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*Note*

# Simple Synthesis of 5,9-Dimethylated Long-Chain Alkanes, the Sex Pheromones of Leaf Miner Moths

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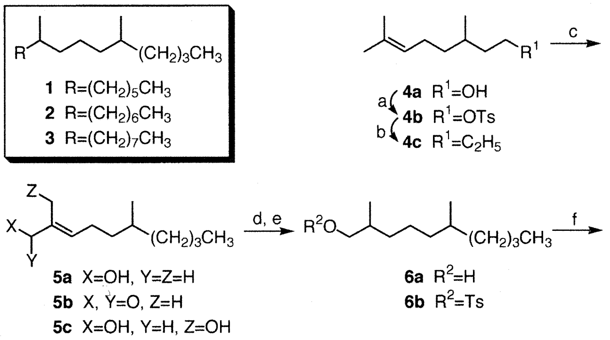
**Each stereoisomeric mixture of 5,9-dimethylpentadecane and 5,9-dimethylhexadecane, the major and the minor sex pheromone components of *Perileucoptera coffeella*, respectively, was synthesized in about 25% overall yield through 6 steps from β-citronellol. 5,9-Dimethylheptadecane, the major sex pheromone component of *Leucoptera malifoliella*, was also synthesized analogously as a stereoisomeric mixture in a 22% overall yield.**

**Key words:** sex pheromone; *Perileucoptera coffeella*; 5,9-dimethylpentadecane; 5,9-dimethylheptadecane; 5,9-dimethylhexadecane

The leaf miner moths, *Leucoptera malifoliella* and *Perileucoptera coffeella* are important pests of apple and pear trees in many temperate regions of Europe and coffee trees in Brazil, respectively.[1,2] The isolation of the sex pheromone of *L. malifoliella* as a mixture of 5,9-dimethylheptadecane (**3**, the main component), 5,9-dimethylhexadecane (**2**), and 5,9-dimethyloctadecane[1-3] prompted the synthesis of these compounds either as stereoisomeric mixtures[1-3] or as optically active forms,[4-6] aiming the pest management by the pheromones. These efforts brought about the findings that (5*S*,9*S*)-**3** has the substantial pheromonal activity and 5,9-dimethyloctadecane is synergistic, while 5,9-dimethylhexadecane and the other stereoisomers of **3** have virtually no effect on the activity. On the other hand, the female-produced sex pheromone of *P. coffeella* was proposed to consist of 5,9-dimethylpentadecane (**1**) and 5,9-dimethylhexadecane (**2**) as the major and the minor components, respectively, and the syntheses of these compounds as stereoisomeric mixtures were also reported.[2] Since a stereoisomeric mixture of **3**, which was prepared by the Kolbe coupling of (±)-4-methyldodecanoic acid and (±)-3-methylheptanoic acid followed by purification by GLC, is known, in a field trapping test to *L. malifoliella*, to have nearly the same pheromonal activity as its pure (5*S*,9*S*)-isomer at a four times higher dosage,[4] a stereoisomeric mixture of **1** was also considered to be effective as an attractant toward male *P. coffeella*. Thus, we planned a more efficient and simple synthesis of **1** and **3** as stereoisomeric mixtures from a standpoint of the practical use of the pheromones in monitoring and controlling the leaf miner moths. Furthermore, the synthesis of **2** was also tried in order to evaluate its effect on the pheromonal activity of **1** toward *P. coffeella*.

Commercially available (±)-β-citronellol (**4a**) was tosylated and the resulting tosylate (**4b**) was coupled with ethylmagnesium bromide in tetrahydrofuran in the presence of dilithium tetrachlorocuprate[7] to give olefin **4c** in a 77% yield for the two steps. Allylic oxidation of **4c** with a mixture of selenium dioxide and *t*-butylhydroperoxide in dichloromethane[8] afforded a mixture of allylic alcohol **5a**, α,β-unsaturated aldehyde **5b**, and alkenediol **5c** in a ratio of 5.5:1.7:1.0. Both **5a** and **5b** contained in the mixture were reduced under a hydrogen atmosphere using platinum dioxide as catalyst in refluxing ethanol to give **6a** as a diastereomeric mixture in a 49% yield for



