Rearrangement approaches to sesquiterpenes containing multiple contiguous quaternary carbon atoms. Total synthesis of (±)-myltayl-8(12)-ene and (±)-6-epijunicedranol

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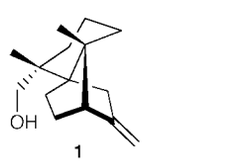
Details of the first total syntheses of the sesquiterpenes myltayl-8(12)-ene and 6-epijunicedran-8-ol are described. The aldehyde **13**, obtained by Claisen rearrangement of cyclogeraniol, was transformed into the dienones **12** and **18**. Boron trifluoride–diethyl ether mediated cyclization and rearrangement transformed the dienones **12** and **18** into the tricyclic ketones **16** and **17**, efficiently creating three and four contiguous quaternary carbon atoms, respectively. Wittig methylenation of **16** furnished (±)-myltayl-8(12)-ene (**11**), whereas reduction of the ketone **17** furnished (±)-6-epijunicedranol (**23**).

The creativity of Nature in devising varied molecular architecture is revealed through the isolation of a wide range of natural products with remarkable skeletal build-up and multifarious functionalities. Among the natural products, terpenoids occupy a special position on account of their widespread occurrence and the bewildering array of carbocyclic skeleta that they embody. Sesquiterpenes, biogenetically derived from farnesyl pyrophosphate, are assembled in acyclic, monocyclic, bicyclic, tricyclic and even tetracyclic structures containing small, medium and large rings and a wide range of functionalities.[1] Because of this phenomenal structural diversity, this class of natural products holds special appeal to synthetic chemists and provides a fertile ground for developing and testing new synthetic strategies, particularly those directed towards the carbocyclic ring construction. As a result, synthetic activity in this area continues to flourish.[2] Even though there are several methods developed for the creation of a quaternary carbon atom, the presence of two or more quaternary carbon atoms in contiguous manner in sesquiterpenes makes them challenging synthetic targets.



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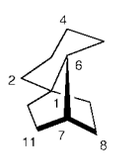
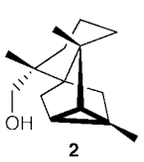


Tricyclo[5.2.2.0^{1,6}]-undecane



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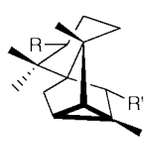
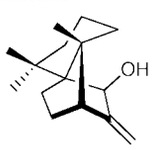


