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Synthesis of Four Possible Isomers of 9-(Bromomethylene)-1,2,5-trimethylspiro[5.5]undeca-1,7-dien-3-one: Structure Elucidation of a Brominated Rearranged Chamigrane-Type Sesquiterpene[1)]

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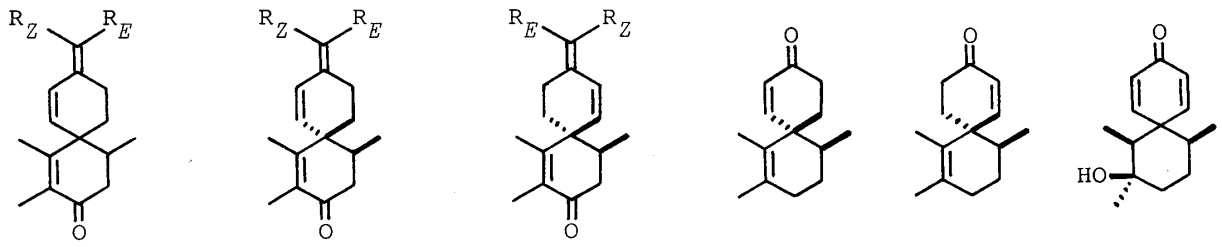
The first total synthesis of (5*R**,6*R**)- and (5*R**,6*S**)-9-(bromomethylene)-1,2,5-trimethylspiro[5.5]undeca-1,7-dien-3-one (**1a** and **1b**) was achieved stereoselectively. The relative configuration of C-5 and C-6 of the natural product *Z*-**1** was elucidated as 5*R** and 6*R** by comparison with our synthetic samples.

Keywords——9-(bromomethylene)-1,2,5-trimethylspiro[5.5]undeca-1,7-dien-3-one; halogenated rearranged chamigrane-type sesquiterpene; total synthesis; structure elucidation; hydroxyspirodienone; regioselective reduction; bromomethylenation; allylic oxidation

A number of halogenated sesquiterpenes of chamigrane type and rearranged chamigrane type have been isolated from the red algae of genus *Laurencia* and the molluscs of genus *Aplysia*.[2)] Nevertheless, few synthetic studies have been reported on these halogenated sesquiterpenes.[3)] 9-(Bromomethylene)-1,2,5-trimethylspiro[5.5]undeca-1,7-dien-3-one (*Z*- and *E*-**1**), one such rearranged chamigrane-type sesquiterpene, has been isolated from *Aplysia dactylomela*, and the *E*-isomer *E*-**1** has been suggested to be an artifact of isolation. However, the relative configuration between C-5 and C-6 is not known.[4)]

In the previous paper,[5)] we have reported a useful regioselective reduction in the spirocyclic system (neighboring hydroxyl group-participating metal–ammonia reduction and intramolecular Michael-type addition of the hydroxyl group). In this paper, we wish to report the synthesis of the four possible isomers of **1**, *i.e.*, *Z*-**1a** (5*R**,6*R**,9*Z*), *E*-**1a** (5*R**,6*R**,9*E*), *Z*-**1b** (5*R**,6*S**,9*Z*), and *E*-**1b** (5*R**,6*S**,9*E*) *via* the key intermediates **2a** and **2b**, which were



1 (5*R**,6*R**) **1a** (5*R**,6*S**) **1b** **2a** **2b** **3**

Z: R_Z=Br, R_E=H

E: R_Z=H, R_E=Br

Fig. 1

stereoselectively prepared from the common hydroxyspirodienone **3** by utilizing our method. The structure of the natural product *Z*-**1** could be assigned as 5*R** and 6*R** (*Z*-**1a**) by comparison of the ^{1}H-nuclear magnetic resonance (NMR) spectra.

