Pergamon

Tetrahedron 54 (1998) 14803–14810

TETRAHEDRON

Synthesis of Angular Triquinanes from (+)-β-Cedrol

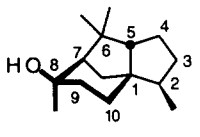
Marie-Christine Pierre, Alphonse Tenaglia* and Maurice Santelli*

ESA 6009 and UMR 6516 (CNRS), Faculté de St-Jérôme, 13397 Marseille Cedex 20, France

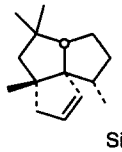
Received 23 July 1998; accepted 5 October 1998

Abstract: Angular triquinanes such as (+)-silphinan-3,5-dione, silphin-3-en-3,5-dione or 2-bromosilphin-3-en-3,5-dione have been obtained from (+)-β-cedrene in seven steps and an overall yield of 8%.

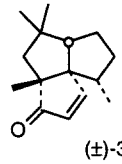
Highly condensed polycyclopentanoids (polyquinanes) represent a class of natural products of increasing importance.[1] Among them, angularly-fused sesquiterpenes such as silphinene,[2] isolated from *Silphium perfoliatum* roots, as well as (±)-3-oxosilphinene[3] and (±)-1-oxosilphinen-3,5-diol[4] features the intriguing tricyclo[6.3.0.0^{1,5}]undecane (triquinane) structure.[5] Most of the syntheses of these substrates were reported for racemic compounds.[6] Successfull access to this class of compounds is based on methodologies involving the construction of stereodefined fused cyclopentanoid systems.[7] It turns out that obtention of enantiomerically pure derivatives by semisynthetis from readily available and inexpensive natural compounds are rare.[8] In an ongoing project directed towards new synthetic approaches to quinanes we planned the multistep syntheses of structural analogs of silphinene from (+)-cedrol **1**.



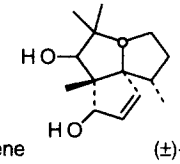
1



Silphinene



(±)-3-Oxosilphinene

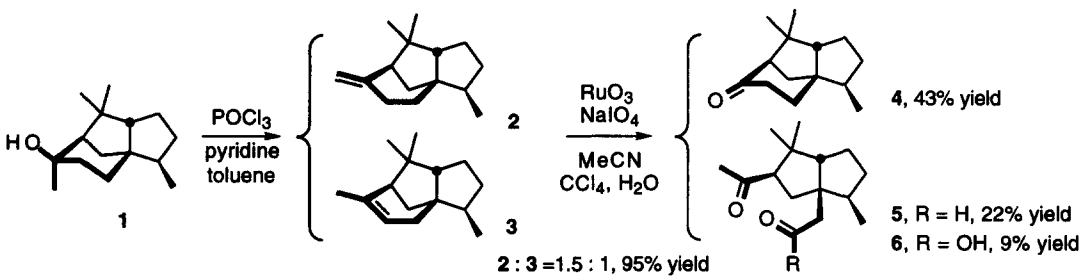


(±)-1-Silphinen-3,5-diol

In the tricyclic structure of **1**, we note the interesting 2,2,5-trimethylbicyclo[3.3.0]octane substructure which could be available as enantiomerically pure building block for further transformation to the triquinane system. Indeed, Asakawa[8] reported the synthesis of a triquinane, the epimer of the alleged senoxydene,[7e] in a low overall yield from **1**. In the key transformations, C(7) in **1** was hydroxylated using MCPBA (1.5% yield), and the resulting α-diol was subsequently cleaved with $NaIO_4$ affording the key 1,6-diketone. Such a cleavage should also be possible by the ring-opening of an appropriate lactone **7**, which in turn would derive from norcedranone **4**, provided a regioselective Baeyer-Villiger (BV) oxidation can be carried out. The requisite norcedranone **4**[9] was obtained by known methods from (+)-cedrol **1** in an 43% overall yield from **1**. Dehydration of (+)-cedrol **1** using $POCl_3$[10] afforded a 1.5:1 mixture of (+)-β-cedrene **2** and (−)–α-cedrene **3**.

Fax: (33) (0)4 91 98 38 65; e-mail: m.santelli@lso.u-3mrs.fr

0040-4020/98/$ - see front matter
PII: S0040-4020(98)00928-4



Without any attempts to separate **2** from **3**, the mixture was subjected to ozonolysis providing the desired ketone **4** in low yield (15%). When using $KMnO_4$ dispersed on silica gel[11] for oxidative cleavage only 6% of **4** formed. Rewardingly, RuO_4 generated in situ[12] yielded **4** in an acceptable isolated yield of 43% (72% based on β-cedrene), and easily separated from the accompanying ketoaldehyde **5** (22%) and ketoacid **6** (9%).

Next, the Baeyer-Villiger oxidation of **4** was investigated in detail with different reagents (Table 1). First, oxidation with *m*-chloroperbenzoic acid in refluxing CH_2Cl_2 led to an inseparable mixture of lactones **7** and **8** (50% yield) in a 1.3:1 ratio (entry 1). The presence of boron trifluoride allowed the reaction to proceed at room temperature with slightly increased yield (60%) and better regioselectivity (1.5:1) (entry 2). Finally, the best transformation (81%) occured in the presence of $NaHCO_3$ (entry 3) though the regioselectivity decreased. The other oxidizing reagents which were examined (entry 4-8) proved unsatisfactory since they proceeded with a reversed regioselectivity. On the other hand, the exclusive formation of the known diacid **9**[18] (64%), presumably via the non isolated lactone **8**, was observed when using CAN (entry 9).

