Pheromone Synthesis, CLXXV<sup>[ $\diamond$ ]</sup>

## Synthesis of Koiganal I and II, the Sex Pheromone Components of the Webbing Clothes Moth

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Received July 10, 1996

Keywords: Koiganal I / Koiganal II / Pheromone / Tineola bisselliella

Koiganal I [(E)-2-octadecenal (1)] and II [(2E,13Z)-2,13-octadecadienal (2)], the female-produced pheromone components of the webbing clothes moth (Tineola bisselliella), were synthesized.

In 1985 Yamaoka et al. isolated 6 µg of koiganal I and 12 µg of koiganal II from the extract of ca. 25000 adult females of the webbing clothes moth, Tineola bisselliella Hummel (Lepidoptera; Tineidae. common name in Japanese = koiga), and determined their structures as 1 and 2, respectively, by mass spectrometry and synthesis<sup>[1]</sup>. However, experimental details of this synthesis are not available. T. bisselliella is a pest which causes damage by larvae feeding on wool, fur and other products of animal origin, especially in museums. In order to use 1 and 2 for the purpose of monitoring the population of T. bisselliella, we synthesized 1 and 2.

Scheme 1 summarizes our synthesis of koiganal I and II, which is simple and straightforward. Oxidation of 1-hexadecanol (3) with pyridinium chlorochromate (PCC) gave hexadecanal (4)<sup>[2]</sup>, which was subjected to the Horner-type Wittig reaction to furnish 5. Reduction of 5 with diisobutylaluminium hydride afforded (E)-2-octadecen-1-ol (6), whose oxidation with PCC gave koiganal I (1). The overall

Scheme 1. Synthesis of koiganal I and II<sup>[a]</sup>



<sup>[a]</sup> Reagents: (a) PCC, CH<sub>2</sub>Cl<sub>2</sub> (86% for 4; 93% for 1; 75% for 8; 95% for 2). – (b)  $(EtO)_2P(O)CH_2CO_2Et$ , NaH, THF (68% for 5; 93% for 9). - (c) *i*Bu<sub>2</sub>AIH, toluene (94% for 6; 96% for 10).

[<sup>()</sup>] Part CLXXIV: K. Mori, H. Horikiri, Liebigs Ann. 1996, 501 - 505.

yield of 1 was 51% based on 3 (4 steps). The synthesis of koiganal II started from (Z)-11-hexadecen-1-ol (7), whose PCC oxidation gave the aldehyde 8. Treatment of 8 with the anion generated from triethyl phosphonoacetate yielded 9. The corresponding alcohol 10 was oxidized with PCC to give koiganal II (2). The overall yield of 2 was 64% based on 7 (4 steps).

In conclusion, koiganal I and II were prepared in amounts sufficient for a detailed bioassay.

We thank Drs. J. Chambers and D. B. Pinniger, Central Science Laboratory, MAFF, U.K., for their suggestion to undertake the present project. Financial support of the project by Kumagai Science Foundation and Nitto Denko Co. is gratefully acknowledged. We also thank Mr. Ri-ichiro Kawaguchi for his help in the experiments.

## **Experimental Section**

Boiling points and melting points: uncorrected values. - IR: Perkin-Elmer 1640. - <sup>1</sup>H NMR: Hitachi R-24 B (60 MHz), Jeol JNM-EX 90A (90 MHz) and Jeol JNM-EX 270L (270 MHz) (TMS at  $\delta = 0.00$  or CHCl<sub>3</sub> at  $\delta = 7.26$  as an internal standard).  $- {}^{13}C$ NMR: Jeol JNM-EX 90A (22.5 MHz, TMS as an internal standard).

Hexadecanal (4): To a suspension of PCC (16.2 g, 75.2 mmol) in dry dichloromethane (150 ml), a solution of 3 (12.1 g, 50.0 mmol) in dry dichloromethane (150 ml) was added and this mixture was stirred for 5 h at room temperature. Diethyl ether (100 ml) and MgSO<sub>4</sub> (10 g) were added to the reaction mixture. The resulting mixture was filtered through a column of silica gel (300 g). The filtrate was concentrated in vacuo, and the residue was purified by chromatography on silica gel (300 g, hexane/ethyl acetate, 100:1) to give 10.4 g (86%) of 4 as waxy crystals, m.p. 33.5-34.0 °C (ref.<sup>[3]</sup> m.p. 34.0 °C). – IR (KBr disk):  $\tilde{v}_{max} = 1710 \text{ cm}^{-1}$  (s, C=O). – <sup>1</sup>H NMR (CDCl<sub>3</sub>, 60 MHz):  $\delta = 0.89$  (t, J = 6.3 Hz, 3H, 16-H<sub>3</sub>), 1.09-1.60 (m, 26 H, 3,4,5,6,7,8,9,10,11,12,13,14,15-H<sub>2</sub>), 2.42 (q, J = 7.2 Hz, 2H, 2-H<sub>2</sub>), 9.61 (t, J = 3 Hz, 1H, 1-H).

