Functionalization of *trans*-Decalin. V. A Synthesis of (±)-Nootkatone and (±)-Valencene from 4β,4aβ-Dimethyl-$\Delta^{6,7}$-octalin-1-one Ethylene Acetal

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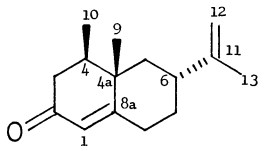
(Received July 17, 1981)

A synthesis of (±)-nootkatone (**1**) and (±)-valencene (**18**) starting from 4β,4aβ-dimethyl-$\Delta^{6,7}$-octalin-1-one ethylene acetal (**2**) is described. Epoxidation of the double bond of **2** followed by regiospecific reduction of the oxirane ring at the C-6 position gave the corresponding C-7 alcohol **4**. Oxidation of **4** and subsequent methoxycarbonylation at the C-6 position afforded methyl 1,1-ethylenedioxy-4β,4aβ-dimethyl-7-oxodecalin-6-carboxylate (**6**) in good yield. The keto ester **6** was converted to methyl 1,1-ethylenedioxy-4β,4aβ-dimethyldecalin-6α-carboxylate (**10b**) by the reduction with $NaBH_4$ followed by dehydration and subsequent hydrogenation over PtO_2 and epimerization of the 6β-methoxycarbonyl group with MeONa in MeOH. Deacetalization of **10b** followed by reduction and dehydration afforded methyl 4β,4aβ-dimethyl-$\Delta^{1(8a)}$-octalin-6α-carboxylate (**15**). The conversion of **15** into (±)-**18** was carried out directly by the reaction with salt-free methylenetriphenylphosphorane in refluxing tetrahydrofuran (76%) or by hydrolysis of **15** followed by methylation with MeLi, and subsequent Wittig reaction (60%). The allylic oxidation of (±)-**18** with $CrO_3 \cdot (pyridine)_2$ complex gave the desired (±)-**1**, smoothly.

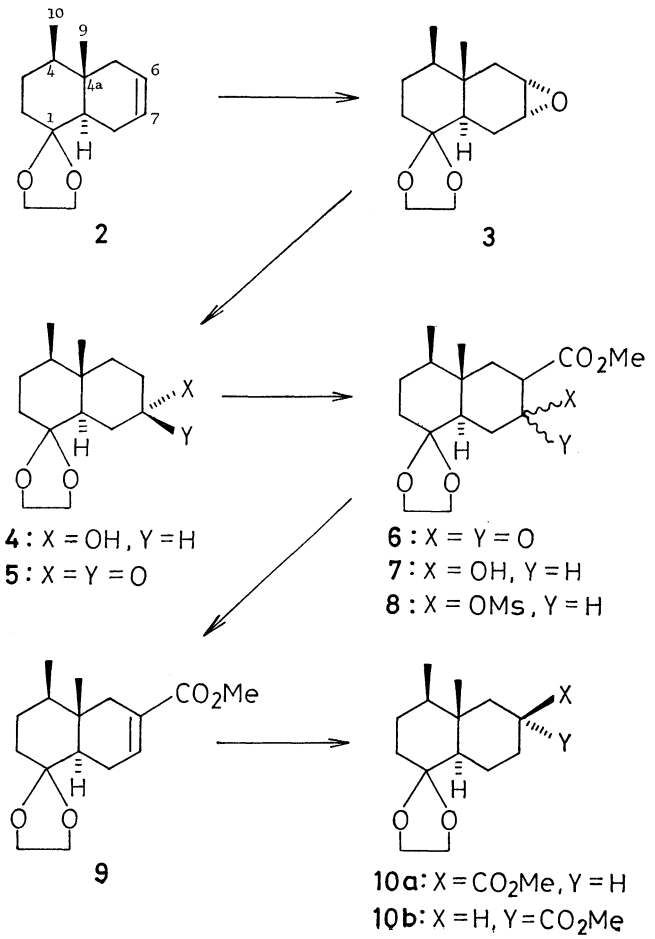
The stereoselective introduction of 4β,4aβ-dimethyl groups of valencene (**18**) is an essential strategy for the nootkatone synthesis.[1] Most of Robinson-type annelation procedures[1f-h,j] for the preparation of (±)-nootkatone (**1**) except for cyclopentenone annulation by Nazarov-type reaction[1k] lack the stereoselectivity on introducing the 4β,4aβ-dimethyl groups in the $\Delta^{1(8a)}$-octalin skeleton. However, an exquisite procedure for the stereoselective synthesis of **1** has been devised by employing a Diels-Alder type reaction.[1l] In connection with preparative investigations of eremophilane-type sesquiterpenes,[2] we have also developed the stereo-controlled construction of *trans*-4β,4aβ-dimethyl-$\Delta^{6,7}$-octalin-1-one ethylene acetal (**2**) by Diels-Alder reaction of 4-methyl-3-methoxycarbonyl-2-cyclohexen-1-one with butadiene.[2b] The present work is concerned with the stereoselective synthesis of the flavoring sesquiterpenes **1** and **18**[3] from the adduct **2**.



