Synthesis of (1*R*,3*S*,5*S*)-1,3,8-Trimethyl-2,9-dioxabicyclo[3.3.1]non-7-ene, the Male Pheromone of a Hepialid Moth, *Endoclita excrescens*, and Its Enantiomer[‡]

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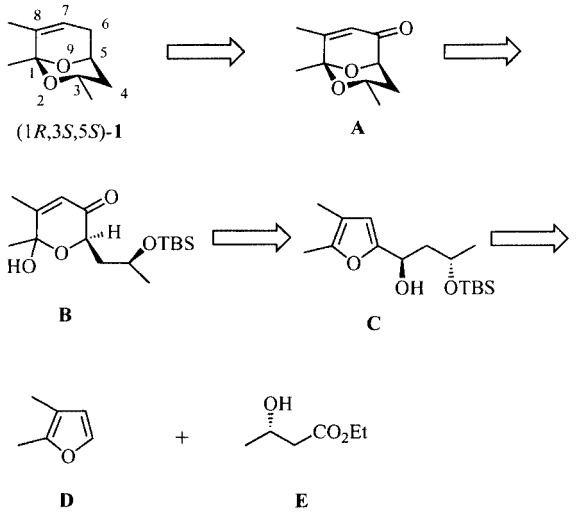
The (1*R*,3*S*,5*S*)- and (1*S*,3*R*,5*R*)-isomers of 1,3,8-trimethyl-2,9-dioxabicyclo[3.3.1]non-7-ene were synthesized from the (*S*)- and (*R*)-isomers of ethyl 3-hydroxybutanoate. The (1*R*,3*S*,5*S*)-isomer was identified as the pheromone produced by the male Japanese hepialid moth, *Endoclita excrescens*.

Introduction

Endoclita excrescens, a hepialid moth, damages herbal and woody plants in Japan by boring into their stems and/or trunks. In 2001 Nakashima reported the isolation of a compound from the hexane extract of the brush organ in the hind legs of male *E. excrescens*.[1] This compound induced an electroantennographic detection (EAD) response in female antennae, and was found to be the pheromone of the hepialid moth. The chemical structure of the pheromone was proposed as 1,3,8-trimethyl-2,9-dioxabicyclo[3.3.1]non-7-ene (**1**, Scheme 1) mainly on the basis of its mass spectral analysis.[1] A number of cyclic acetals and spiroacetals have been synthesized because of their pheromone activities.[2] We thus became interested in synthesizing the enantiomers of **1** so as to clarify the absolute configuration of the natural pheromone. Only (1*R*,3*S*,5*S*)-**1** showed pheromone activity when bioassayed by Nakashima. This paper reports the details of our synthesis of **1**, which has been published as a preliminary communication.[3]



Scheme 1. Structure and retrosynthetic analysis of the male pheromone [(1*R*,3*S*,5*S*)-**1**] of *Endoclita excrescens*

Results and Discussion

Burke's successful application[4] of ring-closing olefin metathesis[5] in the synthesis of *exo*- and *endo*-brevicomins, the well-known acetal pheromone isomers, prompted us to utilize a similar approach for the synthesis of **1**. Unfortunately, all our attempts were unsuccessful.

We therefore turned our attention to the more classical retrosynthetic analysis as shown in Scheme 1. This analysis was essentially the same as that employed by us in our 1986 synthesis of 1,8-dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]-non-7-ene, one of the pheromone components of the male swift moth, *Hepialus hecta*.[6] Similar strategies were also adopted for the construction of 2,9-dioxabicyclo[3.3.1]non-7-ene systems by Ziegler[7] and DeShong.[8] Accordingly, **1** can be prepared from **A** by reducing its carbonyl group to a methylene group. The ketone **A** is obtained by intramolecular acetalization of **B** after removal of its *tert*-butyldime-