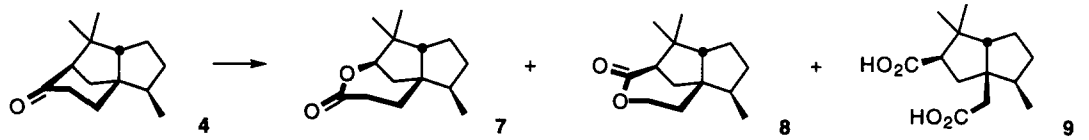


Table 1. Baeyer-Villiger Oxidation of Cedranone 4.

Entry	Reagents	Conditions	Results* (Isolated yields are reported)
1	*m*CPBA, CH_2Cl_2	reflux, 2 days	50 % yield, **7** : **8** = 1.32 : 1
2	*m*CPBA, BF_3-Et_2O, CH_2Cl_2	25 °C, 1 day	60 % yield, **7** : **8** = 1.56 : 1
3	*m*-CPBA, $NaHCO_3$, CH_2Cl_2	reflux, 1 day	81 % yield, **7** : **8** = 1.22 : 1
4	$(CF_3CO)_2O$, H_2O_2, Na_2HPO_4, CH_2Cl_2	25 °C, 2.5 days	20 % yield, **7** : **8** = 0.35 : 1
5	2 $KHSO_5$, $KHSO_4$, K_2SO_4/Alumina, CH_2Cl_2,[13]	reflux, 1 day	14 % yield, **7** : **8** = 0.28 : 1
6	AcOH, H_2O_2 (30 %), AcONa,[14]	50 °C, 5 days	0 % yield
7	PhCHO, O_2, Fe_2O_3, benzene,[15]	25 °C, 7 days	16 % yield, **7** : **8** = 0.31 : 1
8	PhCHO, O_2, MnO_2, $CH_2H_4Cl_2$,[16]	25 °C, 6 days	10 % yield, **7** : **8** = 0.31 : 1
9	CAN, H_2O, MeCN,[17]	70 °C, 1 h	**9**,[18] 64 % yield.

Since Baeyer-Villiger oxidation of bicyclo[3.2.1]octan-2-ones proceeds as expected to produce 2-oxabicyclo[4.2.1]nonan-3-ones,[19, 20] the low regioselectivity observed with cedranone **4** was disappointing.

Calculations performed using the PM3 method[21] reveal that the more stable regioisomer is **7** (**7**, ΔH_f = −118.6 kcal/mol; **8**, ΔH_f = −117.2 kcal/mol), although the energy difference is too little to favour the formation of **7** ($\delta\Delta H_f$ = −1.4 kcal/mol).

Nucleophilic addition of a peracid to the carbonyl group is known to occur selectively from the sterically less hindered side.[22] In the case of ketone **4**, the gem dimethyl located at C(6) disfavour equatorial attack of the incoming nucleophile and the transposition occurs on intermediate **A** (Criegee intermediate).[23] Two conformations **A1** et **A2** have to be taken into account. The conformation **A1** would lead to lactone **7** whereas **A2** will afford **8**. Semi-empirical calculations of **A** (PM3 method) show that conformation **A2** is more stable than conformation **A1** ($\delta\Delta H_f = -1.2$ kcal/mol) that is approximately the same level of difference observed for lactones **7** and **8**. Moreover, these calculations indicated that O(2)-O(3) bond is very long (O-O bond length of endoperoxides, 1.467 Å),[24] and that the C(7)-C(8) bond antiperiplanar to O(2)-O(3) is lengthened.

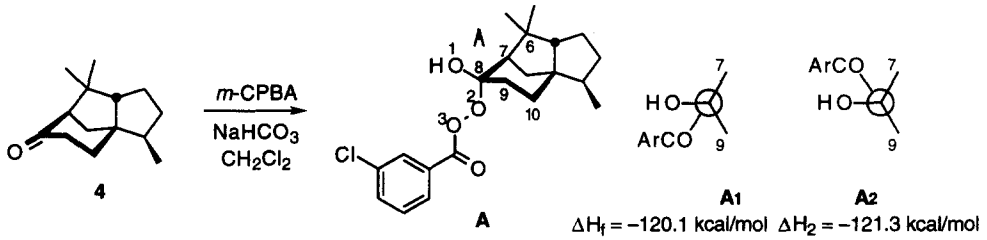
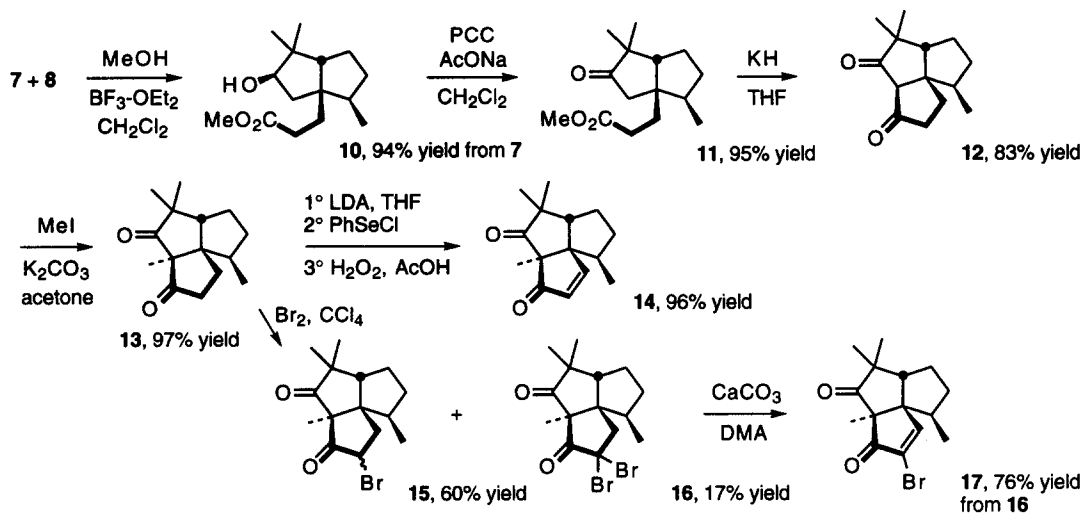