The preparation of the hydroxyspirodienone **3** started with the known lactone **4**.[6] Hydrogenolysis of **4** over palladium–carbon (Pd–C), in the presence of hydrochloric acid, afforded the methyl ester **5** in 80% yield. Demethylation of **5** with hydroiodic acid in acetic acid afforded the phenolic carboxylic acid **6**. Transformation of **6** to the phenolic α-diazoketone **7** (4 steps; acetylation, treatment with thionyl chloride, treatment with diazoethane, and hydrolysis) and subsequent copper(II) chloride-catalyzed cyclization of **7** to the spirodienone **8** were achieved in 85% and 27% yields, respectively, according to the procedure described before.[3c] The infrared (IR) spectrum of **8**, obtained as the single product, shows an absorption due to a six-membered ring ketone at 1715 cm^{-1} and dienone bands at 1650 and 1630 cm^{-1}. The stereochemistry of **8** was confirmed by the ^{1}H-NMR chemical shifts of the C_7- and C_{11}-methyl signals at 0.77 and 0.79 ppm. This indicates that these two methyl groups are situated in the shielding region of the dienone moiety, *i.e.*, they are equatorial. The stereochemistry of **8** can be rationalized by initial formation of the cyclopropane derivative followed by cleavage of the cyclopropane ring and concomitant formation of the enolate as shown in Chart 1. Treatment of **8** with methylmagnesium iodide at 0 °C stereoselectively afforded the desired hydroxyspirodienone **3**[7] in 64% yield based on consumed starting material **8**. The axial configuration of the hydroxyl group in **3** was confirmed by the ^{1}H-NMR chemical shift of the C_1-olefinic proton at 7.59 ppm.[8]

The hydroxyspirodienone **3** was regioselectively reduced with lithium in liquid ammonia at −78 °C to afford the hydroxyenone **9** in 74% yield.[5] The stereochemistry of **9** was confirmed by the disappearance of the C_1-olefinic proton signal which was observed at 7.59 ppm in **3**. Compound **9** was dehydrated with thionyl chloride and pyridine in toluene at −78 °C to afford the key intermediate **2a** in 89% yield. The direction of this dehydration was confirmed by the ^{1}H-NMR signals of vinyl methyl protons at 1.60 ppm (6H, m) and the mass spectral (MS) peak at *m/z* 162 (retro Diels–Alder fission). Transformation of **2a** to **1a** was carried out by the method described before as follows.[3c] Bromomethylenation by means of the Witting reaction[9] afforded an inseparable mixture of the bromomethylene derivative **10a** in 86% yield (*Z*:*E*=*ca.* 3:4 based on ^{1}H-NMR[10]). Compound **10a** was oxidized with chromium trioxide and 3,5-dimethylpyrazole[11] to afford in 54% yield a *ca.* 2:3 mixture of *Z*- and *E*-**1a**, which could be separated by preparative thin layer chromatography (PTLC).

On the other hand, treatment of the hydroxyspirodienone **3** with sodium amide in liquid ammonia afforded the tricyclic enone **11** in 63% yield (81% yield based on consumed starting material **3**). The structure of **11** was confirmed by the ^{1}H-NMR signals of the C_6- and C_7-olefinic protons at 5.98—6.63 ppm (AB type) and the C_{9a}-proton at 4.32 ppm (dd, J=8, 10 Hz) and the absorptions in the IR spectrum at 1670 and 1610 cm^{-1} due to an enone. Compound **11** was hydrogenated over Pd–C to afford the tricyclic ketone **12** in quantitative yield. Ether ring-opening reaction of **12** by β-elimination with fluoride anion or other bases[5] did not give a satisfactory result. This difficulty of ring opening may be due to the *gem*-dialkyl effect caused by the C_{10}-methyl group.[12] Finally the key intermediate **2b** could be obtained in one pot and in good yield (91% yield) under the conditions reported by Fujita *et al.* ($AlCl_3$–NaI–acetonitrile).[13] The structure of **2b** was confirmed by the ^{1}H-NMR signals of the vinyl methyl protons at 1.67 ppm (6H, m) and MS peak at *m/z* 162 (retro Diels–Alder fission). The enone **2b** was transformed to **1b** according to a procedure similar to that described for the synthesis of **1a**. Bromomethylenation of **2b** (89% yield) followed by allylic oxidation (49% yield) afforded a *ca.* 2:3 mixture of *Z*- and *E*-**1b**, which could be separated by PTLC.

