

## Syntheses of (4E, 6E, 11Z)-4, 6, 11-hexadecatrienyl acetate and (4E, 6E, 11Z)-4, 6, 11-hexadecatrienal, female sex pheromones of eri-silkworm, *Samia cynthia ricini* (Lepidoptera: Saturniidae)

VASUNDHARA SINGH, RAKESH VIG, VISHV MOHINI,  
I R TREHAN and G L KAD\*

Department of Chemistry, Panjab University, Chandigarh 160014, India

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**Abstract.** Syntheses of (4E, 6E, 11Z)-4, 6, 11-hexadecatrienyl acetate (1) and (4E, 6E, 11Z)-4, 6, 11-hexadecatrienal (2), female sex pheromones of eri-silkworm, *Samia cynthia ricini* have been achieved through Claisen ortho ester rearrangement of (6).

**Keywords.** Pheromones; Claisen orthoester rearrangement; LAH reduction.

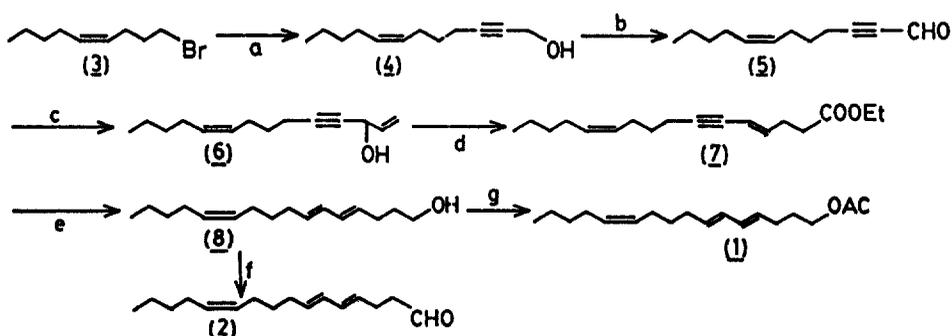
### 1. Introduction

The eri-silkworm moth *Samia cynthia ricini* Donovan is indigenous to China and South-East Asia and is often used in electrophysiological investigations because of its easy rearing, availability, and the size of its antennae. Females of the eri-silkworm moth emit a sex pheromone which attracts conspecific males. Recently (Bestmann *et al* 1989) isolated the major components of the female sex pheromone of the eri-silkworm, *Samia cynthia ricini* (Lepidoptera: Saturniidae). On the basis of GC and GCMS analysis, structures (4E, 6E, 11Z)-4, 6, 11-hexadecatrienyl acetate (1) and (4E, 6E, 11Z)-4, 6, 11-hexadecatrienal (2) have been assigned to these pheromones. Literature reports a synthesis of (1) and (2) (Bestmann *et al* 1989). We report therein a simple synthesis of (1) and (2) using Claisen orthoester rearrangement (Yadav *et al* 1986).

### 2. Results and discussion

The reaction strategy utilized in the synthesis of (1) and (2) is described in figure 1.

1-Bromo-4-nonene (3) was prepared in three steps as reported in the literature (Chattopadhyay *et al* 1984; Reddy and Yadav 1984). Alkylation of (3) with the dianion of propargyl alcohol in the presence of Li/Liq.NH<sub>3</sub> and a catalytic amount of Fe(NO<sub>3</sub>)<sub>3</sub> and THF as co-solvent afforded (4). Alcohol (4) was submitted to oxidation with PCC in CH<sub>2</sub>Cl<sub>2</sub> in the presence of sodium acetate (fused) to furnish aldehyde 5 (Corey and Suggs 1975). (Z)-7-Dodecen-2-yn-1-ol (5) on Grignard reaction with vinyl magnesium bromide in dry THF furnished (6). The Claisen orthoester rearrangement of (6) afforded (7) in 81% yield. The *trans*-geometry was confirmed from the IR spectra