Table 2. PM3 Calculations of **A1** and **A2**.

	A1	A2
ΔH_f (kcal/mol)	−120.13	−121.30
d(C(7)-C(8))	1.5715 Å	1.5593 Å
d(C(8)-C(9))	1.5515 Å	1.560 Å
d(C(8)-O(1))	1.4041 Å	1.404 Å
d(C(8)-O(2))	1.412 Å	1.415 Å
d(O(2)-O(3))	1.569 Å	1.560 Å

With lactone **7** in hand, several new, enantiomerically pure angular triquinanes were readily obtained using standard transformations. For instance, dione **12** was obtained in 8.1% overall yield from **1** with the following selective reactions. The Lewis acid (BF_3) catalyzed selective ring opening of lactone **7**, from an inseparable mixture of isomeric lactones **7** + **8**, in methanol afforded selectively hydroxyester **10**, leaving unchanged lactone **8**.[25] This reaction allows a facile separation of **10** at this stage. Oxidation of **10** with PCC and subsequent intramolecular Claisen alkylation[26] delivers dione **12**. The latter was easily alkylated with methyl iodide to silphinan-3,5-dione **13**. Oxidation of cyclopentanone nucleus to the cyclopentenone was achieved in high yield (96%) using Reich's procedure[27] affording 1-silphinen-3,5-dione **14** precursor of silphinen-3-one and 1-silphinen-3,5-diol. Bromination of **13** afforded a mixture of monobrominated **15** (60%) and dibrominated **16** (17%). With the latter, dehydrobromination in the presence of $CaCO_3$ give 1-bromo-1-silphinen-3,5-dione **17**.



Conclusion: We have shown that the 2,2,5-trimethylbicyclo[3.3.0]octane structure, easily obtained in enantiomerically pure form using standard procedures from naturally occuring and abundant (+)-β-cedrol, (worldwide annual production amounts to 1500–2000 t)[28] is an excellent precursor for the elaboration of new unnatural angular triquinanes in **seven steps and an overall yield of 8%.**

EXPERIMENTAL SECTION

General. All reactions were run under argon in an oven-dried glassware. ^1H (200 MHz) and ^{13}C NMR (50 MHz) spectra were recorded on a Bruker AC 200 spectrometer in $CDCl_3$ solutions. Chemical shift (δ) are reported in ppm with tetramethylsilane as internal standard. IR spectra were recorded on a Perkin-Elmer 1600 spectrophotometer. Flash chromatography was performed on silica gel (Merk 60 GF_{254} 230-400 mesh) and TLC on silica gel (Merck 60 F_{254}).

Material. All solvents were distilled before used, CH_2Cl_2 and $CHCl_3$ from P_2O_5, MeOH under $Mg(OMe)_2$, THF over sodium/benzophenone.

α- and β-Cedrene (2 and 3). To a stirred solution of cedrol **1b** (733 mg, 3.3 mmol), pyridine (18 mL) and toluene (20 mL) was slowly added phosphorus oxychlorure (3.6 mL). After 16 h at room temperature, CH_2Cl_2 was added (50 mL) and the pyridine was removed by washing with saturated solution of $CuSO_4$. The organic layer was dried ($MgSO_4$). Concentration in vacuo gave the crude product that was subjected to chromatography on silica gel to afford a 1.5:1 mixture of **2** and **3** (639 mg, 95% yield).

