NOVEL CONVENIENT SYNTHESIS OF (Z/E)-8-DODECENYL ACETATES, COMPONENTS OF THE Grapholitha molesta SEX PHEROMONE

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Components of the Grapholitha molesta sex pheromone, (Z/E)-8-dodecenyl acetates (1, 2), were synthesized in five steps in 20% overall yield using 10-hydroxydecanoic acid (3) as starting material.

Key words: sex pheromone, Grapholitha molesta, 8-dodecenyl acetate, ozonolysis.

Grapholitha molesta, or Oriental fruit moth, is a pest of peaches, apples, pears, apricots, etc. About 40 years ago its pheromone component was isolated [1] and identified [2] as (Z)-8-dodecenyl acetate (1, Scheme 1). Many researchers found that sex pheromone 1 that contains from 5 to 10% of the (E)-isomer (2) is still biologically active [3, 4].



a) pyridine, Ac₂O, room temperature, 24 h; *b*) HgO, Br₂, CCl₄, irradiation by tungsten lamps, 200 W, 4 h; *c*) LiBr, Li₂CO₃, DMF, 130°C, 6 h; *d*) O₃, CH₂Cl₂, then Zn/H₂O/CH₃COOH; *e*) BuLi, *n*-butyltriphenylphosphonium bromide, dry THF, 18-25°C.

Compounds **1** and **2** can be used as attractants of other insects such as *Cryptophlebia batrachopa*, *G. leucotreta*, *G. funebrana*, *G. lobarzewskii*, *Eucosma notanthes*, etc. [5-8]. Leal et al. discovered in 2001 that the (*E*)-isomer is the main component of the sex pheromone of *Ecdytolopha aurantiana* [9].

The synthesis of components of *G. molesta* sex pheromone has been reported [3, 4, 10-15]. The shortest pathway to the acetylene compounds consists of Wittig olefination of 8-acetoxyoctanal by *n*-butyltriphenylphosphonium bromide. The difficulty in this instance is the preparation of 8-acetoxyoctanal. The synthesis of the pheromones used 1,8-octanediol, which is monoacetylated for use as a precursor in the synthesis of the target molecule. Then this compound is oxidized by pyridinium chlorochromate. However, the monoacetylation of 1,8-octanediol is difficult to carry out successfully because the diacetyl derivative can be produced simultaneously with the monoacetyl derivative. Another drawback is the contamination of the reaction mixture with pyridinium chlorochromate.

Herein we report a more efficient method for synthesizing components of *G. molesta* sex pheromone. Scheme 1 shows the total synthesis of 1 and 2, which includes five steps. The (*Z*)- and (*E*)-components were synthesized starting from 10-decanoic acid (3), which was prepared by the literature method [16]. After protection of the hydroxyl in 3, esterification with acetic anhydride in pyridine produced 10-acetoxydecanoic acid (4). Then a classical Hunsdiecker reaction of 4 gave

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alkylbromide **5**. Elimination of HBr upon reaction of **5** with LiBr and Li_2CO_3 produced **6** with a terminal methylene, ozonolysis of which gave key intermediate **7** (8-acetoxyoctanal), from which reaction with *n*-butyltriphenylphosphonium bromide under conditions for *n*-butyllithium produced **1** and **2**.

Thus, we demonstrated a novel and convenient pathway to the target compounds. Furthermore, **7** can be used to prepare a series of 8-alkenylacetates.

EXPERIMENTAL

IR spectra were recorded in KBr disks on an Bruker Equinox 55 spectrophotometer. PMR spectra in CDCl_3 were obtained on a Varian 400 spectrophotometer with TMS internal standard. Column chromatography used silica gel (200-300 mesh) from Yantai Jiangyou Silica Development Co. Ltd. All solvents were analytically pure.

10-Acetoxydecanoic Acid. 10-Hydroxydecanoic acid (9.4 g, 0.05 mol) was acetylated by acetic anhydride (10 mL) in pyridine (10 mL) with stirring at room temperature for 24 h. The reaction mixture was poured into icewater (50 mL) and extracted with ether. The organic layer was washed with water (20 mL) and saturated brine (20 mL), dried over anhydrous Na₂SO₄, and evaporated in vacuo. The reaction products were purified by flash chromatography with elution by petroleum ether:ethylacetate (30:1) to afford **4** (10.69 g, 93%), colorless oil. PMR spectrum (CDCl₃, δ , ppm, J/Hz): 1.31 [10H, m, –(CH₂)₅-], 1.62 (4H, m, 3-CH₂, 9-CH₂), 2.05 (3H, s, COCH₃), 2.35 (2H, t, J = 7.6, CH₂COO), 4.05 (2H, t, J = 6.8, CH₂OAc). The COOH proton was not observed because of rapid exchange with water of the solvent.