The ^{1}H-NMR and IR spectra of authentic *Z*- and *E*-**1**[4] were identical with those of the synthetic *Z*- and *E*-**1a**, respectively, but the ^{1}H-NMR spectra of the (5*R**,6*S**)-isomer *Z*- and

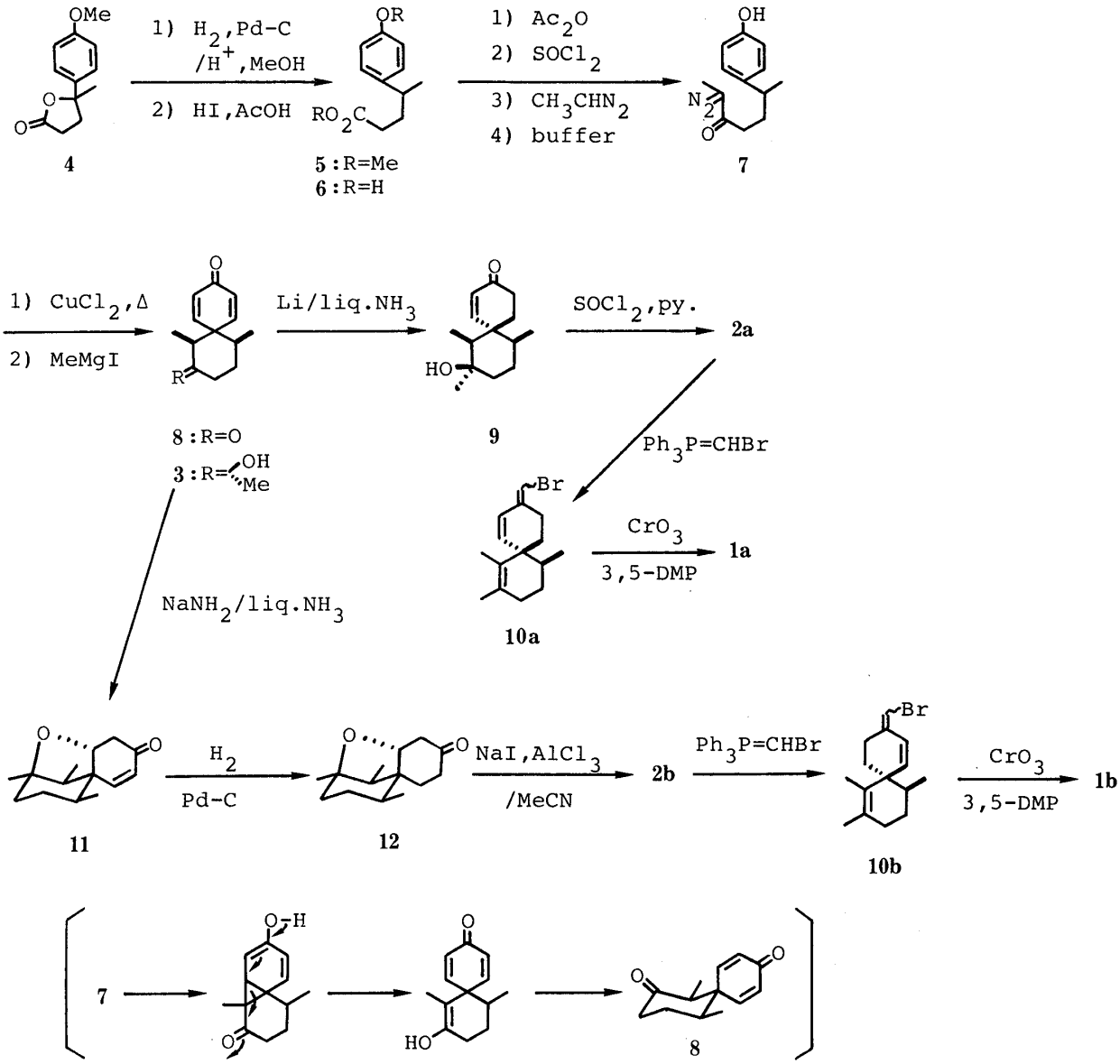


Chart 1

TABLE I. ^{1}H-NMR Data for Natural and Synthetic **1**[a]