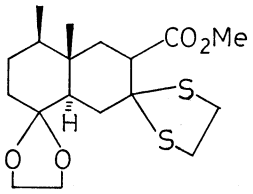
1

The strategy of leading **2** to the targets **1** and **18** involves the introduction of a methoxycarbonyl group at the C-6 carbon of **2**. Epoxidation of **2** with *m*-chloroperbenzoic acid at −60—10 °C gave the corresponding 6α,7α-epoxide **3** in 97% yield. The following reduction of the epoxy ring at the C-6 position of **3** based on the axial ring opening rule[4] with lithium in liquid ammonia afforded the 7α-alcohol **4** in 96% yield. Oxidation of **2** with pyridinium chlorochromate (PCC)[5] gave the ketone **5**, and subsequent methoxycarbonylation at the C-6 position of **5** with sodium hydride in refluxing dimethyl carbonate gave the keto ester **6** in 81% yield (from **4**).[6] The completely enolized form of **6** was characterized by two singlet signals at δ 95.7 and δ 171.5 due to the C-6 and C-7 carbons in homogeneous sixteen peaks in the ^{13}C NMR spectra.[7]

The hydrogenolysis of the ethylene dithioacetal[8] and the lithium metal reduction of methoxymethyl ether in liquid ammonia[9] were explored for the reduction of the β-keto esters. However, we have encountered some difficulties in obtaining the ethylene dithioacetal **11** on treatment of **6** with 1,2-ethanedithiol–boron trifluoride etherate, since the acetal-thioacetal



exchange occurred at the C-1 position of **6**, giving **12** exclusively. The lithium metal reduction of **6** was not feasible due to the reduction of the ester moiety to a hydroxymethyl group.



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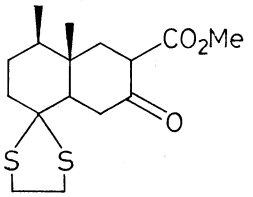

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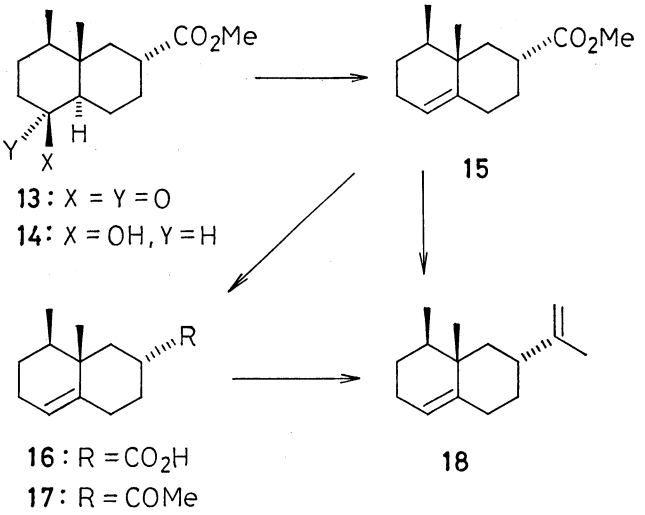
Because of the above results, stepwise transformation of **6** to **10** by ways of the dehydration of **7** and subsequent catalytic hydrogenation of **9** seemed to be promising for the present purpose. Reduction of **6** with sodium borohydride gave the epimeric alcohols **7** in 82% yield, and subsequent dehydration of the corresponding mesylates **8** with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) in refluxing benzene afforded α,β-unsaturated ester **9** in 64% yield (from **7**).[10] Catalytic hydrogenation of **9** over platinum oxide gave **10a** bearing the desired 6β-methoxycarbonyl group in 98% yield, as the result of preferential attack of hydrogen to the α side of the $\Delta^{6,7}$-double bond. The ^{13}C NMR spectra of **10a** showed homogeneous peaks, and the assigned configuration was also confirmed by the conversion of **10a** into the thermodynamically favorable 6α-isomer, **10b** on treatment with sodium methoxide at 85—90 °C in methanol (93% yield). The assigned stereochemistry at the C-6 position of **10b** can be rationally interpreted on the basis of downfield shift of ^1H NMR signals due to the angular C-4a methyl protons (δ 0.87) in comparison with that of **10a** (δ 0.72). This is due to the absence of shielding effects of the carbonyl group for a pair of axial and equatorial ester groups.[11]

