7,7-Dimethyltricyclo[3.3.0.0^{2,8}]octan-3-ones as Synthetic Intermediates. V.[1] An Improved Synthesis of (±)-Pentalenene

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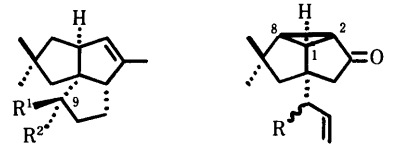
Improved synthetic routes to (±)-pentalenene (1) and (±)-9-epipentalenene (6) were developed. Intramolecular alkylation of a tricyclic halo ester (7), obtained from 3, by treatment with lithium hexamethyldisilazide in tetrahydrofuran gave 14 and 15 in a ratio of 74:26. Compound 14 was successfully converted into the key intermediate (16) for (±)-1. On the other hand, catalytic hydrogenation of 8 afforded 20, a key intermediate for (±)-6, along with 16 (20:16=86:14).

Keywords pentalenene; 9-epipentalenene; formal synthesis; tricyclo[3.3.0.0^{2,8}]octane; tetracyclo[6.3.0.0^{2,11}.0^{4,8}]undecane; intramolecular alkylation; catalytic hydrogenation; kinetic control

In the preceding paper,[2] we reported a total synthesis of (±)-pentalenene (**1**),[3] an angular triquinane sesquiterpene, *via* a regioselective C_2–C_8 cyclopropane bond cleavage of a tricyclo[3.3.0.0^{2,8}]octan-3-one (**2**). Nevertheless, the synthesis was non-stereoselective because the intermediate (**2**) was only prepared as a *ca.* 1:1 diastereomeric mixture. On the other hand, we also reported a regioselective C_1–C_2 bond cleavage of the tricyclooctanone (**3**) to give compound **4**, which was successfully transformed into (±)-descarboxyquadrone (**5**).[4] This paper deals with a stereoselective synthesis of (±)-pentalenene (**1**) and its isomer, (±)-9-epipentalenene (**6**), utilizing **3** as the common starting material.

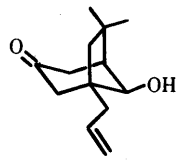
The present synthetic plan involves two crucial steps. One is a stereoselective intramolecular alkylation of the bromo ester (**7**) and the other a catalytic hydrogenation of the *exo*-methylene intermediate (**8**).

First of all, compound **7** was prepared from **3** as follows. Base-induced alkylation of the tricyclo[3.3.0.0^{2,8}]octan-3-one ring system is well-known to afford the C_4-alkylated product because regioselectivity of the enolate formation is strictly controlled by the cyclopropane ring adjacent to the



1 : R^1=Me, R^2=H
6 : R^1=H, R^2=Me

2 : R=Me
3 : R=H



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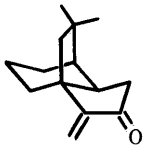

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Chart 1

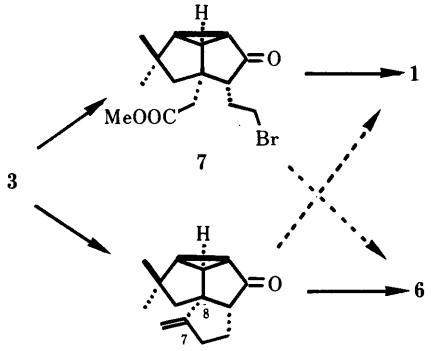

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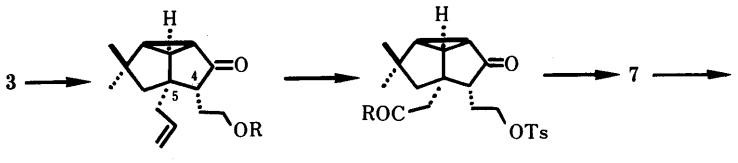
Chart 2



9 : R=THP
10 : R=H
11 : R=Ts

12 : R=H
13 : R=OMe

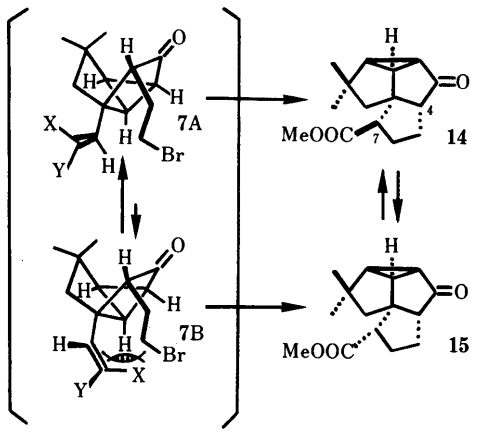


Chart 3

carbonyl. Furthermore, the alkylation proceeds exclusively from the same side of the C_5-substituent for steric reasons.[5] Treatment of **3** with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) in the presence of hexamethylphosphoric triamide (HMPA) at −78 °C followed by reaction with 2-[(tetrahydropyran-2-yl)oxy]ethyl bromide[6] afforded the desired product (**9**) as a sole alkylated compound in 64% yield along with the starting material (24%).

Detetrahydropyranylation of **9** to **10** and subsequent tosylation in the usual manner gave **11** (80% from **9**), which was subjected to ozonolysis followed by reductive work-up to afford the aldehyde (**12**) in 89% yield. Oxidation of **12** with chromic trioxide and then treatment with diazomethane in ether afforded the ester (**13**) in 60% yield. Compound **13** was quantitatively converted into the bromide (**7**) on reaction with lithium bromide in acetone.