	Z-**1**[b]	*Z*-**1a**	*Z*-**1b**	*E*-**1**[b]	*E*-**1a**	*E*-**1b**
C_1-H	6.78 (dd, J=10.2, 1.0)	6.79 (dd, J=10, 1)	6.68 (d, J=10)	6.35 (dd, J=10.1, 0.5)	6.35 (br d, J=10)	6.24 (d, J=10)
C_9=CHBr	6.01 (dd, J=1.5, 1.1)	6.00 (t-like, J=1)	5.98 (m)	6.23 (m)	6.22 (m)	6.18 (m)
C_2-H	5.62 (dd, J=10.1, 1.5)	5.62 (dd, J=10, 1)	5.88 (br d, J=10)	5.45 (d, J=9.9)	5.44 (d, J=10)	5.72 (d, J=10)
C_1- and C_2-CH_3	1.85 (d, J=1.1) 1.77 (d, J=0.9)	1.85 (d, J=1) 1.78 (d, J=1)	1.81 (br s) 1.78 (br s)	1.84 (d, J=0.9) 1.77 (d, J=0.9)	1.84 (br s) 1.77 (br s)	1.81 (br s) 1.78 (br s)
C_5-CH_3	0.97 (d, J=6.4)	0.97 (d, J=6)	1.02 (d, J=6)	0.97 (d, J=6.4)	0.98 (d, J=6)	1.00 (d, J=7)

a) The spectra were taken in $CDCl_3$ with tetramethylsilane as an internal standard. *b*) Quoted from ref. 4.

E-**1b** were not identical with those of authentic *Z*- and *E*-**1**, as shown in Table I.

Experimental

Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. IR and ultraviolet (UV) spectra were recorded on a Hitachi 215 spectrometer and a Hitachi 124 spectrophotometer, respectively. ^{1}H-NMR spectra were recorded on a Hitachi R-22 (90 MHz) and/or a JEOL JNM-FX90Q (90 MHz). ^{1}H-NMR spectra were obtained with tetramethylsilane as an internal standard, and the following abbreviations are used; s = singlet, d = doublet, m = multiplet, and br = broad. MS were obtained with a JEOL JMS-D 300 and/or a Shimadzu GCMS-QP1000. High-resolution mass spectra (High MS) were obtained with a JEOL JMS-D 300. For silica gel PTLC and column chromatography, Merck Kieselgel PF_{254} and Merck Kieselgel 60 (70—230 mesh) were used, and for alumina column chromatography Merck Aluminumoxid 90 (70—230 mesh) was used. High pressure liquid chromatography (HPLC) was carried out on a Waters Associates high-pressure liquid chromatograph with an M6000A pump, a U6K septumless injector, and a Series R401 differential refractometer. Two silica packed columns [Waters Associates, μ-Porasil (7.8 mm i.d. × 30 cm length)] were connected and used at a flow rate of 5 ml/min.

Methyl 4-(4-Methoxyphenyl)pentanoate (5)——A mixture of Norit A (1 g) and palladium chloride (410 mg) in methanol (30 ml) was shaken under 3 atm pressure of hydrogen at room temperature for 1 h. A solution of the lactone **4** (34.7 g) in methanol (70 ml) was added and the whole mixture was shaken under 3 atm pressure of hydrogen at room temperature for 24 h. After filtration to remove the catalyst and evaporation of methanol, the residue was dissolved in ether and the ethereal solution was washed with water and brine, dried (Na_2SO_4) and concentrated. The crude ester was purified by distillation under reduced pressure (bp 123—125 °C/0.025 mmHg) to give pure **5** (29.8 g) in 80% yield. IR ($CHCl_3$): 2960, 1725, 1610 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.27 (1H, d, J=7 Hz, $-CH_3$), 1.76—2.88 (5H, m, C_2-, C_3-, and C_4-H), 3.68, 3.85 (each 3H, s, $-OCH_3$ and $-COOCH_3$), 6.85—7.27 (4H, AA'BB' type, aromatic protons). MS *m/z*: 222 (M^+, 5.6). *Anal.* Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.08; H, 8.03.

4-(4-Hydroxyphenyl)pentanoic Acid (6)——A solution of **5** (26.5 g) in 57% hydroiodic acid (80 ml) and acetic acid (100 ml) was refluxed for 7 h. After evaporation of the acetic acid *in vacuo*, water (250 ml) and ethyl acetate (150 ml) were added. The organic phase was separated and the aqueous phase was extracted with ethyl acetate (100 ml × 2). The combined ethyl acetate layers were washed with water, 10% sodium thiosulfate solution, water and brine, dried (Na_2SO_4) and concentrated *in vacuo* to give **6** (23.5 g) as a viscous oil. An analytically pure sample was obtained by distillation under high vacuum [bp 180—190 °C (bath temperature)/0.003 mmHg] and crystallized on standing, mp 66—71 °C. IR ($CHCl_3$): 3580, 3550—2380, 1705, 1615, 1595 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.22 (3H, d, J=7 Hz, $-CH_3$), 1.57—2.90 (5H, m, C_2-, C_3-, and C_4-H), 6.76—7.16 (4H, AA'BB' type, aromatic H), 8.52 (2H, br s, –COOH and –OH). MS *m/z*: 194 (M^+, 17.5). *Anal.* Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.10; H, 7.13.