(1*S*, 2*R*, 5*S*, 7*R*)-2,6,6-Trimethyltricyclo[5.3.1.0^{1,5}]undecan-8-one (4). A mixture of **2** and **3** (3.67 g, 18 mmol), CCl_4 (35 mL), acetonitrile (35 mL), $NaIO_4$ (19 g, 89 mmol) in water (55 mL) and $RuCl_3.3H_2O$ (223 mg, 0.89 mmol) were stirred at room temperature for 5h. After cooling to 0 °C, isopropanol (5 mL) was slowly added and the solution was extracted with ether, dried over $MgSO_4$, concentrated in vacuo and chromatographed on silica gel to give recovered **2** (129 mg, 0.63 mmol), **4** (1.59 g, 43% yield), **5** (1.04 g, 22%) and **6** (475 mg, 9%). **4**: $[\alpha]_{578}$ +99° (*c* 1.0, CH_2Cl_2); IR ν 1700, 912 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (d, *J* = 7.0 Hz, 3H), 1.00 (s, 6H), 1.10-2.03 (m, 10H), 2.30 (m, 2H), 2.40 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 15.3 (q), 25.3 (t), 25.6 (q), 26.0 (q), 31.8 (t), 36.4 (t), 36.6 (t), 41.1 (t), 41.4 (d), 42.6 (s), 54.2 (s), 56.6 (d), 66.9 (d), 213.9 (s). **(1*R*, 3*R*, 5*S*, 8*R*)-3-Acetyl-1-(2-oxoethyl)-4,4,8-trimethylbicyclo[3.3.0]octane (5).** $[\alpha]_{578}$ −61° (*c* 1.0, CH_2Cl_2); IR ν 1710, 1365 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (s, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 1.12 (s, 3H), 1.20-1.82 (m, 7H), 2.12 (s, 3H), 2.15 (t, *J* = 12.9, 1H), 2.38 (dd, *J* = 15.6, 3.0 Hz, 1H), 2.43 (dd, *J* = 15.6, 2.7 Hz, 1H), 2.75 (dd, *J* = 12.5, 6.3 Hz, 1H), 9.83 (dd, *J* = 3.0, 2.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.6 (q), 24.7 (q), 25.3 (q), 28.7 (t), 31.6 (q), 33.7 (t), 38.6 (t), 43.8 (s), 46.2 (d), 49.9 (s),

52.2 (t), 58.7 (d), 62.7 (d), 203.4 (d), 209.5 (s). **(1*R*, 3*R*, 5*S*, 8*R*)-3-Acetyl-1-carboxymethyl-4,4,8-trimethylbicyclo[3.3.0]octane (6).** $[\alpha]_{578}$ –63° (*c* 1.0, CH_2Cl_2); IR ν 3056, 1703, 1367, 1265 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (s, 3H), 0.93 (d, *J* = 6.4 Hz, 3H), 1.08 (s, 3H), 1.12-1.80 (m, 8H), 2.05 (t, *J* = 9.0 Hz, 1H), 2.11 (s, 3H), 2.20 (d, *J* = 14.8 Hz, 1H), 2.38 (d, *J* = 14.8 Hz, 1H), 2.68 (dd, *J* = 12.7, 6.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.7 (q), 24.5 (q), 24.8 (q), 28.3 (t), 31.3 (q), 33.1 (t), 37.7 (t), 41.2 (t), 43.5 (s), 46.2 (d), 50.2 (s), 58.8 (d), 60.7 (d), 178.9 (s), 210.3 (s).

(1*S*, 2*R*, 5*R*, 7*R*)-2,6,6-Trimethyl-8-oxatricyclo[5.4.1.0^{1,5}]dodecan-9-one (7). To ketone **4** (84 mg, 0.41 mmol) in CH_2Cl_2 (12 mL) was added $NaHCO_3$ (84 mg, 1 mmol) and *m*-CPBA (173 mg, 1 mmol). The mixture was refluxed for 1 d with exclusion of light. After cooling to room temperature, a 10% solution of $NaHSO_3$ (10 mL) was added. After 15 min of stirring, the mixture was extracted with CH_2Cl_2 (5 x 5 mL). The organic layer were washed with brine and dried over $MgSO_4$. After removal of the solvent in vacuo, the crude product was purified by chromatography on silica gel to give **4** (16 mg, 19% yield) and an inseparable mixture of **7** and **8** (73 mg, 81% yield). **7**: IR ν 1727, 1210, 1122, 1086 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (d, *J* = 6.9 Hz), 0.97 (s, 3H), 1.11 (s, 3H), 1.22-2.05 (m, 10H), 2.65 (ddd, *J* = 14.9, 11.7, 6.1 Hz, 1H), 2.85 (dt, *J* = 14.9, 4.5 Hz, 1H), 4.25 (d, *J* = 6.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.4 (q), 26.3 (t), 26.8 (q), 28.7 (q), 30.6 (t), 36.2 (t), 37.1 (t), 45.3 (d), 45.5 (t), 46.3 (s), 57.3 (s), 57.9 (d), 94.3 (d), 178.0 (s). **(1*R*, 2*R*, 5*S*, 7*R*)-2,6,6-Trimethyl-9-oxatricyclo[5.4.1.0^{1,5}]dodecan-8-one (8).** IR ν 1727, 1210, 1122, 1086 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (d, *J* = 6.9 Hz, 3H), 1.08 (s, 3H), 1.20 (s, 3H), 1.22-1.95 (m, 9H), 2.05 (br t, *J* = 8.3 Hz, 1H), 2.90 (dd, *J* = 5.5, 1.7 Hz, 1H), 4.31 (d, *J* = 8.3 Hz, 1H), 4.35 (br. d, *J* = 8.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.6 (q), 26.5 (t), 26.8 (q), 28.7 (q), 36.2 (t), 37.2 (t), 41.8 (t), 44.1 (s), 45.3 (d), 57.3 (s), 58.1 (d), 63.5 (d), 66.7 (t), 177.9 (s).

