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Absolute configuration of gomadalactones A, B and C, the components of the contact sex pheromone of *Anoplophora malasiaca*☆

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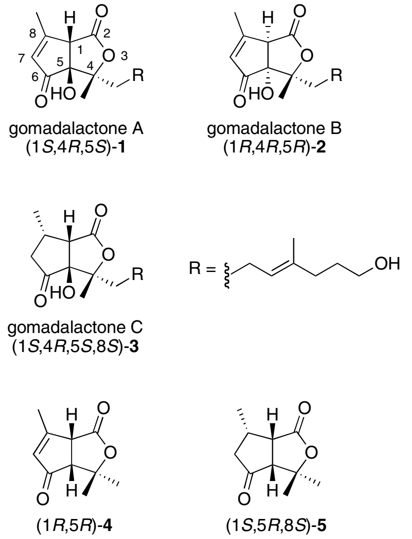
Abstract—Absolute configuration of gomadalactones A (**1**), B (**2**) and C (**3**), the pheromone components of the white-spotted longicorn beetle (*Anoplophora malasiaca*) was assigned as (1*S*,4*R*,5*S*)-**1**, (1*R*,4*R*,5*R*)-**2** and (1*S*,4*R*,5*S*,8*S*)-**3** by comparing their published CD spectra with those of (1*R*,5*R*)-(+)-4,4,8-trimethyl-3-oxabicyclo[3.3.0]oct-7-ene-2,6-dione (**4**) and (1*S*,5*R*,8*S*)-(+)-4,4,8-trimethyl-3-oxabicyclo[3.3.0]octane-2,6-dione (**5**) prepared from (*R*)-(−)-carvone (**6**).

Yasui et al. recently clarified the structures of gomadalactones A (**1**, Scheme 1), B (**2**) and C (**3**), the components of the contact sex pheromone of the female white-spotted longicorn beetle, *Anoplophora malasiaca*.[2] Their unique structures as novel 3-oxabicyclo[3.3.0]-octanes attracted our attention, especially because their absolute configuration remained unknown. Since the CD spectra of **1**, **2** and **3** have been published,[2] assignment of their absolute configuration seems feasible, if we can synthesize and measure the CD spectra of the optically active **1**–**3** or their close relatives.

This Letter describes the synthesis and CD measurements of (1*R*,5*R*)-4,4,8-trimethyl-3-oxabicyclo[3.3.0]oct-7-ene-2,6-dione (**4**) and (1*S*,5*R*,8*S*)-4,4,8-trimethyl-3-oxabicyclo[3.3.0]octane-2,6-dione (**5**). CD spectral comparison of **4** and **5** with **1**, **2** and **3** allowed us to assign the absolute configuration of the latter pheromone components as (1*S*,4*R*,5*S*)-**1**, (1*R*,4*R*,5*R*)-**2** and (1*S*,4*R*,5*S*,8*S*)-**3** as detailed below.



Scheme 1. Structures of gomadalactones A (**1**), B (**2**) and C (**3**), and the model compounds **4** and **5**.

Scheme 2 summarizes our synthesis of **4** and **5** from (*R*)-(−)-carvone (**6**). Wallach converted (*R*)-**6** to (1*R*,5*R*)-(+)-carvenolide (**8**) via tribromide **7** as early as in 1899.[3] Oxidation of **8** with chromic anhydride-3,5-dimethylpyrazole complex[4,5] in dichloromethane furnished α,β-unsaturated ketone (1*R*,5*R*)-**4**.[6] Its structure as **4** was supported by its IR, ^{1}H and ^{13}C NMR spectral data,[6] and its absolute configuration was thought to be as depicted in **4**, because its (*R*)-stereochemistry at C-5 originated from that of (*R*)-(−)-carvone (**6**). Finally, hydrogenation of **4** over palladium–charcoal delivered

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Keywords: *Anoplophora malasiaca*; Carvenolide; CD spectra; Gomadalactone; Pheromone.

☆ Pheromone synthesis, Part 234. For Part 233, see Ref. 1.