In the intramolecular alkylation of **7**, there must be two different transition states **7A** and **7B**: **7A** is the transition state for **14** possessing the same stereochemistry as pentalenene (**1**) and **7B** is that for **15**. From inspection of the Dreiding model, the former (**7A**) is easily expected to be more stable than the latter because **7B** has a severe $A^{1,3}$-strain. This consideration brings us to the assumption that the desired compound **14** would be formed more easily than **15** by intramolecular alkylation of **7**, at least under kinetically controlled conditions.

The intramolecular alkylation of **7** was examined under various conditions. The positive results are summarized in Table I. Two diastereomeric tetracyclic compounds (**14** and **15**) were produced as a mixture in all runs and were separable from each other by high-performance liquid chromatography (HPLC). The stereochemistry of the products was confirmed by their proton nuclear magnetic resonance (^{1}H-NMR) spectra. The C-4 proton signal in **14** appeared at 3.09 ppm (triplet, J=5 Hz), whereas that in **15** resonated at 2.65 ppm. This phenomenon could be attributed to the *cis* relationship between the C-4 proton and C-7 methoxycarbonyl group in **14**. Starting from each isomer, the same equilibrium mixture (**14**:**15**=*ca.* 45:55) was reached in the presence of sodium methoxide in boiling methanol. A similar equilibrium result was also reported in the case of the angular triquinane ring system.[7] The data in Table I are consistent with the following conclusions.

1) The ratio of the two products (**14**:**15**) in run 1 or 3 is almost the same as that in the equilibrium mixture mentioned above and therefore the reactions are controlled thermodynamically. In other words, the initially formed products isomerized to each other within the reaction time under the conditions employed.

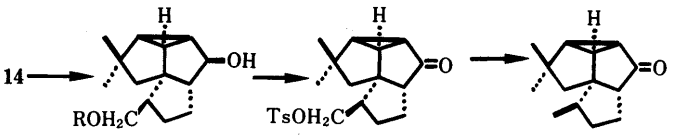
2) The ratio obtained in run 2 or 4 is compatible with the above argument. These results should be due to kinetically controlled intramolecular alkylation.

3) In run 2, the use of a less bulky base (LDA in a nonpolar solvent) seems to have caused side reactions, which may be initiated to a large extent by abstraction of the C-4 hydrogen, and consequently the yield of the normally cyclized products (**14** and **15**) is very low.

4) The desired compound (**14**) was effectively obtainable (**14**:**15**=*ca.* 3:1, total yield 90%) in run 4.

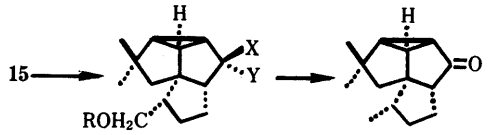
Transformation of **14** into a key intermediate (**16**) was straightforward, as follows. Reduction of **14** with lithium aluminum hydride (LAH) in ether at room temperature afforded the diol (**17**) as a single diastereomer. Tosylation of **17** in the usual manner afforded **18** (75% yield), which was subjected to oxidation with pyridinium chlorochromate (PCC) to produce the ketone (**19**) quantitatively. Reductive removal of the tosyloxy group in **19** was accomplished by treatment with zinc dust and sodium iodide in boiling dimethoxyethane (DME)[8] to give **16** (83% yield), which was previously converted into (±)-pentalenene (**1**) in a 3-step sequence by us.[2] Compound **15** was also converted into the isomer (**20**) similarly (**15**→**21**→**22**→**23**→**20**).

On the other hand, the *exo*-methylene ketone (**8**) was prepared from the aldehyde (**12**) as shown in Chart 5:



17 : R=H
18 : R=Ts

19 16



21 : R=H, X=OH, Y=H
22 : R=Ts, X=OH, Y=H
23 : R=Ts, X+Y=O

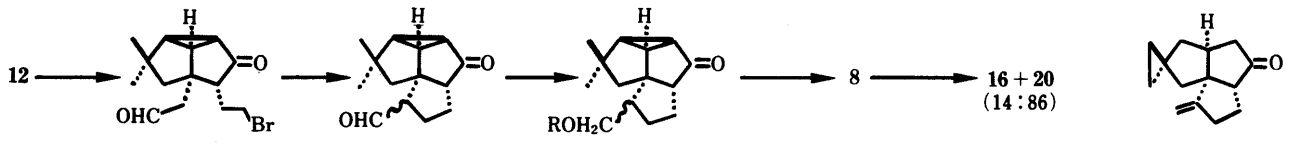
20

Chart 4

Table I. Intramolecular Alkylation of 7

Run	Reaction conditions	Yield (%)	Ratio (**14**:**15**)[a,b]
1	*tert*-BuOK, THF, 0 °C, 2 h	85	47:53
2	LDA, THF, −78 °C, 1 h	16	78:22
3	LDA, HMPA, THF, −78 °C, 30 min	77	39:61
4	LHMDS, THF, −78 °C, 1 h	90	74:26

a) The ratios were determined by capillary GLC analysis. *b*) The same equilibrium mixture (**14**:**15**=45:55) was obtained from each isomer on treatment with NaOMe in MeOH.