3a. R = OH; R = H
3b. R = O-caffeate; R' = H
4a. R = R' = H
4b. R = H; R' = OH



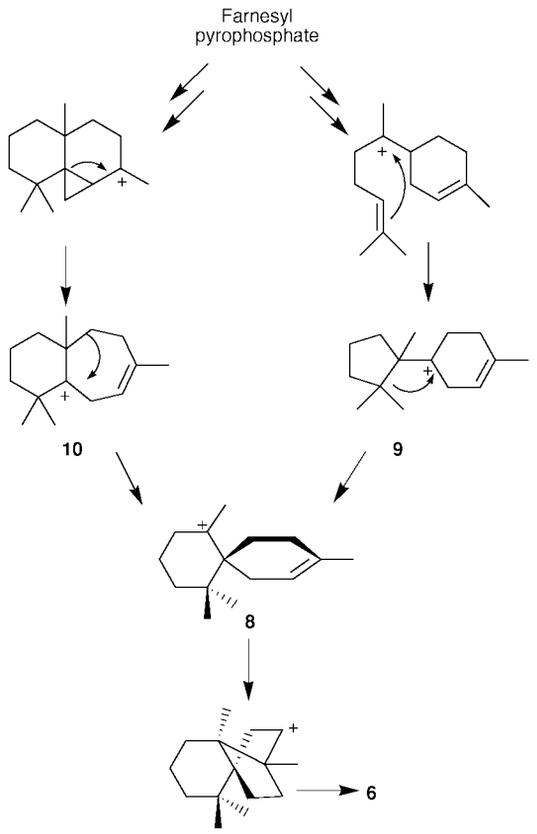
5

6. R = H
7. R = Ac

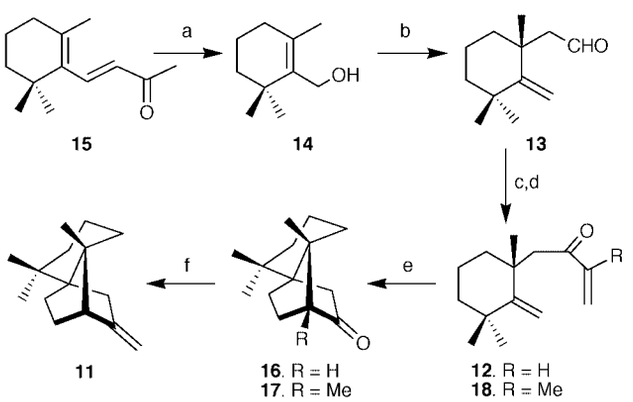
Matsuo and co-workers in 1985 and 1988 reported[3] the isolation of novel, irregular sesquiterpene alcohols, myltaylenol **1** and cyclomyltaylenol **2** from the liverwort *Mylia taylorii* (Hook, S. Gray) and identified the new carbon frameworks present in them as myltaylane and cyclomyltayalanes. In 1991, Asakawa and co-workers reported[4] the isolation of cyclomyltaylenol **3a** and its caffeate ester **3b** from the liverwort *Bazzania japonica*. Later, Wu and co-workers reported[5] the isolation of cyclomyltaylene **4a** from the Taiwanese liverwort *Bazzania tridens* and cyclomyltaylenol **4b** from *Reboulia hemisphaerica*. In 1996, Asakawa and co-workers reported[6] the isolation of myltaylenol **5** from the French liverwort *Bazzania trilobata*. A characteristic of the structure of the myltaylane and cyclomyltaylanes is the presence of a 2,2,6,8-tetramethyltricyclo[5.2.2.0^{1,6}]undecane carbon framework comprising three contiguous quaternary carbon atoms. Recently, Barrero and co-workers reported[7] the isolation of the crystalline sesquiterpene, junicedranol **6** from the essential oil of the wood of *Juniperus oxycedrus* sp. *macrocarpa*, comprising a 2,2,6,7-tetramethyltricyclo[5.2.2.0^{1,6}]undecane carbon framework incorporating four contiguous quaternary carbon atoms (C-1, 2, 6 and 7). The relative stereostructure of junicedranol (**6**) was established by using various 2D NMR correlation techniques on junicedranol (**6**) and its acetate **7**. Biosynthetically junicedranol (**6**) is very interesting. A possible biosynthetic pathway to junicedranol (**6**) was proposed[7] by Barrero and co-workers as depicted in Scheme 1. The chamigrenyl cation **8** was postulated as the precursor of the junicedrane carbon skeleton. The chamigrenyl cation **8** might be formed from either the cuparenyl cation **9**, or the widdrenyl cation **10**. Cyclization of the chamigrenyl cation **8** *via* an intramolecular anti-Markovnikov addition leads to the junicedrane framework.

Interesting structural features, particularly the presence of the tricyclo[5.2.2.0^{1,6}]undecane carbon framework comprising three and four contiguous quaternary carbon atoms in myltaylane and junicedranes, respectively, made them challenging synthetic targets. As part of our ongoing efforts on the synthesis of sesquiterpenes containing multiple contiguous carbon atoms,[8] we have developed a novel approach to myltaylane and junicedranes.[9,10] Subsequent to our report on the first total synthesis[9] of myltaylene **11**, Winterfeldt and co-workers reported[11] an enatioselective synthesis of (−)-myltaylenol **1** by employing an intramolecular Diels–Alder cycloaddition reaction based strategy. Herein we describe the details of our first total synthesis[9] of myltayl-8(12)-ene[12] **11** and its extension to the first total synthesis[10] of a junicedrane.

A biogenetically patterned cation mediated cyclization and rearrangement of the dienone **12** was explored for the synthesis of myltaylene **11**. The synthetic sequence is depicted in Scheme 2. It was conceived that the dienone **12** could be prepared from the aldehyde **13**, which in turn could be obtained from cyclogeraniol **14** *via* the Claisen rearrangement. The requisite starting material, cyclogeraniol **14** was obtained from

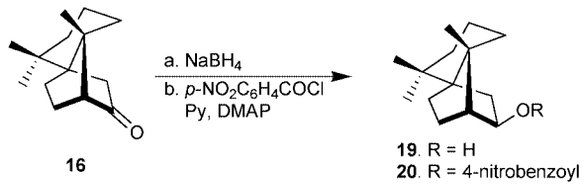


Scheme 1

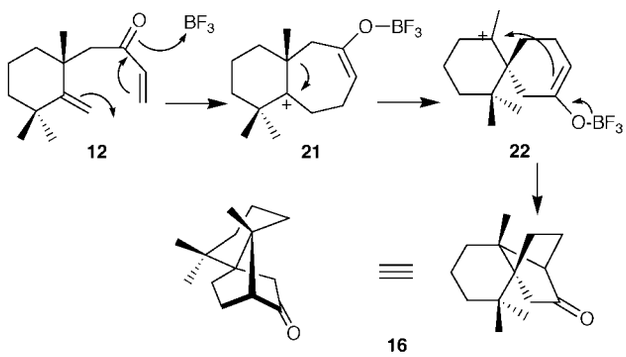


Scheme 2 *Reagents and conditions*: (a) O_3/O_2, MeOH; $NaBH_4$; (b) CH_2=CH–OEt, $Hg(OAc)_2$; Δ; (c) CH_2=C(R)–MgBr; (d) PCC, NaOAc; (e) $BF_3{\cdot}OEt_2$; (f) Ph_3P=CH_2.