a) Liq.  $\text{NH}_3$ ,  $\text{Fe}(\text{NO}_3)_3$ ,  $\text{HC}\equiv\text{CCH}_2\text{OH}$ , THF. b) PCC,  $\text{CH}_2\text{Cl}_2$ . c) Mg,  $\text{H}_2\text{C}=\text{CH}-\text{Br}$ ,  $(\text{C}_2\text{H}_5)_2\text{O}$   
 d)  $(\text{C}_2\text{H}_5\text{O})_3\text{CCH}_3$ ,  $\text{CH}_3\text{CH}_2\text{COOH}$ ,  $140^\circ$  e)  $\text{LiAlH}_4$ , diglyme f) PCC,  $\text{CH}_2\text{Cl}_2$   
 g)  $(\text{CH}_3\text{CO})_2\text{O}$ ,  $\text{CH}_2\text{Cl}_2$

Figure 1. The reactions involved in the synthesis of 1 and 2.

( $970\text{ cm}^{-1}$ ) and also supported by ample precedent (Yadav *et al* 1986). LAH reduction of (7) in diglyme furnished the alcohol (8) (Rossi and Carpita 1977). Acetylation of (8) with acetic anhydride and pyridine gave (1) in 84% yield. The alcohol (8) on oxidation with PCC in  $\text{CH}_2\text{Cl}_2$  afforded the pheromone (2). The IR and PMR spectral data of the pheromones (1) and (2) confirmed the structures.

### 3. Experimental

The boiling points are uncorrected. IR spectra ( $\nu_{\text{max}}$  in  $\text{cm}^{-1}$ ) were run as thin films on a Perkin-Elmer spectrophotometer model 337 and PMR spectra in  $\text{CCl}_4$  on a Varian EM-390 spectrophotometer using TMS as an internal standard. Silica gel (ASC, Bombay) impregnated with  $\text{CaSO}_4$  was used for TLC. Unless otherwise stated, all organic extracts were dried over anhydrous sodium sulphate.

#### 3.1 (*Z*)-7-Dodecen-2-yn-1-ol (4)

To a well-stirred suspension of lithium amide, prepared from lithium metal (0.63 g, 90 mmol) in liq. ammonia (1 litre) containing a crystal of ferric nitrate, propargyl alcohol (1.68 g, 30 mmol) was added over a period of 15 min. The solution was stirred for 3 h, then 3 (6.15 g, 30 mmol) in dry THF (10 ml) was introduced dropwise in the next 30 min and the whole stirred further for 3 h. The reaction was quenched with a saturated solution of  $\text{NH}_4\text{Cl}$  (50 ml), the residue dissolved in water, then extracted with diethyl ether ( $3 \times 50\text{ ml}$ ) and the ethereal extract dried. The solvent was evaporated and the crude product on purification over silica gel column using light petroleum diethyl ether (7:3) afforded 4 (3.50 g, 65%). IR (film):  $3500\text{--}3300$ , 2950, 1650, 1470, 1350 and  $725\text{ cm}^{-1}$ , NMR ( $\text{CCl}_4$ ):  $\delta$  0.9 (t, 3H,  $-\text{CH}_3$ ), 1.3–1.7 (m, 6H,  $-\text{CH}_2-$ ), 1.7–2.2 (m, 6H, allylic and acetylenic methylenes), 3.4–3.6 (m, 3H,  $-\text{CH}_2-\text{OH}$ ), 5.4–5.6 (t, 2H, olefinic protons,  $J = 5.4\text{ Hz}$ ). (Found: C, 80.04; H, 11.10.  $\text{C}_{12}\text{H}_{20}\text{O}$  requires, C, 79.94; H, 11.18%).