24 25 26 : R=H
27 : R=Ts

28

Chart 5

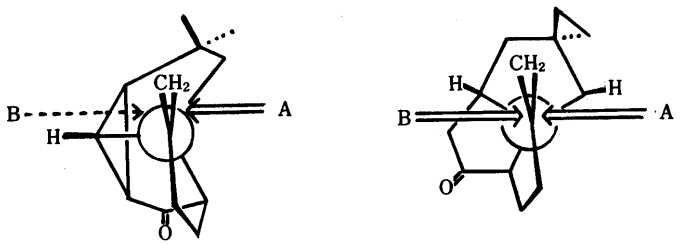


Fig. 1. Newman Projections of **8** and **28** Viewing the Molecules from C-7 along the C_7–C_8 Bond

replacement of the tosyloxy group with bromine (**12**→**24**), intramolecular alkylation (**24**→**25**), reduction of the aldehyde with sodium borohydride (**25**→**26**), tosylation (**26**→**27**), and treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and sodium iodide[9] (**27**→**8**). Compound **8**, possessing a tetracyclo[6.3.0.0.^{2,11}.$0^{4,8}$]undecane ring system, exists in a rigid conformation as depicted in Fig. 1, which indicates that addition reaction to the carbon–carbon double bond of **8** would predominantly occur from the less hindered side (A) rather than the B-side. In fact, catalytic hydrogenation of **8** over 5% palladium on carbon in methanol under atmospheric pressure of hydrogen at room temperature gave the expected product (**20**), which was also converted into (±)-9-epipentalenene (**6**),[10] along with a small amount of its isomer (**16**) (**20**:**16**=86:14). In comparison with the finding that hydrogenation of compound **28**, a 2,11-seco congener of **8**, gave only a *ca.* 1:1 diastereomeric mixture,[11] the present result is quite interesting.

In conclusion, the key intermediates (**16** and **20**) for (±)-pentalenene (**1**) and (±)-epipentalenene (**6**) were both stereoselectively synthesized from the common starting material (**3**) *via* an intramolecular alkylation of **7** and catalytic hydrogenation of **8**, respectively.

Experimental

Melting points are uncorrected. The infrared (IR) spectra were recorded with a Hitachi 260-10 spectrometer. ^{1}H-NMR spectra were measured with a Hitachi R-22 (90 MHz) or a JEOL FX-90Q (90 MHz) with tetramethylsilane as an internal standard. The mass spectra (MS) and high-resolution MS (High MS) were obtained with a Shimadzu QP-1000 or a JEOL JMS-D300 mass spectrometer. For column chromatography, Silica gel 60 (E. Merck) was used. Capillary gas-liquid chromatography (capillary GLC) was run on a Shimadzu GC-14A with a CBP-M25-025 column.

(1*RS*,2*SR*,4*SR*,5*RS*,8*SR*)-7,7-Dimethyl-5-(2-propen-1-yl)-4-[2-[(tetrahydropyran-2-yl)oxy]ethyl]tricyclo[3.3.0.0^{2,8}]octan-3-one (9) A solution of **3** (475 mg, 2.5 mmol) in THF (5 ml) was added dropwise to a THF solution of LDA [prepared from *n*-BuLi (1.6 M, 3.9 ml, 5.5 mmol) and diisopropylamine (iso-Pr_2NH) (556 mg, 5.5 mmol) in THF (10 ml)] at −78 °C under stirring. Stirring was continued at this temperature for 20 min and HMPA (2 ml) was added. After 15 min, a solution of 2-[(tetrahydropyran-2-yl)oxy]ethyl bromide (1.05 g, 5.0 mmol) in THF (5 ml) was added dropwise, and the reaction temperature was gradually raised to room temperature. Saturated NH_4Cl solution was added to the reaction mixture and the whole was extracted with ether. The extract was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (10:1) to give the starting material (115 mg) and **9** (507 mg, 64%) as a colorless oil. IR (CCl_4) cm^{-1}: 3080, 3040, 3010, 1720, 1640, 1050, 985, 920. ^{1}H-NMR (CCl_4) δ: 1.10 and 1.18 (each 3H, s, 7-Me×2), 3.2—4.0 (4H, m, CH_2O–CH–OCH_2–), 4.51 (1H, m, O–CH–O–), 4.9—5.3 (2H, m, CH=CH_2), 5.4—6.0 (1H, m, CH=CH_2). MS *m/z* (%): 318 (M^+, 0.15), 190 (100). High MS Calcd for $C_{20}H_{30}O_3$: 318.2192. Found: 318.2189.

(1*RS*,2*SR*,4*SR*,5*RS*,8*SR*)-4-(2-Hydroxyethyl)-7,7-dimethyl-5-(2-propen-1-yl)tricyclo[3.3.0.0^{2,8}]octan-3-one (10) A mixture of **9** (436 mg, 1.4 mmol), acetone (20 ml), and 1 N HCl (20 ml) was stirred at room temperature for 12 h. The acetone was evaporated off, and the residue was extracted with ether. The extract was washed with saturated $NaHCO_3$ and brine, dried, and evaporated. The crude product was chromatographed on silica gel with hexane–AcOEt (2:1) to give **10** (320 mg, 100%) as a colorless oil. IR ($CHCl_3$) cm^{-1}: 3600, 3450, 3080, 3040, 1705, 1640, 1080, 1040, 980, 920. ^{1}H-NMR ($CDCl_3$) δ: 1.10 and 1.20 (each 3H, s, 7-Me×2), 1.40 and 2.05 (each 1H, d, *J*=14 Hz, 6-CH_2), 2.65 (1H, br, OH), 3.74 (2H, m, CH_2OH), 5.0—5.3 (2H, m, CH=CH_2), 5.5—6.0 (1H, m, CH=CH_2). MS *m/z* (%): 234 (M^+, 0.69), 190 (100). High MS Calcd for $C_{15}H_{22}O_2$: 234.1620. Found: 234.1628.