the commercially available β-ionone **15**. Thus, controlled ozonation[8c,13] of β-ionone **15** followed by reduction of the ozonide with sodium borohydride furnished cyclogeraniol **14**. One-pot Claisen rearrangement of cyclogeraniol **14** using ethyl vinyl ether and mercuric acetate at 170 °C in a sealed tube furnished the aldehyde[14] **13** in 65% yield. Addition of vinylmagnesium bromide to the aldehyde **13** furnished an epimeric mixture of the corresponding allyl alcohol, which on oxidation with pyridinium chlorochromate (PCC)[15] and sodium acetate generated the key intermediate of the sequence, the dienone **12**, in 65% overall yield. Treatment of the dienone **12** with a catalytic amount of boron trifluoride–diethyl ether in methylene chloride furnished normyltaylanone **16**, in 60% yield, whose structure was established from its spectral data. To confirm the structure of normyltaylanone **16**, the ketone in **16** was reduced to the alcohol **19**, and was converted into the *p*-nitrobenzoate derivative **20**, mp 156–157 °C. The single



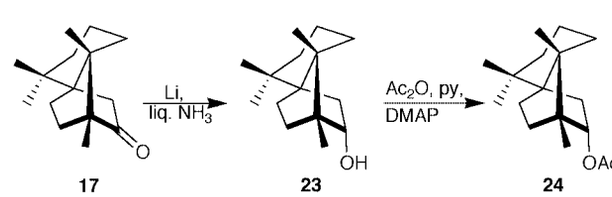
crystal X-ray analysis[9] of **20** unambiguously established the structure of normyltaylanone **16**. Finally, Wittig methylenation of normyltaylanone **16** with methylenetriphenylphosphorane furnished myltayl-8(12)-ene **11**. Formation of normyltaylanone **16** from the dienone **12** can be explained as depicted in Scheme 3. First, acid catalyzed cyclization of the dienone **12** generates



Scheme 3

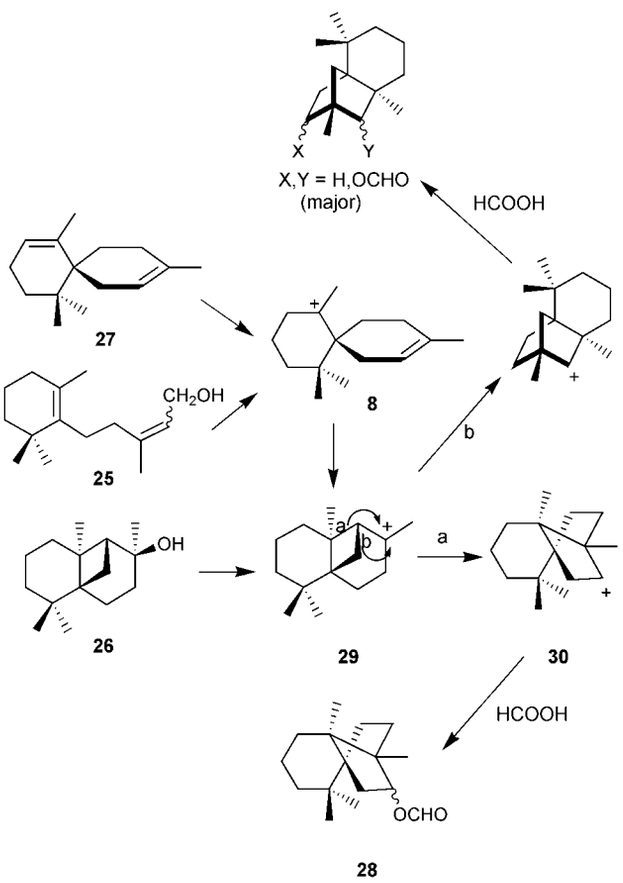
the bicyclic tertiary carbonium ion **21**, which rearranges to the spiro system **22**. Reketonization of **22** *via* cyclization from the α-face of the carbonium ion centre furnishes normyltaylanone **16** with methyl group at C-6 and the ketone *anti* to each other.

