*, which led to the identification of a tetranortriterpene limonoid dumsin **1** possessing remarkably potent insect antifeedant activity.[1a] The structure was secured on the basis of detailed spectroscopic analysis and ultimately by single crystal X-ray diffraction analysis. Subsequently, a number of dumsin analogues (Fig. 1) were isolated from various extracts of *C. jatrophoides*[1] and also from the root bark of *Turraea wakefieldii*,[2a] and *Walsura robusta*,[2b] all possessing excellent antifeedant activity. Structurally, dumsin and its analogues possess an interesting tetranortriterpene framework with an A-ring rearranged to a spiro system. In many of them, a new A′ heterocyclic ring formed through either hemiacetal or ether or peroxy acetal linkage. Limonoids are attractive biologically active substances because they possess anti-HIV activity, antimalarial activity, and cytotoxicity against cancer cell lines in addition to insect antifeedant activity.[1e] However, not much synthetic efforts have been reported in the literature on the synthesis of dumsin and its analogues. So far there is no report in the literature on either the total synthesis or the construction of the complete ring system of any of the dumsins. In 1994, Paquette had reported the first synthetic efforts to dumsin by constructing the AB ring system of dumsin.[3a] Subsequently (in 2003 and 2007), enantioselective synthesis of the functionalised AA′B ring system (mentioned as the ABC ring system) of dumsin is reported by employing a very long sequence.[3b,c] Herein, we report a very rapid, short and efficient enantiospecific approach to the functionalized ABC ring system of dumsin and its analogues.

2. Results and discussion

We have envisioned the synthesis of the ABC-ring system **2** by employing (*R*)-carvone **3** as the chiral starting material, Scheme 1. It was readily visualized that carvone **3** can serve as the B-ring of dumsins, and spirocyclopentannulation at the C-6 carbon and cyclohexannulation at the C-1, C-2 bond of carvone would lead to an ABC ring system **2** of dumsins.

The synthetic sequence is depicted in Scheme 2. First, the construction of the AB-ring system of dumsins was addressed *via* a spirocyclopentannulation at the C-6 carbon of carvone, employing RCM reaction of 6,6-bis-allyl carvone **4** as the key step. Thus, kinetic allylation of carvone **3** with lithium diisopropylamide and allyl bromide[4] generated a 1:5 *cis-trans* mixture of 6-allylcarvone **5** in 95% yield, which on second allylation using the same conditions furnished 6,6-bis-allylcarvone **4** in 87% yield. The RCM reaction[5] of bis-allylcarvone **4** with Grubbs' first generation catalyst $Cl_2(PCy_3)_2Ru{=}CHPh$ in refluxing methylene chloride furnished the spiroenone **6** in 99% yield, containing the AB ring system of dumsins, whose structure was deduced from its spectral data.

For the annulation of the C-ring to the AB ring system, the introduction of two allyl groups at the C-6 C-7 carbons of the spiroenone **6** was conceived. An allyl group was introduced at the C-6 carbon atom by employing a 1,3-enone transposition methodology.[6] Sonochemically accelerated Barbier reaction of the spiroenone **6** with zinc and allyl bromide generated the *tert*-alcohol **7**, in quantitative yield, which on oxidation with PCC and silica gel furnished the enone **8**. A reductive allylation was explored for the stereoselective introduction of the second allyl group at the

* Corresponding author. Tel.: +91 80 22 932 215; fax: +91 80 23 600 529.
E-mail address: ask@orgchem.iisc.ernet.in (A. Srikrishna).