(1*RS*,2*SR*,4*SR*,5*RS*,8*SR*)-7,7-Dimethyl-5-(2-propen-1-yl)-4-[2-(*p*-tosyloxy)ethyl]tricyclo[3.3.0.0^{2,8}]octan-3-one (11) A solution of **10** (1.2 g, 5.1 mmol), triethylamine (Et_3N) (3.0 ml), dimethylaminopyridine (DMAP) (20 mg), and *p*-toluenesulfonyl chloride (*p*-TsCl) (1.95 g, 10.2 mmol) in methylene chloride (60 ml) was stirred at room temperature for 16 h. The reaction mixture was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (5:1) to give **11** (1.6 g, 80%) as colorless needles, mp 84.0—85.0 °C (from hexane). IR (CCl_4) cm^{-1}: 1720, 1640, 1600, 1195, 1185, 980, 920. ^{1}H-NMR (CCl_4) δ: 1.02 and 1.13 (each 3H, s, 7-Me×2), 2.42 (3H, s, aromatic Me), 3.9—4.2 (2H, m, –CH_2O–), 4.9—5.2 (2H, m, CH=CH_2), 5.3—5.9 (1H, m, CH=CH_2), 7.22 and 7.68 (each 2H, d, *J*=8 Hz, aromatic H×4). MS *m/z* (%): 388 (M^+, 2.4), 233 (100). *Anal.* Calcd for $C_{22}H_{28}O_4S$: C, 68.01; H, 7.26; S, 8.25. Found: C, 67.76; H, 7.47; S, 8.06.

(1*RS*,2*SR*,4*SR*,5*SR*,8*SR*)-7,7-Dimethyl-3-oxo-4-[2-(*p*-tosyloxy)ethyl]tricyclo[3.3.0.0^{2,8}]octane-5-acetaldehyde (12) Dry ozone was passed into a solution of **11** (1.1 g, 2.8 mmol) in methylene chloride (30 ml) at −78 °C until the starting material had disappeared on thin layer chromatography (TLC). Then excess ozone was removed by flushing the reaction mixture with dry N_2. Zinc dust (1.0 g, 15 mmol) and acetic acid (2.0 ml) were added, and the whole was stirred at 0 °C for 2 h. After removal of the solids by filtration, the filtrate was washed thoroughly with saturated $NaHCO_3$ and then brine, dried, and evaporated. The crude product was chromatographed on silica gel with hexane–AcOEt (1:1) to give **12** (952 mg, 89%) as a colorless oil. IR (CCl_4) cm^{-1}: 1725, 1195, 1180. ^{1}H-NMR ($CDCl_3$) δ: 1.04 and 1.20 (each 3H, s, 7-Me×2), 2.42 (3H, s, aromatic Me), 2.82 (2H, m, CH_2CHO), 4.0—4.3 (2H, m, CH_2OTs), 7.33 and 7.73 (each 2H, d, *J*=8 Hz, aromatic H×4), 9.82 (1H, t, *J*=1 Hz, CHO). MS *m/z* (%): 390 (M^+, 0.99), 218 (100). High MS Calcd for $C_{21}H_{26}O_5S$: 390.1498. Found: 390.1483.

Methyl (1*RS*,2*SR*,4*SR*,5*SR*,8*SR*)-7,7-Dimethyl-4-[2-(*p*-tosyloxy)ethyl]tricyclo[3.3.0.0^{2,8}]octane-5-acetate (13) The Jones reagent[12] was added dropwise to a solution of **12** (952 mg, 2.4 mmol) in purified acetone (30 ml) until the color of the reagent persisted for more than 5 min. Excess reagent was decomposed by addition of 2-propanol, then the solvent was removed *in vacuo*. Water was added to the residue, and the whole was extracted with ether. The extract was washed with brine, dried and evaporated to give a carboxylic acid as a colorless oil. IR ($CHCl_3$) cm^{-1}: 3500—2500, 1715, 1380, 1175. ^{1}H-NMR ($CDCl_3$) δ: 1.06 and 1.20 (each 3H, s, 7-Me×2), 1.67 and 2.02 (each 1H, d, *J*=14 Hz, 6-CH_2), 2.40 (3H, s, aromatic Me), 2.70 and 2.73 (each 1H, d, *J*=17 Hz, CH_2COOH), 4.15 (2H, t, *J*=7 Hz, CH_2OTs), 7.29 and 7.55 (each 2H, d, *J*=9 Hz, aromatic H×4), 8.92 (1H, br, COOH). MS *m/z* (%): 406 (M^+, 1.3), 234 (100). An ethereal solution of diazomethane was added in excess to a solution of the carboxylic acid in ether, and the mixture was stirred for 30 min. Evaporation of the excess reagent and solvent left a crude product, which was chromatographed on silica gel with hexane–AcOEt (2:1) to give **13** (620 mg, 60%) as colorless needles, mp 96.0—97.0 °C (from benzene–hexane). IR (CCl_4) cm^{-1}: 1740, 1720, 1370, 1190, 1180. ^{1}H-NMR (CCl_4) δ: 1.04 and 1.18 (each 3H, s, 7-Me×2), 1.57 and 1.96 (each 1H, d, *J*=14 Hz, 6-CH_2), 2.44 (3H, s, aromatic Me), 2.56 and 2.70 (each 1H, d, *J*=16 Hz, CH_2COOMe), 3.64 (3H, s, COOMe), 3.9—4.3 (2H, m, CH_2OTs), 7.30 and 7.72 (each 2H, d, *J*=8 Hz, aromatic H×4). MS *m/z* (%): 420 (M^+, 8.9), 248 (100). *Anal.* Calcd for $C_{22}H_{28}O_6S$: C, 62.84; H, 6.71; S, 7.62. Found: C, 62.81; H, 6.73; S, 7.63.