The remarkable similarity of the mechanism depicted in Scheme 3 for the formation of normyltaylanone **16** to the proposed[7] biosynthesis of junicedranol (*cf.* Scheme 1) is worth noting. A close perusal of the two schemes, particularly the last step, indicates that the cyclization of the chamigrenyl cation **8** could lead to an isomeric junicedranyl carbonium ion **30** as the cyclization places the C-6 methyl group and the cationic centre *anti* to each other, analogous to **16**. This prompted us to investigate the synthesis of junicedranol employing the same strategy as that used for myltaylene **11**, which led to the first total synthesis of 6-epijunicedranol (or 11-junicedranol) **23**. For the synthesis of epijunicedranol **23**, based on the synthesis of myltylene **11**, it was anticipated that epijunicedran-8-one **17** could be obtained *via* a Lewis acid mediated cyclization of the dienone **18**, Scheme 2. Thus, reaction of the aldehyde **13** with isopropenylmagnesium bromide in THF at room temperature generated a 3:1 epimeric mixture of the corresponding allylic alcohol. Oxidation of this secondary alcohol with pyridinium chlorochromate,[15] sodium acetate and 4 Å molecular sieves powder in methylene chloride at room temperature furnished the dienone **18** in 82% yield. Treatment of the dienone **18** in methylene chloride with a catalytic amount of boron trifluoride–diethyl ether for 30 min at 0 °C, as expected, furnished 6-epijunicedran-8-one **17** in 60% yield. The structure of **17** was established by comparison of the ^1H and ^{13}C NMR spectral data with those of normyltaylanone **16**. Finally,



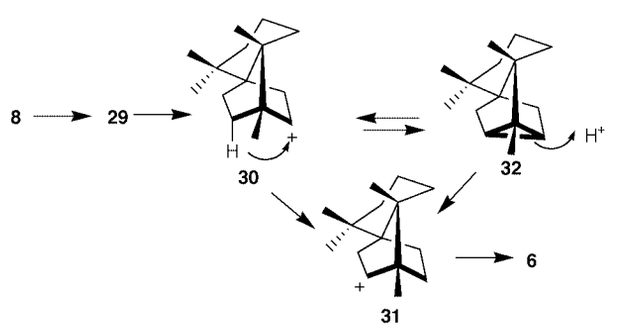
treatment of the ketone **17** with lithium in liquid ammonia and THF furnished 6-epijunicedranol (**23**), which on acetylation with acetic anhydride and pyridine in the presence of a catalytic amount of DMAP furnished the corresponding acetate **24**.

Very recently,[16] Frater and co-workers have reported the formation of the 6-epijunicedran-8-yl formate **28** as a minor product in the acid catalyzed formolysis reaction of either β-monocyclofarnesol **25** or the tertiary alcohol **26** or chamigrene **27** *via* the carbonium ion **29** and junicedranyl carbonium ion **30**, Scheme 4. The formate **28** was converted into 6-



Scheme 4

epijunicedran-8-one **17** *via* hydrolysis and oxidation. Formation of 6-epijunicedranone **17** from the dienone **18** in our synthesis, and formation[16] of the formate **28** from **26** and **27** is worth noting in comparison to the biogenetic formation of junicedranol (*cf*. Scheme 1) from the same chamigrenyl carbonium ion **8** (difference in stereochemistry at C-6). Alternatively one can consider two possibilities for the biogenetic transformation of the chamigranyl cation **8** into junicedranol (**6**) *via* the formation of the junicedranyl cation **30**, Scheme 5. First, cyclization



Scheme 5

of chamigranyl cation **8** generates tricyclic cation **29**, which rearranges to the junicedranyl cation **30** (*cf.* Scheme 4). A 1,3-hydride shift[16,17] in the cation **30** generates the isomeric cation **31** leading to junicedranol **6**. The second possibility is the formation of the cyclopropane ring from the cation **30** to form cyclojunicedrane **32**, which reopens to generate the junicedranyl cation **31** leading to junicedranol **6**. The concept of cyclojunicedrane is supported by the existense of myltaylane and cyclomyltaylenes;[5,6] seychellene and cycloseychellenes; *etc.*[1] type of sesquiterpenes in Nature.

In conclusion, we have achieved the first total synthesis of (±)-myltaylene (**11**) and (±)-6-epijunicedranol (**23**) starting from the readily available cyclogeraniol (**14**), employing biogenetically patterned acid catalyzed carbonium ion mediated cyclization and rearrangement of the dienones **12** and **18**, in which three and four contiguous quaternary carbon atoms were efficiently generated, respectively.

Experimental

2-(1,3,3-Trimethyl-2-methylenecyclohexyl)acetaldehyde (13)

A solution of cyclogeraniol (**14**, 800 mg, 5.2 mmol), ethyl vinyl ether (2.4 mL, 26.0 mmol) and a catalytic amount (40 mg) of mercuric acetate was placed in a Carius tube and heated to 170 °C for 24 h in an oil bath. The reaction mixture was cooled, diluted with ether (15 mL), washed with brine and dried (Na_2SO_4). Evaporation of the solvent and purification of the product on a silica gel (8 g) column using ethyl acetate–hexane (1:20 to 1:10) as eluent furnished the aldehyde[14] **13** (600 mg, 64%) as an oil. IR (neat): ν_{max} 2720, 1715, 1620, 900 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + CCl_4): δ 9.67 (1 H, t, J = 3.0 Hz), 5.10 (1 H, s), 4.90 (1 H, s), 2.64 (1 H, dd, J = 15 and 3 Hz), 2.30 (1 H, dd, J = 15.0 and 3.0 Hz), 1.70–1.40 (6 H, m), 1.26 (3 H, s), 1.16 (6 H, s). ^{13}C NMR (75 MHz, DEPT, $CDCl_3$ + CCl_4): δ 203.4 (CH), 159.5 (C), 109.7 (CH_2), 53.1 (CH_2), 40.9 (CH_2), 40.3 (CH_2), 38.5 (C), 36.5 (C), 32.3 (CH_3), 30.6 (CH_3), 30.3 (CH_3), 18.6 (CH_2). Mass: *m*/*z* 180 (M^+, 1%), 153 (30), 137 (25), 123 (33), 107 (25), 95 (25), 73 (100).