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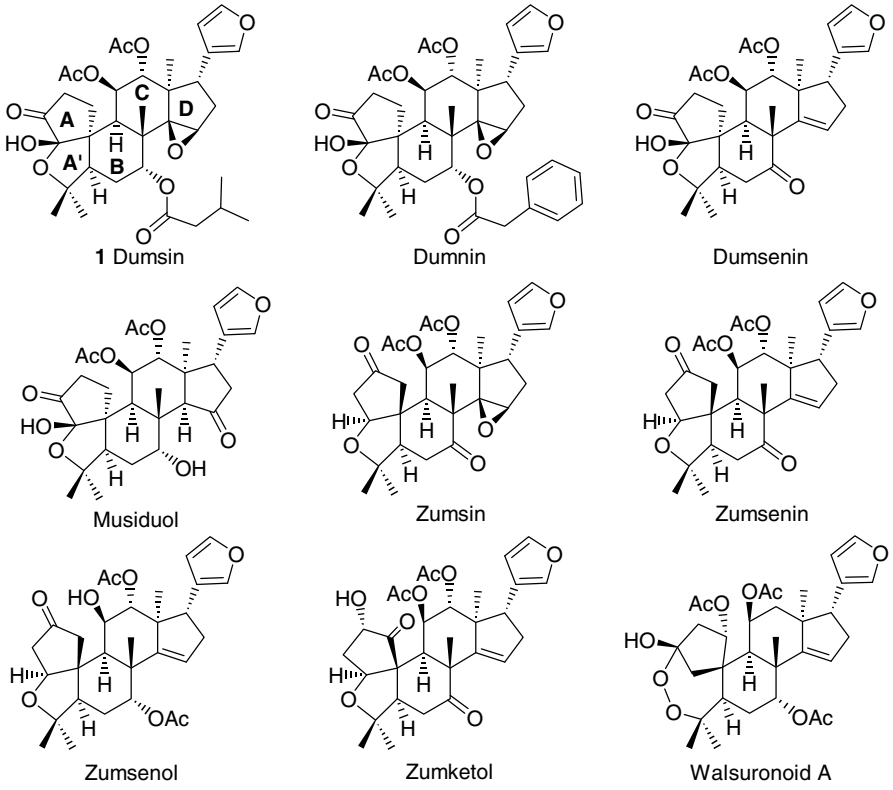
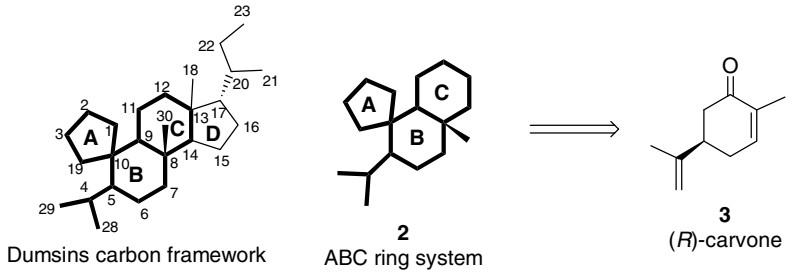


Figure 1.



Scheme 1.

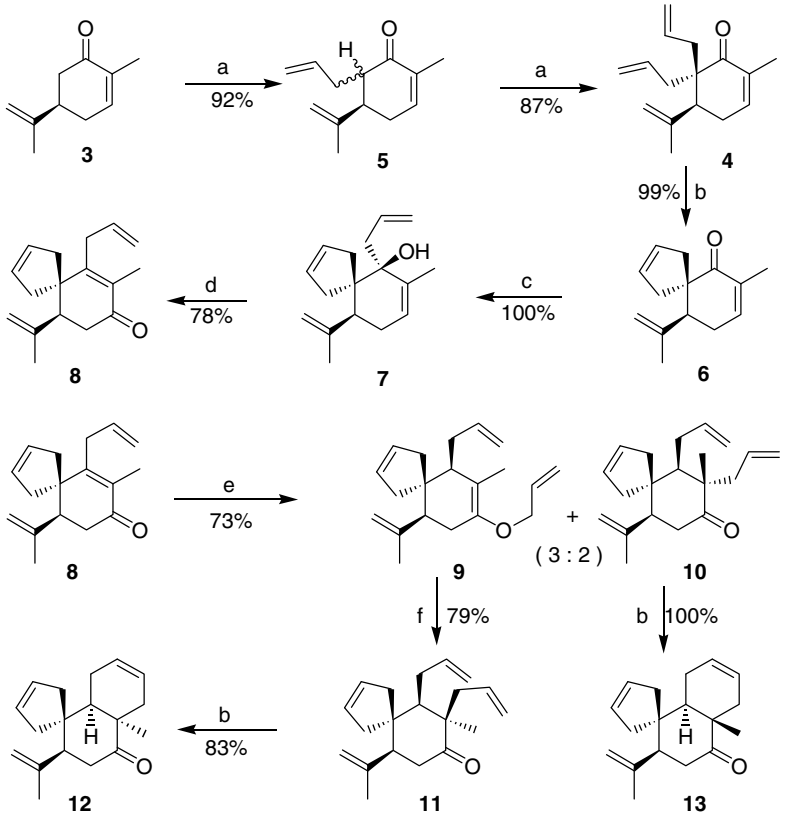
C-7 position. Treatment of the spiroenone **8** with lithium in liquid ammonia followed by alkylation with allyl bromide furnished a 3:2 mixture of O- and C-allylated products **9** and **10** in 73% yield, which were separated by column chromatography on silica gel. The stereochemistry at the C-6 centre was assigned on the basis of thermodynamic considerations in analogy to the reduction of carvone derivatives.[7] It was further supported by the single crystal X-ray diffraction analysis of the ketone **10** (an ORTEP is depicted in Fig. 2). The *O*-allyl compound **9** on thermal Claisen rearrangement at 180 °C in a sealed tube, contrary to the expectation, furnished the stereoisomer **11** in 79% yield.[8] RCM reaction of the bisallyl compound **11** with Grubbs' catalyst $Cl_2(PCy_3)_2Ru{=}CHPh$ in methylene chloride at room temperature, followed by purification on a silver nitrate impregnated silica gel column furnished the spiroenone **12** in 83% yield, containing the ABC ring system of dumsins (containing a BC-*cis* ring fusion). On the other hand, the RCM reaction of the bisallyl compound **10** with Grubbs' catalyst $Cl_2(PCy_3)_2Ru{=}CHPh$ in methylene chloride at room temperature furnished the spiroenone **13** in quantitative yield, containing the ABC ring system of dumsins (containing also a BC-*trans* ring fusion as in dumsins), whose structure was deduced from its spectral data.