Methyl (1*RS*,2*SR*,4*SR*,5*SR*,8*SR*)-4-(2-Bromoethyl)-7,7-dimethyltricyclo[3.3.0.0^{2,8}]octane-5-acetate (7) A suspension of **13** (604 mg, 1.4 mmol) and LiBr (250 mg, 2.9 mmol) in acetone (15 ml) was refluxed for 15 h. The acetone was evaporated off, then water was added, and the whole was extracted with ether. The extract was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (7:1) to give **7** (443 mg, 94%) as colorless crystals, mp 115.0—116.0 °C (from hexane). IR ($CHCl_3$) cm^{-1}: 1720. ^{1}H-NMR ($CDCl_3$) δ:

1.11 and 1.21 (each 3H, s, 7-Me × 2), 1.68 and 2.02 (each 1H, d, J=13 Hz, 6-CH_2), 2.68 and 2.73 (each 1H, d, J=15 Hz, CH_2COOMe), 3.40—3.65 (2H, m, CH_2Br), 3.68 (3H, s, COOMe). MS m/z (%): 330 (M^+ for ^{81}Br, 1.4), 328 (M^+ for ^{79}Br, 1.3), 74 (100). *Anal.* Calcd for $C_{15}H_{21}BrO_3$: C, 54.83; H, 6.51; Br, 24.27. Found: C, 54.83; H, 6.51; Br, 24.09.

Intramolecular Cyclization of 7 a) With Potassium *tert*-Butoxide (*tert*-BuOK) (Run 1): *tert*-BuOK (128 mg, 1.14 mmol) was added portionwise to a solution of **7** (313 mg, 0.95 mmol) in THF (5 ml) at 0 °C, and the mixture was stirred for 2 h at 0 °C. Saturated NH_4Cl solution was added, and the whole was extracted with ether. The extract was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (5:1) to give a mixture of methyl (1*RS*,2*SR*,4*SR*,7*SR*,8*SR*,11*SR*)- and (1*RS*,2*SR*,4*SR*,7*RS*,8*SR*,11*SR*)-10,10-dimethyl-3-oxotetracyclo[6.3.0.0^{2,11}.0^{4,8}]octane-7-carboxylate (**14** and **15**) (total 200 mg, 85%). The ratio of **14** and **15** was determined to be 47:53 by means of a capillary GLC analysis (retention times were 7.2 min for **14** and 7.5 min for **15** at 200 °C). Each component was separable by HPLC (Waters, μ-Porasil semiprep.) with hexane–AcOEt (5:1). **14**: white amorphous solid. IR (CCl_4) cm^{-1}: 1740, 1720. ^{1}H-NMR (CCl_4) δ: 1.07 and 1.24 (each 3H, s, 10-Me × 2), 1.52 and 2.07 (each 1H, d, J=13 Hz, 9-CH_2), 2.56 (1H, dd, J=12, 5 Hz, CHCOOMe), 3.09 (1H, t, J=5 Hz, 4-H), 3.67 (3H, s, COOMe). MS m/z (%): 248 (M^+, 88), 188 (100). High MS Calcd for $C_{15}H_{20}O_3$: 248.1411. Found: 248.1427. **15**: colorless oil. IR (CCl_4) cm^{-1}: 1740, 1720. ^{1}H-NMR (CCl_4) δ: 1.06 and 1.23 (each 3H, s, 10-Me × 2), 1.46 and 2.35 (each 1H, d, J=13 Hz, 9-CH_2), 2.65 (1H, t, J=5 Hz, 4-H), 2.78 (1H, dd, J=10, 7 Hz, CHCOOMe), 3.77 (3H, s, COOMe). MS m/z (%): 248 (M^+, 18), 188 (100). High MS Calcd for $C_{15}H_{20}O_3$: 248.1411. Found: 248.1411.

b) With LDA in THF (Run 2): A solution of **7** (50 mg, 0.15 mmol) in THF (1 ml) was added to a THF (3 ml) solution of LDA (0.30 mmol) at −78 °C, and the mixture was stirred for 1 h. Saturated NH_4Cl solution was added, and the whole was extracted with ether. The extract was washed with brine, dried, and evaporated. The residue was purified as described above to give a mixture of **14** and **15** (total 6 mg, 16%) in 78:22 ratio.

c) With LDA in THF–HMPA (Run 3): HMPA (0.3 ml) and a solution of **7** (50 mg, 0.15 mmol) in THF (1 ml) was added to a THF solution of LDA (0.20 mmol) at −78 °C, and the mixture was stirred for 30 min. Work-up as described above gave a mixture of **14** and **15** (total 29 mg, 77%) in 39:61 ratio.

d) With Lithium Hexamethyldisilazide (LHMDS) in THF (Run 4): LHMDS (0.5 M, 1.2 ml) was added to a solution of **7** (50 mg, 0.15 mmol) in THF (1 ml) at −78 °C, and the mixture was stirred for 1 h. Work-up as described above gave a mixture of **14** and **15** (total 34 mg, 90%) in 74:26 ratio.