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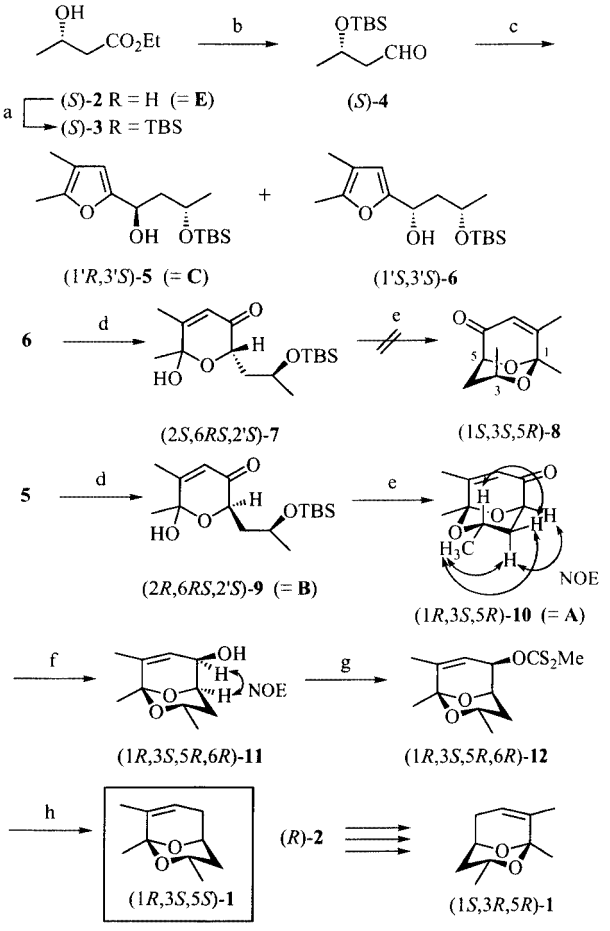
thylsilyl (TBS) group. It should be added that (±)-**A** is a known compound.[8] The hemiacetal ketone **B** is the oxidation product of **C**, while **C** can be synthesized from **D** and **E**. Although this strategy was less innovative than the unsuccessful olefin metathesis approach, we were confident that the synthesis would be successful, since 2,3-dimethylfuran (**D**) and the enantiomers of ethyl 3-hydroxybutanoate (**E**) are both commercially available.

Scheme 2 summarizes the synthesis of the enantiomers of **1**. Protection of the hydroxy group of the commercially available ethyl (*S*)-3-hydroxybutanoate (**2**, 96.7% *ee*) as its TBS ether gave (*S*)-**3**, which was reduced with diisobutylaluminum hydride (DIBAL-H) to afford the known aldehyde (*S*)-**4**.[9] Addition of (*S*)-**4** to the anion generated from 2,3-dimethylfuran by treatment with *tert*-butyllithium in THF/HMPA afforded a mixture of two diastereoisomeric alcohols (1′*R*,3′*S*)-**5** and (1′*S*,3′*S*)-**6** in a ratio of almost 1:1 as shown by the ^{1}H NMR spectrum, reflecting almost no *syn*/*anti*-stereoselection. Careful chromatographic purification of the mixture gave less polar (1′*R*,3′*S*)-**5** (35% yield) and more polar (1′*S*,3′*S*)-**6** (27%), whose stereochemistries were deduced by the subsequent conversion of **5** to **10**.

Oxidation of the more polar (1′*S*,3′*S*)-**6** with *m*-chloroperbenzoic acid (MCPBA) yielded an epimeric mixture of hemiacetal **7** as an oil. Neither hydrofluoric acid nor boron trifluoride/diethyl ether[6] could convert **7** to the 2,9-dioxabicyclo[3.3.1]non-7-ene derivative **8**, presumably because of the instability of **8** with severe 1,3-diaxial interactions between the methyl group at C-3 and the substituents at C-1 or C-5. Oxidation of the less polar **5** with MCPBA yielded hemiacetal **9** as a crystalline mixture of two epimers (m.p. 68−74 °C). Treatment of **9** with 48% hydrofluoric acid in acetonitrile[6] afforded the cyclized product **10** in 79% yield. Cyclization took place readily due to the equatorial nature of the methyl group at C-3. The stereochemistry of **10** as depicted in the formula was supported by the NOE correlations.

In order to remove the oxygen functionality at C-6, the ketone **10** was first reduced with sodium borohydride in the presence of cerium(III) chloride[10] to give the allylic alcohol **11** in 94% yield. Although the splitting pattern of the signal due to the proton at C-6 of **11** could not be analyzed in the ^{1}H NMR spectrum, the NOE correlation as shown in the formula of **11** in Scheme 2 suggested an *R* configuration at C-6. The hydroxy group at C-6 of **11** could now be removed by Barton's radical deoxygenation method.[11] Accordingly, alcohol **11** was converted to the corresponding methyl xanthate **12** by successive treatments of **11** with *n*-butyllithium, carbon disulfide and methyl iodide.