2-Diazo-6-(4-hydroxyphenyl)-3-heptanone (7)——Acetic anhydride (4.5 ml) was added dropwise to a stirred solution of **6** (8.5 g) in 5% NaOH (73 ml) at 0 °C. After being stirred for 1 h, the mixture was adjusted with acetic acid to pH 5, and the resulting mixture was extracted with benzene. The organic phase was washed with water, dried (Na_2SO_4), and concentrated *in vacuo* to give an acetate. This acetate was transformed to an acid chloride by treatment with thionyl chloride (10 ml) in dry benzene (100 ml) according to the usual procedure. The acid chloride dissolved in dry ether (100 ml) was added to an ethereal solution of diazoethane (about 5-fold excess) at 0 °C with stirring. The mixture was stirred for 3 h, then the solvent was evaporated off *in vacuo* to give the diazoketone. This was dissolved in methanol (400 ml), then water (225 ml), sodium bicarbonate (20 g), and sodium carbonate (22.5 g) were added. The mixture was stirred overnight at room temperature. After evaporation of most of the methanol *in vacuo*, the residue was neutralized with saturated oxalic acid solution, and extracted with benzene. The extract was washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The water remaining in the residue was removed azeotropically *in vacuo* with dry benzene (100 ml × 2). The crude phenolic α-diazoketone **7** (8.6 g) was obtained as an unstable yellow oil, which was used immediately for the annelation reaction without purification. IR ($CHCl_3$): 3590, 3330, 2960, 2070, 1615 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.23 (3H, d, J=7 Hz, $-CH_3$), 1.95 (3H, s, $-C(N_2)CH_3$), 6.80—7.20 (4H, AA'BB' type, aromatic H).

(7*R,11*R**)-7,11-Dimethylspiro[5.5]undeca-1,4-diene-3,8-dione (8)**——A chloroform solution (50 ml) of **7** (8.5 g) was added dropwise to a boiling suspension of cupric chloride (5 g) in chloroform (1 l) over 20 min and the reaction mixture was refluxed for a further 5 min. After rapid cooling, the reaction mixture was filtered through Florisil and concentrated *in vacuo* to give a brown oil, which was purified by alumina column chromatography ($CHCl_3$: hexane = 1 : 1) to give **8** (2.0 g) in 27% yield, mp 105.0—106.5 °C (colorless crystals from ethyl acetate). IR ($CHCl_3$): 1715, 1650, 1630 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.77, 0.79 (each 3H, d, J=7 Hz, C_7- and C_{11}-CH_3), 6.25—6.80 (4H, ABCD type, olefinic H). UV λ_{max}^{EtOH} nm (ε): 239 (11500). MS *m/z*: 204 (M^+, 32.8). *Anal.* Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.14; H, 7.96.

(7*R,8*S**,11*R**)-8-Hydroxy-7,8,11-trimethylspiro[5.5]undeca-1,4-dien-3-one (3)**——Ethereal methylmagnesium iodide solution (1 M, 1.6 ml) was added dropwise to a stirred solution of **8** (293 mg) in ether (8 ml) and tetrahydrofuran (THF) (2 ml) at 0 °C. The mixture was stirred for 20 min at 0 °C, and ether saturated with water (50 ml) and then saturated ammonium chloride solution (10 ml) were added with stirring. The organic phase was separated and the

aqueous phase was extracted with ether. The combined ethereal phase was washed with water and brine, dried (Na_2SO_4), and concentrated to give a pale yellow oil, which was purified by silica gel PTLC (ether : petr. ether = 3 : 1) to give **3** (153.2 mg) in 48% yield (64% yield based on consumed starting material) with recovery of the starting material **8** (72.1 mg) in 25% yield. **3**, mp 99—100 °C (colorless crystals from ethyl acetate). IR ($CHCl_3$): 3600, 3400, 1660, 1617 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.73 (6H, d, J = 7 Hz, C_7- and C_{11}-CH_3), 1.24 (3H, s, C_8-CH_3), 6.21—6.64 (ABC part in ABCM, C_1-, C_2-, and C_4-H), 7.59 (1H, dd, J = 3, 11 Hz, C_5-H). UV λ_{max}^{EtOH} nm (ε): 244 (16800). MS m/z: 220 (M^+, <1). *Anal.* Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.23; H, 9.40.