3. Conclusion

In conclusion, we have developed a rapid and efficient enantiospecific synthesis of the ABC ring system of dumsin and its analogues, containing functionality in all the three rings. The isopropenyl group in **12** and **13** serves as a latent A′ ring of the dumsins. A spirocyclopentannulation at the C-6 carbon and a cyclohexannulation at the C-1 to C-2 carbons of carvone employing two efficient RCM reactions have been employed as the key steps. Extension of the methodology for further elaboration to dumsins is currently under investigation.

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



Scheme 2. Reagents and conditions: (a) LDA, THF, $BrCH_2CH{=}CH_2$; (b) $Cl_2(PCy_3)_2Ru{=}CHPh$ (5 mol %), CH_2Cl_2; (c) Zn, $BrCH_2CH{=}CH_2$, THF,))); (d) PCC, silica gel, CH_2Cl_2; (e) Li, liq. NH_3, THF, ^{t}BuOH, $BrCH_2CH{=}CH_2$; (f) sealed tube, 180 °C.

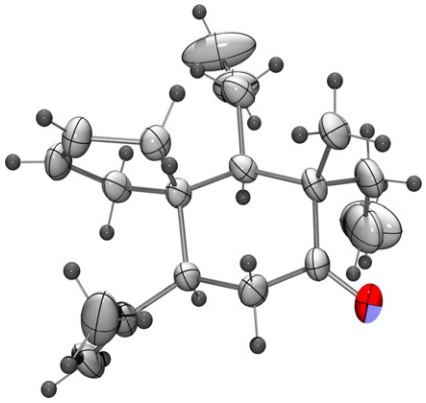


Figure 2. ORTEP diagram of **10**.

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 ^{1}H) or the central line (77.0 ppm) of $CDCl_3$ (for ^{13}C). In the ^{13}C NMR, the nature of the 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 a Micromass Q-TOF micro mass spectrometer using electron spray 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 a 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 gram of crude material).

4.1. (5*S*)-6,6-Bis-allyl-5-isopropenyl-2-methylcyclohex-2-enone 4

To a cold (0 °C), magnetically stirred solution of diisopropylamine (0.52 ml, 3.7 mmol) in anhydrous THF (3 ml) was slowly added a solution of *n*-BuLi (2.5 M in hexane, 1.4 ml, 3.5 mmol) over a period of 5 min and stirred for 10 min. To the LDA thus formed was added dropwise a solution of 6-allylcarvone[4] **5** (500 mg, 2.63 mmol) in anhydrous THF (2 ml) over a period of 10 min and stirred for 45 min at the same temperature. The enolate was then treated with allyl bromide (0.32 ml, 3.7 mmol) and stirred for 10 h at rt. The reaction mixture was then diluted with water and extracted with ether (3 × 5 ml). The combined organic 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 (1:10) as eluent furnished bis-allylcarvone **4** (526 mg, 87%) as an oil. $[\alpha]_D^{23} = -47.5$ (*c* 10, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3076, 2978, 2949, 2920, 1668, 1639, 1439, 1376, 1189, 1074, 997, 912; ^{1}H 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: Calcd for $C_{16}H_{23}O$ (M+H): 231.1749. Found: 231.1749.