Hydrolysis of the ethylene acetal of **10b** with perchloric acid and subsequent reduction of **13** with sodium borohydride provided the 1β-alcohol **14** in 95% yield (from **10b**). Dehydration of the hydroxyl group of **14** *via* the corresponding mesylate afforded **15** in 73% yield, the key precursor for the valencene synthesis.

The previous methods reported in the literature for the conversion of an ester into an isopropenyl group comprise the following two methods: one involves hydrolysis of the ester with an aqueous base, and treatment of the produced acid with methyllithium, giving the corresponding methyl ketone, and its subsequent treatment with methylenetriphenylphosphorane, giving the desired product.[1f,k] The other deals with the novel reaction of the ester with an excess of methylenetriphenylphosphorane, giving directly isopropenyl derivatives.[12] The reaction of **15** with an excess of salt-free methylenetriphenylphosphorane in tetrahydrofuran under reflux afforded the desired **18** in 76% yield. Meanwhile, the reaction of the acid **16** prepared by hydrolysis of **15** gave with methyllithium the ketone **17**, and subsequent olefination of **17** by Wittig reaction with methylenetriphenylphosphorane provided **18** (60% yield from **15**). The allylic oxidation of **18** with a slurry of the anhydrous chromium trioxide complex[13] furnished (±)-nootkatone (**1**) in 80% yield.[14]



13: X = Y = O
14: X = OH, Y = H
15
16: R = CO_2H
17: R = COMe
18

Experimental

Melting points are uncorrected and boiling points are indicated without correction by the air bath temperature. IR spectra were determined on a JASCO IRA-1 grating spectrometer. ^1H NMR (60 MHz) spectra were obtained on a Hitachi R-24 spectrometer and ^{13}C NMR (25.05 MHz) spectra on a JEOL FX-100 spectrometer. Samples were dissolved in $CDCl_3$ and the chemical shift values (δ) are expressed in parts per million downfield from the internal standard Me_4Si. Elemental analyses were performed in our laboratory.

6α,7α-Epoxy-1,1-ethylenedioxy-4β,4aβ-dimethyl-trans-*decalin (**3**).* To a solution of *m*-CPBA (324 mg, 1.88 mmol) in CH_2Cl_2 (10 ml) was added a solution of **2** (320 mg, 1.44 mmol) in CH_2Cl_2 (10 ml) at −60 °C. After 1 h, the mixture was allowed to be warmed to 10 °C during 5 h, at which temperature it was stirred for 2 h. The mixture was filtered and the filtrate was washed with aqueous 20% KOH and aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated to give 332 mg (97%) of **3** after chromatography (SiO_2, hexane–AcOEt 5:1): bp 119—121 °C/2 Torr;† IR (neat) 1297, 1277, 1197, 1162, 1150, 1085, 1041 cm^{-1}; ^1H NMR δ 0.75 (s, 3, CH_3), 0.79 (d, J=6 Hz, 3, CH_3), 1.05—2.22 (m, 10, CH_2, CH), 2.80—3.11 (m, 2, CH–O), 3.51—3.96 (m, 4, CH_2O); ^{13}C NMR δ 13.2 (q, C-9), 15.1 (q, C-10), 20.2 (t, C-8), 28.0 (t, C-3), 34.9 (s, C-4a), 35.5 (t, C-2), 39.7 (t, C-5), 42.6 (d, C-4), 42.9 (d, C-8a), 50.3 (d, C-7), 52.7 (d, C-6), 64.0, 65.3 (t, CH_2O), 110.0 (s, C-1). Found: C, 70.65; H, 9.47%. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30%.