(6*R,7*R**,8*S**,11*R**)-8-Hydroxy-7,8,11-trimethylspiro[5.5]undec-1-en-3-one (9)**——A THF solution (3 ml) of **3** (150 mg) was added in one portion to a stirred solution of lithium (11.9 mg) in liquid ammonia (*ca.* 30 ml) at −78 °C. Immediately dry powdered ammonium chloride (*ca.* 300 mg) was added portionwise and ammonia was evaporated off. Water was added to the residue and the resulting solution was extracted with ethyl acetate. The extract was washed with saturated sodium bicarbonate solution, water and brine, then dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified by silica gel PTLC (ether : petr. ether = 5 : 1) to give **9** (112.4 mg) as a colorless oil in 74% yield. IR ($CHCl_3$): 3600, 3420, 1665, 1620 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.92, 0.99 (each 3H, d, J = 5 Hz, C_7- and C_{11}-CH_3), 1.18 (3H, s, C_8-CH_3), 5.98—6.31 (2H, AB type, C_1- and C_2-H). MS m/z: 222 (M^+, 2.2). High MS m/z: 222.160 (M^+, Calcd for $C_{14}H_{22}O_2$: 222.162).

(6*R,11*R**)-7,8,11-Trimethylspiro[5.5]undeca-1,7-dien-3-one (2a)**——Thionyl chloride (0.072 ml) was added to a stirred solution of **9** (110 mg) and pyridine (0.2 ml) in toluene (5 ml) at −78 °C. After being stirred for 15 min at −78 °C, the reaction mixture was poured into saturated sodium bicarbonate solution containing crushed ice and extracted with ether. The extract was washed with saturated sodium bicarbonate solution, water and brine, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by silica gel PTLC (ether : petr. ether = 5 : 1) to give **2a** (89.6 mg) as a colorless oil in 89% yield, bp 85 °C (bath temperature)/0.001 mmHg. IR ($CHCl_3$): 3000, 2955, 1665 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.98 (3H, d, J = 6 Hz, C_{11}-CH_3), 1.60 (6H, m, C_7- and C_8-CH_3), 5.98—6.55 (2H, AB type, C_1- and C_2-H). MS m/z: 204 (M^+, 61.3), 162 (retro Diels–Alder fission, 18.5). *Anal.* Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.21; H, 10.16.

(5*R,6*R**)-9-(Bromomethylene)-1,2,5-trimethylspiro[5.5]undeca-1,7-diene (10a)**——A THF solution of lithium piperidide, which was prepared by adding a 15% hexane solution of butyllithium (0.70 ml) to a stirred THF solution (1.5 ml) of piperidine (0.11 ml) at 0 °C and stirring for 10 min at 0 °C, was added dropwise to a stirred suspension of bromomethyltriphenylphosphonium bromide (509 mg) in THF (2.5 ml) at 0 °C. The resulting yellow solution was stirred for 5 min at 0 °C and a THF solution (1 ml) of **2a** (77 mg) was added at 0 °C. After being stirred for 1 h at 0 °C, the reaction mixture was diluted with ether, washed with water and brine, dried (Na_2SO_4), and concentrated *in vacuo*. The residual yellow oil was purified by silica gel PTLC (hexane) to give **10a** (91.4 mg) in 86% yield as an inseparable mixture (Z : E = *ca.* 3 : 4, based on ^{1}H-NMR). IR ($CHCl_3$): 3000, 2930, 1620, 1580 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.87 (3H, d, J = 7 Hz, C_5-CH_3), 1.51 (3H, m, C_1- or C_2-CH_3), 1.59 (3H, br s, C_1- or C_2-CH_3), 6.07, 5.84 (total 1H, each m, E- and Z-C$\underline{H}$Br = C_9), 5.39, 5.54 (total 1H, each br d, J = 10 Hz, E- and Z-C_7-H), 6.18, 6.60 (total 1H, d, J = 10 Hz, E-C_8-H and dd, J = 1, 10 Hz, Z-C_8-H). MS m/z: 280, 282 (M^+, 47.4, 48.0). High MS m/z: 280.082 (M^+, Calcd for $C_{15}H_{21}{}^{79}Br$: 280.082).