Base-Catalyzed Isomerization of 14 and 15 Each ester (*ca.* 10 mg) was treated with *ca.* 10 eq of NaOMe in MeOH under reflux for 2.5 h. The reaction mixture was neutralized with acetic acid, and the MeOH was evaporated off. The residue was extracted with ether and the extract was washed with brine, dried, and evaporated. Each crude product was found to contain **14** and **15** in the same ratio (45:55) by means of HPLC analysis.

(1*RS*,2*SR*,3*SR*,4*SR*,7*SR*,8*RS*,11*SR*)-7-Hydroxymethyl-10,10-dimethyltetracyclo[6.3.0.0^{2,11}.0^{4,8}]undecan-3-ol (17) LAH (28 mg, 0.74 mmol) was added portionwise to a stirred solution of **14** (92 mg, 0.37 mmol) in ether (5 ml) at 0 °C, and the mixture was stirred for 12 h at room temperature. Saturated Rochelle salt solution was slowly added in small portions at 0 °C to the well-stirred reaction mixture until the greyish precipitates turned white. After the precipitates had been filtered off, the filtrate was dried, and concentrated. The residue was chromatographed on silica gel with hexane–AcOEt (1:1) to give **17** (57 mg, 69%) as a colorless oil. IR ($CHCl_3$) cm^{-1}: 3620, 3450, 3020. ^{1}H-NMR ($CDCl_3$) δ: 1.21 and 1.35 (each 3H, s, 10-Me × 2), 2.42 (2H, s, OH × 2), 3.26 (1H, dd, J=10, 9 Hz, one of CH_2OH), 3.49 (1H, dd, J=10, 6 Hz, one of CH_2OH), 4.46 (1H, dd, J=2.5 Hz, 3-H). MS m/z (%): 220 (M^+, 1.3), 173 (100). High MS Calcd for $C_{14}H_{22}O_2$: 222.1619. Found: 222.1619.

(1*RS*,2*SR*,3*SR*,4*SR*,7*SR*,8*RS*,11*SR*)-10,10-Dimethyl-7-[(*p*-tosyloxy)methyl]tetracyclo[6.3.0.0^{2,11}.0^{4,8}]undecan-3-ol (18) *p*-TsCl (148 mg, 0.78 mmol), DMAP (catalytic amount), and Et_3N (0.1 ml) were added to a solution of **17** (57 mg, 0.26 mmol) in methylene chloride (5 ml), and the whole was stirred at room temperature for 12 h. *p*-TsCl (148 mg, 0.78 mmol), DMAP (catalytic amount), and Et_3N (0.1 ml) were added again, and the mixture was stirred for 12 h. This procedure was repeated 3 times. The reaction mixture was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (3:1→1:1) to give **18** (72 mg, 75%) as a colorless oil. IR ($CHCl_3$) cm^{-1}: 3610, 3040, 3000, 1600, 1500, 1370, 1190, 1180. ^{1}H-NMR ($CDCl_3$) δ: 1.17 and 1.31 (each 3H, s, 10-Me × 2), 2.42 (3H, s, aromatic Me), 3.70 (1H, dd, J=10, 8 Hz, one of CH_2OH), 3.85 (1H, dd, J=10, 6 Hz, one of CH_2OH), 4.42 (1H, dd, J=5, 2 Hz, 3-H), 7.29 and 7.70 (each 2H, d, J=9 Hz, aromatic H × 4). MS m/z (%): 376 (M^+, 0.2), 186 (100). High MS Calcd for $C_{21}H_{28}O_4S$: 376.1709. Found: 376.1724.

(1*RS*,2*SR*,4*SR*,7*SR*,8*RS*,11*SR*)-10,10-Dimethyl-7-[(*p*-tosyloxy)methyl]tetracyclo[6.3.0.0^{2,11}.0^{4,8}]undecan-3-one (19) PCC (50 mg, 0.23 mmol) was added portionwise to a solution of **18** (72 mg, 0.19 mmol) in methylene chloride (5 ml) at room temperature, and the whole was stirred for 1.5 h. The mixture was diluted with ether, and passed through a Florisil column. The eluate was concentrated and chromatographed on silica gel with hexane–AcOEt (2:1) to give **19** (72 mg, 100%) as a colorless oil. IR ($CHCl_3$) cm^{-1}: 3040, 3010, 1710, 1600, 1500, 1370, 1190, 1180. ^{1}H-NMR ($CDCl_3$) δ: 1.01 and 1.18 (each 3H, s, 10-Me × 2), 2.45 (3H, s, aromatic Me), 3.78 (1H, dd, J=10, 8 Hz, one of CH_2OTs), 3.95 (1H, dd, J=10, 6 Hz, one of CH_2OTs), 7.30 and 7.71 (each 2H, d, J=8 Hz, aromatic H × 4). MS m/z (%): 374 (M^+, 10.6), 202 (100). High MS Calcd for $C_{21}H_{26}O_4S$: 374.1550. Found: 374.1525.