3.2 (*Z*)-7-Dodecen-2-yn-1-ol (5)

To a solution of pyridinium chlorochromate (3.62 g, 16.5 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (100 ml) was added alcohol 4 (2.0 g, 11.0 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (10 ml) at  $0^\circ$ . The reaction mixture was stirred for 3 h and then diluted with anhydrous diethyl ether (100 ml). The supernatant layer was decanted from the gummy residue and then passed through a column of neutral alumina, eluting aldehyde with light petroleum: diethyl ether (9:1) to yield 5 (1.2 g, 60%) after removal of solvent IR (neat): 2900, 2850, 1710, 1650, 1470 and  $720\text{ cm}^{-1}$ . NMR ( $\text{CCl}_4$ ):  $\delta$  0.9 (t, 3H,  $-\text{CH}_3$ ), 1.2–1.5 (m, 6H,  $-\text{CH}_2-$ ), 2.0–2.1 (m, 6H, allylic and acetylenic methylenes), 5.4–5.5 (t, 2H, olefinic protons,  $J = 5.4\text{ Hz}$ ), 9.8 (s, 1H,  $-\text{CHO}$ ). (Found: C, 80.81; H, 10.31.  $\text{C}_{12}\text{H}_{18}\text{O}$  requires C, 80.85; H, 10.25%).

3.3 (1, 9*Z*)-Tetradecadien-4-yn-3-ol (6)

To a Grignard reagent, prepared from vinyl bromide (1.2 g, 14.0 mmol) and activated magnesium turnings (0.34 g, 14.0 mmol) in anhydrous ether (100 ml) at room temperature, was added a solution of 5 (2.0 g, 11.2 mmol) in anhydrous ether (10 ml) at  $0^\circ$  dropwise and the contents stirred for 12 h. The resulting solution was decomposed with a saturated solution of ammonium chloride, extracted with ether ( $4 \times 25\text{ ml}$ ) and dried. Evaporation of the solvent followed by column chromatography afforded pure 6 (1.60 g, 70%). IR (neat): 3500–3300, 2900, 1470,  $720\text{ cm}^{-1}$ . NMR ( $\text{CCl}_4$ ):  $\delta$  0.9 (t, 3H,  $-\text{CH}_3$ ), 1.2–1.6 (m, 6H,  $-\text{CH}_2-$ ), 2.0–2.3 (m, 6H, allylic and acetylenic methylenes), 3.9–4.1 (m, 2H,  $-\text{C}$ , 4.9–5.6 (m, 4H, olefinic protons), 5.7–6.1 (m, 1H,  $=\text{HC}-\text{CH}_2$ ). (Found: C, 81.43; H, 10.79.  $\text{C}_{14}\text{H}_{22}\text{O}$  requires C, 81.50; H, 10.75%).

3.4 Ethyl(4*E*, 11*Z*)-hexadecadien-6-yn-1-oate (7)

A mixture of 6 (2.0 g, 9.7 mmol), propionic acid (0.5 g, 6.8 mmol) and triethyl orthoacetate (11.4 g, 68.0 mmol) was heated at  $140^\circ$  for 2 h under nitrogen atmosphere with distillative removal of ethanol. The solution was poured into ether (100 ml), washed with  $\text{NaHCO}_3$  (15 ml) solution, brine and dried. The excess of triethyl orthoacetate was removed under reduced pressure and the crude residue was purified through silica gel column chromatography to afford pure 7 (2.1 g, 81%) as a sweet-smelling liquid. IR (neat): 2900, 1730, 1650, 1470, 970,  $720\text{ cm}^{-1}$ . NMR ( $\text{CCl}_4$ ):  $\delta$  1.0 (t, 6H, 3X- $\text{CH}_3$ ), 1.4–1.6 (bs, 6H, 3X- $\text{CH}_2-$ ), 1.8–2.2 (m, 8H, allylic and acetylenic methylenes), 3.4 (m, 2H,  $-\text{CH}_2-\text{CO}-$ ), 4.0 (q, 2H,  $-\text{COOCH}_2-$ ), 5.2–5.6 (m, 4H, olefinic protons). Found: C, 78.17; H, 10.28.  $\text{C}_{18}\text{H}_{28}\text{O}_2$  requires C, 78.26; H, 10.21%).