1-(1,3,3-Trimethyl-2-methylenecyclohexyl)but-3-en-2-one (12)

To a cold (0 °C), magnetically stirred solution of vinylmagnesium bromide [prepared from magnesium (186 mg, 7.6 mmol) and vinyl bromide (0.72 mL, 10.2 mmol) and a catalytic amount of iodine in 4 mL of dry THF] was added dropwise a solution of the aldehyde **13** (640 mg, 3.6 mmol) in 3 mL of dry THF. The reaction mixture was slowly warmed up to room temp. and stirred for 2 h. It was then poured into saturated aq. NH_4Cl solution and extracted with ether (2 × 10 mL). The ether extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent furnished an epimeric mixture of the intermediate secondary alcohol (480 mg, 65%) as an oil. IR (neat): ν_{max} 3430, 1625, 900 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, peaks due to the major isomer): δ 5.90–5.80 (1 H, m), 5.25–5.00 (2 H, m), 5.11 (1 H, s), 5.01 (1 H, s), 4.16 (1 H, t, J = 7.7 Hz), 2.30–1.25 (9 H, m), 1.23 (3 H, s), 1.14 (3 H, s), 1.09 (3 H, s). Peaks due to the minor isomer: δ 5.90–5.80 (1 H, m), 4.30 (1 H, t, J = 7.7 Hz), 1.21 (3 H, s), 1.18 (3 H, s), 1.15 (3 H, s). ^{13}C NMR (75 MHz, $CDCl_3$, peaks due to the major isomer): δ 160.5 (C), 142.7 (CH), 113.0 (CH_2), 109.7 (CH_2), 71.3 (CH), 46.6 (CH), 41.3 (CH_2), 41.2 (CH_2), 39.6 (CH_2), 36.5 (C), 32.8 (C), 30.4 (CH_3), 29.8 (CH_3), 18.6 (CH_3).

To a magnetically stirred solution of the alcohol (440 mg, 2.11 mmol) in 5 mL of dry CH_2Cl_2 was added a homogeneous mixture of PCC (910 mg, 4.2 mmol) and NaOAc (420 mg, 2.02 mmol) and the mixture was stirred vigorously for 30 min at room temp. It was then filtered through a small silica gel column and eluted with excess CH_2Cl_2. Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate–hexane (1:4) as eluent furnished the

dienone **12** (270 mg, 65%) as an oil. IR (neat): ν_{max} 1690, 1620, 900 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 6.35 (1 H, dd, J = 17.7 and 10.8 Hz), 6.14 (1 H, d, J = 17.7 Hz), 5.68 (1 H, d, J = 10.8 Hz), 5.00 (1 H, s), 4.85 (1 H, s), 2.80 and 2.72 (2 H, AB q, J = 14.7 Hz), 1.80–1.25 (6 H, m), 1.22 (3 H, s), 1.16 (3 H, s), 1.14 (3 H, s). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ 199.6 (C), 161.0 (C), 137.9 (CH), 126.9 (CH_2), 108.2 (CH_2), 50.4 (CH_2), 40.5 (C), 39.2 (CH_2), 38.4 (CH_2), 36.1 (C), 32.3 (CH_3), 31.0 (CH_3), 29.5 (CH_3), 18.3 (CH_2). Mass: *m*/*z* 206 (M^+, 8%), 191 (8), 137 (80), 121 (100), 95 (95). HRMS: Calcd. for $C_{14}H_{22}O$ *m*/*z* 206.1670. Found: 206.1640.

2,2,6-Trimethyltricyclo[5.2.2.0^{1,6}]undecan-8-one (16)