(1*RS*,2*SR*,4*SR*,7*SR*,8*SR*,11*SR*)-7,10,10-Trimethyltetracyclo[6.3.0.0^{2,11}.0^{4,8}]undecan-3-one (16) from 19 A suspension of **19** (42 mg, 0.11 mmol), NaI (83 mg, 0.55 mmol), and Zn (72 mg, 1.10 mg-atom) in DME (3 ml) was refluxed for 1 h. After filtration, the filtrate was washed with $Na_2S_2O_3$ solution and brine, then dried, and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (10:1) to give **16** (19 mg, 83%) as a colorless oil, which was identical with an authentic sample.[2]

(1*RS*,2*SR*,3*SR*,4*SR*,7*RS*,8*RS*,11*SR*)-7-Hydroxymethyl-10,10-dimethyltetracyclo[6.3.0.0^{2,11}.0^{4,8}]undecan-3-ol (21) Compound **15** (135 mg) was converted into **21** (62 mg, 52%) in a manner similar to that described for **14**→**17**. Colorless needles, mp 62.0—65.0 °C. IR ($CHCl_3$) cm^{-1}: 3620, 3020. ^{1}H-NMR ($CDCl_3$) δ: 1.18 and 1.35 (each 3H, s, 10-Me × 2), 1.57 and 2.04 (each 1H, d, J=13 Hz, 9-H_2), 2.67 (2H, s, OH × 2), 3.71 (1H, dd, J=10, 8 Hz, one of CH_2OH), 3.87 (1H, dd, J=10, 4 Hz, one of CH_2OH), 4.44 (1H, dd, J=5, 2 Hz, 3-H). MS m/z (%): 222 (M^+, 3.0), 173 (100). High MS Calcd for $C_{14}H_{22}O_2$: 222.1617. Found: 222.1600.

(1*RS*,2*SR*,3*SR*,4*SR*,7*RS*,8*RS*,11*SR*)-10,10-Dimethyl-7-[(*p*-tosyloxy)methyl]tetracyclo[6.3.0.0^{2,11}.0^{4,8}]undecan-3-ol (22) Compoun **21** (62 mg) was converted into **22** (86 mg, 82%) in a manner similar to that described for **17**→**18**. A colorless oil. IR ($CHCl_3$) cm^{-1}: 3620, 3020, 1600, 1500, 1370, 1190, 1180. ^{1}H-NMR ($CDCl_3$) δ:1.16 and 1.32 (each 3H, s, 10-Me × 2), 1.53 and 1.93 (1H, d, J=13 Hz, 9-H_2), 2.44 (3H, s, aromatic Me), 4.16 (1H, dd, J=10, 8 Hz, one of CH_2OTs), 4.21 (1H, dd, J=10, 6 Hz, one of CH_2OTs), 4.38 (1H, dd, J=6, 2 Hz, 3-H), 7.30 and 7.75 (each 2H, d, J=8 Hz, aromatic H × 4). MS m/z (%): 376 (M^+, 0.2), 186 (100).

(1*RS*,2*SR*,4*SR*,7*RS*,8*RS*,11*SR*)-10,10-Dimethyl-7-[(*p*-tosyloxy)methyl]tetracyclo[6.3.0.0^{2,11}.0^{4,8}]undecan-3-one (23) Compound **22** (86 mg) was converted into **23** (76 mg, 89%) in a manner similar to that described for **18**→**19**. A colorless oil. IR (CCl_4) cm^{-1}: 3040, 1720, 1600, 1500, 1380, 1190, 1180. ^{1}H-NMR ($CDCl_3$) δ: 1.04 and 1.20 (each 3H, s, 10-Me × 2), 1.49 and 2.18 (each 1H, d, J=13 Hz, 9-H_2), 2.44 (3H, s, aromatic Me), 4.18 and 4.24 (each 1H, dd, J=10, 6 Hz, CH_2OTs), 7.28 and 7.71 (each 2H, d, J=8 Hz, aromatic H × 4). MS m/z (%): 374 (M^+, 21.5), 202 (100).

(1*RS*,2*SR*,4*SR*,7*RS*,8*SR*,11*SR*)-7,10,10-Trimethyltetracyclo[6.3.0.0^{2,11}.0^{4,8}]undecan-3-one (20) from 23 Compound **23** (74 mg) was converted into **20** (14 mg, 35%) in a manner similar to that described for **19**→**16**. Compound **20** was identical with an authentic sample.[2]

(1*RS*,2*SR*,4*SR*,5*SR*,8*SR*)-4-(2-Bromoethyl)-7,7-dimethyl-3-oxotricyclo[3.3.0.0^{2,8}]octane-5-acetaldehyde (24) A suspension of **12** (148 mg, 0.38 mmol) and LiBr (99 mg, 1.14 mmol) in acetone (10 ml) was refluxed for 3 h. The acetone was evaporated off, and the residue was extracted with ether. The extract was washed with brine, dried, and evaporated. The crude product was chromatographed on silica gel with hexane–AcOEt (3:1) to give **24** (100 mg, 88%) as a colorless oil. IR (CCl_4) cm^{-1}: 2730, 1725. ^{1}H-NMR (CCl_4) δ: 1.12 and 1.21 (each 3H, s, 7-Me × 2), 2.78 (2H, d-like, J=5 Hz, CH_2CHO), 3.2—3.6 (2H, m, CH_2Br), 9.83 (1H, s-like, CHO). MS m/z (%): 300 (M^+ for ^{81}Br, 4.1), 298 (M^+ for ^{79}Br, 3.7), 106 (100). High MS Calcd for $C_{14}H_{19}{}^{81}BrO_2$ and $C_{14}H_{19}{}^{79}BrO_2$: 300.0546 and 298.0568. Found: 300.0525 and 298.0593.