Deoxygenation of **12** proceeded smoothly when it was heated with tri(*n*-butyl)tin hydride in dry toluene with 2,2′-azobisisobutyronitrile (AIBN), affording the desired acetal (1*R*,3*S*,5*S*)-**1** {$[\alpha]_D^{22}$ = +116 (*c* = 1.04, $CHCl_3$)} in 44% yield after chromatographic purification and distillation. GC analysis of (1*R*,3*S*,5*S*)-**1** on Chirasil−DEX® revealed it to be of 96.8% *ee*, and the MS of **1** was in good agreement with that of the natural pheromone. The overall yield of (1*R*,3*S*,5*S*)-**1** was 8% based on (*S*)-**2** (8 steps). Similarly,



Scheme 2. Synthesis of the male pheromone [(1*R*,3*S*,5*S*)-**1**] of *Endoclita excrescens* and its enantiomer; reagents: (a) TBSCl, imidazole, DMF (91%); (b) DIBAL-H, CH_2Cl_2 (88%); (c) 2,3-dimethylfuran, *t*BuLi, Et_2O/HMPA (35% of **5** and 27% of **6**); (d) MCPBA, CH_2Cl_2 (96% of **7** and 89% of **9**); (e) 48% HF aq., MeCN (79%); (f) $NaBH_4$, $CeCl_3{\cdot}7H_2O$, MeOH (94%); (g) *n*BuLi, CS_2, MeI, THF (98%); (h) $(n\text{Bu})_3\text{SnH}$, AIBN, toluene (76%)

(1*S*,3*R*,5*R*)-**1** {$[\alpha]_D^{23}$ = −116 (*c* = 1.01, $CHCl_3$)} was synthesized from (*R*)-**2** in a 7% overall yield (8 steps). Electroantennographic (EAG) and behavioral studies of the enantiomers of **1** by Nakashima showed (1*R*,3*S*,5*S*)-**1** to be the naturally occurring pheromone. The opposite enantiomer, (1*S*,3*R*,5*R*)-**1**, was biologically inactive.

In conclusion, (1*R*,3*S*,5*S*)-1,3,8-trimethyl-2,9-dioxabicyclo[3.3.1]non-7-ene (**1**) was proved to be the male pheromone of the moth *E. excrescens.* Hence the Japanese hepialid moth *E. excrescens* shares the same absolute configuration as that of a European swift moth, *Hepialus hecta*, i.e. (1*R*,3*S*,5*S*)-1,8-dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]-non-7-ene.[12]

Experimental Section

Boiling points and melting points: Uncorrected values. IR: Jasco FT/IR-410. ^{1}H NMR: Jeol JNM-LA 400 (400 MHz), Jeol JNM-LA 500 (500 MHz), (TMS at δ = 0.00 ppm or $CHCl_3$ at δ = 7.26 ppm as an internal standard). ^{13}C NMR: JNM-LA 400 (100 MHz),

Jeol JNM-LA 500 (126 MHz), ($CDCl_3$ at δ = 77.0 ppm as an internal standard). MS: Jeol JMS-SX 102A and Hitachi M-80B. Optical rotation: Jasco P-1020. M.p.: Yanaco MP-S3. CC: Merck Kieselgel 60 Art 1.07734. TLC: 0.25 mm Merck silica gel plates (60F−254).

5-(3′-*tert*-Butyldimethylsilyloxy-1′-hydroxybutyl)-2,3-dimethylfuran (1′*R*,3′*S*)-5 and (1′*S*,3′*S*)-6: *t*BuLi (1.43 M in *n*-pentane, 115 mL, 164 mmol) was added dropwise to a stirred solution of 2,3-dimethylfuran (99%, 13.2 g, 136 mmol) in dry diethyl ether (300 mL) at 0 °C over 30 min under Ar. The mixture was stirred for 2 h at 0 °C and then cooled to −78 °C before a solution of (*S*)-**4**[9] (11.0 g, 54.4 mmol) in dry diethyl ether (130 mL) was added over 10 min, followed by HMPA (60 mL). The resulting mixture was stirred for 30 min at −78 °C then warmed to −60 °C over 1 h. The mixture was poured onto crushed ice and water, saturated with NaCl, stirred for 10 min, and extracted with diethyl ether. The extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by chromatography over silica gel (300 g) with *n*-hexane/ethyl acetate (30:1) yielding (1′*R*,3′*S*)-**5** and (1′*S*,3′*S*)-**6** (14.5 g, 90%) as a pale yellow oil. The diastereomeric ratio of **5** and **6** (1:1) was determined by ^1H NMR spectroscopy. This mixture was purified by chromatography over spherical silica gel (Kanto Silica Gel 60 N: 40−50 μm) eluting the less polar (1′*R*,3′*S*)-**5** (5.74 g, 35%) oil with *n*-hexane/ethyl acetate (30:1) and the more polar (1′*S*,3′*S*)-**6** (4.34 g, 27%) oil with *n*-hexane/ethyl acetate (20:1).