(1*R*, 3*R*, 5*S*, 8*R*)-1-Carboxymethyl-4,4,8-trimethylbicyclo[3.3.0]octane-3-carboxylic acid (9). To a solution of ketone **4** (63 mg, 0.3 mmol) in acetonitrile (1 mL) was added cerium ammonium nitrate (CAN) (1.6 g, 2.4 mmol) in H_2O (2 mL). After stirring and heating (70 °C) for 1 h, cooling to room temperature, H_2O (2 mL) was added. The solution was filtered through celite, extracted with CH_2Cl_2, dried over $MgSO_4$ and concentrated. The crude solid was purified by chromatography on silica gel to give **9** (50 mg, 64% yield). Mp 167–168 °C; IR ν 3150, 1703, 1237, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.76 (s, 3H), 0.89 (d, *J* = 6.4 Hz, 3H), 1.07 (s, 3H), 1.11-2.71 (m, 11H); ^{13}C NMR ($CDCl_3$) δ 13.6 (q), 24.2 (q), 24.7 (q), 28.6 (t), 31.0 (t), 32.8 (t), 32.9 (t), 36.1 (t), 40.6 (t), 43.7 (s), 46.3 (d), 50.9 (s), 51.6 (d), 58.7 (d), 180.5 (s), 182.0 (s).

(1*S*, 3*R*, 5*R*, 8*R*)-1-[2-(Methoxycarbonyl)ethyl]-4,4,8-trimethylbicyclo[3.3.0]octan-3-ol (10). To a solution of the mixture **7** and **8** (31 mg, 0.14 mmol) in CH_2Cl_2 was added BF_3-Et_2O (17μL, 0.14 mmol) and anhydrous methanol (6 μL, 0.1 mmol). After 6 h at room temperature, a saturated solution of $NaHCO_3$ was added. After usual work up, the crude product was chromatographed on silica gel to give **8** (16 mg) and **10** (17 mg, 94% yield). **10**: IR ν 3449, 1731, 1267, 1175 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (s, 3H), 0.94 (s, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 1.15-1.80 (m, 11H), 2.27-2.38 (m, 2H), 3.65 (s, 3H), 3.77 (dd, *J* = 10.4, 6.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1 (q), 22.4 (q), 22.7 (q), 28.0 (t), 31.2 (t), 32.3 (t), 33.7 (t), 42.1 (t), 42.7 (s), 46.5 (d), 48.1 (s), 51.5 (q), 57.3 (d), 78.4 (d), 174.6 (s). Anal. calcd. for $C_{15}H_{26}O_3$: C, 70.80; H, 10.30. Found: C, 70.91; H, 10.37.

(1*S*, 5*R*, 8*R*)-1-[2-(Methoxycarbonyl)ethyl]-4,4,8-trimethylbicyclo[3.3.0]octan-3-one (11). A mixture of celite (300 mg), pyridinium chlorochromate (508 mg, 2.36 mmol), sodium acetate (96 mg, 1.2 mmol) was suspended in CH_2Cl_2 (50 mL) and stirred for 15 min. Then alcool **10** (300 mg, 1.18 mmol) was added. After 6 h of stirring, Et_2O was added (10 mL) and the mixture was filtered through celite and silicagel to

give **11** (283 mg, 95% yield). IR (neat) ν 1737, 1457, 1380, 1172 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (d, J = 6.6 Hz, 3H), 0.95 (s, 3H), 1.04 (s, 3H), 1.13-1.84 (m, 8H), 2.08 (d, J = 18.0 Hz, $1H_2$), 2.35 (d, J = 18.0 Hz, 1H), 2.03-2.32 (m, 2H), 3.65 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 13.8 (q), 21.8 (q), 25.1 (t), 28.6 (q), 28.9 (t), 30.2 (t), 32.5 (t), 44.7 (t), 45.5 (s), 48.2 (d), 48.5 (s), 51.7 (q), 55.0 (d), 174.4 (s), 223.1 (s). Anal. calcd. for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.22; H, 9.51.

(1*S*, 2*R*, 5*R*, 8*S*)-2,6,6-Trimethyltricyclo[6.3.0.0^{1,5}]octan-7,9-dione (12). Ketoester **11** (283 mg, 1.12 mmol) in THF (1 mL) was added to a cooled (0 °C) slurry of pentane-washed (4 x 5 mL) potassium hydride (35% dispersion in mineral oil, 200 mg, 1.7 mmol) in THF (7 mL). The resulting clear solution was stirred at room temperature for 1 h. The reaction mixture was quenched by addition of acetic acid (97μL, 1.17 mmol) and H_2O (30 mL). After removal of THF *in vacuo* the mixture was extracted with Et_2O (5 x 8 mL), dried over $MgSO_4$ and concentrated. The crude product was purified by chromatography on silica gel to give **12** (194 mg, 83% yield) as a white crystalline solid. **12**, mp 67-68 °C; $[\alpha]_{578}$ +56.3° (*c* 1, $CHCl_3$); IR (CCl_4) ν 1760, 1713, 1461, 1078 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (d, J = 6.9 Hz, 3H), 1.01 (s, 3H), 1.02 (s, 3H), 1.23-2.10 (m, 8H), 2.20 (m, 1H), 2.28 (dd, J = 8.3, 7.4 Hz, 1H), 2.91 (s, 1H); ^1H NMR (C_6D_6) δ 0.68 (d, J = 6.6 Hz, 3H), 0.94 (s, 3H), 0.98 (s, 3H), 1.10-1.80 (m, 8H), 1.80 (dd, J = 8.7, 5.4 Hz, 1H), 2.04 (dd, J = 8.7, 7.1 Hz, 1H), 2.76 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 14.6 (q), 22.4 (q), 25.1 (t), 27.4 (t), 27.7 (q), 34.1 (t), 38.4 (t), 42.3 (d), 50.0 (s), 56.3 (s), 58.0 (d), 68.0 (d), 209.3 (s), 213.7 (s). Anal. calcd. for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.39; H, 8.99.