1,1-Ethylenedioxy-4β,4aβ-dimethyl-trans-*decalin-7α-ol (**4**).* To a blue solution of Li (55 mg, 7.93 mmol) in liquid NH_3 (45 ml) was added a solution of **3** (350 mg, 1.47 mmol) in THF (5 ml) at −70 °C. After being stirred for 3 h at −70 °C and for 1.5 h at −33 °C, the mixture was quenched with NH_4Cl (500 mg), allowed to stand at room temperature until the liquid NH_3 was removed, and worked up in the usual manner to give 340 mg (96%) of **4** after chromatography (SiO_2, hexane–AcOEt 3:1): bp 157—159 °C/0.035 Torr; IR (neat) 3400 (OH) cm^{-1}; ^1H NMR δ 0.80 (m, 3, CH_3), 0.82 (s, 3, CH_3), 1.00—2.10 (m, 12, CH_2, CH), 3.17

† 1 Torr≈133.322 Pa.

(br, 1, OH), 3.54—4.00 (m, 4, CH_2O), 4.11 (complex t, J=2.5, 1 Hz, 1, CH–O); ^{13}C NMR δ 11.5 (q, C-9), 14.8 (q, C-10), 27.1 (t), 28.2 (t), 28.4 (t,) 33.7 (t, C-5), 35.8 (t, C-2), 37.7 (s, C-4a), 42.5 (d, C-4), 44.7 (d, C-8a), 64.0, 65.2 (t, CH_2O), 66.0 (d, C-7), 110.5 (s, C-1). Found: C, 69.87; H, 10.17%. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07%.

1,1-Ethylenedioxy-4β,4aβ-dimethyl-trans-*declain-7-one* (**5**). To a suspension of $Py \cdot CrO_3 \cdot HCl$ (1.06 g, 3.96 mmol) and AcONa (550 mg, 6.70 mmol) in CH_2Cl_2 (15 ml) was added a solution of **4** (320 mg, 1.33 mmol) in CH_2Cl_2 (5 ml). After being stirred for 3 h at 5 °C and for 3 h at room temperature, the mixture was diluted with ether (20 ml) and filtered. The concentrated filtrate was chromatographed (SiO_2, hexane–AcOEt 3:1) to give 294 mg (93%) of **5**: mp 59—61 °C; IR (Nujol) 1705 cm^{-1} (C=O); ^1H NMR δ 0.91 (m, 3, CH_3), 1.04 (s, 3, CH_3), 1.12—2.14 (m, 8, CH_2, CH), 2.15—2.57 (m, 4, CH_2CO), 3.57—4.10 (m, 4, CH_2O); ^{13}C NMR δ 11.7 (q, C-9), 15.3 (q, C-10), 28.3 (t, C-3), 35.6 (t, C-2), 36.4 (t), 37.1 (s, C-4a), 37.7 (t), 39.1 (t, C-5), 42.1 (d, C-4), 50.9 (d, C-8a), 64.1, 65.4 (t, CH_2O), 109.3 (s, C-1), 211.8 (s, C-7). Found: C, 70.63; H, 9.11%. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30%.