**Scheme.** Synthesis of the Pheromones of Leaf Miner Moths.

Reagents: a) TsCl, Py; b) EtMgBr, $Li_2CuCl_4$, THF (77%, 2 steps); c) $SeO_2$, *t*-BuOOH, salicylic acid, $CH_2Cl_2$; d) $H_2$, $PtO_2$, EtOH (49%, 2 steps); e) TsCl, Py; f) $CH_3(CH_2)_4MgBr$, $CH_3(CH_2)_5MgBr$, or $CH_3(CH_2)_6MgBr$, $Li_2CuCl_4$, THF (59–67%, 2 steps).

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the two steps after chromatographic removal of a diol derived from **5c**. The diastereomeric ratio of **6a** was *ca.* 1:1 by its 500 MHz $^1$H-NMR analysis (see Experimental). Finally, the alcohol (**6a**) was converted to tosylate **6b**, which was then coupled with pentylmagnesium bromide, hexylmagnesium beomide or heptylmagnesium bromide in the presence of dilithium tetrachlorocuprate to give the desired hydrocarbons **1**, **2** or **3** in yields of 67%, 66%, or 59%, respectively.

This synthesis of **1**, **2**, and **3** accomplished through 6 steps in about 22–25% overall yields from a commercially available and cheap starting material, (±)-$\beta$-citronellol, is considered to be operationally easier than the previous syntheses, and could be practically useful for large-scale production of these pheromones. Field trapping tests with **1** are now well underway in Brazil (Prof. Vilela, Universidade Federal de Vicosa) and the results will be published elsewhere.

## Experimental

IR spectra were measured with a Jasco FT/IR-5000 spectrometer. $^1$H-NMR spectra (500 MHz) were recorded with TMS as an internal standard in $CDCl_3$ by a Jeol JNM-A500 spectrometer. High-resolution mass spectra (70 eV) were measured with a Shimadzu GCMS 9020-DF spectrometer. Merck silica gel 60 Art 7734 was used for silica gel column chromatography.

*2,6-Dimethyl-2-decene* (**4c**). To a stirred solution of (±)-$\beta$-citronellol (**4a**) (10.0 g, 64.0 mmol) in pyridine (36 ml) was added portionwise *p*-toluenesulfonyl chloride (16.4 g, 83.2 mmol) at 0°C. After 1 h, the mixture was allowed to warm gradually to room temperature, and stirred overnight. To the mixture was added water (5 ml), and the resulting mixture was stirred for 20 min. The mixture was poured into water and extracted with ether. The ethereal solution was successively washed with 2 M HCl aq., sat. $NaHCO_3$ aq. and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 19.4 g of crude **4b**. The tosylate (**4b**) (19.4 g, 62.5 mmol) was dissolved in THF (250 ml) and cooled to −78°C. To the solution was added successively a solution of ethylmagnesium bromide in THF (1.00 M, 89.0 ml, 89.0 mmol) and a solution of dilithium tetrachlorocuprate in THF (0.1 M, 5.92 ml, 0.592 mmol). After 30 min, the mixture was allowed to warm gradually to room temperature and stirred for 14 h. The mixture was poured into sat. $NH_4Cl$ aq. and extracted with ether. The ethereal solution was successively washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed over silica gel (100 g, hexane) and distilled to give 8.03 g (77%) of **4c**, b.p. 82–84°C (20 Torr). IR $\nu_{max}$ cm$^{-1}$: 2960 (s), 2930 (s), 29860 (s), 1460 (m), 1380 (m), 1090 (w), 1020 (w), 825 (w); $^1$H-NMR $\delta$: 0.86 (3H, d, $J=6.5$ Hz, 6-$CH_3$), 0.89 (3H, t, $J=6.9$ Hz, 10-$H_3$), 1.07–1.16 (2H, m, 9-$H_2$), 1.19–1.34 (6H, m, 5-$H_2$, 7-$H_2$ and 8-$H_2$), 1.35–1.42 (1H, m, 6-H), 1.60 (3H, br s, C=C-$CH_3$), 1.68 (3H, br s, C=C-$CH_3$), 1.90–2.03 (2H, m, 4-$H_2$), 5.10 (1H, tm, $J=7.1$ Hz, 3-H). HRMS *m/z* ($M^+$): calcd. for $C_{12}H_{24}$, 168.1877; found, 168.1901.