5: R_f = 0.80 (hexane/ethyl acetate, 3:1); n_D^{24} = 1.4652. $[\alpha]_D^{24}$ = +27.4 (*c* = 0.95, $CHCl_3$). IR: (film): $\tilde{\nu}_{max}$ = 3435 cm^{-1} (s, O−H), 1255 (s, Si−CH_3), 1005 (s, Si−O), 835 (s), 775 (s). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.09, 0.11 (each s, total 6 H, Si−CH_3), 0.90 (s, 9 H, *t*Bu), 1.25 (d, *J* = 6.4 Hz, 3 H, 4′-CH_3), 1.81 (ddd, *J* = 14.6, 6.4, 3.2 Hz, 1 H, 2′-H), 1.90, (s, 3 H, 3-CH_3), 2.02 (ddd, *J* = 14.6, 10.4, 3.6 Hz, 1 H, 2′-H), 2.18 (s, 3 H, 2-CH_3), 3.29 (d, *J* = 3.2 Hz, 1 H, 1′-OH), 4.20 (ddq, *J* = 6.4, 3.6, 6.4 Hz, 1 H, 3′-H), 4.90 (dt, *J* = 10.4, 3.2 Hz, 1 H, 1′-H), 5.99 (s, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −4.5, −3.6, 9.8, 11.3, 18.0, 23.2, 25.9, 43.0, 64.5, 66.9, 108.7, 114.3, 146.6, 153.9 ppm. $C_{16}H_{30}O_3Si$ (298.5): calcd. C 64.38, H 10.13; found C 64.40, H 10.26.

6: R_f = 0.75 (hexane/ethyl acetate, 3:1). n_D^{24} = 1.4651. $[\alpha]_D^{24}$ = +14.8 (*c* = 0.97, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3420 cm^{-1} (s, O−H), 1255 (s, Si−CH_3), 1000 (s, Si−O), 835 (s), 775 (s). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.095, 0.10 (each s, total 6 H, Si−CH_3), 0.90 (s, 9 H, *t*Bu), 1.20 (d, *J* = 6.4 Hz, 3 H, 4′-CH_3), 1.84−1.94, (m, 1 H, 2′-H), 1.90 (s, 3 H, 3-CH_3), 1.95−2.07 (m, 1 H, 2′-H), 2.18 (s, 3 H, 2-CH_3), 3.38 (br. s, 1 H, 1′-OH), 4.07 (ddq, *J* = 9.2, 4.0, 6.4 Hz, 1 H, 3′-H), 4.76 (dd, *J* = 8.8, 4.0 Hz, 1 H, 1′-H), 6.00 (s, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −5.0, −3.6, 9.8, 11.3, 18.0, 24.3, 25.7, 43.1, 67.0, 68.9, 108.8, 112.4, 146.6, 153.9 ppm. $C_{16}H_{30}O_3Si$ (298.5): calcd. C 64.38, H 10.13; found C 64.13, H 10.47.

5-(3′-*tert*-Butyldimethylsilyloxy-1′-hydroxybutyl)-2,3-dimethylfuran (1′*S*,3′*R*)-5 and (1′*R*,3′*R*)-6: Using the procedure described above, (*R*)-**4** (17.5 g, 86.0 mmol) was converted into 23.2 g (96%) of a mixture of (1′*S*,3′*R*)-**5** and (1′*R*,3′*R*)-**6** as a pale yellow oil. This mixture was purified by chromatography to give the less polar (1′*S*,3′*R*)-**5** (8.08 g, 31%) and the more polar (1′*R*,3′*R*)-**6** (6.43 g, 25%) as oils.

(1′*S*,3′*R*)-**5:** n_D^{23} = 1.4651. $[\alpha]_D^{24}$ = −27.9 (*c* = 1.10, $CHCl_3$). IR and NMR spectra are identical to those of **5**. $C_{16}H_{30}O_3Si$ (298.5): calcd. C 64.38, H 10.13; found C 64.61, H 10.24.

(1′*R*,3′*R*)-**6**: n_D^{24} = 1.4638. $[\alpha]_D^{24}$ = −13.8 (*c* = 1.06, $CHCl_3$). IR and NMR spectra are identical to those of **6**. $C_{16}H_{30}O_3Si$ (298.5): calcd. C 64.38, H 10.13; found C 64.41, H 9.87.