4.2. (10*S*)-10-Isopropenyl-7-methylspiro[4.5]deca-2,7-dien-6-one 6

To a magnetically stirred solution of enone **4** (50 mg, 0.22 mmol) in anhydrous CH_2Cl_2 (11 ml, 0.02 M) was added Grubbs' first generation catalyst (13 mg, 7 mol %). The reaction mixture was refluxed for 4 h and the catalyst was filtered off through a short silica gel column. Evaporation of the solvent and purification of the residue on a silica gel column using CH_2Cl_2–hexane (1:4) as eluent furnished the spiro enone **6** (43 mg, 99%) as an oil. $[\alpha]_D^{25} = -179.2$ (*c* 1.3, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3055, 2920, 2846, 1670, 1434, 1377, 1361, 1188, 1072, 1058, 895; ^1H NMR (300 MHz, $CDCl_3$): δ 6.52 (1H, s, H-8), 5.60 and 5.49 (2H, 2 × dt, *J* 6.0 and 2.1 Hz, H-2 and H-3), 4.76 (1H, s) and 4.62 (1H, s) [C=C*H*$_2$], 2.90–2.50 (5H, m), 2.45–2.25 (2H, m), 1.79 (3H, s) and 1.64 (3H, s) [2 × olefinic–CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$): δ 200.9 (C, C=O), 146.4 (C, *C*=CH_2), 140.8 (CH, C-8), 134.0 (C, C-7), 129.4 (CH), 127.0 (CH), 114.0 (CH_2, *C*H_2=C), 54.5 (C, C-5), 51.8 (CH, C-10), 41.8 (CH_2), 37.8 (CH_2), 29.0 (CH_2), 22.0 (CH_3), 16.9 (CH_3); HRMS: Calcd for $C_{14}H_{18}ONa$ (M+Na): 225.1255. Found: 225.1257.

4.3. (6*S*,10*S*)-6-Allyl-10-isopropenyl-7-methylspiro[4.5]deca-2,7-dien-6-ol 7

To a sonochemically activated suspension of Zn (196 mg, 3 mmol) in dry THF (2 ml) in a round-bottom flask was slowly added a solution of spiroenone **6** (60 mg, 0.3 mmol) and allyl bromide (363 mg, 3 mmol) in THF (1 ml) over a period of 5 min and irradiated sonochemically for 45 min. The reaction mixture was then quenched with aq NH_4Cl and extracted with 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 on a silica gel column using CH_2Cl_2–hexane (1:4) as eluent furnished the tertiary alcohol **7** (72 mg, 100%). $[\alpha]_D^{24} = +3.0$ (*c* 2.7, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3573, 3070, 2920, 2845, 1633, 1436, 1375, 1060, 1003, 893, 814, 768, 662; ^1H NMR (300 MHz, $CDCl_3$): δ 5.93 (1H, ddt, *J* 16.8, 9.0 and 7.2 Hz), 5.68–5.60 (1H, m), 5.60–5.50 (1H, m), 5.34 (1H, br s), 5.17–5.10 (2H, m), 4.72 (1H, s), 4.70 (1H, s), 2.77 (1H, dd, *J* 11.1 and 6.6 Hz), 2.60–2.20 (8H, m), 2.05–1.94 (1H, m), 1.71 (3H, s) and 1.69 (3H, s) [2 × olefinic–CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.2 (C, *C*=CH_2), 139.8 (C, C-7), 135.7 (CH), 130.9 (CH), 129.9 (CH), 121.9 (CH), 117.9 (CH_2), 114.3 (CH_2), 78.0 (C, C-6), 52.6 (C, C-5), 47.3 (CH, C-10), 44.6 (CH_2), 37.9 (CH_2), 36.5 (CH_2), 28.6 (CH_2), 20.6 (CH_3), 20.0 (CH_3); HRMS: Calcd for $C_{17}H_{24}ONa$ (M+Na): 267.1725. Found: 267.1721.

