A Wittig Route to (Z)-13-Eicosen-10-one, the Pheromone of the Peach Fruit Moth, and Its Biological Activity Test

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(Received October 24, 1984)

Introduction

(Z)-13-Eicosen-10-one, an active component of sex pheromone of the peach fruit moth, Carposina niponensis Walsingham, a major economic pest of apple, peach and other fruits was isolated by Tamakino in 1977. Structurally, while most lepidopterous pheromones were characterized as unsaturated alcohols, acetals, or aldehydes of 12-, 14-, 16-, or 18-carbon chain length, the sex pheromone of the peach fruit moth is an exceptional unsaturated aliphatic ketone. Several syntheses of (Z)-13-eicosen-10-one have been reported. In 1982, Yoshida reported the synthesis of (Z)-13-eicosen-10-one via salt-free Wittig reaction of heptyldienetriphenylphosphonium ylide and 4-oxo-tridecan-1-al(2). 4-Oxo-tridecan-1-al(2) was prepared from 1-(p-tolylsulfonyl) nonane and methyl 4,4-dimethoxybutanoate. Recently, 4-oxo-tridecan-1-al(2) was synthesized by Hernandez by addition of n-nonyllithium to γ-butyrolactone followed by PCC oxidation of the resulting alcohol in his synthesis of (Z)-13-eicosen-10-one(1). In 1981, Naoshima reported a synthesis of (Z)-13-eicosen-10-one via the Wittig olefination of 4-oxo-tridecan-1-al(2) with heptyldienetriphenylphosphonium ylide in toluene in the presence of 12-crown-4-ether. In this report, 4-oxo-tridecan-1-al(2) was prepared from diethyl 2-oxo-glutarate in five steps.

Institute of Agricultural Sciences in Suwon, Korea needed a fair amount of the pheromone of the peach fruit moth to conduct field test experiments in Korea. We therefore undertook to develop some practical methods for the synthesis of the pheromone of the peach fruit moth.

We wish to report a practical synthesis of (Z)-13-eicosen-10-one(1) via the Wittig olefination of 4-oxo-tridecan-1-al(2) with heptyldienetriphenylphosphonium ylide. The key intermediate, 4-oxo-tridecan-1-al(2) was prepared by three different synthetic methods. Also we wish to report the results of the biological activity test as attractant for males of the peach fruit moth.

Results and Discussion

It has been well established that the Wittig reaction when carried out between aliphatic aldehyde and aliphatic non-stabilized triphenylphosphonium ylide in salt-free, nonpolar solvent or in polar aprotic solvents such as DMF, DMSO or HMPA gives Z-alkenes stereoselectively. It has been known that only aldehyde reacts with phosphonium ylide in the presence of ketone. A simple retrosynthetic analysis (Scheme 1) reveals that 4-oxo-tridecan-1-al(2) is the key intermediate.

We have prepared 4-oxo-tridecan-1-al(2), the key intermediate by three different methods and synthesized the pheromone of the peach fruit moth by olefination reaction of 4-oxo-tridecan-1-al(2).

(I) Grignard Route. 4-Oxo-tridecan-1-al(2) was prepared from commercially available acrolein and decanoyl chloride (Scheme 2).

1,4-Addition of HBr to acrolein, followed by protection of the aldehyde portion with 1,3-propanediol afforded 2-(2-bromoethyl)-1,3-dioxane(3). Grignard reagent from 2-(2-bromoethyl)-1,3-dioxane and Mg in THF was added to
Scheme 1.

\[
\begin{align*}
\text{2-(3-oxodecanyl)-1,3-dioxane (4)} 
\end{align*}
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Decanoyl chloride at dry ice temperature \((-78^\circ C)\) gave 2-(3-oxodecanyl)-1,3-dioxane(4) with no more than a trace of tertiary alcohol. Deprotection of the ketone acetal(4) with oxalic acid and water gave 4-oxo-tridecan-1-ol(8), which was converted to (Z)-13-eicos-10-one(1).