Ethyl (E)-2-Octadecenoate (5): NaH (60% suspension in oil, 0.2 g, 5 mmol) was suspended in dry THF (10 ml). Triethyl phosphonoacetate (1.5 ml, 7.5 mmol) was added to the slurry with stirring under argon. After the addition, the solution was stirred at room temperature for 1 h until hydrogen gas evolution had ceased.

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A solution of 4 (1.2 g, 5.0 mmol) in dry THF (10 ml) was added to the solution and stirred for 1 h at room temperature. Water was added to the reaction mixture, the organic phase was separated, and the aqueous phase was extracted with diethyl ehter (50 ml). The combined organic solutions were washed with water, a saturated aqueous NH<sub>4</sub>Cl solution and brine, dried with MgSO<sub>4</sub>, and concentrated in vacuo. The residue was purified by chromatography on silica gel (30 g, hexane/ethyl acetate, 300:1) to give 1.11 g (68%) of **5** as an oil,  $n_{\rm D}^{22} = 1.4539$ . – IR (film):  $\tilde{v}_{\rm max} = 1720$  cm<sup>-1</sup> (S, C=O), 1650 (m, C=C), 1180 (m, C-O). - <sup>1</sup>H NMR (CDCl<sub>3</sub>, 90 MHz):  $\delta = 0.89$  (t, J = 6.3 Hz, 3H, 18-H<sub>3</sub>), 1.09-1.60 (m, 29 H,  $5,6,7,8,9,10,11,12,13,14,15,16,17-H_2$ , 2'-H<sub>3</sub>), 2.18 (q, J = 7.2 Hz, 2 H, 4-H<sub>2</sub>), 4.18 (q, J = 7.2 Hz, 2 H, 1'-H<sub>2</sub>), 5.81 (dt, J = 16.2 Hz, J' = 2.6 Hz, 1 H, 2-H), 6.95 (dt, J = 16.2 Hz, J' = 7.2 Hz, 1 H, 3-H). - C<sub>20</sub>H<sub>38</sub>O (310.5): calcd. C 77.36, H 12.34; found C 77.59, H 12.42.

(*E*)-2-Octadecen-1-ol (**6**): To a stirred and cooled solution of **5** (0.40 g, 1.3 mmol) in dry toluene (10 ml), diisobutylaluminium hydride (1.01 M in toluene, 8 ml, 8 mmol) was added dropwise at  $-78 \,^{\circ}$ C under argon. After stirring for 1 h at  $-78 \,^{\circ}$ C, the reaction was quenched with methanol. The mixture was diluted with diethyl ether, filtered through Celite, and concentrated in vacuo. The residue was purified by chromatography on silica gel (7.0 g, hexane/ethyl acetate, 40:1) to give 0.33 g (94%) of **6** as a waxy solid, m.p. 45.5-46.0 °C. – IR (KBr disk):  $\tilde{v}_{max} = 3300 \, \text{cm}^{-1}$  (s, O–H), 1080 (m, C–O). – <sup>1</sup>H NMR (CDCl<sub>3</sub>, 270 MHz):  $\delta = 0.88$  (t, J = 6.6 Hz, 3H, 18-H<sub>3</sub>), 1.26–1.42 (m, 27 H, 5,6,7,8,9,10,11,12,13,14, 15,16,17-H<sub>2</sub>, -OH), 2.04 (q, J = 6.4 Hz, 2H, 4-H<sub>2</sub>), 4.09 (d, J = 5.0 Hz, 2H, 1-H<sub>2</sub>), 5.65 (dt, J = 15.5 Hz, J' = 5.0 Hz, 1H, 2-H), 5.68 (dt, J = 15.5 Hz, J' = 5.4 Hz, 1H, 3-H). – C<sub>18</sub>H<sub>36</sub>O (268.5): caled. C 80.53, H 13.52; found C 80.39, H 13.80.