4.4. (10*S*)-6-Allyl-10-isopropenyl-7-methylspiro[4.5]deca-2,6-dien-8-one 8

To a magnetically stirred solution of the tertiary alcohol **7** (100 mg, 0.41 mmol) in anhydrous CH_2Cl_2 (2 ml) was added a homogeneous mixture of PCC (440 mg, 2.1 mmol) and silica gel (440 mg) and stirred vigorously for 1 day at rt. The reaction mixture was then filtered through a small silica gel column and the column eluted with excess CH_2Cl_2. Evaporation of the solvent and purification of the residue on a silica gel column using CH_2Cl_2–hexane (1:4) as eluent furnished the enone **8** (79 mg, 78%) as an oil. $[\alpha]_D^{25} = +7.8$ (*c* 1.8, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3055, 2926, 2856, 1670, 1637, 1612, 1438, 1377, 1344, 910; ^1H NMR (300 MHz, $CDCl_3$): δ 5.80 (1H, ddt, *J* 16.8, 10.5 and 5.7 Hz), 5.66 (2H, s, H-2 and H-3), 5.13–4.98 (2H, m), 4.80 (1H, s) and 4.72 (1H, s) [C=CH_2], 2.97 (2H, d, *J* 5.7 Hz), 2.80–2.40 (7H, m), 1.75 (3H, s) and 1.67 (3H, s) [2 × olefinic–CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.6 (C, C=O), 159.4 (C, C-6), 146.0 (C, *C*=CH_2), 134.3 (CH), 131.6 (C, C-7), 129.9 (CH), 129.7 (CH), 116.8 (CH_2), 114.9 (CH_2), 52.3 (CH, C-10), 49.7 (C, C-5), 45.0 (CH_2), 40.0 (2C, CH_2), 35.2 (CH_2), 22.4 (CH_3), 11.7 (CH_3); HRMS: Calcd for $C_{17}H_{22}ONa$ (M+Na): 265.1568. Found: 265.1566.

4.5. (6*R*,10*S*)-6-Allyl-10-isopropenyl-7-methyl-8-(prop-2-enyloxy)spiro[4.5]deca-2,7-diene 9 and (6*R*,7*S*,10*S*)-6,7-bis-allyl-10-isopropenyl-7-methylspiro[4.5]dec-2-en-8-one 10

To freshly distilled liquid ammonia (50 ml) was added Li metal (17.2 mg, 2.46 mmol). To the resulting blue-coloured solution was added a solution of the enone **8** (50 mg, 0.246 mmol) and *tert*-butyl alcohol (0.23 ml, 2.46 mmol) in dry THF (4 ml) over a period of 10 min. The reaction mixture was stirred for 15 min and quenched with a solution of allyl bromide (0.22 ml, 2.46 mmol) in dry THF (1 ml). It was then slowly warmed up to rt and stirred for 3 h. Water (5 ml) was added to the reaction mixture and extracted with ether (3 ml × 3). The ether extract was washed with brine (5 ml) and dried over Na_2SO_4. Evaporation of the solvent followed by purification on a silica gel column using CH_2Cl_2–hexane (1:9) first furnished O-allylated product **9** (26 mg, 44%). $[\alpha]_D^{20} = -38.6$ (*c* 5.4, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3072, 3052, 2977, 2914, 2855, 1688, 1637, 1439, 1376, 1349, 1164, 994, 908, 894; ^1H NMR (300 MHz, $CDCl_3$): δ 6.05–5.80 (2H, m), 5.65–5.45 (2H, m), 5.30 (1H, dd, *J* 17.1 and 1.5 Hz), 5.17 (1H, dd, *J* 10.8 and 1.5 Hz), 5.00 (1H, d, *J* 17.7 Hz), 4.92 (1H, d, *J* 9.6 Hz), 4.75 (1H, s) and 4.69 (1H, s) [C=C*H*$_2$], 4.20 (2H, d, *J* 5.7 Hz, O–C*H*$_2$), 2.65–2.55 (2H, m), 2.40–2.30 (4H, m), 2.20–1.80 (4H, m), 1.69 (3H, s) and 1.65 (3H, s) [2 × olefinic–CH_3]; ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.0 (C), 146.1 (C), 139.7 (CH), 135.0 (CH), 129.9 (CH), 129.2 (CH), 119.0 (C, C-7), 116.5 (CH_2), 114.7 (CH_2), 113.9 (CH_2), 69.3 (CH_2, O*C*H_2), 52.3 (CH), 48.2 (C, C-5), 45.6 (CH), 41.5 (CH_2), 40.0 (CH_2), 37.8 (CH_2), 28.9 (CH_2), 21.2 (CH_3), 16.4 (CH_3); HRMS: Calcd for $C_{20}H_{28}ONa$ (M+Na): 307.2038. Found: 307.2043.