To a cold (0 °C) magnetically stirred solution of the dienone **12** (250 mg, 1.21 mmol) in dry CH_2Cl_2 (5 mL) was added $BF_3{\cdot}Et_2O$ (0.015 mL, 0.12 mmol), and the reaction mixture was stirred for 20 min at the same temperature. It was then quenched with aq. $NaHCO_3$ solution and extracted with CH_2Cl_2 (2 × 8 mL). The organic layer was washed with saturated aq. $NaHCO_3$ solution and water, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate–hexane (1 : 20) as eluent furnished normyltaylanone **16** (123 mg, 60%) as an oil. IR (neat): ν_{max} 1745 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 2.50 (1 H, dd, J = 18.6 and 3.3 Hz), 2.40–1.00 (12 H, m), 1.09 (3 H, s), 1.03 (3 H, s), 0.84 (3 H, s). ^{13}C NMR (22.5 MHz, $CDCl_3$): δ 216.3 (s), 61.8 (d), 52.6 (s), 46.1 (t), 35.8 (2 C, t and s), 33.5 (s), 30.2 (t), 28.6 (q), 26.7 (t), 23.0 (q), 22.3 (t), 18.7 (2 C, t and q). Mass: *m*/*z* 206 (M^+, 100%), 191 (20), 163 (35), 150 (45), 121 (65), 95 (70). HRMS: Calcd. for $C_{14}H_{22}O$ *m*/*z* 206.1670. Found: 206.1665. 2,4-DNP derivative: mp 161 °C. Anal. Calcd. for $C_{20}H_{26}N_4O_4$ C 62.16; H 6.78; N 14.5. Found C 61.96; H 6.72; N 14.19%.

2,2,6-Trimethyl-8-methylenetricyclo[5.2.2.0^{1,6}]undecane (myltayl-8(12)-ene 11)

To a cold (0 °C), magnetically stirred suspension of methyltriphenylphosphonium bromide (690 mg, 1.92 mmol) in benzene (5 mL) was added potassium *tert*-amyl oxide [prepared from potassium (80 mg, 2 mmol) in 2.0 mL *tert*-amyl alcohol] in benzene (1 mL) and the resultant yellow reaction mixture was stirred for 20 min at room temp. To the methylenetriphenylphosphorane thus formed, was added a solution of the ketone **16** (80 mg, 0.39 mmol) in benzene (2 mL) and stirred at room temp. for 1.5 h. The reaction mixture was then quenched with water (1 mL) and extracted with ether (2 × 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 hexane as eluent furnished myltaylene[12] **11** (57 mg, 71%). IR (neat): ν_{max} 1660 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 4.71 (1 H, br s), 4.52 (1 H, br s), 2.54 (1 H, br d, J = 16.5 Hz), 2.10–1.15 (10 H, m), 1.00 (3 H, s), 0.96 (3 H, s), 0.81 (3 H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.7, 101.3, 57.7, 52.8, 46.9, 40.4, 36.5, 33.6, 30.2, 28.7, 27.9, 27.6, 23.2, 19.2, 19.1. Mass: *m*/*z* 204 (M^+, 15%), 189 (25), 175 (6), 161 (25), 133 (35), 119 (50), 108 (100).

1-(1,3,3-Trimethyl-2-methylenecyclohexyl)-3-methylbut-3-en-2-one (18)

Reaction of isopropenylmagnesium bromide [prepared from magnesium (60 mg, 2.5 mmol) and isopropenyl bromide (304 mg, 0.22 mL, 2.5 mmol) and a catalytic amount of iodine] with the aldehyde **13** (300 mg, 1.68 mmol) in 6 mL of dry THF for 8 h, as described for the preparation of compound **12**, furnished a 3 : 1 epimeric mixture of the intermediate secondary alcohol (300 mg, 81%) as an oil. IR (neat): ν_{max} 3380, 1620, 890 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) peaks due to the major isomer: δ 5.06 (1 H, s), 4.97 (1 H, s), 4.81 (1H, s), 4.67 (1 H, s), 4.07 (1 H, d, J = 9.0 Hz), 1.69 (3 H, s), 2.10–1.15 (9 H, m), 1.17 (3 H, s), 1.07 (3 H, s), 1.02 (3 H, s). Peaks due to the minor isomer: δ 4.88 (1 H, s), 4.72 (1 H, s), 1.16 (3 H, s), 1.12 (3 H, s), 1.08 (3 H, s). Mass: *m*/*z* 222 (M^+, 3%), 138 (30), 123 (100). HRMS: Calcd. for $C_{15}H_{26}O$ *m*/*z* 222.1984. Found: 222.1985.

To a magnetically stirred solution of the alcohol (43 mg, 0.2 mmol) in 1.5 mL of dry CH_2Cl_2 was added a homogeneous mixture of PCC (83 mg, 0.4 mmol), NaOAc (21 mg, 0.4 mmol) and 4 Å molecular sieves powder (85 mg) and the mixture was stirred vigorously for 45 min at room temp. The reaction mixture was then filtered through a small silica gel column and eluted with an excess of CH_2Cl_2. Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate–hexane (1 : 4) as eluent furnished the dienone **18** (35 mg, 82%) as an oil, which was found to decompose slowly on standing and hence was used immediately in the next reaction. IR (neat): ν_{max} 1660, 895 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 5.90 (1 H, s), 5.73 (1 H, s), 5.00 (1 H, s), 4.86 (1 H, s), 2.97 and 2.84 (2 H, AB q, J = 14.8 Hz), 1.90–1.20 (6 H, m), 1.86 (3 H, s), 1.20 (3 H, s), 1.15 (6 H, s). Mass: *m*/*z* 220 (M^+, 17%), 205 (13), 137 (95), 122 (100), 109 (35).