Methyl 1,1-Ethylenedioxy-4β,4aβ-dimethyl-7-oxo-trans-*decalin-6-carboxylate* (**6**). A mixture of **5** (340 mg, 1.43 mmol) and NaH (65 mg, 2.71 mmol) in dimethyl carbonate (1.7 ml) was heated under reflux for 3 h and quenched with cold aqueous $NaHCO_3$. The mixture was extracted with benzene–AcOEt (1:1) and the extract was worked up in the usual manner to give 369 mg (87%) of **6** after chromatography (SiO_2, hexane–AcOEt 2:1): mp 99—102 °C; IR (Nujol) 1655 (COO), 1621 cm^{-1} (C=C); ^1H NMR δ 0.78 (s, 3, CH_3), 0.89 (m, 3, CH_3), 1.05—2.00 (m, 6, CH_2, CH), 2.04—2.48 (m, 4, CH_2), 3.72 (s, 3, OCH_3), 3.80—4.12 (m, 4, CH_2O), 12.11 (s, 1, OH); ^{13}C NMR δ 11.8 (q, C-9), 15.3 (q, C-10), 25.4 (t, C-8), 28.1 (t, C-3), 35.5 (t, C-2), 36.4 (s, C-4a), 38.2 (t, C-5), 42.4 (d, C-4), 47.0 (d, C-8a), 51.3 (q, OCH_3), 64.1, 65.5 (t, CH_2O), 95.7 (s, C-6), 109.4 (s, C-1), 171.5 (s, C-7), 173.1 (s, COO). Found: C, 64.93; H, 8.31%. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16%.

Methyl 1,1-Ethylenedioxy-7-hydroxy-4β,4aβ-dimethyl-trans-*decalin-6-carboxylate* (**7**). To a solution of **6** (462 mg, 1.58 mmol) in MeOH (25 ml) was added a solution of $NaBH_4$ (59 mg, 1.56 mmol) in H_2O (1 ml) at 0 °C. The mixture was stirred for 12 h at room temperature, poured into aqueous $NaHCO_3$, and extracted with AcOEt–benzene (1:1). The extract was worked up in the usual manner to give 381 mg (82%) of **7** after chromatography (SiO_2, hexane–AcOEt 1:1): bp 143—145 °C/0.025 Torr; IR (neat) 3500 (OH), 1740 (COO), 1710 cm^{-1} (COO); ^1H NMR δ 0.71, 0.90 (s, 3, CH_3), 0.81 (m, 3, CH_3), 1.05—2.60 (m, 11, CH_2, CH), 2.90 (br, 1, OH), 3.46—4.40 (m, 5, CH_2O, CH–O), 3.66 (s, 3, OCH_3). Found: C, 64.69; H, 8.79%. Calcd for $C_{16}H_{26}O_5$: C, 64.41; H, 8.78%.

Methyl 1,1-Ethylenedioxy-7-methylsulfonyloxy-4β,4aβ-dimethyl-trans-*decalin-6-carboxylate* (**8**). To a solution of **7** (438 mg, 1.47 mmol) and Et_3N (1.04 g, 2.94 mmol) in ether (10 ml) was added $MeSO_2Cl$ (337 mg, 2.94 mmol) at 0 °C. The mixture was stirred for 2 h at 0 °C and for 1 h at room temperature, poured into cold aqueous $NaHCO_3$, and taken up in AcOEt–benzene (1:1). The extract was worked up in the usual manner to give 480 mg (87%) of **8**: mp 123—126 °C; IR (Nujol) 1718 cm^{-1} (COO); ^1H NMR δ 0.85 (m, 3, CH_3), 0.91 (s, 3, CH_3), 1.00—2.85 (m, 11, CH_2, CH), 2.99 (s, 3, SO_2CH_3), 3.50—4.15 (m, 4, CH_2O), 3.70 (s, 3, OCH_3), 4.50—5.00 (m, 1, CH–O). Found: C, 54.07; H, 7.52%. Calcd for $C_{17}H_{28}SO_7$: C, 54.25; H, 7.50%.