*A mixture of (E)-2,6-dimethyl-2-decen-1-ol* (**5a**), *(E)-2,6-dimethyl-2-decenal* (**5b**), *and 2-(4-methyloctylidene)-1,3-propanediol* (**5c**). To a mixture of selenium dioxide (0.40 g, 3.63 mmol) and salicylic acid (0.63 g, 4.54 mmol) in dichloromethane (15 ml) was added successively a solution of *t*-BuOOH in dichloromethane [about 3 M, 60 ml, *ca.* 180 mmol; prepared by drying a mixture of 70% *t*-BuOOH aq. (50 ml) and dichloromethane (100 ml) with $MgSO_4$] and a solution of **4c** (8.03 g, 48.6 mmol) in dichloromethane (15 ml) at 0°C. After the mixture was stirred at room temperature for 9 h, selenium dioxide (0.10 g, 0.91 mmol) was added again, and the mixture was stirred for an additional 9 h. The mixture was diluted with ether and water, and cooled to 0°C. To the mixture was added ferrous sulfate heptahydrate (80 g) and the resulting mixture was stirred for 10 min. The ether layer was separated and the water layer was extracted with ether. The combined extracts were successively washed with water, sat. $NaHCO_3$ aq. and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give a mixture (9.8 g) containing **5a**, **5b**, and **5c**, the $^1$H-NMR analysis of which revealed the ratio of the components to be 5.5:1.0:1.7. Each component isolated by silica gel column chromatography showed the following physical properties. **5a**: IR $\nu_{max}$ cm$^{-1}$: 3340 (m), 2960 (s), 2925 (s), 2860 (s), 1460 (m), 1380 (m), 1010 (m); $^1$H-NMR $\delta$: 0.87 (3H, d, $J=6.5$ Hz, 6-$CH_3$), 0.89 (3H, t, $J=7.0$ Hz, 10-$H_3$), 1.08–1.18 (2H, m, 9-$H_2$), 1.18–1.34 (6H, m, 6-H, 7-$H_2$, 8-$H_2$ and OH), 1.34–1.44 (2H, m, 5-$H_2$), 1.67 (3H, br s, C=C-$CH_3$), 1.93–2.10 (2H, m, 4-$H_2$), 4.00 (2H, br s, 1-$H_2$), 5.40 (1H, tm, $J=7.1$ Hz, 3-H). HRMS *m/z* ($M^+$): calcd. for $C_{12}H_{24}O$, 184.1826; found, 184.1819. **5b**: IR $\nu_{max}$ cm$^{-1}$: 2960 (s), 2930 (s), 2860 (m), 2710 (w), 1690 (vs), 1645 (m), 1460 (m), 1380 (m), 1240 (w), 1080 (w), 1000 (w); $^1$H-NMR $\delta$: 0.88 (3H, t, $J=6.5$ Hz, 6-$CH_3$), 0.91 (3H, d, $J=6.8$ Hz, 10-$H_3$), 1.10–1.35 (6H, m, 7-$H_2$, 8-$H_2$ and 9-$H_2$), 1.40–1.55 (3H, m, 5-$H_2$ and 6-H), 2.28–2.42 (2H, m, 4-$H_2$), 6.49 (1H, tm, $J=7.4$ Hz, 3-H), 9.39 (1H, s, 1-H). HRMS *m/z* ($M^+$): calcd. for $C_{12}H_{22}O$, 182.1670; found, 182.1684. **5c**: IR $\nu_{max}$ cm$^{-1}$: 3350 (s), 2970 (s), 2940 (s), 2880 (s), 1460 (m), 1380 (m), 1010 (s); $^1$H-NMR $\delta$: 0.87 (3H, d, $J=6.5$ Hz, 6-$CH_3$), 0.89 (3H, t, $J=6.9$ Hz, 10-$H_3$), 1.09–1.33 (7H, m, 6-H, 7-$H_2$, 8-$H_2$ and 9-$H_2$), 1.33–1.45 (2H, m, 5-$H_2$), 1.97 (2H, br, OH × 2), 2.02–2.16 (2H, m, 4-$H_2$), 4.22 (2H, s, O-$CH_2$), 4.33 (2H, s, O-$CH_2$), 5.56 (1H, t, $J$=7.5 Hz, 3-H). HRMS $m/z$ ($M^+$): calcd. for $C_{12}H_{24}O_2$, 200.1775; found, 200.1798.