(2) Umpolung Route. The key intermediate(2) could also be prepared from 1-decanal using alkylation reaction of the protected cyanohydrin by Umpolung (Scheme 3).

Decyloxyanhydrin(5) from 1-decanal and HCN was allowed with ethyl vinyl ether under the catalysis of POCI₃, ethoxymethyl ether was afforded. The carbanion of protected cyanohydrin generated by reacting with LDA in HMPA/THF was alkylated with 3-bromopropanol THF ether to produce the fully protected dioi cyanide(7). Sequential treatment with acid \((\text{H}_2\text{SO}_4/\text{MeOH})\) and with base \((0.5N \text{NaOH})\) gave 4-oxo-tridecan-1-ol(8), which was oxidized with PCC to afford 4-oxo-tridecan-1-ol(2).

(3) Imine Route. The ketoaldehyde(2) was prepared from commercially available undecan2-one (Scheme 4).

2-Undecanone cyclohexylimine(9) was obtained by refluxing a solution of 2-undecanone, cyclohexylamine, and p-TsOH in dry benzene while trapping water with Dean–Stark water separator. The carbanion of 2-undecanone cyclohexylimine(9), generated upon treatment of the imine with 1 equiv. of LDA was selectively alkylated at less hindered carbon with allyl bromide in HMPA/THF followed by acidic hydrolysis to give the keto olefin(10*). The OsO₄/NaIO₄ cleavage of the keto olefin afforded 4-oxo-tridecan-1-ol(2).

The above synthetic methods described were considered to be convenient and economical. Especially, Grignard route involves routine reaction conditions which are amenable to large-scale preparations.

**Biological Activity**

The biological activity test of the synthetic pheromone as attractant for the male peach fruit moth was conducted in 1983 at the Horticultural Experiment Station in Suwon, Korea. In this test, 18 pheromone vials at a concentration of 3 mg per polyethylene capsule were tested on 107 consecutive nights from June 1 to September 15 using water traps with covers (Figure 1). A total of 1873 male moths were caught in 18 traps (Table 1). Most of the male peach fruit moth were caught from June 26 to July 5 and from August 6 to August 31. From the above results, the synthetic pheromone was tested as active from males of the peach fruit moth.

The biological activity test of the synthetic pheromone as attractant for the male peach fruit moth was conducted in 1984 at several districts of Korea. From the Table 2, it could be concluded that the numbers of moths trapped were proportional to the percentage of the fruits damaged. In Suwon, Yesan, Naju, and Jinju, a total of 134, 11, 28, 453 male moths were
TABLE 1: The Attractant Effect of the Males of the Peach Fruit Moth for the Synthetic Pheromone

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caught, respectively. In Chungju and Daegu, no male moth of the peach fruit moth was caught. This synthetic pheromone could be used not only as mass trapping of the peach fruit moth, but also as a tool for the forecasting the population of the peach fruit moth. After preliminary trapping of the male moths using this synthetic pheromone, pesticides can be applied to control the peach fruit moth in the field.

Experimental

Infrared spectra were recorded with Shimadzu IR-440 Spectrophotometer. Proton NMR were taken on a BRUKER WP 80 SY 80MHz NMR Spectrophotometer, using tertamethylsilane as an internal reference. All solvents and liquids were distilled before use.