(E)-2-Octadecenal (1): To a suspension of PCC (189 mg, 0.88 mmol) in dry dichloromethane (10 ml), a solution of 6 (157 mg, 0.58 mmol) in dry dichloromethane (5 ml) was added, and the mixture was stirred for 3 h at room temperature. Diethyl ether (5 ml) and MgSO<sub>4</sub> (1 g) were added to the reaction mixture. The obtained mixture was filtered through a column of silica gel (40 g). The filtrate was concentrated in vacuo, and the residue was purified by chromatography on silica gel (10 g, hexane/ethyl acetate, 80:1) to give 144 mg (93%) of 1 as a white solid, m.p. 43.5-44.0°C. - IR (KBr disk):  $\tilde{v}_{max} = 1700 \text{ cm}^{-1}$  (s, C=O), 1670 (m, C=C).  $- {}^{1}\text{H}$ NMR (CDCl<sub>3</sub>, 270 MHz):  $\delta = 0.88$  (t, J = 6.6 Hz, 3H, 18-H<sub>3</sub>), 1.26-1.29 (m, 24 H, 6,7,8,9,10,11,12,13,14,15,16,17-H<sub>2</sub>), 1.51 (quint, J = 7.1 Hz, 2H, 5-H<sub>2</sub>), 2.34 (q, J = 7.2 Hz, 2H, 4-H<sub>2</sub>), 6.11 (ddt, J = 15.8 Hz, J' = 7.9 Hz, J'' = 1.5 Hz, 1H, 2-H), 6.86 (dt, J = 15.5 Hz, J' = 6.8 Hz, 1H, 3-H), 9.51 (d, J = 7.9 Hz, 1H, 1-H).  $-{}^{13}$ C NMR (CDCl<sub>3</sub>, 22.5 MHz):  $\delta = 14.7, 23.3, 28.5, 29.8,$  $30.0, 30.1, 30.3, 32.5, 33.3, 135.6, 159.5, 194.6. - C_{18}H_{34}O$  (266.5): calcd. C 81.13, H 12.86; found C 80.85, H 12.74.

(Z)-11-Hexadecenal (8): To a suspension of PCC (1.5 g, 7.1 mmol) in dry dichloromethane (50 ml), a solution of 7 (1.1 g, 4.8 mmol) in dry dichloromethane (10 ml) was added and the mixture was stirred for 5 h at room temperature. Diethyl ether (10 ml) and MgSO<sub>4</sub> (1 g) were added to the reaction mixture, and the resulting mixture was filtered through a column of silica gel (100 g). The residue was concentrated in vacuo, and purified by chromatography on silica gel (20 g, hexane/ethyl acetate, 100:1) to give 0.85 g (75%) of 8 as an oil,  $n_{\rm D}^{23} = 1.4523$ . – IR (film):  $\tilde{v}_{\rm max} = 2730$  (w, C–H) cm<sup>-1</sup>, 1730 (s, C=O). – <sup>1</sup>H NMR (CDCl<sub>3</sub>, 90 MHz):  $\delta = 0.89$  (t, J = 6 Hz, 3H, 16-H<sub>3</sub>), 1.05–1.76 (m, 18H, 3,4,5,6,7,8,9,14,15-H<sub>2</sub>), 1.93 (m, 4H, 10, 13-H<sub>2</sub>), 2.38 (dt, J = 7 Hz, J' = 3 Hz, 2H, 2-H<sub>2</sub>),

5.27 (m, 2H, 11,12-H), 9.63 (t, J = 3 Hz, 1H, 1-H). This oil was employed for the next step without further purification.

Ethyl (2E,13Z)-Octadecadienoate (9): NaH (60% suspension in oil, 0.13 g, 3.3 mmol) was suspended in 10 ml of dry THF. Triethyl phosphonoacetate (0.6 ml, 3.2 mmol) was added to the slurry with stirring under argon. After the addition, the solution was stirred at room temperature for 30 min until hydrogen gas evolution had ceased. A solution of 8 (0.48 g, 2.0 mmol) in dry THF (20 ml) was added to the solution and the mixture was stirred for 1 h at room temperature. Water was added to the reaction mixture, the organic phase was separated, and the aqueous phase was extracted with diethyl ether (50 ml). The combined organic phases were washed with water, a saturated aqueous  $NH_4Cl$  solution and brine, dried with MgSO<sub>4</sub>, and concentrated in vacuo. The residue was purified by chromatography on silica gel (30 g, hexane/ethyl acetate, 100:1) to give 0.57 g (93%) of **9** as an oil,  $n_D^{22} = 1.4637$ . – IR (film):  $\tilde{v}_{max} = 1730 \text{ cm}^{-1}$  (s, C=O), 1660 (m, C=C), 1180 (m, C-O). -<sup>1</sup>H NMR (CDCl<sub>3</sub>, 90 MHz):  $\delta = 0.89$  (m, 3H, 18-H<sub>3</sub>), 1.26-1.38 (m, 18H, 5,6,7,8,9,10,11,16,17-H<sub>2</sub>), 1.45 (t, J = 7.0 Hz, 2H, 2'-H<sub>3</sub>), 2.01 (m, 4H, 12,15-H<sub>2</sub>), 2.19 (br. q, J = 7.6 Hz, 2H, 4-H<sub>2</sub>), 4.18  $(q, J = 7.0 \text{ Hz}, 2\text{ H}, 1'-\text{H}_2), 5.35 \text{ (m, 2H, 13,14-H)}, 5.81 \text{ (dt, } J =$ 15.5 Hz, J' = 1.7 Hz, 1H, 2-H), 6.96 (dt, J = 15.5 Hz, J' = 6.9Hz, 1H, 3-H). –  $C_{20}H_{36}O$  (308.5): calcd. C 77.87, H 11.76; found C 77.96, H 11.93.