(1*S*, 2*R*, 5*R*, 8*S*)-5,7,7,11-Tetramethyltricyclo[6.3.0.0^{1,5}]octan-4,6-dione (13). A mixture of dione **12** (16 mg, 0.07 mmol), acetone (3 mL), anhydrous K_2CO_3 (14 mg, 0.1 mmol) and methyl iodide (25 μL, 0.04 mmol) was stirred at room temperature for 24 h. The reaction mixture was filtered through celite and concentrated *in vacuo*. Chromatography on silica gel (Et_2O/petroleum ether 12/88) afforded the desired product **13** (16 mg, 97% yield) as a white crystalline solid. **13**, mp 66-67 °C; $[\alpha]_{578}$ +81.4° (*c* 1, CH_2Cl_2); IR (CCl_4) 1754, 1713, 1288, 1019 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (s, 3H), 0.96 (s, 3H), 0.99 (d, J = 6.3 Hz, 3H), 1.14 (s, 3H), 1.45-2.20 (m, 8H), 2.42 (dd, J = 9.8, 3.3 Hz, 1H), 2.44 (d, J = 9.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 15.7 (q), 16.1 (q), 22.4 (q), 23.4 (t), 24.2 (t), 28.5 (q), 34.5 (t), 36.0 (t), 37.6 (d), 48.3 (s), 56.3 (d), 60.3 (s), 67.9 (s), 213.3 (s), 217.0 (s). Anal. calcd. for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.79; H, 9.48.

(1*R*, 5*S*, 8*R*, 11*R*)-5,7,7,11-Tetramethyltricyclo[6.3.0.0^{1,5}]octan-2-en-4,6-dione (14). To a solution of diisopropylamine (20 μL, 0.12 mmol) in anhydrous THF (1 mL) stirred at -78 °C, was added *n*-butyllithium (75 μL, 1.5 M in hexane, 0.12 mmol). After 15 min, a solution of dione **13** (23 mg, 0.098 mmol) in THF (1 mL) was added and then a solution of phenylselenyl chloride (23 mg, 0.12 mmol) in THF (1 mL). The solution was allowed to warm to room temperature and acetic acid (12μL), H_2O (60 μL), 30% H_2O_2 (50 μL) were successively added. After 0.5 h, the reaction mixture was pourred into a saturated solution of Na_2CO_3 and extracted with Et_2O (5 x 3 mL). The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by chromatography on silica gel (Et_2O/petroleum ether 12/88) to give **14** (22 mg, 96 %) as a colorless oil. Mp 37-38 °C; $[\alpha]_{578}$ –382° (*c* 1, $CHCl_3$); IR (CCl_4) ν 1744, 1700, 1456, 1019 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (s, 3H), 0.95 (d, J = 7.1 Hz, 3H), 1.00, (s, 3H), 1.22 (s, 3H), 1.27-2.18 (m, 5H), 2.25 (dd, J = 11.3, 7.2 Hz, 1H), 6.06 (d, J = 5.6 Hz, 1H), 7.78 (d, J = 5.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 16.6 (q), 17.8 (q), 21.5 (q), 28.5 (q), 30.0 (t), 35.1 (t), 38.8 (d), 49.7 (s), 56.7 (d), 62.6 (s), 65.4 (s), 129.1 (d), 170.5 (d), 204.7 (s), 215.1 (s). Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.42; H, 8.54.

(1*S*, 5*R*, 8*R*, 11*R*)-3-Bromo-5,7,7,11-tetramethyltricyclo[6.3.0.0^{1,5}]octan-4,6-dione (15). Bromine (3 μL, 0.06 mmol) was added to a solution of dione **1** (14 mg, 0.06 mmol) in CCl_4 (4 mL). After 2 h,

the solution was clear and a 10% aqueous solution of $Na_2S_2O_3$ (3 mL) was added. The aqueous phase was extracted with CH_2Cl_2, and the combined organic phase dried over $MgSO_4$ and concentrated. The crude product was purified by chromatography on silica gel, eluting with Et_2O/petroleum ether (10/90) to afford **16** (4 mg, 17% yield) and **15** (11 mg, 60% yield). **15** (2 diastereomers, axial Br : equat. Br = 2 : 1): IR ($CHCl_3$) ν 1764, 1720, 1454, 1017, 755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (s, 3H), 0.98 (s, 3H), 1.00 (d, J = 6.4 Hz, 2H), 1.15 (d, J = 6.4 Hz, 1H), 1.27 (s, 2/3x3H), 1.29 (s, 1/3x3H), 1.41-2.81 (m, 8H), 4.40 (dd, J = 9.1, 4.0 Hz, 2/3x1H), 4.49 (dd, J = 11.4, 8.3 Hz, 1/3x1H). Anal. Calcd for $C_{15}H_{21}BrO_2$: C, 57.52; H, 6.76. Found: C, 57.49; H, 6.75. **(1*S*, 5*R*, 8*R*, 11*R*)-3,3-Dibromo-5,7,7,11-tetramethyltricyclo[6.3.0.0^{1,5}]octan-4,6-dione (16)**. ^1H NMR ($CDCl_3$) δ 1.00 (s, 3H), 1.11 (s, 3H), 1.43 (s, 3H), 1.00 (d, J = 6.2 Hz, 3H), 1.15-2.20 (m, 6H), 2.93 (d, J = 16.0 Hz, 1H), 3.23 (d, J = 16.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 16.2 (q), 19.7 (q), 23.6 (t), 23.8 (q), 26.9 (q), 34.7 (t), 39.5(d), 49.4 (s), 49.7 (t), 56.6 (d), 57.0 (s), 58.4 (s), 62.5 (s), 215.1 (s), 218.7 (s). Anal. Calcd for $C_{15}H_{20}Br_2O_2$: C, 45.95; H, 5.14. Found: C, 45.79; H, 5.08.