Further elution of the column with CH_2Cl_2-hexane (1:4) furnished *C*-allylated product **10** (17 mg, 29%) as a gummy solid, which was recrystallised from methanol. Mp 99–101 °C; $[\alpha]_D^{20} = +13.2$ (*c* 4.8, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3074, 3054, 2972, 2868, 1707, 1637, 1458, 1431, 1376, 1275, 1240, 998, 910, 715, 667; ^1H NMR (300 MHz, $CDCl_3$): δ 5.92–5.60 (2H, m), 5.57 (2H, s), 5.15–4.85 (4H, m), 4.75 (1H, s), 4.73 (1H, s), 2.91 (1H, t, *J* 14.4 Hz), 2.80–2.00 (10H, m), 1.92 (1H, t, *J* 4.2 Hz), 1.69 (3H, s, olefinic–CH_3), 1.09 (3H, s, *tert*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 213.2 (C, C=O), 145.3 (C, *C*=CH_2), 140.2 (CH), 135.6 (CH), 130.5 (CH), 130.2 (CH), 118.1 (CH_2), 115.0 (CH_2), 114.7 (CH_2), 54.6 (CH), 53.3 (C), 50.7 (CH), 49.2 (C), 44.6 (CH_2), 40.8 (CH_2), 40.3 (CH_2), 35.8 (CH_2), 31.2 (CH_2), 21.9 (CH_3), 20.8 (CH_3); HRMS: Calcd for $C_{20}H_{28}ONa$ (M+Na): 307.2038. Found: 307.2032. Anal. Calcd for $C_{20}H_{28}O$, C, 84.45; H, 9.92. Found: C, 84.42; H, 9.72.

4.6. X-ray analysis data of 10

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 F^2 using SHELXL-97. The non-hydrogen atoms were refined anisotropically whereas hydrogen atoms were refined isotropically. Mol. for $C_{20}H_{28}O$; M_W = 284.42; colourless; crystal system: trigonal; space group R3; cell parameters, a = 25.309(5) Å, b = 25.309(5) Å, c = 7.2440(15) Å; α 90.00, β 90.00, γ 120.00, V = 4018.6(14) Å^3, Z = 9, D_c = 1.058 g cm^{-3}, F(000) = 1404, μ = 0.063 mm^{-1}. Total

number of l.s. parameters = 192, R_1 = 0.0644 for 2015 $F_0 > 2\sigma(F_0)$ and 0.1146 for all 3500 data. wR_2 = 0.1673, GOF = 1.022, restrained GOF = 1.022 for all data. An ORTEP diagram is depicted in Figure 2. Crystallographic data have been deposited with Cambridge Crystallographic Data Centre (CCDC 681247).

4.7. (6*R*,7*R*,10*S*)-6,7-Bis-allyl-10-isopropenyl-7-methylspiro-[4.5]dec-2-en-8-one 11

Allyl enol ether **9** (42 mg, 0.15 mmol) was taken in a sealed tube and heated to 180 °C for 6 h. It was cooled and purified on a silica gel column using CH_2Cl_2–hexane (1:4) to give enone **11** (32 mg, 79%) as an oil. $[\alpha]_D^{24} = +3.7$ (*c* 1.9, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3076, 2974, 2929, 2860, 1707, 1639, 1446, 1378, 1124, 994, 912, 676; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.85–5.75 (2H, m), 5.65–5.55 (2H, m), 5.10–4.90 (4H, m), 4.81 (1H, s), 4.61 (1H, s), 2.80–2.55 (3H, m), 2.54–2.42 (3H, m), 2.40–2.20 (4H, m), 2.18–2.10 (2H, m), 1.68 (3H, s, olefinic–CH_3), 1.11 (3H, s, *tert*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 214.4 (C, C=O), 147.0 (C, *C*=CH_2), 140.3 (CH), 133.8 (CH), 129.7 (CH), 129.0 (CH), 117.6 (CH_2), 114.7 (CH_2), 114.4 (CH_2), 53.2 (CH), 52.5 (CH), 48.9 (2C, C), 44.4 (CH_2), 43.0 (CH_2), 40.4 (CH_2), 39.1 (CH_2), 32.4 (CH_2), 23.6 (CH_3), 21.9 (CH_3); HRMS: Calcd for $C_{20}H_{28}ONa$ (M+Na): 307.2038. Found: 307.2035.