(2E,13Z)-Octadecadien-1-ol (10): To a stirred and cooled solution of 9 (0.3 g, 1 mmol) in dry toluene (10 ml), diisobutylaluminium hydride (1.01 M in toluene, 6 ml, 6 mmol) was added dropwise at -78 °C under argon. After stirring for 1 h at -78 °C, the reaction was quenched with methanol, the obtained mixture was diluted with diethyl ether, filtered through Celite, and concentrated in vacuo. The residue was purified by chromatography on silica gel (20 g, hexane/ethyl acetate, 25:1) to give 0.26 g (96%) of 10 as an oil,  $n_D^{22} = 1.4699$ . – IR (film):  $\tilde{v}_{max} = 3320$  cm<sup>-1</sup> (s, O–H). – <sup>1</sup>H NMR (CDCl<sub>3</sub>, 90 MHz):  $\delta = 0.89$  (t, J = 5.7 Hz, 3H, 18-H<sub>3</sub>), 1.10–1.38 (m, 19 H, 5,6,7,8,9,10,11,16,17-H<sub>2</sub>, -OH), 2.02 (m, 6 H, 4,12,15-H<sub>2</sub>), 4.08 (d, J = 4.0 Hz, 2H, 1-H<sub>2</sub>), 5.35 (m, 2H, 13,14-H), 5.66 (t, J = 4.5 Hz, 2H, 2,3-H). – C<sub>18</sub>H<sub>34</sub>O (266.5): calcd. C 81.13, H 12.86; found C 81.33, H 12.48.

(2E,13Z)-Octadecadienal (2): To a suspension of PCC (160 mg, 0.74 mmol) in dry dichloromethane (10 ml), a solution of 10 (132 mg, 0.49 mmol) in dry dichloromethane (5 ml) was added, and the mixture was stirred for 3 h at room temperature. Diethyl ether (5 ml) and  $MgSO_4$  (1 g) were added to the reaction mixture, which was filtered through a column of silica gel (30 g). The residue was concentrated in vacuo, and purified by chromatography on silica gel (20 g, hexane/ethyl acetate, 60:1) to give 125 mg (95%) of 2 as an oil,  $n_{\rm D}^{24} = 1.4697$ . – IR (film):  $\tilde{v} = 2730$  (w, C–H) cm<sup>-1</sup>, 1700 (s, C=O), 1640 (m, C=C). - <sup>1</sup>H NMR (CDCl<sub>3</sub>, 90 MHz):  $\delta =$  $0.90 \text{ (m, 3H, 18-H_3)}, 1.29-1.43 \text{ (m, 18H, 5,6,7,8,9,10,11,16,17-}$ H<sub>2</sub>), 1.49 (t, J = 6.9 Hz, 2H, 4-H<sub>2</sub>), 2.02 (m, 4H, 12,15-H<sub>2</sub>), 5.35 (m, 2H, 13,14-H), 6.09 (ddt, J = 16.3 Hz, J' = 7.9 Hz, J'' = 1.5Hz, 1-H, 2-H), 6.86 (dt, J = 16.3 Hz, J' = 6.9 Hz, 1H, 3-H), 9.51 (d, J = 7.9 Hz, 1 H, 1-H).  $- {}^{13}$ C NMR (CDCl<sub>3</sub>, 22.4 MHz):  $\delta =$ 14.6, 23.0, 27.6, 27.8, 28.5, 29.8, 29.9, 30.0, 30.1, 30.4, 32.6, 33.4, 130.48, 130.54, 133.6, 159.6, 194.7. –  $C_{18}H_{32}O$  (264.5): calcd. C 81.95, H 12.20; found C 81.44, H 12.25,

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<sup>[2]</sup> Dictionary of Natural Products, vol. 3, 2754-2755, Chapman & Hall, London, 1994.

<sup>[3]</sup> Dictionary of Organic Compounds, 5th ed., vol. 3, p. 2895, Chapman & Hall, London, 1982.