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A Practical Synthesis of (Z)-7-Eicosen-11-one and (Z)-7-Nonadecen-11-one, the Pheromone of Peach Fruit Moth, and Its Biological Activity Test

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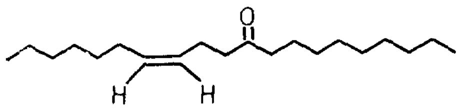
A new practical method is described for the synthesis of (Z) 7-eicosen-11-one (1) and (Z)-7-nonadecen-11-one (2), the active principles of the sex pheromone of the peach fruit moth. Lithium anion of 1-octyne (from acetylene and 1-bromohexane) was alkylated with 3-bromo-1-propanol tetrahydropyranyl ether and deprotected to afford 4-undecyn-1-ol, which was oxidized with pyridinium chlorochromate to 4-undecyn-1-al. 4-Undecyn-1-al was treated with 1-nonylmagnesiumbromide or 1-octylmagnesiumbromide to yield 7-eicosyn-11-ol and 7-nonadecyn-11-ol. Jones oxidation, followed by Lindlar catalytic hydrogenation afforded the target compounds. Biological activity of the synthetic pheromones as attractants for males of the peach fruit moth was tested in the field using polyethylene capsules as containers. For each vial containing about 3.0 mg of the synthetic pheromone, the number of trapped moths were counted.

Introduction

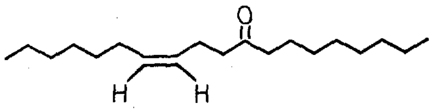
In 1977, Tamaki *et al*[1] isolated (Z)-7-eicosen-11-one (**1**) and (Z)-7-nonadecen-11-one (**2**) (Figure 1) as active components of the female sex pheromone of the peach fruit moth, Carposina niponensis Walsingham, a major economic pest of apple, peach and other fruits. Structurally, most lepidopterous pheromones are characterized as unsaturated alcohols, acetates or aldehydes of $C_{12,14,16,18}$ chain length, the sex pheromone of the peach fruit moth is an exceptional unsaturated aliphatic ketones. Activity is synergistically enhanced by mixing the two compounds in the ratio of 20:1 of (Z)-7-eicosen-11-one and (Z)-7-nonadecen-11-one, even if (Z)-7-eicosen-11-one alone exerts a pheromonal effect. Field test on the atractiveness of synthetic pheromones has been done with polyethylene capsules or caps by Tamaki *et al.*[2] Generally, pheromonal acitivity is sensitive to insect species, place, and climate. It is worthwhile to test the activity of the peach fruit moth in this country (Korea). Three syntheses have been reported by Y. Tamaki *et al*[1]., K. Mori *et al*[3]., and Y.Naoshima *et al*[4]. Using similar methodology reported by Y. Tamaki, we developed a practical synthesis of (Z)-7-eicosen-11-one (**1**) and (Z)-7-nonadecen-11one (**2**).

Results and Discussion

Sodium acetylide can be easily reacted with 1-bromohexane to give 1-octyne[5], presumably because of good solubility and nucleophilicity in liquid ammonia. In our prelimiary experiments, lithium 1-octynide[6] could not be alkylated with various alkylating agents, such as dib romoethane, chloroethyl p-toluenesulfonate and 1-bromo-1-chloroethane even in dipolar aprotic solvents (DMF, DMSO, HMPA and THF), but smoothly alkylated with 3-bromo-1-propanol THP ether in a mixture of HMPA and THF[7], and the product was deprotected with p-toluenesulfonic acid to afford 4-undecyn-1-ol. 4-Undecyn-1-ol was oxidized with pyridinium chlorochromate (PCC)[8] in dry methylene chloride to 4-undecyn-1-al in 84 % yield. Y. Tamaki obtained 4-un-



(Z)-7-Eicosen-11-one (1)



(Z)-7-Nonadecen-11-one (2)

Figure 1.

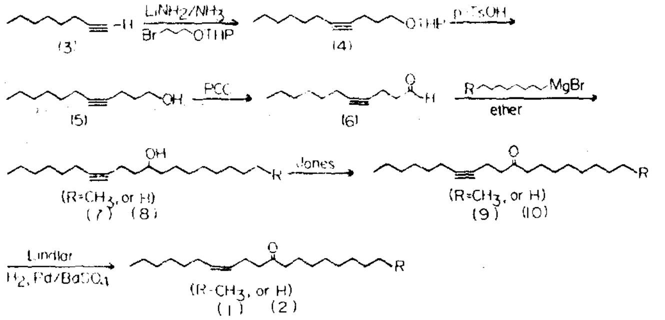


Figure 2.