Methyl 1,1-Ethylenedioxy-4β,4aβ-dimethyl-$\Delta^{6,7}$-trans-*octalin-6-carboxylate* (**9**). A mixture of **8** (460 mg, 1.22 mmol) and DBU (1.36 g, 8.93 mmol) in benzene (20 ml) was heated at reflux for 12 h, poured into aqueous $NaHCO_3$, worked up in the usual manner to give 255 mg (74%) of **9** after chromatography (SiO_2, hexane–AcOEt 5:1): mp 79—81 °C; IR (Nujol) 1718 (COO), 1650 cm^{-1} (C=C); ^1H NMR δ 0.76 (s, 3, CH_3), 0.93 (m, 3, CH_3), 1.10—2.55 (m, 10, CH_2, CH), 3.70 (s, 3, OCH_3), 3.90 (m, 4, CH_2O), 6.95 (m, 1, HC=C); ^{13}C NMR δ 11.8 (q, C-9), 15.2 (q, C-10), 22.4 (t, C-8), 28.3 (t, C-3), 35.5 (t, C-2), 36.1 (s, C-4a), 40.0 (t, C-5), 42.6 (d, C-4), 46.9 (d, C-8a), 51.4 (q, OCH_3), 64.0, 65.5 (t, CH_2O), 109.7 (s, C-1), 128.2 (s, C-6), 138.7 (d, C-7), 167.9 (s, COO). Found: C, 68.50; H, 8.89%. Calcd for $C_{16}H_{24}O_4$: C, 68.55; H, 8.63%.

Methyl 1,1-Ethylenedioxy-4β,4aβ-dimethyl-trans-*decalin-6β-carboxylate* (**10a**). A mixture of **9** (123 mg, 0.44 mmol) and PtO_2 (40 mg) in AcOEt (7 ml) was treated with excess H_2 for 4 d at room temperature, filtered, and concentrated to give 122 mg (98%) of **10a**: bp 110—111 °C/0.017 Torr; IR (neat) 1730 cm^{-1} (COO); ^1H NMR δ 0.72 (s, 3, CH_3), 0.82 (m, 3, CH_3), 1.00—2.70 (m, 13, CH_2, CH), 3.67 (s, 3, OCH_3), 3.86 (m, 4, CH_2O); ^{13}C NMR δ 12.5 (q, C-9), 14.9 (q, C-10), 16.8 (t, C-8), 26.3 (t, C-7), 28.2 (t, C-3), 35.9 (t, C-2), 37.4 (d, C-4), 38.1 (s, C-4a), 41.2 (t, C-5), 43.0 (d, C-8a), 51.4 (q, OCH_3), 52.7 (d, C-6), 64.3, 65.4 (t, CH_2O), 109.9 (s, C-1), 176.4 (s, COO). Found: C, 70.52; H, 9.46%. Calcd for $C_{16}H_{26}O_4$: C, 70.56; H, 9.30%.

Epimerization of **10a** *to* **10b**. **10a** (110 mg, 0.39 mmol) was heated in MeOH (6 ml) containing MeONa (540 mg, 10 mmol) at 85—90 °C for 12 h. The mixture was poured into aqueous 5% tartaric acid and extracted with AcOEt–benzene (1:1). The crude product obtained after the usual workup was treated with excess CH_2N_2, giving 102 mg (93%) of **10b**: bp 121—123 °C/0.015 Torr; IR (neat) 1730 cm^{-1} (COO); ^1H NMR δ 0.86 (m, 3, CH_3), 0.87 (s, 3, CH_3), 1.10—2.75 (m, 13, CH_2, CH), 3.64 (s, 3, OCH_3), 4.87 (m, 4, CH_2O); ^{13}C NMR δ 12.7 (q, C-9), 14.8 (q, C-10), 19.0 (t, C-8), 28.4 (t), 28.9 (t), 35.8 (t, C-2), 37.7 (s, C-4a), 38.9 (d, C-4), 42.5 (t, C-5), 42.6 (d, C-8a), 51.4 (q, OCH_3), 51.9 (d, C-6), 64.2, 65.3 (t, CH_2O), 110.0 (s, C-1), 176.7 (s, COO). Found: C, 70.65; H, 9.51%. Calcd for $C_{16}H_{26}O_4$: C, 70.56; H, 9.30%.

