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TETRAHEDRON

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

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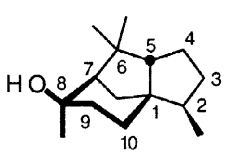
Abstract: Angular triquinanes such as (+)-silphinan-3,5-dione, silphin-3-en-3,5-dione or 2-bromosilphin-3-en-3,5-dione have been obtained from (+)-β-cedrene in seven steps and an overall yield of 8%.

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**.



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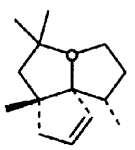
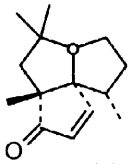
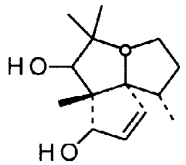


Silphinene



(±)-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,[7c] 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**.

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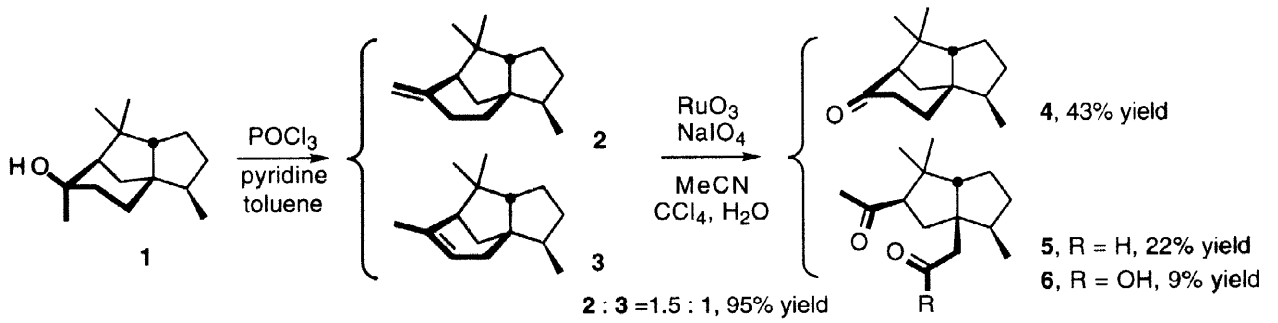


Without any attempts to separate **2** from **3**, the mixture was subjected to ozonolysis providing the desired ketone **4** in low yield (15%). When using $KMnO_4$ dispersed on silica gel[11] for oxidative cleavage only 6% of **4** formed. Rewardingly, RuO_4 generated in situ[12] yielded **4** in an 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).

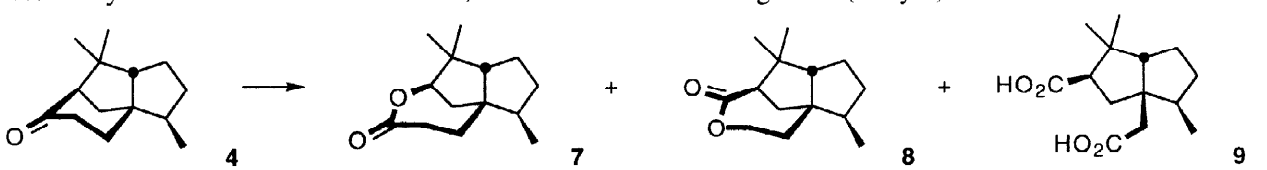


Table 1. Baeyer-Villiger Oxidation of Cedranone 4.

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.

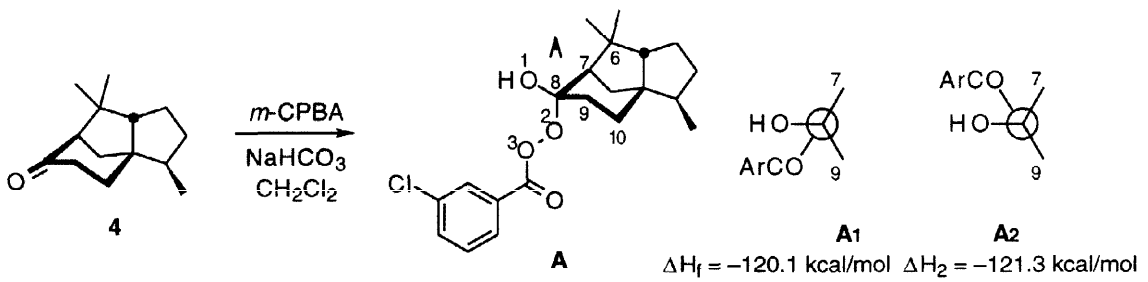
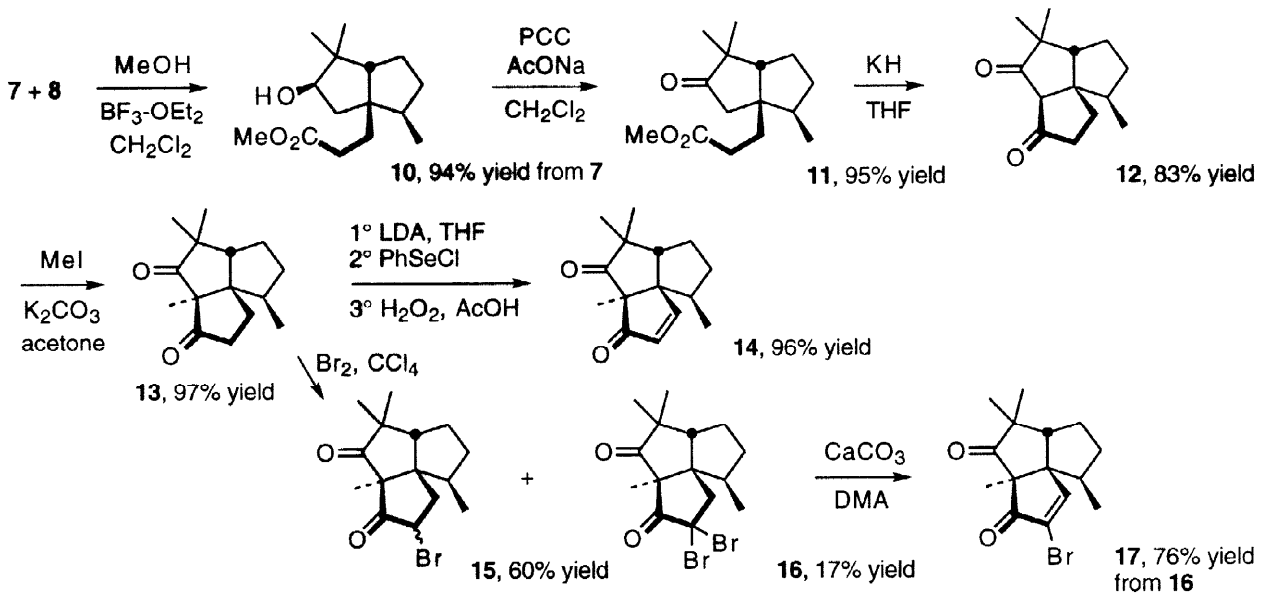


Table 2. PM3 Calculations of **A1** and **A2**.

	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 $RuCl_3$.3 H_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.

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