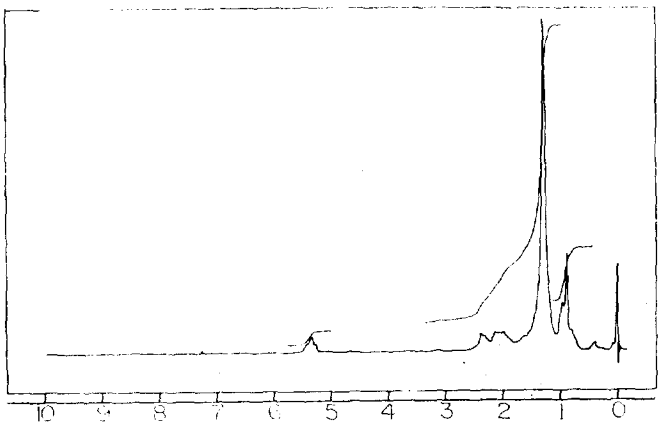


Figure 3. NMR spectrum of (Z)-7-Eicosen-11-one.

decyn-1-al in a poor yield (17 %) using CrO_3 pyridine as oxidizing agent. 4-Undecyn-1-al was treated with 1-nonylmagnesiumbromide in dry ether to afford 7-eicosyn-11-ol, which was purified by Florisil columns. This secondary alcohol was oxidized to 7-eicosyn-11-one by Jones oxidation[9], which was stereoselectively reduced with Lindlar catalyst ($Pd/BaSO_4$)[10] to afford the target compound, (*Z*)-7-eicosen-11-one (1) (Figures 2, 3). The second active compound (2) was also synthesized in the comparable yield *via* the route already described above for (1).

Biological Activity

Preliminary test was conducted at Horticultural Experiment Station in Suwon to establish that the synthetic sex pheromone was attractive to males of the peach fruit moth. In this exiperiment, only (Z)-7-eicosen-11-one was used as an attractant for the peach fruit moth. 10 Pheromone vials at a concentration of 3 mg per polyethene capsules were tested on 30 consecutive nights from June 18 to July 17 without renewal using water traps with covers. A total of 434 male moths were caught in 10 traps (Table 1). One trap averaged the catch rate of 7 males per 5 days. A daily peak amounted to 7 males during one night July 8 and 12. From the above results, the synthetic pheromone was tested as active for males of the peach fruit moth.

TABLE 1: The Attractant Effect of the Males of the Peach Fruit Moth for the Synthetic Pheromone

Date	The numbers of males which were caught in 10 traps										Total
	1	2	3	4	5	6	7	8	9	10	
6.18-6.22	9	0	3	3	1	1	4	10	1	5	37
6.23-6.26	1	2	1	3	10	0	4	3	3	2	29
6.27-7. 3	6	4	6	0	0	11	25	8	11	16	87
7.4 -7. 7	13	9	3	4	16	3	13	8	7	23	99
7.8 -7.12	13	7	3	1	15	4	10	6	13	34	106
7.13-7.17	9	3	2	1	8	2	16	12	7	16	76
											434

Experimental

Infrared spectra were recorded with Beckman IR-33 grating infrared spectrophotometer. Proton NMR were taken on a Varian 60-MHz spectrophotometer, using tetramethylsilane as an internal reference. Gas chromatography was performed with column 10 % OV-101 on Varian 3700. All solvents and liquids were distilled before use.

4-Undecyn-1-ol tetrahydropyranyl ether (**4**). Lithium (0.7 g) and excess liquid ammonia (200 m*l*) was stirred for 30 minutes under dry nitrogen atmosphere. Extra ammonia was evaporated and added THF (60 m*l*) and HMPA (60 m*l*). To this solution was added dropwise 1-octyne (3) (11.0 g) in THF (20 m*l*) and stirred for 2 hours at room temperature. 3-Bromopropan-1-ol THP ether (15.6 g) in HMPA (20 m*l*) was added dropwise slowly and stirred for 2 days at room temperature. The mixture was extracted with ether, washed with water and dried over Na_2SO_4. Concentration and vacuum distillation (5 mmHg) gave (4) (15.2 g, 88 %) IR : 1040, 1200 cm^{-1}; NMR δ : 0.90 (3H), 1.60 (16H), 2.10 (4H), 4.80 (1H).

4-Undecyn-1-ol (**5**). To 4-undecyn-1-ol THP ether (4) (4.0 g) was added THF (50 m*l*), ethanol (40 m*l*), H_2O (7 ml) and *p*-TsOH (0.13 g). The mixture was stirred for 18 hours and then added H_2O (200 m*l*). The organic layer was extracted with ether, washed with saturated sodium bicarbonate solution, dried over Na_2SO_4 and concentrated *in vacuo*. Vacuum distillation (5 mmHg) gave (**5**) (2.65 g, 99 %) IR: 3300 cm^{-1}; NMR δ: 0.90 (3H), 1,15-1.90 (8H), 2.00-2.70 (6H), 9.35 (1H).

4-Undecyn-1-al (**6**). To a stirred solution of pyridinium chlorochromate (1.60 g) in dry dichloromethane (10 m*l*) was added in one portion, 4-undecyn-1-ol (**5**) (0.92 g) in dry dichloromethane (1 m*l*). The mixture was stirred at room temperature for 2 hours. The reactants were 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 $MgSO_4$ and concentrated *in vacuo* to give 4-undecyn-1-al (**6**). (0.76 g, 84 %) IR: 2960, 1730, 1460 cm^{-1}; NMR δ: 0.90 (3H), 1.15-

1.90 (8H), 2.00–2.70 (6H), 9.35 (1H).