*2,6-Dimethyl-1-decanol* (**6a**). The mixture of **5a**, **5b**, and **5c** obtained above (9.8 g) was dissolved in ethanol (100 ml) and stirred vigorously at reflux with platinum dioxide (0.71 g) under a hydrogen atmosphere for 36 h, with more platinum dioxide (2 × 0.23 g) being added after 12 and 24 h. The mixture was filtered through a Celite pad, and the filtrate was concentrated *in vacuo*. The residue was chromatographed over silica gel (100 g, hexane-ether = 30:1) and distilled to give 4.35 g (49% from **4c**) of **6a**, b.p. 126–130°C (30 Torr). IR $\nu_{max}$ cm$^{-1}$: 3350 (s), 2960 (s), 2930 (s), 2870 (s), 1460 (m), 1380 (m), 1035 (m), 990 (w), 730 (w); $^1$H-NMR $\delta$: 0.846 (3 × 0.5H, d, $J$=6.7 Hz, 6-$CH_3$), 0.848 (3 × 0.5H, d, $J$=6.7 Hz, 6-$CH_3$), 0.89 (3H, t, $J$=7.0 Hz, 10-$H_3$), 0.918 (3 × 0.5H, d, $J$=6.8 Hz, 2-$CH_3$), 0.922 (3 × 0.5H, d, $J$=6.8 Hz, 2-$CH_3$), 1.04–1.14 (3H, m), 1.18–1.34 (8H, m), 1.22 (1H, t, $J$=5.8 Hz, OH), 1.34–1.42 (2H, m), 1.58–1.65 (1H, m, 2-H), 3.42 (1H, ddd, $J$=10.5, 6.2, 5.8 Hz, 1-H), 3.510 (1 × 0.5H, dt, $J$=10.5, 5.8 Hz, 1-H), 3.514 (1 × 0.5H, dt, $J$=10.5, 5.8 Hz, 1-H). HRMS $m/z$ ($M^+$): calcd. for $C_{12}H_{26}O$, 186.1982; found, 186.1943.

*2,6-Dimethyldecyl tosylate* (**6b**). To a solution of **6a** (4.13 g, 22.2 mmol) in pyridine (14 ml) was added portionwise *p*-toluenesulfonyl chloride (5.67 g, 28.9 mmol) at 0°C. After the mixture was stirred at 0°C for 1 h and then at room temperature overnight, water (5 ml) was added to the mixture. The mixture was stirred for 20 min, poured into water, and then extracted with ether. The ethereal solution was successively washed with 2 M HCl aq. and water, dried ($MgSO_4$) and concentrated *in vacuo* to give 7.32 g of crude **6b**. IR $\nu_{max}$ cm$^{-1}$: 2960 (s), 2930 (s), 2860 (m), 1600 (w), 1465 (m), 1365 (s), 1190 (s), 1180 (s), 1095 (m), 965 (s), 810 (s), 670 (s), 550 (s). This tosylated product was used for the next step without further purification.