2,2,6,7-Tetramethyltricyclo[5.2.2.0^{1,6}]undecan-8-one (6-epijunicedran-8-one 17)

To a cold (0 °C) magnetically stirred solution of the dienone **18** (10 mg, 0.05 mmol) in dry CH_2Cl_2 (0.4 mL) was added $BF_3{\cdot}Et_2O$ (15 μL), and the reaction mixture was stirred for 30 min at the same temperature. It was then quenched with 10% aq. NH_3 solution and extracted with CH_2Cl_2 (2 × 5 mL). The organic layer was washed with saturated aq. $NaHCO_3$ solution and water, and dried (Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate–hexane (1 : 20) as eluent furnished junicedranone **17** (6 mg, 60%) as an oil. IR (neat): ν_{max} 1740 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.43 (1 H, dd, J = 18.6 and 3.5 Hz), 2.00–0.90 (10 H, m), 1.80 (1 H, d, J = 18.6 Hz), 1.05 (3 H, s), 0.99 (3 H, s), 0.88 (3 H, s), 0.83 (3 H, s). ^{13}C NMR (100 MHz, Spin Echo FT, $CDCl_3$): δ 218.4 (C), 60.9 (C), 52.5 (C), 48.1 (C), 45.4 (CH_2), 36.1 (CH_2), 33.7 (C), 30.1 (CH_2), 28.9 (CH_2), 28.8 (CH_3), 27.4 (CH_2), 23.5 (CH_3), 18.8 (CH_2), 16.5 (CH_3), 9.3 (CH_3). Mass: *m*/*z* 220 (M^+, 90%), 205 (12), 177 (25), 163 (25), 150 (45), 135 (100), 124 (50), 121 (46), 109 (70). HRMS: Calcd. for $C_{15}H_{24}O$ *m*/*z* 220.1827. Found: 220.1816.

exo-2,2,6,7-Tetramethyltricyclo[5.2.2.0^{1,6}]undecan-8-ol (6-epijunicedran-8-ol 23)

To a solution of lithium (3 mg) in 25 mL of freshly distilled (over Na) ammonia was added, dropwise, a solution of the ketone **24** (6 mg, 0.03 mmol) in 1 mL of dry THF. The reaction mixture was stirred for 10 min and then quenched with ammonium chloride. Ammonia was evaporated, and the reaction mixture was diluted with water and extracted with ether (2 × 4 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 ethyl acetate–hexane (1 : 20 to 1 : 10) as eluent furnished 6-epijunicedranol **23** (3 mg, 50%) as an oil. IR (neat): ν_{max} 3360 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.88 (1 H, ddd, J = 10.3, 4.0 and 2.0 Hz), 2.32 (1 H, ddd, J = 14.0, 10.3 and 4.0 Hz), 1.81 (1 H, ddd, J = 13.4, 9.0 and 4.2 Hz), 1.70–0.70 (11 H, m), 0.89 (3 H, s), 0.85 (3 H, s), 0.76 (3 H, s), 0.70 (3 H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 75.5, 53.3, 52.2, 49.0, 41.8, 36.3, 33.9, 28.6, 28.5, 27.6, 25.5, 23.7, 19.2, 17.5 and 13.7. Mass: *m*/*z* 222 (M^+, 23%), 204 (20), 163 (53), 150 (65), 135 (40), 123 (100), 109 (75), 95 (80). HRMS: Calcd. for $C_{15}H_{26}O$ *m*/*z* 222.1984. Found: 222.1999.

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References

1 (*a*) B. M. Fraga, *Nat. Prod. Rep.*, 1985, **2**, 147; 1986, **3**, 273; 1987, **4**, 473; 1988, **5**, 497; 1990, **7**, 61; 1992, **9**, 217; 557; 1993, **10**, 397; 1994, **11**, 533; 1995, **12**, 303; 1996, **13**, 307; 1997, **14**, 145; 1998, **15**, 73; (*b*) G. W. Gribble, in *Progress in the Chemistry of Organic Natural Products*, Eds. W. Herz, G. W. Kirby, R. E. Moore, W. Steglich and Ch. Tamm, Springer, Vienna, New York, 1996, Vol. 68, pp. 1–87; (*c*) S. B. Christensen, A. Andersen, U. V. Smitt, in *Progress in the Chemistry of Organic Natural Products*, Eds. W. Herz, G. W. Kirby, R. E. Moore, W. Steglich and Ch. Tamm, Springer, Vienna, New York, 1997, Vol. 71, 129–167; (*d*) Y. Asakawa, in *Progress in the Chemistry of Organic Natural Products*, Eds. W. Herz, G. W. Kirby, R. E. Moore, W. Steglich and Ch. Tamm, Springer, Vienna, New York, 1995, Vol. 65, pp. 1–296.