7-Eicosyn-11-ol (**7**). To 90 mg of magnesium turnings with catalytic of iodine under dry nitrogen atmosphere was added *n*-nonyl bromide (0.77 g) in dry ether (3 m*l*) for 1 hour to prepare the Grignard reagent. A solution of 4-undecyn-1-al (**6**) (0.68 g) in dry ether (2 m*l*) was added dropwise to the Grignard reagent during 2 hours and the mixture was stirred overnight at noom temperature and heated to reflux for 1hour. At O °C, the reaction mixture was acidified with 6N hydrochloric acid and stirred for one hour at room temperature. The reaction mixture was extracted with ether and the extract was washed with water and saturated sodium chloride solution, dried over $MgSO_4$, and concentrated *in vacuo* to afford 7-eicosyn-11-ol (**7**) (1.10 g, 92 %). IR: 3450, 2930, 1470 cm^{-1}; NMR: 0.90 (6H), 1.05–1.07 (20H), 1.80–2.75 (8H), 3.40–3.90 (2H).

7-Nonadecyn-11-ol (**8**). *n*-Octylmagnesium bromide was prepared from magnesium turnings (45 mg) with catalitic amounts of iodine and *n*-octyl bromide (0.31 g) in dry ether (1.5 m*l*) and a solution of 4-undecyn-1-al (**6**) (0.34 g) in dry ether (1 m*l*). Subsequent work-up as for (**7**) gave (**8**) (0.50 g, 88 %). IR: 3400, 2935, 1470 cm^{-1}; NMR δ: 0.90 (6H), 1.05–1.70 (20H), 1.80–2.75 (8H), 3.40–3.90 (2H).

7-Eicosyn-11-one-(**9**). To prepare the Jones reagent, 0.23 g of chromium trioxide was dissolved in 0.5 m*l* of H_2O, added 0.21 m*l* of concentrated sulfuric acid in an ice bath, and followed by 1 m*l* of H_2O. This reagent was added dropwise to a solution of 7-eicosyn-11-ol (**7**) (1.10g) in acetone (2.5 m*l*) in an ice bath. The mixture was vigorously stirred for 2 hours, extracted with ether, and the extract was washed with saturated sodium bisulfite solution, 6 *N* NaOH, water and saturated sodium chloride solution. The organic solution was dried over $MgSO_4$ and concentrated *in vacuo* to give (**9**) (0.80 g, 73 %). IR: 2260, 1720, 1450 cm^{-1}; NMR δ: 0.90 (6H), 1.05–1.75 (22H), 1.90–2.60 (8H).

7-Nonadecyn-11-one (**10**). Chromium trioxide (0.11 g) was dissolved in H_2O (0.25 m*l*) added concentrated sulfuric acid (0.1 ml) in an ice bath and followed by 0.5 m*l* of H_2O. To a solution of 7-nonadecyn-11-ol (**8**)(0.49 g)in acetone (1.25 m*l*) was added dropwise the Jones reagent.The following procedure is the same as that of 7-eicosyn-11-one (**9**). The product gave 0.35 g of 7-nonadecyn-11- one (**10**) (73 %). IR: 2940, 1720, 1470 cm^{-1}; NMR δ: 0.88 (6H), 1.08–1.65 (20H), 1.70–2.70 (8H).

(Z)-7-Eicosen-11-one (**1**). To a solution of 7-eicosyn-11-one (**9**) (0.75 g) in methanol (17.7 ml) was added 5 % palladium on barium sulfate (38.5 mg) and quinoline (2 drops). The mixture was stirred under hydrogen atmosphere for 12 hours. The reactant mixture was filtered to remove the catalyst and methanol was evaporated *in vacuo*. The ressdue was extracted with ether and washed 6 *N* hydrochloric acid, water and saturated sodium chloride solution. The organic solution was dried over $MgSO_4$ and concentrated *in vacuo* to afford the target product (**1**) (0.73 g, 97 %) The ratio of *cis* and *trans* isomer of 7-eicosen-one (**1**) was 20:1 by gas chromatography 10 % OV-101 on Varian 3700. IR: 2960, 1760, 1470 cm^{-1} NMR δ: 0.90 (6H), 1.10–1.70 (22H), 1.80–2.75 (8H), 5.35 (2H)

(Z)-7-Nonadecen-11-one (**2**). 5 % Palladium on barium sulfate (38mg) and quinoline (1 drop) were added to a solution of 7-nonadecyn-11-one (**10**) (0.34 g) in methanol (10 m*l*) and hydrogenated as described for 7-eicosen-11-one (**1**) to give 0.29g (85 %) of 7-nonadecen-11-one (**2**). IR: 2940, 1725, 1475 cm^{-1}; NMR δ: 0.90 (6H), 1.05–18.5 (20H), 1.95–2.50 (8H), 5.30 (2H).

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