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A FACILE SYNTHESIS OF THE SEX PHEROMONE OF *Grapholitha molesta*

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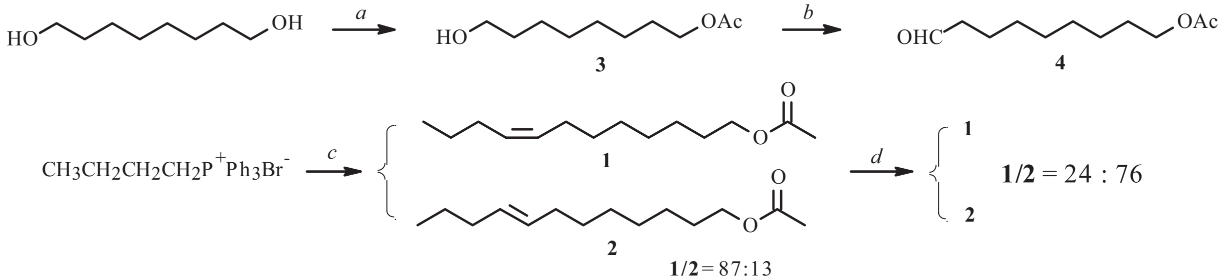
The sex pheromone of Grapholitha molesta, *(*Z/E*)-8-dodecylen-1-ol acetate, was easily synthesized in an overall yield of 41.5% with 1,8-octanediol as starting material via mono-esterification, PCC oxidation, and Witting reactions. The* Z/E *ratio is 83:17. Configuration transformation of* Z/E *83:17 compound with sodium nitrite and nitric acid resulted in the production of a compound with* Z/E *24:76. The products were confirmed by IR, ^{1}H NMR, and MS spectral data.*

Keywords: sex pheromone, 1,8-octanediol, *Grapholitha molesta*, 8-dodecenyl acetate, Wittig reaction.

Grapholitha molesta (or Oriental fruit moth) is a pest that damage peaches, apples, pears, apricots, etc. Its pheromone was isolated [1] and identified as (*Z*/*E*)-8-dodecenyl acetate by Roelofs in 1969 [2]. It has been reported by Leal and other researchers that an (*E*)-isomer content in the range of 5% to 10% in (*Z*/*E*)-8-dodecenyl acetate (**1** and **2**) is more biologically active [3, 4]. A mixture of **1** and **2** can be used as attractant to capture insects such as *Cryptophlebia batrachopa*, *G. leucotreta*, *G. funebrana*, *G. lobarzewskii*, *Eucosma notanthes*, etc [5, 6].

Several synthetic methods for the sex pheromone of *G. molesta* have been reported [7–14]. However, there are some disadvantages in the synthetic routes. The expensive cost of material, harsh reaction conditions, and long reaction steps are the main disadvantages in the reported methods. Thus, it is important to explore more economical and easier synthetic routes.

Continuing our previous study [15, 16], herein we report a more facile and economical method for synthesizing the *G. molesta* sex pheromone (Scheme 1). In this route, we use the low-cost 1,8-octanediol as starting material, via mono-esterification, PCC oxidation, and Witting reactions, to obtain the sex pheromone of *Grapholitha molesta* in an overall yield of 41.5%, with a *Z*/*E* ratio of 83:17. Subsequently, the mixture with *Z*/*E* 83:17 was stirred in a solution of sodium nitrite and nitric acid at 70–75°C under nitrogen gas to obtain a mixture with a low *Z*/*E* ratio of 24:76. The products were confirmed by the ^{1}H NMR and MS spectral data.



a. AcOH/conc. H_2SO_4 (cat.), $C_6H_5CH_3$/reflux; *b*. PCC, CH_2Cl_2; *c*. 1) *t*-BuOK/THF, 0°C, 2) **4**/THF, –15°C; *d*. $NaNO_2$ (sol.), HNO_3 (sol.)

Scheme 1

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EXPERIMENTAL

All melting points were determined on a Yanaco MP-300 micromelting point apparatus, and values are uncorrected. Thin layer chromatography (TCL) was performed on silica gel F_{254} sheet and monitored by iodine vapor. ^{1}H NMR spectral data were recorded on a Varian Inova-400 spectrometer using tetramethylsilane (TMS) as an internal reference and $CDCl_3$ as solvent; ESI-MS were performed on an HP1100LC/MS spectrometer. The chemicals are commercially available and used without further purification. THF was distilled from sodium and benzophenone before used.

8-Hydroxyoctan-1-ol Acetate (3). To a solution of 1,8-octanediol (36.5 g, 0.25 mol) in toluene (430 mL) was added 0.68 mL conc. H_2SO_4 and 14.4 mL acetic acid (diluted with 50 mL toluene) at 75°C. The mixture was refluxed for 15 h. The completion of the reaction was monitored by TLC. The mixture was evaporated under reduced pressure. Then the residue was poured into 300 mL ice water, neutralized with saturated sodium carbonate solution, and extracted with ethyl acetate (50 mL × 3). The organic layer was dried over sodium sulfate and purified by column chromatography (petroleum ether–EtOAc, 5:1) to give **3** (41.68 g) in 89% yield. Colorless oil. IR: 3456 (-OH), 2950–2832 (C-H), 1745 (C=O), 1011 (C-O). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.25–1.29 (8H, m, $(CH_2)_4$), 1.54–1.62 (4H, m, 2-CH_2, 7-CH_2), 2.04 (3H, s, $OCOCH_3$), 2.27 (1H, s, OH), 3.63 (2H, t, J = 6.6, $HOCH_2$), 4.03 (2H, t, J = 6.8, CH_2OAc).