9-Bromononyl Acetate (5). A mixture of 10-acetoxydecanoic acid (**4**, 4.6 g, 0.02 mol), HgO (6.5 g, 0.035 mol), and Br₂ (1.5 mL) in CCl₄ (120 mL) was irradiated by two tungsten lamps (100 W) with stirring on a magnetic stirrer. The reaction was carried out under N₂ for 4 h in a flask equipped with a reflux condenser. The resulting solution was cooled to room temperature; washed with aqueous NaHSO₃ (10%, 3×10 mL), saturated aqueous NaHCO₃ (3×10 mL), and brine (2×20 mL); dried over anhydrous Na₂SO₄; and evaporated in vacuo. The product was purified by flash chromatography with elution by petroleum ether:ethylacetate (30:1) to afford **5** (4.13 g, 78%), yellow oil. PMR spectrum (CDCl₃, δ , ppm, J/Hz): 1.31 [10H, m, –(CH₂)₅–], 1.62 (2H, m, 8-CH₂), 1.85 (2H, m, 2-CH₂), 2.05 (3H, s, COCH₃), 3.41 (2H, t, J = 6.4, CH₂Br), 4.05 (2H, t, J = 6.4, CH₂OAc).

8-Nonenyl Acetate (6). A stirred suspension of dry LiBr (0.4 g) and Li₂CO₃ (0.26 g) in dry DMF (15 mL) at 120°C was treated with **5** (1.92 g, 0.007 mol). The reaction was carried out under N₂ for 6 h. The resulting mixture was cooled, poured into dilute acetic acid, and extracted with CH₂Cl₂. The extract was washed with water (2 × 10 mL) and brine (2 × 10 mL), dried over anhydrous Na₂SO₄, and evaporated in vacuo. The product was purified by flash chromatography with elution by petroleum ether:ethylacetate (100:1) to afford **6** (1.04 g, 81%), colorless oil. PMR spectrum (CDCl₃, δ , ppm, J/Hz): 1.36 [8H, m, –(CH₂)₄–], 1.62 (2H, m, 8-CH₂), 2.03 (5H, m, 7-CH₂, COCH₃), 4.05 (2H, t, J = 6.4, CH₂OAc), 4.95 (2H, m, CH₂CH), 5.80 (1H, m, CH₂CH).

8-Acetoxyoctan-1-al (7). A solution of **6** (1.82 g, 0.01 mol) in CH₂Cl₂ (25 mL) was placed in a three-necked roundbottomed flask, cooled to -40°C in liquid N₂, and ozonized with a stream of O₃ (50 mL/min, 5 g/h). The completion of the reaction was determined by testing with KI starch paper. Then the flask with the reaction mixture was purged with N₂ for 10 min to remove the excess of O₃. The cooling bath was removed. The reaction mixture was stirred; purged with N₂; treated with Zn dust (2.7 g, 0.042 mol), acetic acid (2mL), and water (6 mL); and slowly brought to room temperature. The solution was filtered. The aqueous layer was extracted with ethylacetate (3 × 10 mL). The organic layer was washed with saturated aqueous NaHCO₃, water, and brine; dried over anhydrous Na₂SO₄, and evaporated in vacuo. The product was purified by flash chromatography with elution by petroleum ether:ethylacetate (30:1) to afford **7** (1.32 g, 71%), colorless oil. PMR spectrum (CDCl₃, δ , ppm, J/Hz): 1.32 [6H, m, –(CH₂)₃–], 1.59 (4H, m, 3-CH₂, 7-CH₂), 2.02 (3H, s, COCH₃), 2.40 (2H, tt, CH₂CHO), 4.02 (2H, t, J = 6.8, CH₂OAc), 9.74 (1H, t, J = 1.6, CHO).

(*Z/E*)-8-Dodecenyl Acetates (1 and 2). A suspension of *n*-butyltriphenylphosphonium bromide (10.6 g, 0.027 mol) in dry THF (40 mL) at 18°C under N₂ was treated with *n*-butyllithium in hexane (2.5 M, 11 mL, 0.027 mol). The mixture was stirred at 18°C for 2 h, treated with 7 (3.16 g, 0.017 mol), stirred at 18°C for 2 h and overnight at room temperature. The reaction mixture was saturated with saturated NH₄Cl solution and filtered. The organic layer was washed with water and brine, dried over anhydrous Na₂SO₄, and evaporated in vacuo. The product was purified by chromatography with elution by petroleum ether:ethylacetate (100:1) to afford 1 and 2 (1.85 g), yellowish oil. GC of the components determined that the ratio of *Z*- and

E-isomers was 72.5:27.5. Overall yield 48.2%. IR spectrum (v_{max} , cm⁻¹): 3005, 2929, 2856, 1743, 1462, 1366, 1239, 1041, 970, 723. PMR spectrum (CDCl₃, δ , ppm, J/Hz): 0.905 (3H, t, J = 7.6, 12-CH₃), 1.36 [10H, m, 11-CH₂, -(CH₂)₄-], 1.60 (2H, m, 2-CH₂), 2.00 (7H, m, COCH₃, 7-CH₂, 10-CH₂), 4.05 (2H, t, J = 6.8, CH₂OAc), 5.36 (2H, m, CH=CH).

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