(1*S*, 5*R*, 8*R*, 11*R*)-3-Bromo-5,7,7,11-tetramethyltricyclo[6.3.0.0^{1,5}]octan-2-en-4,6-dione (17). Dione **16** (83 mg, 0.21 mmol) in N,N-dimethylacetamide (5 mL) containing $CaCO_3$ (50 mg, 0.5 mmol) was heated at 140 °C for 3h. After cooling to the room temperature, the solution was washed with brine, dried over $MgSO_4$. The crude product was purified by chromatography on silica gel (ether/petroleum ether 10/90) to afford **17** (50 mg, 76% yield) as a white crystalline solid. **17**, mp 121-122 °C; $[\alpha]_{578}$ –228° (*c* 1, $CHCl_3$); IR ($CHCl_3$) ν 1750, 1711, 1453, 1215 cm^{-1} ; ^1H NMR ($CDCl_3$) δ 0.89 (s, 3H), 0.97 (d, J = 7.4 Hz, 3H), 0.99 (s, 3H), 1.14 (s, 3H), 1.25 (s, 3H), 1.10-1.66 (m, 2H), 1.85-1.99 (m, 2H), 2.16 (dd, J = 11.9, 6.8 Hz, 1H), 2.28 (dd, J = 11.3, 7.4 Hz, 1H), 7.84 (s, 1H); $^{13}CNMR$ ($CDCl_3$) δ 16.7 (q), 18.1 (q), 21.4 (q), 28.2 (q), 29.9 (t), 34.9 (t), 38.9 (d), 49.5 (s), 56.7 (d), 62.2 (s), 64.1 (s), 120.9 (s), 167.3 (d), 213.6 (s), 217.9 (s). Anal. Calcd for $C_{15}H_{19}BrO_2$: C, 57.89; H, 6.15. Found: C, 57.83; H, 6.17.

Acknowledgement. We thank Dr R. Faure for his assistance in NMR measurements and Dr D. Joulain (Robertet, 06 Grasse, F) for helpful comments and his continuous interest. We thank the CNRS and the "Région Provence Alpes Côtes d'Azur" Council for a fellowship to MCP.

References and Notes

1. (a) Paquette, L. A. *Top. Cur. Chem.* **1979**, *79*, 41–73. (b) Paquette, L. A.; Doherty, A. M. *Polyquinane Chemistry, Syntheses and Reactions*, Springer: Berlin, 1987. (c) Mehta, G.; Srikrishna, A. *Chem. Rev.* **1997**, *97*, 671–719.
2. (a) Bohlmann, F.; Jakupovic, J. *Phytochemistry* **1980**, *19*, 259–265. (b) Shizuri, Y.; Ohkubo, M.; Yamamura, S. *Tetrahedron Lett.* **1989**, *30*, 3797–3798.
3. (a) Ihara, M.; Kawaguchi, A.; Ueda, H.; Chihiro, M.; Fukumoto, K.; Kametani, T. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1331–1337. (b) Ue, M.; Ohnishi, Y.; Kobiro, K.; Kakiuchi, K.; Tobe, Y.; Odaira, Y. *Chem. Lett.* **1990**, 149–150. (c) Bohlmann, F.; *J. Nat. Prod.* **1984**, *47*, 658.
4. Bohlmann, F. *Phytochemistry* **1982**, *21*, 139–142 and **1985**, *24*, 3048–3050.
5. Vandewalle, M.; De Clercq, P. *Tetrahedron* **1985**, *41*, 1767–1831 and references therein.
6. (a) Paquette, L. A.; Leone-Bay, A. *J. Org. Chem.* **1983**, *47*, 4173–4174. (b) Tsunoda, T.; Kodama, M.; Itô, S. *Tetrahedron Lett.* **1983**, *24*, 83–86. (c) Sternbach, D. D.; Hughes, J. W.; Burdi, D. F.; Banks, B. A. *J. Am. Chem. Soc.* **1985**, *107*, 2149–2153. (d) Wender, P. A.; Ternansky, R. J. *Tetrahedron Lett.* **1985**, *26*, 2625–2628. (e) Crimmins, M. T.; Mascarella, S. W. *Tetrahedron Lett.* **1987**, *28*, 5063–5066. (f) Rao, Y. K.; Nagarajan, M. *Tetrahedron Lett.* **1988**, *29*, 107–108.
7. (a) **Radical fragmentation:** Enholm, E. J.; Jia, Z. *Tetrahedron Lett.*, **1996**, *37*, 1177-1178; Lange, G. L.; Gottardo, C. *J. Org. Chem.*, **1995**, *60*, 2183-2187. (b) **Reductive fragmentation:** Rawal, V. H.;