2-(2-Bromoethyl)-1,3-dioxane (3). Bromine (9.81ml) was added dropwise to dry tetralin (3.01g) and swirled at room temperature from time to ensure a continuous evolution of hydrogen bromide. An excess of hydrogen bromide was bubbled into a solution of acrolein (2.00g) in dichloromethane (11.0ml) at room temperature. 1,3-Propanediol (2.71g) and p-toluene sulfonic acid hydrate (0.036g) were added to the crude 3-bromopropanol and the reaction mixture was stirred at room temperature for 8 hr. The resulting solution was neutralized with saturated sodium hydrogen carbonate, and washed with water. The organic layer was dried over anhydrous potassium carbonate, concentrated and the residual product was distilled in vacuo to afford 2-(2-bromoethyl)-1,3-dione (2) (0.08g, 74%): bp 68-70°C (3.0mmHg); IR cm⁻¹: 2900, 2850, 2710, 1140; NMRd: 1.30 (m, 1H), 2.10 (m, 3H), 3.36 (t, 2H), 3.90(m, 4H), 4.57 (t, 1H).

2-(3-Oxodecanyl)-1,3-dioxane (4). To a solution of thionyl chloride (1.43g) in dry benzene (1.0ml) was added decanoic acid (1.72g) in dry benzene (5.0ml). The reaction mixture was heated at reflux for 7h. The volatiles were evaporated and the residue was distilled on Kugelrohr (1.52g, 80%): bp 110-140°C (25mmHg); IR cm⁻¹: 2930, 2850, 1710, 1465; NMRd: 0.90 (t, 3H), 1.10-1.90 (m, 14H), 2.36 (t, 2H).

To the magnesium turnings (0.13g) with catalytic amount of iodine in dry THF (4.0ml) under nitrogen atmosphere was added 2-(2-bromoethyl)-1,3-dioxane (3) (0.78g) in dry THF (1.0ml). The reaction mixture was heated at reflux until the magnesium turnings were dissolved. After cooling to room temperature, the solution was drawn up into a syringe, leaving the excess magnesium behind. At -78°C, the Grignard reagent solution prepared was added dropwise to a solution of decanoyl chloride (0.64g) in dry THF (4.0ml), and warmed to room temperature over 55min. The reaction mixture was quenched with ammonium chloride solution and then evaporated under reduced pressure. The residue was extracted with ether, washed with water and saturated sodium chloride solution. The organic layer was dried over anhydrous potassium carbonate and concentrated in vacuo. The residue was passed through a short column of silica gel eluting with 10% ethyl acetate in cyclohexane to afford 2-(3-oxodecanyl)-1,3-dioxane (4) (0.68g, 75%); IR cm⁻¹: 2900, 2850, 2710, 1140; NMRd: 0.80~2.20 (m, 21H), 2.50 (m, 4H), 2.90 (m, 4H), 4.55 (t, 1H).

4-Oxo-tridecan-1-1 (2). To a 2-(3-oxodecanyl)-1,3-dioxane (0.12g) was added oxalic acid (0.067g) and water (2.0ml). The reaction mixture was vigorously heated at reflux for 6h. After cooling, the organic layer was extracted with ether, washed
with water, aqueous sodium bicarbonate, and saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The residual oil was passed through a short column of silicon gel using benzene-hexane (5:5) as eluent to give 4-oxo-tridecan-1-ol (2) (0.074 g, 77%). 

Decylicyano hydrin (5). To a solution of decylaldehyde (5.28 g) in ether (10.0 ml) was added sodium cyanide (5.94 g). To the reaction mixture in an ice bath was slowly added concentrated hydrochloric acid (10.3 ml) over 1 h. After the ice bath was removed, the reaction mixture was stirred at room temperature for 2 h. The organic layer was extracted with ether and washed with 6 N hydrochloric acid solution, water and saturated sodium chloride solution. The organic solution was dried over anhydrous magnesium sulfate and concentrated in vacuo to give decylicyano hydrin (5) (5.76 g, 93%). 

4-Oxy-tridecan-1-ol (8). To a solution of pyridinium chlorochromate (0.48 g) in dry dichloromethane (4.0 ml) was added in one portion, 4-oxo-tridecan-1-ol (8) (0.43 g) in dry dichloromethane (1.0 ml). The reaction mixture was stirred at room temperature for 4 h. The reaction mixture was dissolved in ether and washed thoroughly from the black gum. Ether and dry dichloromethane were evaporated and the residue was extracted with ether and the extract was washed with saturated sodium bicarbonate solution, water and saturated sodium chloride solution. The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo to afford 4-oxo-tridecan-1-ol (8) (0.52 g, 82%).
cm⁻¹: 920, 1715, 1450; NMRd: 0.90 (6H), 1.15–1.50 (22H), 1.80–2.50 (8H), 5.20–5.50 (2H).