(2*R*,6*RS*,2′*S*)-2-(2′-*tert*-Butyldimethylsilyloxypropyl)-6-hydroxy-5,6-dimethyl-2*H*-pyran-3-one (9): MCPBA (70%, 8.60 g, 34.9 mmol) was added to a stirred solution of (1′*R*,3′*S*)-**5** (5.20 g, 17.4 mmol) in dry CH_2Cl_2 (100 mL) at 0 °C. The mixture was stirred for 1 h, poured into a sat. Na_2SO_3 solution and stirred for 30 min. It was then poured into sat. $NaHCO_3$ solution and stirred for a further 30 min. The mixture was then extracted with diethyl ether. The organic layers were washed with sat. Na_2SO_3 solution and brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by chromatography over silica gel (100 g) with *n*-hexane/ethyl acetate (5:1) yielding **9** (4.59 g, 89%) as a colorless solid. (diastereomeric mixture; major/minor = 4:1) This was further purified by recrystallization from *n*-pentane to give pure **9** as colorless needles, m.p. 68−74 °C. $[\alpha]_D^{24}$ = +19.9 (*c* = 1.08, $CHCl_3$). IR (nujol): $\tilde{\nu}_{max}$ = 3430 cm^{-1} (s, O−H), 1660 (m, C=O), 1255 (m, Si−CH_3), 1140 (s, C−O), 1025 (s, Si−O), 835 (s), 780 (s). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.07 (s, 6 H, Si−CH_3), 0.87 (s, 9 H, *t*Bu), 1.15 (d, *J* = 6.1 Hz, 3 H, 3′-CH_3), 1.50, 1.68 [each ddd, *J* = 14.3, 10.5, 2.9 Hz, total 1 H (4:1), 1′-H], 1.59, 1.60 [each s, total 3 H (1:4), 6-CH_3], 2.02 (br. s, 3 H, 5-CH_3), 2.08, 2.16 [each ddd, *J* = 14.3, 9.8, 2.7 Hz, total 1 H (1:4), 1′-H], 2.59 (br. s, 1 H, 6-OH), 4.00−4.13 (m, 1 H, 2-H), 5.85 (br. s, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −4.6, −4.1, 18.0, 19.4, 24.4, 25.8, 27.1, 39.7, 64.2, 71.3, 94.9, 124.3, 158.7, 197.4 ppm. $C_{16}H_{30}O_4Si$ (314.5): calcd. C 61.11, H 9.61; found C 60.60, H 9.91.

(2*S*,6*RS*,2′*S*)-2-(2′-*tert*-Butyldimethylsilyloxypropyl)-6-hydroxy-5,6-dimethyl-2*H*-pyran-3-one (7): Using the procedure described for the preparation of **9**, **6** (3.60 g, 12.1 mmol) was converted into 3.44 g (96%) of **7** as a pale yellow oil, n_D^{24} = 1.4678. $[\alpha]_D^{24}$ = +48.2 (*c* = 1.02, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3405 cm^{-1} (s, O−H), 1675 (s, C=O), 1255 (s, Si−CH_3), 1105 (s, C−O), 1010 (s, Si−O), 835 (s), 775. ^1H NMR (400 MHz, $CDCl_3$): δ = −0.01, 0.01 (each s, total 6 H, Si−CH_3), 0.83 (s, 9 H, *t*Bu), 1.15 (d, *J* = 6.1 Hz, 3 H, 3′-H), 1.57, 1.58 [each s, total 3 H (1:4), 6-CH_3], 1.73, 1.84 [each ddd, *J* = 13.7, 7.3, 6.4 Hz, total 1 H (4:1), 1′-H], 1.93−2.08 (m, 1 H, 1′-H), 1.99 (br. s, 3 H, 5-CH_3), 3.38 (br. s, 1 H, 6-OH), 4.03−4.16 (m, 1 H, 2′-H), 4.26, 4.52 [each dd, *J* = 7.3, 4.9 Hz, total 1 H (1:4), 2-H], 5.81 (br. s, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = −4.8, −4.7, 14.1, 18.0, 19.4, 23.6, 25.9, 39.4, 65.5, 71.3, 94.9, 124.2, 158.9, 197.3 ppm. $C_{16}H_{30}O_4Si$ (314.5): calcd. C 61.11, H 9.61; found C 60.75, H 9.65.

(2*S*,6*RS*,2′*R*)-2-(2′-*tert*-Butyldimethylsilyloxypropyl)-6-hydroxy-5,6-dimethyl-2*H*-pyran-3-one (9): Using the procedure described for the preparation of **9**, (1′*S*,3′*R*)-**5** (8.00 g, 26.8 mmol) was converted into 6.61 g (78%) of (2*S*,6*RS*,2′*R*)-**9** as a colorless solid. This was further purified by recrystallization from *n*-pentane to give pure (2*S*,6*RS*,2′*R*)-**9** as colorless needles, m.p. 68−73 °C. $[\alpha]_D^{24}$ = −18.3 (*c* = 1.13, $CHCl_3$). IR and NMR spectra are identical to those of **9**. $C_{16}H_{30}O_4Si$ (314.5): calcd. C 61.11, H 9.61; found C 61.05, H 9.67.

