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-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-dimethylpentadecane (3, the main component), 5,9-dimethylhexadecane (2), and 5,9-dimethyloctadecane3) prompted the synthesis of these compounds either as stereoisomeric mixtures or as optically active forms,4,5) aiming the pest management by the pheromones. These efforts brought about the findings that (S,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 synthesis 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-methyldecanoic 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 (S,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 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 dichloromethane6) 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, Li2CuCl4, THF (77%, 2 steps); c) SeO2, t-BuOOH, salicylic acid, CH2Cl2; d) H2, PtO2, EIOH (49%, 2 steps); e) TsCl, Py; f) CH2(CH2)5MgBr, CH2(CH2)5MgBr, or CH2(CH2)5MgBr, Li2CuCl4, 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 1H-NMR analysis (see Experimental). Finally, the alcohol (6a) was converted to tosylate 6b, which was then coupled with pentylmagnesium bromide, hexylmagnesium bromide 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, (±)-β-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 Vicsa) and the results will be published elsewhere.

Experimental

IR spectra were measured with a Jasco FT/IR-5000 spectrometer. 1H-NMR spectra (500 MHz) were recorded with TMS as an internal standard in CDCl3 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 (±)-β-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 ether solution was successively washed with 2 M HClaq., sat. NaHCO3aq. and brine, dried (MgSO4) 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 ml, 89.0 ml, 89.0 mmol) and a solution of dilithium tetrachlorocuprate in THF (0.1 ml, 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. NH4Claq. and extracted with ether. The ether solution was successively washed with water and brine, dried (MgSO4) 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 νmax cm⁻¹: 2960 (s), 2930 (s), 29860 (s), 1460 (m), 1380 (m), 1090 (w), 1020 (w), 825 (w); 1H-NMR δ: 0.86 (3H, d, J = 6.5 Hz, 6-CH3), 0.89 (3H, t, J = 6.9 Hz, 10-CH3), 1.07-1.16 (2H, m, 9-H2), 1.19-1.34 (6H, m, 5-H2, 7-H2 and 8-H2), 1.35-1.42 (1H, m, 6-H), 1.60 (3H, br s, C=C-CH3), 1.68 (3H, br s, C=C-CH3), 1.90-2.03 (2H, m, 4-H2), 5.10 (1H, tm, J = 7.1 Hz, 3-H). HRMS m/z (M⁺): calcd. for C14H26, 186.1787; 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-methylcyclohexadiene)-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 ml, 60 ml, ca. 180 mmol); prepared by drying a mixture of 70% t-BuOOHaq. (50 ml) and dichloromethane (100 ml) with MgSO4] 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 ferric 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. NaHCO3aq. and brine, dried (MgSO4) and concentrated in vacuo to give a mixture (9.8 g) containing 5a, 5b, and 5c, the 1H-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 νmax cm⁻¹: 3340 (m), 2960 (s), 2925 (s), 2860 (s), 1460 (m), 1380 (m), 1010 (m); 1H-NMR δ: 0.87 (3H, d, J = 6.5 Hz, 6-CH3), 0.89 (3H, t, J = 7.0 Hz, 10-CH3), 1.08-1.18 (2H, m, 9-H2), 1.18-1.34 (6H, m, 6-H, 7-H2, 8-H2 and OH), 1.34-1.44 (2H, m, 5-H2), 1.67 (3H, br s, C=C-CH3), 1.93-2.10 (2H, m, 4-H2), 4.00 (2H, br s, 1-H2), 5.40 (1H, tm, J = 7.1 Hz, 3-H). HRMS m/z (M⁺): calcd. for C15H26O2, 184.1826; found, 184.1819. 5b: IR νmax cm⁻¹: 2960 (s), 2930 (s), 2860 (m), 2710 (w), 1690 (vs), 1645 (m), 1460 (m), 1380 (m), 1240 (w), 1080 (w), 1000 (w); 1H-NMR δ: 0.88 (3H, t, J = 6.5 Hz, 6-CH3), 0.91 (3H, d, J = 6.8 Hz, 10-H2), 1.10-1.35 (6H, m, 7-H2, 8-H2 and 9-H2), 1.40-1.55 (3H, m, 5-H2 and 6-H), 2.28-2.42 (2H, m, 4-H2), 6.49 (1H, tm, J = 7.4 Hz, 3-H), 9.39 (1H, s, 1-H). HRMS m/z (M⁺): calcd. for C15H24O2, 182.1670; found, 182.1684. 5c: IR νmax cm⁻¹: 3350 (s), 2970 (s), 2940 (s), 2880 (s), 1460 (m), 1380 (m), 1010 (s); 1H-NMR δ: 0.87 (3H, d, J = 6.5 Hz, 6-CH3), 0.89 (3H, t, J = 6.9 Hz, 10-CH3), 1.09-1.33 (7H, m, 6-H, 7-H2, 8-H2 and 9-H2), 1.33-1.45 (2H, m, 5-H2).
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References

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