4.8. (1*R*,4*S*,6*R*)-4-Isopropenyl-1-methylbicyclo[4.4.0]decane-spiro[5.1′]cyclopenta-8,3′-dien-2-one 12

The RCM reaction of enone **11** (20 mg, 0.07 mmol) in anhydrous CH_2Cl_2 (7 ml, 0.01 *M*) using Grubbs' first generation catalyst (6 mg, 10 mol %) for 6 h at room temperature and work up as described for the enone **6**, followed by purification on a silica gel column impregnated with silver nitrate using ethyl acetate–hexane (1:30) as eluent furnished the tricyclic enone **12** (15 mg, 83%) as an oil. $[\alpha]_D^{27} = -3.3$ (*c* 0.6, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3052, 3026, 2968, 2912, 1705, 1455, 1433, 1375, 1272, 1231, 953, 894, 666; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.68 (2H, s), 5.59 (2H, s), 4.82 (1H, s), 4.59 (1H, s), 2.88–2.75 (2H, m), 2.70–2.60 (2H, m), 2.50–2.00 (8H, m), 1.68 (3H, s, olefinic–CH_3), 1.21 (3H, s, *tert*-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 215.3 (C, C=O), 147.1 (C, *C*=CH_2), 129.6 (CH), 128.9 (CH), 125.9 (CH), 123.9 (CH), 114.4 (CH_2, C=*C*H_2), 53.1 (CH), 48.2 (C), 47.6 (C), 45.0 (CH), 43.7 (CH_2), 42.1 (CH_2), 39.6 (CH_2), 33.4 (CH_2), 24.3 (CH_2), 23.82 (CH_3), 23.79 (CH_3); HRMS: Calcd for $C_{18}H_{24}ONa$ (M+Na): 279.1725. Found: 279.1725.

4.9. (1*S*,4*S*,6*R*)-4-Isopropenyl-1-methylbicyclo[4.4.0]-decanespiro[5.1′]cyclopenta-8,3′-dien-2-one 13

The RCM reaction of enone **10** (20 mg, 0.07 mmol) in anhydrous CH_2Cl_2 (7 ml, 0.01 M) using Grubbs' first generation catalyst (6 mg, 10 mol %) for 4 h at room temperature followed by purification on a silica gel column using CH_2Cl_2–hexane (1:4) as eluent furnished the RCM product **13** (18 mg, 100%) as an oil. $[\alpha]_D^{21} = +25.7$ (*c* 2.5, $CHCl_3$); IR (neat): ν_{max}/cm^{-1} 3051, 3024, 2924, 2856, 1709, 1656, 1635, 1460, 1433, 1373, 1346, 1270, 1230, 1080, 895, 676, 662; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.61 (2H, br s), 5.60–5.50 (2H, m), 4.76 (1H, s), 4.72 (1H, s), 3.00 (1H, t, *J* 14.1 Hz), 2.70–2.45 (3H, m), 2.40–2.20 (3H, m), 2.20–1.90 (4H, m), 1.80 (1H, dd, *J* 10.5 and 5.7 Hz), 1.72 (3H, s, olefinic–CH_3), 1.12 (3H, s, *tert*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 214.4 (C, C=O), 145.2 (C, *C*=CH_2), 129.6 (2C, CH), 125.2 (CH), 124.8 (CH), 114.9 (CH_2, C=*C*H_2), 56.2 (CH), 49.9 (CH), 47.4 (2C, C), 44.1 (CH_2), 40.2 (CH_2), 36.2 (CH_2), 34.1 (CH_2), 24.3 (CH_2), 21.2 (CH_3), 19.0 (CH_3); HRMS: Calcd for $C_{18}H_{24}ONa$ (M+Na): 279.1725. Found: 279.1725.

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