Acetic Acid 8-Oxo-octyl Ester (4). Pyridinium chlorochromate (PCC) (59.1 g, 275 mmol) was slowly added to a solution of compound **3** (41.5 g, 220 mmol) in 600 mL anhydrous dichloromethane, and the mixture was stirred at room temperature. The completion of the reaction was monitored by TLC. The mixture was filtered, and the filtrate was concentrated under reduced pressure. The residue was dissolved in 500 mL ether, then washed with dilute hydrochloric acid solution (50 mL × 2), saturated sodium bicarbonate solution, and brine. The organic layer was dried over sodium sulfate and concentrated to obtain the crude product **4** (44.5 g), which can be used for the reaction below without further purification.

***Z*/*E*-12-Tetradecen-1-ol Acetates 1 and 2.** Potassium *tert*-butoxide (275 mmol) was slowly added to a solution of butanylthiphenylphosphonium bromide (122.6 g, 308 mmol) in 385 mL anhydrous THF under N_2. When the potassium *tert*-butoxide dissolved completely, a solution of compound **4** (44.0 g) in anhydrous THF was added at –15°C. The mixture was stirred at –15°C for 2 h and then at room temperature overnight. The completion of the reaction was monitored by TLC. A saturated solution of NH_4Cl (50 mL) was added, and the mixture was concentrated under reduced pressure. The residue was extracted with ether (300 mL × 3). The organic layer was dried over sodium sulfate and purified by column chromatography (petroleum ether–EtOAc, 10:1) to give a mixture of **1**, **2**; 26.8 g, colorless oil, yield: 53.8%. IR: 3006, 2926, 2855, 1742 (C=O), 1465, 1365, 1240, 1038, 969 (C=C,*E*), 723 (C=C,*Z*). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 5.36 (2H, m, CH=CH), 4.05 (2H, t, J = 6.8, CH_2OAc), 1.98–2.00 (4H, m, $CH_2C=C-CH_2$), 2.03 (3H, s, $COCH_3$), 1.62 (2H, m, 2-CH_2), 1.27–1.36 (10H, m, 11-CH_2, $(CH_2)_4$], 0.91 (3H, t, J = 7.6, 12-CH_3). The *Z*/*E* ratio of **1**, **2** was confirmed to be 83:17 by GC-MS.

Configuration Transformation of the *Z*/*E* Ratio [17]. A 2.5 mL solution of sodium nitrite (2 mol/L) and 1.7 mL of nitric acid solution (2 mol/L) were added to 22.6 g (0.1 mol) of a mixture of **1**, **2** (*Z*/*E*, 83:17) under N_2, and the whole stirred at 70–75°C for 1 h. Then the reaction mixture was naturally cooled to room temperature. The mixture was neutralized with saturated sodium carbonate solution to pH = 7 and extracted with hexane (100 mL × 3). The organic layer was washed with saturated brine, dried over sodium sulfate, concentrated under reduced pressure, and purified by column chromatography (petroleum ether–EtOAc, 20:1) to obtain 22 g of colorless oil. The *Z*/*E* ratio of **1**, **2** was confirmed to be 24:76 by GC-MS.

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REFERENCES

1. J. A. George, *Can. Entomol.,* **97**, 1002 (1965).
2. W. Roelofs, L. A. Comeau, and R. Selle, *Nature*, **224**, 723 (1969).
3. T. S. Zhong and G. Q. Lin, *Acta Chim. Sin.,* **40** (4), 3815 (1982).
4. G. Z. Huang, J. M. Li, and H. A. Aisa, *Chem. Nat. Comp.,* **42**, 727 (2006).

5. D. R. Hall, P. S. Beevor, A. Cork, and B. F. Nesbitt, *Entomol. Exp. Appl.,* **35** (1), 1570 (1984).
6. H. Arn, B. Delley, M. Baggiolini, and P. J. Charmillot, *Entomol. Exp Appl.,* **19** (2), 139 (1976).
7. T. S. Zhong and G. Q. Lin, *Acta Chim. Sin*., **40** (4), 3815 (1982).
8. S. Li, G. P. Wei, and B. Sheng, *Chin. J. Org. Chem*., **6**, 466 (1986).
9. G. Holan and D. F. O′Keefe, *Tetrahedron Lett*., **14** (9), 673 (1973).
10. S. K. Kang, J. H. Kim, and Y. C. Shin, *Bull. Korean Chem. Soc.,***7** (6), 453 (1986).
11. V. N. Odinokov, G. Y. Ishmuratov, G. G. Balezina, and G. A. Tolstikov, *Chem. Nat. Comp.,* **21**, 372 (1985).
12. V. N. Odinokov, V. R. Akhmetova, K. D. Khasanov, A. A. Abduvakhabov, G. A. Tolstikov, and A. A. Panasenko, *Chem. Nat. Comp.,* **25,** 240 (1989).
13. G. Yuan, *Chin. Chem. Lett.,* **6** (10), 943 (1995).
14. F. C. Liu, Y. W. Li, J. Lin, H. Y. Zhu, and Q. S. Zong, *Chem. J. Chin. Univ.,* **24** (6), 1040 (2003).
15. J. M. Li, J. P. Yong, and H. A. Aisa, *Chem. Nat. Comp.,* **44** (2), 224 (1985).
16. J. M. Li, J. P. Yong, and H. A. Aisa, *Agrochemicals,* **47** (7), 500 (2008).
17. H. B. Chen and Y. J. Du, *Chin. J. Pest. Sci.,* **12** (1), 90 (2010).