2-Undecan-1-one Cyclohexylimine (9). To a solution of 2-undecan-1-one (5.10 g) in dry benzene (50.0 mL) was added cyclohexylimine (4.95 g) and p-toluenesulfonic acid (20.0 mg). The reaction mixture heated at reflux for 3 days until the water (0.9 mL) was trapped by the Dean–Stark apparatus. Benzene was evaporated and the crude ketimine was extracted with ether, washed with water and saturated sodium chloride solution. The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo to afford 2-undecan-1-one, cyclohexylimine (9) (6.42 g, 87%). IR cm⁻¹: 1680, 1620; NMRd: 0.90 (3H), 1.10–1.65 (28H), 1.80 (3H), 2.15 (2H), 2.85 (1H).

1-Tetradecan-5-one (10). At −78 °C, to a solution of dry THF (5.0 mL) and n-butyllithium (0.67 mL) was added isopropylamine (1.54 mL). To this LDA solution was slowly added 2-undecan-1-one cyclohexylimine (9) (2.51 g) in HMPA (2.5 mL). The reaction mixture was stirred for 30 min and then added allyl bromide (1.20 g) in THF (1.2 mL). The reaction mixture was stirred at −78 °C for 2 h. It was warmed to room temperature and stirred for 1 h. The solution was evaporated under reduced pressure. The residue was extracted with ether, washed with water and saturated sodium chloride solution. The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo to give 1-tetradecan-5-one, cyclohexylimine (3.39 g, 82%); IR cm⁻¹: 1695, 1640; NMRd: 0.90 (3H), 1.15–1.80 (24H), 4.78–5.15 (2H), 5.45–6.12 (1H), 3.00 (1H).

To a solution of 1-tetradecan-5-one, cyclohexylimine (0.22 g) in methanol (15 mL) was added hydrochloric acid (0.25 mL). The reaction mixture was heated at reflux for 3 h. Methanol was evaporated and the residue was extracted with ether and the extract was washed with 5% sodium bicarbonate solution and saturated sodium chloride, dried over anhydrous magnesium sulfate, and concentrated in vacuo to afford 1-tetradecan-5-one (10) (0.17 g, 80%); IR cm⁻¹: 1710, 1640; NMRd: 0.90 (3H), 1.10–1.75 (14H), 2.35 (6H), 4.78–5.15 (2H), 5.45–6.12 (1H).

4-Oxo-tridecan-1-al(7). To a solution of THF (2.0 mL) and water (0.5 mL) was added 1-tetradecan-5-one (10) (0.10 g), and stirred at 0 °C for 15 min. To this solution was added dropwise osmiumtetroxide (3.30 mg) in water (1.0 mL) under N₂. After cooling was continued for an additional 30 min at 5 °C, finely powdered sodium metaperiodate (0.26 g) was added to the solution over an hour little by little and stirred for additional 4 h at room temperature. Sodium iodate was filtered off and the residual solution was extracted with ether and washed with a saturated aqueous solution of sodium sulfite, a saturated aqueous solution of sodium hydrogen carbonate, brine. The organic layer was dried over anhydrous magnesium sulfate, and concentrated in vacuo. The residual oil was passed through a short column of silica gel using benzene–hexane (5:5) as eluent to give 4-oxo-tridecan-1-al(2) (0.075 g, 73%); IR cm⁻¹: 1720, 1710; NMRd: 0.90 (3H), 1.10–1.85 (14H), 2.20–2.65 (6H), 9.80 (1H).

References