(5*R,6*R**)-9-(Bromomethylene)-1,2,5-trimethylspiro[5.5]undeca-1,7-dien-3-one (*Z*-1a and *E*-1a)**——3,5-Dimethylpyrazole (195 mg) was added in one portion to a stirred suspension of CrO_3 (203 mg) in CH_2Cl_2 (3 ml) at −20 °C and the whole resulting reaction mixture was stirred for 15 min at −20 °C. A CH_2Cl_2 solution (1 ml) of **10a** (38 mg) was added to the above reagent at −20 °C and the whole resulting reaction mixture was stirred for 4 h at 0 °C, then water and ether were added. The ether extract was washed with saturated sodium bicarbonate solution, water and brine, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified by silica gel PTLC (ether : petr. ether = 3 : 2, developed twice) to give *E*-**1a** ($Rf \fallingdotseq 0.8$, 12.8 mg) in 32% yield and *Z*-**1a** ($Rf \fallingdotseq 0.7$, 8.9 mg) in 22% yield as pale yellow oils. These compounds, *Z*- and *E*-**1a**, were unstable and gradually decomposed on PTLC, so further purification was carried out by HPLC (hexane : ethyl acetate = 10 : 1). *Z*-**1a**, colorless oil. IR (neat): 2930, 1662 cm^{-1}. MS m/z: 294, 296 (M^+, 41.3, 44.8). High MS m/z: 294.063 (M^+, Calcd for $C_{15}H_{19}{}^{79}BrO$: 294.062). *E*-**1a**, colorless oil. IR (neat): 2950, 1662 cm^{-1}. MS m/z: 294, 296 (M^+, 52.3, 53.6). High MS m/z: 294.064 (M^+, Calcd for $C_{15}H_{19}{}^{79}BrO$: 294.062). ^{1}H-NMR data for *Z*- and *E*-**1a** are listed in Table I.

(2*R,5*S**,5a*R**,9a*R**,10*S**)-9*H*-2,3,4,5,5a,9a-Hexahydro-2,5a-methano-2,5,10-trimethyl-1-benzoxepin-8-one (11)**——Ferric chloride (*ca.* 3 mg) was added to a stirred solution of sodium (25 mg) in liquid ammonia (*ca.* 30 ml) at −78 °C and the whole mixture was stirred under reflux until the blue color disappeared. A THF (5 ml) solution of **3** (120 mg) was added dropwise to the sodium amide solution at −78 °C. Stirring was carried out for 2 h at −78 °C, then dry powdered ammonium chloride (*ca.* 300 mg) was added, and ammonia was evaporated off at room temperature. Ether and water were added to the residue. The extract was washed with saturated sodium bicarbonate solution, water and brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (hexane : ethyl acetate = 3 : 1) to give **11** (75.0 mg) as a colorless oil in 63% yield (81% yield based on consumed starting material) and the recovered starting material **3** (27.3 mg) in 23% yield. IR ($CHCl_3$): 2970, 2940, 1670, 1610 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.73 (3H, d, J = 6 Hz, C_5-CH_3), 1.01 (3H, d, J = 7 Hz, C_{10}-CH_3), 1.22 (3H, s, C_2-CH_3), 4.32 (1H, dd, J = 8, 10 Hz, C_{9a}-H), 5.98—6.63 (2H, AB type, C_6- and C_7-H). MS m/z: 220 (M^+, 2.1). High

MS *m/z*: 220.147 (M^+, Calcd for $C_{14}H_{20}O_2$: 220.146).