2 C. H. Heathcock, in *The Total Synthesis of Natural Products 2*, Ed. J. ApSimon, Wiley, New York, 1973; (*b*) C. H. Heathcock, S. L. Graham, M. C. Pirrung, F. Plavac and C. T. White, *The Total Synthesis of Natural Products*, Ed. J. ApSimon, John Wiley, New York, Vol. 5, 1983.

3 D. Takaoka, A. Matsuo, J. Kuramoto, M. Nakayama and S. Hayashi, *J. Chem. Soc.*, *Chem. Commun.*, 1985, 482; D. Takaoka, H. Tani and A. Matsuo, *J. Chem. Res.* (*S*), 1988, 130.

4 Y. Asakawa, M. Toyota, A. Ueda, M. Tori and Y. Fukazawa, *Phytochemistry*, 1991, **30**, 3037.

5 C.-L. Wu and S.-J. Chang, *Phytochemistry*, 1992, **31**, 2150; H.-C. Wei, S.-J. Ma and C.-L. Wu, *Phytochemistry*, 1995, **39**, 91.

6 F. Nagashima, S. Momosaki, Y. Watanabe, S. Takaoka, S. Huneck and Y. Asakawa, *Phytochemistry*, 1996, **42**, 1361.

7 A. F. Barrero, E. Álvarez-Manzaneda and A. Lara, *Tetrahedron Lett.*, 1995, **36**, 6347.

8 (*a*) A. Srikrishna and K. Krishnan, *Tetrahedron Lett.*, 1989, **30**, 6577; (*b*) A. Srikrishna and K. Krishnan, *J. Chem. Soc.*, *Chem. Commun.*, 1991, 1693; (*c*) A. Srikrishna and K. Krishnan, *J. Chem. Soc.*, *Perkin Trans. 1*, 1993, 667; (*d*) A. Srikrishna and K. Krishnan, *J. Org. Chem.*, 1993, **58**, 7751; (*e*) A. Srikrishna, K. Krishnan and S. Nagaraju, *J. Indian Inst. Science*, 1994, **74**, 157; (*f*) A. Srikrishna, T. J. Reddy, P. P. Kumar and D. Vijaykumar, *Synlett*, 1996, 67; (*g*) A. Srikrishna and R. Vishwajanani, *Tetrahedron Lett.*, 1996, **37**, 2863; (*h*) A. Srikrishna and D. Vijaykumar, *J. Chem. Soc.*, *Perkin Trans. 1*, 1997, 3295; (*i*) A. Srikrishna and D. Vijaykumar, *Tetrahedron Lett.*, 1998, **39**, 4901; (*j*) A. Srikrishna and D. Vijaykumar, *J. Chem. Soc.*, *Perkin Trans. 1*, 1999, 1265.

9 A. Srikrishna, C. V. Yelamaggad, K. Krishnan and M. Nethaji, *J. Chem. Soc.*, *Chem. Commun.*, 1994, 2259.

10 A. Srikrishna and P. P. Kumar, *Tetrahedron Lett.*, 1997, **38**, 2005.

11 E. Winterfeldt, S. Doye and T. Hotopp, *Chem. Commun.*, 1997, 1491. For a report on the first total synthesis of cyclomyltaylenol **4b**, see: H. Sakai, H. Hagiwara, Y. Ito, T. Hoshi, T. Suzuki and M. Ando, *Tetrahedron Lett.*, 1999, **40**, 2965.

12 Prior to the report of isolation of myltaylenol,[3] formation of the hydrocarbon **11** as a minor product (5%) in the acid catalyzed dehydration of the tertiary alcohol **30** was reported, see: P. Naegeli and M. Wetli, *Tetrahedron*, 1981, **37** Suppl. 1, 247.

13 M. Jalali-Naini, D. Guillerm and J. Y. Lallemand, *Tetrahedron*, 1983, **39**, 749.

14 (*a*) J. E. McMurry and L. C. Blaszczak, *J. Org. Chem.*, 1974, **39**, 2217; (*b*) G. Buchi and J. D. White, *J. Am. Chem. Soc.*, 1964, **86**, 2884.

15 (*a*) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 1975, 2647; (*b*) L. L. Adams and F. A. Luzzio, *J. Org. Chem.*, 1989, **54**, 5387.

16 G. Frater, U. Muller and P. Kraft, *Helv. Chim. Acta*, 1999, **82**, 522.

17 For example: see, (*a*) H. Tanimoto, H. Kiyota, T. Oritani and K. Matsumoto, *Synlett*, 1997, 121; (*b*) A. G. Martinez, E. T. Vilar, A. G. Fraile, A. H. Fernandez, S. M. Cerero and F. M. Jimenez, *Tetrahedron*, 1998, **54**, 4607.

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