3.5 (4*E*, 6*E*, 11*Z*)-4,6,11-Hexadecatrien-1-ol (8)

To a solution of lithium aluminium hydride (0.69 g, 18.0 mmol) in dry diglyme (50 ml) was added dropwise a solution of 7 (2.20 g, 7.2 mmol) in dry diglyme (25 ml). The reaction mixture was refluxed for 36 h. Thereafter the contents were quenched with a saturated solution of sodium potassium tartrate, extracted with ether ( $4 \times 25\text{ ml}$ ) and dried. Removal of solvent by distillation and purification of the residue by column chromatography afforded 8 (0.87 g, 52%). IR (neat): 3500–3300, 2900, 1450, 1150, 980 and  $725\text{ cm}^{-1}$ . NMR ( $\text{CCl}_4$ ):  $\delta$  0.9 (t, 3H,  $-\text{CH}_3$ ), 1.3–1.5 (m, 8H, 4X- $\text{CH}_2$ ), 2.0–2.3

(*m*, 8H, allylic protons), 3.5–3.7 (*m*, 3H,  $-\text{CH}_2\text{OH}$ ) 5.3–6.1 (*bm*, 6H, olefinic protons). (Found: C, 81.23; H, 12.06.  $\text{C}_{16}\text{H}_{28}\text{O}$  requires C, 81.35; H, 12.00%).

### 3.6 (4*E*, 6*E*, 11*Z*)-4,6,11-Hexadecatrien-1-yl acetate (1)

A solution of 8 (1.0 g, 4.3 mmol) in dry methylene chloride, acetic anhydride (0.54 g, 5.2 mmol), and pyridine (0.52 g, 6.5 mmol) in dry methylene chloride (40 ml) was stirred at room temperature for 5 h. The reaction mixture was extracted with ether and dried. Solvent was expelled followed by column chromatography over silica gel using petroleum ether: ether (9:1) as eluent to afford 1 (1.4 g, 84%). IR (neat): 2900, 1740, 1650, 1470, 1325, 970, 725  $\text{cm}^{-1}$ . NMR( $\text{CCl}_4$ ):  $\delta$  0.9 (*t*, 3H,  $-\text{CH}_3$ ), 1.3–1.5, *m*, 8H,  $-\text{CH}_2-$ ), 1.9–2.2 (*m*, 8H, allylic methylenes), 2.0 (*s*, 3H,  $-\text{COCH}_3$ ), 4.1 (*t*, 2H,  $-\text{CH}_2\text{O}-$ ), 5.3–6.0 (*bm*, 6H, olefinic protons). (Found: C, 77.51; H, 10.72.  $\text{C}_{18}\text{H}_{30}\text{O}_2$  requires C, 77.64; H, 10.86%).

### 3.7 (4*E*, 6*E*, 11*Z*)-4,6,11-Hexadecatrien-1-al (2)

To a well-stirred suspension of pyridinium chlorochromate (1.43 g, 6.3 mmol) in dry methylene chloride (40 ml) was added alcohol 8 (1.0 g, 4.2 mmol) in dry methylene chloride (10 ml) at 0°. The reaction mixture was stirred for 3 h and then diluted with diethyl ether (100 ml). The supernatant layer was decanted from the gummy residue and then passed through a column of neutral alumina, eluting the aldehyde with light petroleum: diethyl ether (9:1) to yield 2 (0.55 g, 56%). IR (neat): 2950, 1710, 1650, 1470, 1350, 970, 725  $\text{cm}^{-1}$ . NMR( $\text{CCl}_4$ ):  $\delta$  0.9 (*t*, 3H,  $-\text{CH}_3$ ), 1.3–1.7 (*m*, 8H,  $-\text{CH}_2-$ ), 1.9–2.2 (*m*, 10H, allylic methylenes  $-\text{CH}_2\text{CO}-$ ), 5.3–6.2 *bm*, 6H, olefinic protons), 9.8 (*s*, 1H,  $-\text{CHO}$ ). (Found: C, 81.20; H, 11.18,  $\text{C}_{16}\text{H}_{26}\text{O}$  requires C, 81.05; H, 11.23%).

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