(2*R,5*S**,5a*S**,9a*R**,10*S**)-9*H*-Octahydro-2,5a-methano-2,5,10-trimethyl-1-benzoxepin-8-one (12)**——Compound **11** (73 mg) in ethyl acetate (2 ml) was hydrogenated in the presence of 10% Pd–C (50 mg) at ordinary pressure until the starting material was no longer detectable on thin layer chromatography (TLC). After separation of the catalyst by filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography (hexane : ethyl acetate = 3 : 1) to give **12** (74.7 mg) as a colorless oil in quantitative yield. IR ($CHCl_3$): 2980, 2945, 1710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.92 (3H, d, J=6 Hz, C_5-CH_3), 1.08 (3H, d, J=8 Hz, C_{10}-CH_3), 1.19 (3H, s, C_2-CH_3), 4.10 (1H, dd, J=6, 11 Hz, C_{9a}-H). MS *m/z*: 222 (M^+, 1.1). High MS *m/z*: 222.162 (M^+, Calcd for $C_{14}H_{22}O_2$: 222.162).

(6*R,11*S**)-7,8,11-Trimethylspiro[5.5]undeca-1,7-dien-3-one (2b)**——Aluminum chloride (89 mg) was added to a stirred solution of **12** (74 mg) and sodium iodide (100 mg) in acetonitrile (5 ml) at room temperature. After being stirred for 3 h at room temperature, the reaction mixture was diluted with saturated sodium bicarbonate solution and extracted with ether. The extract was washed with 10% sodium thiosulfate solution, water and brine, dried (Na_2SO_4) and concentrated *in vacuo*. The residual yellow oil was purified by silica gel PTLC (ether : petr. ether = 1 : 3) to give **2b** (61.7 mg) as a colorless oil in 91% yield. IR ($CHCl_3$): 3000, 2955, 1675 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.99 (3H, d, J= 7 Hz, C_{11}-CH_3), 1.67 (6H, m, C_7- and C_8-CH_3), 6.15—6.93 (2H, AB type, C_1- and C_2-H). MS *m/z*: 204 (M^+, 86.6), 162 (retro Diels–Alder fission, 41.7). High MS *m/z*: 204.150 (M^+, Calcd for $C_{14}H_{20}O$: 204.151).

(5*R,6*S**)-9-(Bromomethylene)-1,2,5-trimethylspiro[5.5]undeca-1,7-diene (10b)**——Compound **10b** (73.8 mg) was obtained in 89% yield from **2b** (60 mg) using bromomethyltriphenylphosphonium bromide (397 mg), butyllithium 1 M hexane solution (0.55 ml), and piperidine (0.087 ml) by the same method as described for the preparation of **10a**. IR ($CHCl_3$): 2955, 2930, 1605, 1580 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, d, J=6 Hz, C_5-CH_3), 1.52 (3H, m, vinyl CH_3), 1.60 (3H, br s, vinyl CH_3), 6.05, 5.83 (total 1H, each m, *E*- and *Z*-C<u>H</u>Br=C_9), 5.67, 5.83 (total 1H, d, J= 10 Hz, *E*-C_7-H and br d, J=10 Hz, *Z*-C_7-H), 6.10, 6.53 (total 1H, each d, J=10 Hz, *E*- and *Z*-C_8-H). MS *m/z*: 280, 282 (M^+, 58.7, 58.5). High MS *m/z*: 282.081 (M^+, Calcd for $C_{15}H_{21}{}^{81}Br$: 282.081).

(5*R,6*S**)-9-Bromomethylene-1,2,5-trimethylspiro[5.5]undeca-1,7-dien-3-one (*Z*-1b and *E*-1b)**——*Z*-**1b** (13.8 mg) in 19% yield and *E*-**1b** (22.0 mg) in 30% yield were obtained from **10b** (70 mg) using CrO_3 (374 mg) and 3,5-dimethylpyrazole (359 mg) by the same method as described for the preparation of *Z*- and *E*-**1a**. Final purification of *Z*- and *E*-**1b** was carried out by HPLC (hexane : ethyl acetate = 10 : 1). *Z*-**1b**, colorless oil. IR (neat): 2840, 1662 cm^{-1}. MS *m/z*: 294, 296 (M^+, 45.3, 45.2). High MS *m/z*: 294.059 (M^+, Calcd for $C_{15}H_{19}{}^{79}BrO$: 294.062). *E*-**1b**, colorless oil. IR (neat): 2840, 1662 cm^{-1}. MS *m/z*: 294, 296 (M^+, 51.1, 51.1). High MS *m/z*: 294.063 (M^+, Calcd for $C_{15}H_{19}{}^{79}BrO$: 294.062). ^{1}H-NMR data for *Z*- and *E*-**1b** are given in Table I.

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References and Notes

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