(2*R*,6*RS*,2′*R*)-2-(2′-*tert*-Butyldimethylsilyloxypropyl)-6-hydroxy-5,6-dimethyl-2*H*-pyran-3-one (7): Using the procedure described for the preparation of **7**, (1′*R*,3′*R*)-**6** (2.44 g, 8.17 mmol) was converted into 1.94 g (75%) of (2*R*,6*RS*,2′*R*)-**7** as a pale yellow oil, n_D^{24} = 1.4657. $[\alpha]_D^{24}$ = −45.7 (*c* = 1.01, $CHCl_3$). IR and NMR spectra are identical to those of **7**. $C_{16}H_{30}O_4Si$ (314.5): calcd. C 61.11, H 9.61; found C 60.91, H 9.79.

(1*R*,3*S*,5*R*)-1,3,8-Trimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-one (10): An aqueous solution of HF (46%, 47.0 mL, 1.09 mol) was added dropwise to a stirred solution of (2*R*,6*RS*,2′*S*)-**9** (4.50 g, 14.3 mmol) in MeCN (120 mL) at 0 °C over 2 min. The mixture

was stirred at 0 °C for 30 min, then added slowly to a sat. K_2CO_3 solution at 0 °C over 5 min with stirring. The organic layer was separated and the aqueous layer was extracted with diethyl ether. The combined organic solution was washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography over silica gel (50 g). Elution with *n*-pentane/diethyl ether (20:1) followed by distillation in the presence of $MgCO_3$ gave pure **10** (2.06 g, 79%) as a colorless oil, b.p. 114 °C/13 Torr. $n_D^{22} = 1.4909$. $[\alpha]_D^{22} = +372$ ($c = 1.07$, $CHCl_3$). IR (film): $\tilde{\nu}_{max} = 1690\ cm^{-1}$ (s, C=O), 1625 (w, C=C), 1125 (s, C−O), 1110 (s, C−O), 955 (s), 880 (s). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.19 (d, $J = 6.1$ Hz, 3 H, 3-CH_3), 1.53 (s, 3 H, 1-CH_3), 1.59 (ddd, $J = 13.6, 3.0, 1.4$ Hz, 1 H, 4-H*a*), 1.85 (ddd, $J = 13.6, 12.0, 6.1$ Hz, 1 H, 4-H*e*), 1.96 (d, $J = 1.4$ Hz, 3 H, 8-CH_3), 3.89 (ddq, $J = 12.0, 3.0, 6.1$ Hz, 1 H, 3-H), 4.30 (br. d, $J = 6.1$ Hz, 1 H, 5-H), 6.14 (s, 1 H, 7-H) ppm. ^{13}C NMR 100 MHz, $CDCl_3$): δ = 19.5, 21.9, 24.8, 34.1, 64.2, 75.0, 96.0, 126.8, 156.9, 197.2 ppm. $C_{10}H_{14}O_3$ (182.2): calcd. C 65.91, H 7.74; found C 65.85, H 7.86.

(1*S*,3*R*,5*S*)-1,3,8-Trimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-one (10): Using the procedure described for the preparation of (1*R*,3*S*,5*R*)-**10**, (2*S*,6*RS*,2′*R*)-**9** (6.46 g, 20.5 mmol) was converted into 2.03 g (54%) of (1*S*,3*R*,5*S*)-**10** as a colorless oil, $n_D^{24} = 1.4897$. $[\alpha]_D^{24} = -371$ ($c = 0.99$, $CHCl_3$). IR and NMR spectra are identical to those of (1*R*,3*S*,5*R*)-**10**. $C_{10}H_{14}O_3$ (182.2): calcd. C 65.91, H 7.74; found C 65.52, H 7.99.

(1*R*,3*S*,5*R*,6*R*)-1,3,8-Trimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-ol (11): $NaBH_4$ (390 mg, 10.4 mmol) was added to a stirred solution of (1*R*,3*S*,5*R*)-**10** (1.90 g, 10.4 mmol) and $CeCl_3{\cdot}7H_2O$ (3.87 g, 10.4 mmol) in MeOH (40 mL) at 0 °C. After 10 min the mixture was diluted with cold H_2O, and extracted with diethyl ether. The diethyl ether solution was washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by chromatography over silica gel (40 g) with *n*-pentane/diethyl ether (1:1) yielding (1*R*,3*S*,5*R*,6*R*)-**11** (1.81 g, 94%) as a colorless oil, $n_D^{22} = 1.4842$. $[\alpha]_D^{22} = +47.2$ ($c = 1.05$, $CHCl_3$). IR (film): $\tilde{\nu}_{max} = 3445\ cm^{-1}$, (s, O−H), 1675 (w, C=C), 1230 (s, C−O), 1100 (s, C−O), 880 (s), 840 (s). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.18 (d, $J = 6.1$ Hz, 3 H, 3-CH_3), 1.41 (s, 3 H, 1-CH_3), 1.53 (br. s, 1 H, 6-OH), 1.55−1.71 (m, 1 H, 4-H), 1.66 (br. s, 3 H, 8-CH_3), 1.89 (dd, $J = 14.1, 3.4$ Hz, 1 H, 4-H), 3.96 (ddq, $J = 11.9, 3.4, 6.1$ Hz, 1 H, 3-H), 4.16 (t, $J = 6.4$ Hz, 1 H, 5-H), 4.59−4.65 (br. m, 1 H, 6-H), 5.70 (br. s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.0, 22.3, 24.6, 30.1, 64.0, 65.8, 70.0, 95.4, 127.7, 134.8 ppm. $C_{10}H_{16}O_3$ (184.2): calcd. C 65.19, H 8.75; found C 64.87, H 8.91.