Methyl 4β,4aβ-Dimethyl-1-oxo-trans-*decalin-6α-carboxylate* (**13**). To a solution of **10b** (122 mg, 0.43 mmol) in THF (6 ml) and H_2O (3 ml) was added 70% $HClO_4$ (0.2 ml). The mixture was stirred for 12 h at room temperature and worked up in the usual manner to give 101 mg (98%) of **13**: mp 68—69 °C; IR (Nujol) 1725 (COO), 1705 cm^{-1} (C=O); ^1H NMR δ 0.66 (s, 3, CH_3), 0.90 (d, J=6 Hz, 3, CH_3), 1.10—2.80 (m, 13, CH_2, CH), 3.65 (s, 3, OCH_3); ^{13}C NMR δ 11.7 (q, C-9), 14.5 (q, C-10), 19.8 (t, C-8), 27.8 (t), 31.3 (t), 38.6 (d, C-4), 40.8 (t), 41.2 (t), 41.4 (s, C-4a), 42.5 (d, C-8a), 51.7 (q, OCH_3), 57.2 (d, C-6), 176.3 (s, COO), 212.0 (s, C-1). Found: C, 70.52; H, 9.46%. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30%.

Methyl 1β-Hydroxy-4β,4aβ-dimethyl-trans-*decalin-6α-carboxylate* (**14**). To a solution of **13** (217 mg, 0.91 mmol) in MeOH (10 ml) was added a solution of $NaBH_4$ (35 mg, 0.92 mmol) in H_2O (0.5 ml) at 0 °C. The mixture was stirred for 3 h at room temperature, quenched with aqueous 10% AcOH, and taken up in AcOEt–benzene (1:1). The extract was worked up in the usual manner to give 213 mg (97%) of **14** after chromatography (SiO_2, hexane–AcOEt 3:1): bp 93—94 °C/0.005 Torr; IR (neat) 3480, 3400 (OH), 1730 (COO), 1715 cm^{-1} (COO); ^1H NMR δ 0.81 (m, 3, CH_3), 0.94 (s, 3, CH_3), 1.00—2.85 (m, 13, CH_2, CH), 1.68

(brs, 1, OH), 3.63 (s, 3, OCH_3), 3.67 (m, 1, CH–O); ^{13}C NMR δ 14.3 (q, C-10), 15.1 (q, C-9), 25.2 (t), 25.7 (t), 29.3 (t), 34.1 (t), 36.5 (s, C-4a), 39.2 (d, C-4), 42.7 (t, C-5), 43.1 (d, C-8a), 48.6 (d, C-6), 51.5 (q, OCH_3), 71.9 (d, C-1), 176.9 (s, COO). Found: C, 69.91; H, 10.08%. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07%.

Methyl 4β,4aβ-Dimethyl-$\Delta^{1(8a)}$-octalin-6α-carboxylate (15). To a solution of **14** (213 mg, 0.89 mmol) and Et_3N (629 mg, 6.22 mmol) in ether (10 ml) was added $MeSO_2Cl$ (203 mg, 1.77 mmol) at 0 °C. The mixture was stirred for 12 h at room temperature, quenched with aqueous $NaHCO_3$, and worked up in the usual manner. Without purification, the crude product was treated with benzene containing DBU (946 mg, 6.21 mmol) for 12 h under reflux. The usual workup and the subsequent chromatography (SiO_2, hexane–AcOEt 5:1) gave 144 mg (73%) of **15**: bp 74—76 °C/0.025 Torr; IR (neat) 1725 cm^{-1} (COO); ^1H NMR δ 0.85 (m, 3, CH_3), 0.93 (s, 3, CH_3), 1.10—2.60 (m, 12, CH_2, CH), 3.64 (s, 3, OCH_3), 5.35 (m, 1, HC=C); ^{13}C NMR δ 15.5 (q, C-10), 18.0 (q, C-9), 25.8 (t), 27.2 (t), 30.4 (t), 31.7 (t), 37.5 (s, C-4a), 39.7 (d), 40.8 (d), 41.9 (t, C-5), 51.4 (q, OCH_3), 121.0 (d, C-1), 141.6 (s, C-8a), 176.4 (s, COO). Found: C, 75.57; H, 9.97%. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97%.

4β,4aβ-Dimethyl-$\Delta^{1(8a)}$-octalin-6α-carboxylic Acid (16). Hydrolysis of **15** (58 mg, 0.26 mmol) in the MeOH (5 ml)–KOH (170 mg, 4.35 mmol)–H_2O (1 ml) system was carried out at room temperature for 24 h, acidified with aqueous 5% HCl, and extracted with AcOEt–benzene (1:1). The usual workup gave 49 mg (91%) of **16**; IR (neat) 3400—2600 (COOH), 1700 cm^{-1} (COO); ^1H NMR δ 0.87 (m, 3, CH_3), 0.93 (s, 3, CH_3), 1.10—2.90 (m, 12, CH_2, CH), 5.35 (m, 1, HC=C), 9.10 (br, 1, OH). Found: C, 75.24; H, 9.87%. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68%.