Dufour, C. *J. Amer. Chem. Soc.* **1994**, *116*, 2913-2614. (c) **Tandem radical cyclization:** Yadav, J. S.; Praveen, K. T. K.; Gadgil, V. R. *Tetrahedron Lett.*, **1992**, *33*, 3687-3690; Schwartz, C. E.; Curran, D. P. *J. Amer. Chem. Soc.*, **1990**, *112*, 9272-9284; Curran, D. P.; Kou, S.-C. *Tetrahedron*, **1987**, *43*, 5653-5661. (d) **Zr-Promoted 1,6-diene Cyclization:** Saitoh, F.; Mori, M.; Okamura, K.; Date, T. *Tetrahedron*, **1995**, *51*, 4439-4446; Meyer, C.; Marek, I.; Normant, J.-F. *Tetrahedron Lett.*, **1996**, *37*, 857-860. (e) **Intramolecular Aldol Cyclization:** Iwata, Chuzo; Takemoto, Yoshiji; Doi, Miyako; Imanishi, Takeshi *J. Org. Chem.*, **1988**, *53*, 1623-1628; Paquette, L. A.; Galemmo, R. A.; Caille, J.-C.; Valpey, R. S. *J. Org. Chem.*, **1986**, *51*, 686-695; Paquette, L. A.; Roberts, R. A.; Drtina, G. J. *J. Amer. Chem. Soc.* **1984**, *106*, 6690-6693. (f) **Intramolecular Conjugate Addition:** Rawal, V. H.; Dufour, C.; Eschbach, A; *J. Chem. Soc., Chem. Commun.* **1994**, 1797-1798. (g) **Wolff rearrangement:** Ihara, M.; Katogi, M.; Fukumoto, K.; Kametani, T. *J. Chem. Soc. Perkin Trans. 1*, **1988**, 2963-2970. (h) **Spiroannulation:** Wu, Y.-J.; Zhu, Y.-Y.; Burnell, D. J. *J. Org. Chem.*, **1994**, *59*, 104-110. (i) **Intramolecular 1,3-Dipolar Cycloaddition of Nitrile Oxide (INOC):** Ihara, M.; Tokunaga, Y.; Taniguchi, N.; Fukumoto, K.; Kabuto, C. *J. Org. Chem.*, **1991**, *56*, 5281-5285. (j) **Silicon-assisted Nazarov Cyclization:** Franck-Neumann, M.; Miesch, M.; Gross, L. *Tetrahedron Lett.*, **1992**, *33*, 3879-3882; Franck-Neumann, M.; Miesch, M.; Lacroix, E. *Tetrahedron Lett.*, **1989**, *30*, 3533-3536.

8. Tori, M.; Matsuda, R.; Asakawa, Y. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2523–2525.
9. (a) Fetizon, M.; Le Bigot, Y.; Rens, J. *Tetrahedron* **1973**, *29*, 2815–2819. (b) Breitholle, E. G.; Fallis, A. G. *J. Org. Chem.* **1978**, *43*, 1964–1968. Norcedranone **4** is also available from α-cedrene **3** with a lower overall yield, see: Kaiser, R.; Lamparsky, D. *Helv. Chim. Acta* **1983**, *66*, 1843–1849.
10. Cocker, J. D.; Halsall, T. G. *J. Chem. Soc.* **1956**, 4262–4271.
11. Ferreira J.; Cruz, W.; Vieera, M., Yonashiro, M. *J. Org. Chem.* **1987**, *52*, 3698–3699.
12. Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936–3938.
13. Hirano, M.; Oose, M.; Morimoto, T. *Chem. Lett.* **1991**, 331-332.
14. Mehta, G.; Pandey, P. N. *Synthesis* **1975**, 404–405.
15. Murahashi, S.-I.; Oda, Y.; Naota, T. *Tetrahedron Lett.* **1992**, *33*, 7557–7560.
16. Inokuchi, T.; Kanazaki, M.; Sugimoto, T.; Torii, S. *Synlett* **1994**, 1037–1038.
17. Soucy, P.; Ho, T. -L.; Deslongchamps, P. *Can. J. Chem.* **1972**, *50*, 2047–2052.
18. Erdtman H., *Acta Chim. Scand.* **1960**, *14*, 2161–2168.
19. Kawamura, M.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1995**, 2403–2404.
20. Watanabe, H.; Mori, K. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2919–2934.
21. Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209–220 and 221–264.
22. Noyori, R.; Kobayashi, H.; Sato, T. *Tetrahedron Lett.* **1980**, *21*, 2573–2576.
23. (a) Criegee, R. *Liebigs Ann. Chem.* **1948**, *560*, 127–135. (b) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*, Pergamon Press: Oxford, 1984, p. 313.
24. (a) Pierrot, M.; El Idrissi, M.; Santelli, M. *Tetrahedron Lett.* **1989**, *30*, 461–462.
25. Deslongchamps, P. *Tetrahedron* **1975**, *31*, 2463–2490.
26. (a) Barco, A.; Benetti, S.; Pollini, G. P. *Synthesis* **1973**, 316. (b) Kataoka, H.; Yamada, T.; Goto, K.; Tsuji, J. *Tetrahedron* **1987**, *43*, 4107–4112.
27. Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Amer. Chem. Soc.* **1975**, *97*, 5434–5447.
28. Bauer, K.; Garbe, D.; Surburg, H. *Common Fragrance and Flavor Materials* Wiley-VCH: Weinheim, 3° Edition, 1997, p. 175.