*5,9-Dimethylpentadecane* (**1**). To a solution of **6b** (2.50 g, 7.47 mmol) in THF (30 ml) was added succesively a solution of pentylmagnesium bromide (1.0 M in THF, 11.2 ml, 11.2 mmol) and a solution of dilithium tetrachlorocuprate (0.1 M in THF, 0.75 ml, 0.075 mmol) at −78°C. After 30 min, the mixture was allowed to warm gradually to room temperature and stirred at room temperature for 14 h and then at 40°C for 4 h. The mixture was poured into sat. $NH_4Cl$ aq. and extracted with ether. The ethereal solution was successively washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed over silica gel (100 g, hexane) and distilled to give 1.18 g (67%) of **1**, b.p. 108–110°C (4 Torr). IR $\nu_{max}$ cm$^{-1}$: 2960 (s), 2930 (s), 2860 (s), 1460 (m), 1380 (m), 1155 (w), 725 (w); $^1$H-NMR $\delta$: 0.84 (6H, br d, $J$=6.7 Hz, 5-$CH_3$ and 9-$CH_3$), 0.883 (6 × 0.75H, t, $J$=7.0 Hz, 1-$H_3$ and 15-$H_3$), 0.888 (6 × 0.25H, t, $J$=7.0 Hz, 1-$H_3$ or 15-$H_3$), 1.02–1.14 (4H, m, 2-$H_2$ and 14-$H_2$), 1.17–1.32 (18H, m), 1.32–1.41 (2H, m, 5-H and 9-H). HRMS $m/z$ ($M^+$): calcd. for $C_{17}H_{36}$, 240.2815; found, 240.2828.

*5,9-Dimethylhexadecane* (**2**). In a similar manner as described for the preparation of **1**, the coupling reaction of tosylate **6b** (2.13 g, 6.26 mmol) and hexylmagnesium bromide (1.0 M in THF, 9.4 ml, 9.4 mmol) in the presence of dilithium tetrachlorocuprate (0.1 M in THF, 0.63 ml, 0.063 mmol) gave 1.05 g (66%) of **2**, b.p. 132–138°C (9 Torr). IR $\nu_{max}$ cm$^{-1}$: 2960 (s), 2930 (s), 2860 (s), 1460 (m), 1380 (m), 1155 (w), 725 (w); $^1$H-NMR $\delta$: 0.84 (6H, br d, $J$=6.7 Hz, 5-$CH_3$ and 9-$CH_3$), 0.884 (6 × 0.75H, t, $J$=7.0 Hz, 1-$H_3$ and 16-$H_3$), 0.889 (6 × 0.25H, t, $J$=7.0 Hz, 1-$H_3$ or 16-$H_3$), 1.01–1.13 (4H, m, 2-$H_2$ and 15-$H_2$), 1.17–1.32 (20H, m), 1.32–1.41 (2H, m, 5-H and 9-H). HRMS $m/z$ ($M^+$): calcd. for $C_{18}H_{38}$, 254.2972; found, 254.2979.

*5,9-Dimethylheptadecane* (**3**). In a similar manner as described for the preparation of **1**, the coupling reaction of **6b** (2.69 g, 7.91 mmol) and heptylmagnesium bromide (1.0 M in THF, 11.9 ml, 11.9 mmol) in the presence of dilithium tetachlorocuprate (0.1 M in THF, 0.79 ml, 0.079 mmol) gave 1.25 g (59%) of 3, b.p. 152–158°C (20 Torr). IR $\nu_{max}$ cm$^{-1}$: 2960 (s), 2930 (s), 2860 (s), 1460 (m), 1380 (m), 1155 (w), 725 (w); $^1$H-NMR $\delta$: 0.84 (6H, br d, $J$=6.7 Hz, 5-$CH_3$ and 9-$CH_3$), 0.882 (6 × 0.75H, t, $J$=7.0 Hzm 1-$H_3$ and 17-$H_3$), 0.888 (6 × 0.25H, t, $J$=7.0 Hz, 1-$H_3$ or 17-$H_3$), 1.01–1.14 (4H, m, 2-$H_2$ and 16-$H_2$), 1.17–1.32 (22H, m), 1.32–1.41 (2H, m, 5-H and 9-H). HRMS $m/z$ ($M^+$): calcd. for $C_{19}H_{40}$, 268.3128; found, 268.3147.

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