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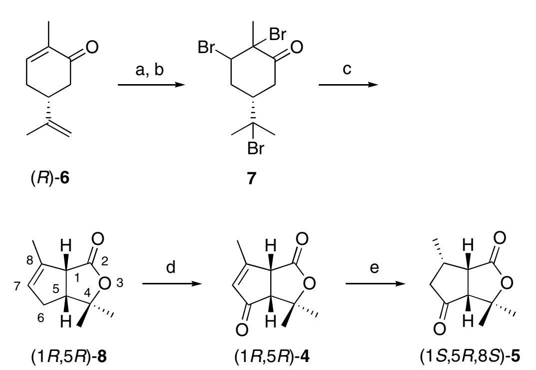

Scheme 2. Synthesis of (1*R*,5*R*)-**4** and (1*S*,5*R*,8*S*)-**5**. Reagents and conditions: (a) 30% HBr in AcOH, 0–5 °C; (b) Br_2, 0–5 °C, 30 min (quant.); (c) THF, 28% NH_3 aq soln, 0 °C—room temperature; steam distillation (15%); (d) CrO_3, 3,5-dimethylpyrazole, CH_2Cl_2, −10 to −20 °C, 2.5 h (16%); (e) H_2, 10% Pd–C, EtOAc, room temperature, 2 h (95%).

the hydrogen atom at C-8 from the less hindered β-side[7–9] to give keto lactone (1*S*,5*R*,8*S*)-**5**.[10]

Figure 1 shows the CD spectra of **4** and **5**. The unsaturated keto lactone (1*R*,5*R*)-**4** showed a positive first Cotton effect at 239.8 nm ($\Delta\varepsilon = +28.2$), and a negative one at 216.5 nm ($\Delta\varepsilon = -34.3$), while the saturated keto lactone (1*S*,5*R*,8*S*)-**5** showed a weak and positive Cotton effect at 304.9 nm ($\Delta\varepsilon = +4.52$). According to Yasui et al., gomadalactone A (**1**) exhibited first positive and second negative Cotton curves, $\lambda_{\text{ext.}}$ 242.8 nm ($\theta = +83.4$ mdeg) and $\lambda_{\text{ext.}}$ 219.2 nm ($\theta = -106.5$ mdeg), while gomadalactone B (**2**) showed a CD curve antipodal to that of **1**.[2] Gomadalactone C (**3**) exhibited a positive Cotton effect at $\lambda_{\text{ext.}}$ 313.0 nm ($\theta = +31.9$ mdeg).[2] Accordingly, gomadalactone A (**1**) and (1*R*,5*R*)-**4** belong to the same stereochemical series, and gomadalactone B (**2**) possesses opposite stereochemistry at C-1 and C-5. Gomadalactone C (**3**) share the same stereochemistry as that of (1*S*,5*R*,8*S*)-**5**. Since the relative stereochemistry of **1**, **2** and **3** had already been settled by Yasui et al.,[2] their absolute stereochemistries were assigned as shown in Scheme 1.

In conclusion, stereostructures of gomadalactones A, B and C were assigned as depicted in **1**, **2** and **3**. The absence of a hydroxy group at C-5 of **4** and **5** seems to be of little importance for the shape of their CD spectra.

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6. *Conversion of (1R,5R)-***8** *to (1R,5R)-***4** *and the physical data of (1R,5R)-***4**: 3.5-Dimethylpyrazole (11.5 g, 120 mmol) was added in one portion to a stirred and cooled suspension of CrO_3 (12.0 g, 120 mmol) in CH_2Cl_2 (90 mL) at −20 °C under Ar. The mixture was stirred at −20 °C for 15 min. A solution of (1*R*,5*R*)-**8** (1.66 g, 10 mmol) in CH_2Cl_2 (10 mL) was then added dropwise to the stirred suspension at −20 °C to −10 °C, and the mixture was stirred for 2.5 h at −20 °C. Subsequently, a solution of NaOH (10 g, 250 mmol) in H_2O (50 mL) was added dropwise at −20 °C to 0 °C. The stirring was continued for 30 min at 0 °C. Then the CH_2Cl_2 layer was separated, successively washed with dil HCl aq, water and brine, dried ($MgSO_4$), and concentrated in vacuo to give a crude product (1.43 g) as a dark oil. This was purified by SiO_2 (20 g) chromatography. Elution with hexane/EtOAc (20:1 to 5:1) gave the recovered **8** (0.3 g), and **4** (240 mg, 16% based on the consumed **8**). Recrystallization from