(1*RS*,2*SR*,4*SR*,8*RS*,11*SR*)-10,10-Dimethyl-3-oxotetracyclo[6.3.0.0^{2,11}.0^{4,8}]undecane-7-carbaldehyde (25) DBU (0.12 ml) was added dropwise to a solution of **24** (30 mg, 0.1 mmol) in benzene (1 ml) under reflux, and the mixture was stirred for 20 min. The mixture was diluted with benzene and washed with diluted HCl solution, saturated $NaHCO_3$ solution, and brine, then dried, and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (3:1) to give **25** (18 mg, 82%) as a

colorless oil. IR (CCl_4) cm^{-1}: 2710, 1715. ^{1}H-NMR (CCl_4) δ: 1.07 and 1.26 (each 3H, s, 10-Me × 2), 9.61 and 10.00 (total 1H, each d, J=2 Hz, CHO). MS m/z (%): 218 (M^+, 27.6), 161 (100). High MS Calcd for $C_{14}H_{18}O_2$: 218.1307. Found: 218.1309.

(1*RS*,2*SR*,4*SR*,8*RS*,11*SR*)-7-Hydroxymethyl-10,10-dimethyltetracyclo-[6.3.0.0^{2,11}.0^{4,8}]undecan-3-one (26) Sodium borohydride (12 mg, 0.32 mmol) was added portionwise to a solution of **25** (136 mg, 0.62 mmol) in MeOH (10 ml) at 0 °C, and stirred for 15 min. The MeOH was evaporated off, water was added, and the mixture was extracted with AcOEt. The extract was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (1 : 1) to give **26** (94 mg, 69%) as a colorless oil. IR ($CHCl_3$) cm^{-1}: 3630, 3450, 1710. ^{1}H-NMR ($CDCl_3$) δ: 1.05, 1.07, 1.22, and 1.24 (total 6H, each s, 10-Me), 3.00 (1H, br, OH), 3.2—4.1 (2H, m, CH_2OH). MS m/z (%): 220 (M^+, 35.7), 133 (100). High MS Calcd for $C_{14}H_{20}O_2$: 220.1463. Found: 220.1479.

(1*RS*,2*SR*,4*SR*,8*RS*,11*SR*)-10,10-Dimethyl-7-[(*p*-tosyloxy)methyl]tetracyclo[6.3.0.0^{2,11}.0^{4,8}]undecan-3-one (27) A mixture of **26** (104 mg, 0.47 mmol), Et_3N (0.1 ml), DMAP (10 mg), *p*-TsCl (179 mg, 0.94 mmol), and methylene chloride (5 ml) was stirred at room temperature for 17 h. The mixture was washed with brine, dried, and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (3 : 1) to give **27** (148 mg, 84%) as a colorless oil. IR (CCl_4) cm^{-1}: 3050, 1720, 1605, 1200, 1185. ^{1}H-NMR (CCl_4) δ: 0.98 and 1.01 (total 3H, each s, 10-Me), 1.17 (3H, s, 10-Me), 2.44 (3H, s, aromatic Me), 3.5—4.4 (total 2H, m, CH_2OTs), 7.28 (2H, d, J=8 Hz, aromatic H), 7.65 and 7.70 (total 2H, each d, J=8 Hz, aromatic H × 4). MS m/z (%): 374 (M^+, 4.1), 58 (100). High MS Calcd for $C_{21}H_{26}O_4S$: 374.1552. Found: 374.1567.

(1*RS*,2*SR*,4*SR*,8*SR*,11*SR*)-10,10-Dimethyl-7-methylenetetracyclo[6.3.-0.0^{2,11}.0^{4,8}]undecan-3-one (8) A mixture of **27** (148 mg, 0.40 mmol), NaI (150 mg, 1.0 mmol), and dimethyl formamide (DMF) (3 ml) was heated at 50—60 °C for 2 h. After cooling of the mixture, DBU (91 mg, 0.60 mmol) was added, and the whole was heated at 90—100 °C for 4 h, then allowed to cool. Water was added, and the whole was extracted with ether. The extract was washed with $Na_2S_2O_3$ solution and brine, then dried, and evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (10 : 1) to give **8** (63 mg, 79%) as a colorless oil. IR (CCl_4) cm^{-1}: 3070, 3040, 1720, 1650, 885. ^{1}H-NMR (CCl_4) δ: 1.09 and 1.29 (each 3H, s, 10-Me × 2), 1.53 and 2.23 (each 1H, d, J=13 Hz, 9-CH_2), 4.96 (2H, m, =CH_2). MS m/z (%): 202 (M^+, 44.1), 58 (100). High MS Calcd for $C_{14}H_{18}O$: 202.1355. Found: 202.1329.

Catalytic Hydrogenation of 8 A mixture of **8** (20 mg, 0.10 mmol), 5% Pd–C (4 mg), and MeOH (3 ml) was stirred for 2 h under H_2 atmosphere at ordinary pressure. The catalyst was filtered off, and the filtrate was evaporated. The residue was chromatographed on silica gel with hexane–AcOEt (10 : 1) to give a mixture of **16** and **20** (total 20 mg, 100%). The ratio was determined to be 14 : 86 by capillary GLC (retention times were 16.0 min for **16** and 16.7 min for **20** at 140 °C, in agreement with those of authentic samples).[2] A colorless oil. IR (CCl_4) cm^{-1}: 1720. ^{1}H-NMR (CCl_4) δ: 0.82 (*ca.* 0.4H, d, J=7 Hz, 7-Me for **16**), 1.11 (*ca.* 2.6H, d, J= 7 Hz, 7-Me for **20**).

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