(1*S*,3*R*,5*S*,6*S*)-1,3,8-Trimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-ol (11): Using the procedure described for the preparation of (1*R*,3*S*,5*R*,6*R*)-**11**, (1*S*,3*R*,5*S*)-**10** (1.75 g, 9.60 mmol) was converted into 1.63 g (92%) of (1*S*,3*R*,5*S*,6*S*)-**11** as a colorless oil, $n_D^{24} = 1.4877$. $[\alpha]_D^{24} = -48.9$ ($c = 1.04$, $CHCl_3$). IR and NMR spectra are identical to those of (1*R*,3*S*,5*R*,6*R*)-**11**. $C_{10}H_{16}O_3$ (184.2): calcd. C 65.19, H 8.75; found C 64.81, H 8.90.

(1*R*,3*S*,5*R*,6*R*)-*O*-1,3,8-Trimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-yl *S*-Methyldithiocarbonate (12): *n*BuLi (1.56 M in *n*-hexane, 5.45 mL, 8.50 mmol) was added dropwise to a stirred solution of (1*R*,3*S*,5*R*,6*R*)-**11** (1.42 g, 7.70 mmol) in dry THF (40 mL) at −78 °C over 5 min under Ar. After stirring at 0 °C for 1 h a solution of CS_2 (99%, 0.920 mL, 15.4 mmol) in dry THF (20 mL) at −20 °C was added over 10 min and the resulting mixture was stirred at 0 °C for 30 min. Then a solution of MeI (1.47 mL, 23.1 mmol) in dry THF (20 mL) was added at 0 °C over 10 min and the mixture was stirred at 0 °C for a further 30 min. After stirring for 1 h at room temperature, the mixture was poured into sat. NH_4Cl solution and extracted with diethyl ether. The residue was purified by chromatography over silica gel (40 g) with *n*-pentane/diethyl ether (40:1) yielding **12** (2.07 g, 98%) as a pale yellow oil, $n_D^{22} = 1.5162$. $[\alpha]_D^{23} = -50.1$ ($c = 0.36$, $CHCl_3$). IR (film): $\tilde{\nu}_{max} = 1205\ cm^{-1}$ (s, C=S), 1125 (s, C−S), 1110 (s, C−S), 1055 (s, C−O), 955 (s), 880 (s). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.20 (d, $J = 6.2$ Hz, 3 H, 3-CH_3), 1.42 (s, 3 H, 1-CH_3), 1.62−1.76 (m, 2 H, 4-H), 1.71 (br. s, 3 H, 8-CH_3), 2.57 (s, 3 H, S-C*H*$_3$), 4.06 (ddq, $J = 11.6, 4.0, 6.2$ Hz, 1 H, 3-H), 4.52 (t, $J = 5.9$ Hz, 1 H, 5-H), 5.78 (br. s, 1 H, 7-H), 6.30−6.38 (m, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.1, 19.3, 22.2, 24.5, 31.3, 63.9, 66.6, 76.5, 95.5, 122.7, 137.5, 215.2 ppm. $C_{12}H_{18}O_3S_2$ (274.4): calcd. C 52.52, H 6.61; found C 52.53, H 6.65.

(1*S*,3*R*,5*S*,6*S*)-*O*-1,3,8-Trimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-yl *S*-Methyldithiocarbonate (12): Using the procedure described for the preparation of (1*R*,3*S*,5*R*,6*R*)-**12**, (1*S*,3*R*,5*S*,6*S*)-**11** (1.58 g, 8.58 mmol) was converted into 2.21 g (94%) of (1*S*,3*R*,5*S*,6*S*)-**12** as a colorless oil, $n_D^{23} = 1.5159$. $[\alpha]_D^{23} = +52.7$ ($c = 1.13$, $CHCl_3$). IR and NMR spectra are identical to those of (1*R*,3*S*,5*R*,6*R*)-**12**. $C_{12}H_{18}O_3S_2$ (274.4): calcd. C 52.52, H 6.61; found C 52.28, H 6.60.