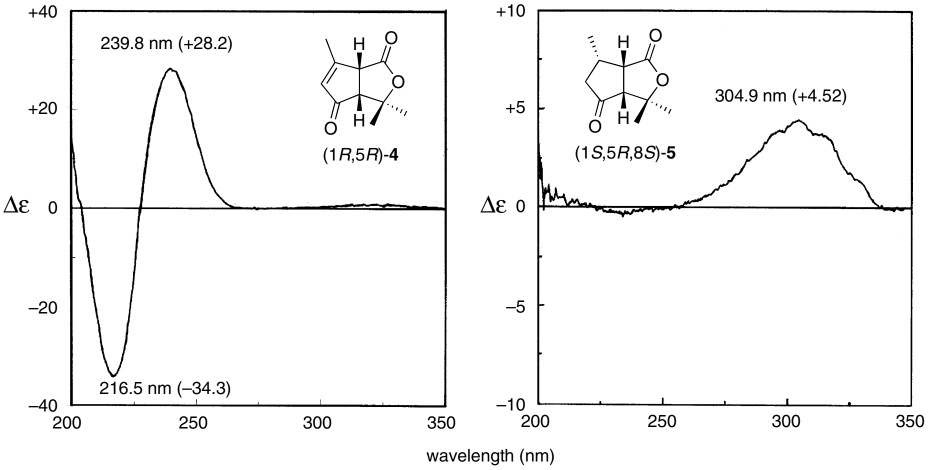

Figure 1. CD spectra of (1*R*,5*R*)-**4** and (1*S*,5*R*,8*S*)-**5**. They were measured in MeOH using a 1 cm cell at the concentrations of 5.4×10^{-5} M (**4**) and 6.6×10^{-5} M (**5**), respectively, on a Jasco J-720 CD spectrometer.

EtOAc/hexane gave colourless rods, mp 52.5–53.0 °C; $[\alpha]_D^{23}$ +292 (*c* 0.957, Et_2O). ν_{max} (Nujol): 1763 (s, C=O), 1689 (s, C=O), 1620 (s, C=C), 1261 (s), 1126 (s); δ_H ($CDCl_3$, 400 MHz): 1.43 (3H, s), 1.56 (3H, s), 2.35 (3H, br s), 2.98 (1H, d, *J* 7.8), 3.87 (1H, d, *J* 7.8), 5.98 (1H, br s); δ_c ($CDCl_3$, 100 MHz): 17.6, 24.8, 31.8, 52.9, 55.2, 84.6, 131.2, 171.6, 173.6, 204.2; CD (Jasco J-720, *c* 5.4×10^{-5} M, MeOH): $\lambda_{ext.}$ 239.8 nm ($\Delta\varepsilon = +28.2$), 216.5 ($\Delta\varepsilon = -34.3$). Anal. Calcd for $C_{10}H_{12}O_3$ (180.2): C, 66.65; H, 6.71. Found: C, 66.59; H, 6.76.

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10. *Conversion of (1R,5R)-***4** *to (1S,5R,8S)-***5** *and the physical data of (1S,5R,8S)-***5**: 10% Palladium–charcoal (120 mg) was added to a solution of **4** (165 mg, 0.92 mmol) in EtOAc (5 mL), and the suspension was stirred under H_2 (balloon) for 2 h at room temperature. The suspension was filtered through SiO_2 (2 g), and Pd–C/SiO_2 was washed with EtOAc. The combined EtOAc solution was concentrated in vacuo to give **5** (159 mg, 95%) as a crystalline solid. Recrystallization from EtOAc/hexane gave colourless needles, mp 83.0–84.0 °C; $[\alpha]_D^{25}$ +319 (*c* 1.014, Et_2O). ν_{max} (Nujol): 1763 (s, C=O), 1740 (s, C=O), 1257 (s), 1169 (s), 1084 (m), 937 (m), 744 (m); δ_H ($CDCl_3$, 400 MHz): 1.41 (3H, d, *J* 6.8), 1.42 (3H, s), 1.45 (3H, s), 1.95 (1H, t-like), 2.45 (1H, m), 2.52 (1H, m), 2.73 (1H, d, *J* 8.8), 3.43 (1H, t, *J* 8.8); δ_C ($CDCl_3$, 100 MHz): 15.7, 24.2, 30.8, 31.9, 46.6, 47.0, 58.2, 83.4, 174.4, 213.2; CD (*c* 6.6×10^{-5} M, MeOH): $\lambda_{ext.}$ 304.9 nm ($\Delta\varepsilon = +4.52$). Anal. Calcd for $C_{10}H_{14}O_3$ (182.2): C, 65.91; H, 7.74. Found: C, 65.83; H, 7.72.