6α-Acetyl-4β,4aβ-dimethyl-$\Delta^{1(8a)}$-octalin (17). To a solution of **16** (54 mg, 0.26 mmol) in ether (5 ml) was added an ethereal solution of 1.05 M MeLi (0.74 ml, 0.78 mmol) at 0 °C. The mixture was stirred for 1 h at 0 °C, quenched with aqueous NH_4Cl, and extracted with AcOEt–benzene (1:1). The extract was worked up in the usual manner to give 43 mg (80%) of **17**: bp 109—112 °C/0.04 Torr (lit,[1h] 100—105 °C/0.02 Torr); IR (neat) 1710 (C=O), 1660 cm^{-1} (C=C); ^1H NMR δ 0.90 (m, 3, CH_3), 0.94 (s, 3, CH_3), 1.00—2.80 (m, 12, CH_2, CH), 2.14 (s, $COCH_3$), 5.32 (m, 1, HC=C).

(±)-Valencene (18) from 15. To a solution of **15** (110 mg, 0.50 mmol) in THF (5 ml) was added a salt-free solution of methylenetriphenylphosphorane prepared from methyltriphenylphosphonium bromide (715 mg, 2.0 mmol) and $NaNH_2$ (200 mg, 5.13 mmol) in THF (4 ml). The mixture was heated for 12 h under reflux and worked up in the usual manner to give 78 mg (76%) of **18**: bp 116—118 °C/14 Torr (lit,[1h] 73—75 °C/0.03 Torr); ^{13}C NMR δ 15.7 (q, C-10), 18.4 (q, C-9), 20.8 (q, C-13), 25.9 (t), 27.2 (t), 32.8 (t), 33.2 (t), 37.9 (s, C-8a), 41.0 (d), 41.1 (d), 45.0 (t, C-5), 108.3 (t, C-12), 120.1 (d, C-1), 143.1 (s, C-8a), 150.6 (s, C-11). IR and ^1H NMR spectra of **18** were identical with those of the reported ones.[3a,15]

Preparation of 18 from 17. To a solution of **17** (62 mg, 0.3 mmol) in benzene (5 ml) was added a benzene solution of 0.5 M methylenetriphenylphosphorane (1.2 ml, 0.6 mmol). The mixture was stirred at room temperature for 5 h, quenched with water, and worked up in the usual manner to give 51 mg (83%) of **18** after chromatography (SiO_2, hexane).

(±)-Nootkatone (1). To a solution of **18** (42 mg, 0.21 mmol) in CH_2Cl_2 (5 ml) was added a slurry of CrO_3·(pyridine)$_2$ complex (553 mg, 3.09 mmol) in CH_2Cl_2 (5 ml). The mixture was stirred for 12 h at room temperature, quenched with aqueous 5% tartaric acid, and worked up in the usual manner to give 36 mg (80%) of **1** after chromatography (SiO_2, hexane–AcOEt 3:1); mp 42—43 °C, crystallized from petroleum ether (boiling range 30—70 °C) at −70 °C (lit,[1f] 44—45 °C); ^{13}C NMR δ 14.9 (q, C-10), 16.8 (q, C-9), 20.8 (q, C-13), 31.7 (t), 33.1 (t), 39.3 (s, C-4a), 40.4 (d), 40.5 (d), 42.1 (t), 43.9 (t), 109.2 (t, C-12), 124.7 (d, C-1), 149.0 (s, C-11), 170.4 (s, C-8a), 199.5 (s, C-2). Except for the optical rotation, the physical data (IR, ^1H and ^{13}C NMR, and TLC analyses) of the product **1** were identical in all respects with those of the authentic sample.[14]

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14) We are grateful to Mr. M. Ishihara, Shiono Koryo Co. Ltd., for a generous gift of natural nootkatone (**1**).

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