(1*R*,3*S*,5*S*)-1,3,8-Trimethyl-2,9-dioxabicyclo[3.3.1]non-7-ene (1): $(n\text{Bu})_3SnH$ (97%, 21.4 mL, 78.0 mmol) was added dropwise to a stirred solution of (1*R*,3*S*,5*R*,6*R*)-**12** (2.06 g, 7.50 mmol) and AIBN (98%, 665 mg, 3.97 mmol) in dry toluene (50.0 mL) over 30 min with stirring and heating at 60 °C for 3 h. The cooled mixture was filtered through silica gel (500 g) and the silica gel was washed with diethyl ether. The concentrated filtrate was purified by chromatography over silica gel (40 g) with *n*-pentane/diethyl ether (10:1) followed by distillation in the presence of $MgCO_3$ yielding pure **1** (559 mg, 44%) as a colorless oil, b.p. 93 °C/22 Torr. $n_D^{22} = 1.4690$. $[\alpha]_D^{22} = +116$ ($c = 1.04$, $CHCl_3$). IR (film): $\tilde{\nu}_{max} = 2970\ cm^{-1}$ (s), 2935 (S), 1435 (m), 1375 (s), 1350 (m), 1325 (m), 1295 (m), 1230 (s), 1200 (m), 1150 (m), 1125 (s), 1115 (s), 1095 (m), 1065 (m), 1005 (m), 955 (s), 875 (m), 855 (s), 795(m). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.16 (d, $J = 6.1$ Hz, 3 H, 3-CH_3), 1.36 (ddd, $J = 13.4, 3.2, 1.2$ Hz, 1 H, 4-H), 1.42 (s, 3 H, 1-CH_3), 1.65 (dt, $J = 2.7, 1.2$ Hz, 3 H, 8-CH_3), 1.78−1.91 (m, 2 H 4-H, 6-H), 2.64 (br. d, $J = 16.6$ Hz, 1 H, 6-H), 4.03 (ddq, $J = 12.0, 3.2, 6.1$ Hz, 1 H, 3-H), 4.29 (t, $J = 6.6$ Hz, 1 H, 5-H), 5.75 (br. s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.6, 22.3, 24.7, 30.3, 38.2, 63.7, 66.5, 95.4, 123.4, 132.9 ppm. MS (EI): *m*/*z* (%) = 43 (100), 71 (16), 81 (22), 93 (15), 109 (59), 125 (5), 153 (7), 168 (17). HRMS (for $C_{10}H_{16}O_2$): calcd. 168.1150; found 168.1144 [M^+]. GC [DB-WAX column (0.25 mm × 60 m), 110 to 250 °C, +5.0 °C/min; He carrier gas at 1.0 kg/cm^2] $t_R = 5.6$ min (**1**, ≈100%); [Chirasil-DEX® (0.25 mm × 25 m), 100 to 250 °C, +3.0 °C/min; He carrier gas at 1.0 kg/cm^2] $t_R = 7.3$ min [(1*S*,3*R*,5*R*)-**1**, 1.6%], $t_R = 7.5$ min (**1**, 98.4%, 96.8% *ee*). MS of **1** correlated well with the reported spectrum of the natural product. Due to high volatility of **1**, its correct combustion analytical data could not be obtained.

(1*S*,3*R*,5*R*)-1,3,8-Trimethyl-2,9-dioxabicyclo[3.3.1]non-7-ene (1): Using the procedure described for the preparation of (1*R*,3*S*,5*S*)-**1**, (1*S*,3*R*,5*S*,6*S*)-**12** (1.92 g, 7.00 mmol) was converted into 591 mg (50%) of (1*S*,3*R*,5*R*)-**1** as a colorless oil, b.p. 86 °C/19 Torr. $n_D^{24} = 1.4671$. $[\alpha]_D^{23} = -116$ ($c = 1.01$, $CHCl_3$). IR, NMR and MS(EI) spectra are identical to those of (1*R*,3*S*,5*S*)-**1**. HRMS (for $C_{10}H_{16}O_2$): calcd. 168.1150; found *m*/*z* = 168.1156 [M^+]. GC [DB-WAX column (0.25 mm × 60 m), 110 to 250 °C, +5.0 °C/min; He carrier gas at 1.0 kg/cm^2] $t_R = 5.6$ min (**1**, 97.0%); [Chirasil-DEX® (0.25 mm × 25 m), 100 to 250 °C, +3.0 °C/min; He carrier gas at 1.0 kg/cm^2] $t_R = 7.2$ min (100%, ≈100% *ee*). The MS of

(1*S*,3*R*,5*R*)-**1** correlated well with the reported spectrum of the natural product. Due to high volatility of (1*S*,3*R*,5*R*)-**1**, its correct combustion analytical data could not be obtained.

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