

Studies on Pheromones of Female Eri-Silk Moth, III.*
Synthesis of (6*Z*, 11*Z*)-6, 11-Hexadecadienal and
Its Activity as Pheromone Mimics toward
Male Eri-Silk Moth

By **Ichiro TOMIDA, Kazumasa TAKAGI, Yoshiaki KATO**
and Hiroshi KAYAHARA

Laboratory of Biological Chemistry, Fac. Agric., Shinshu Univ.

The title compound has electroantennographically exciting activity¹⁾ toward the male eri-silk moth, as does also (6*E*, 11*Z*)-6, 11-hexadecadienal, a component of the pheromone from female *Anthereae polyphemus*²⁾, and has recently been synthesized by Bestmann *et al.*³⁾ As a model compound** for the study of pheromone from female eri-silk moth, *Philosamia cynthia ricini*, we also tried to synthesize the title compound by the following way as was schemed below:

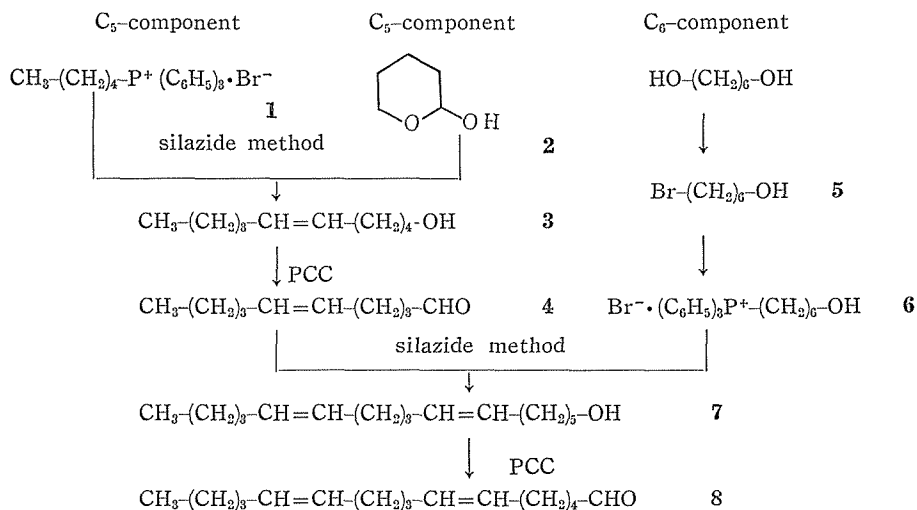


Fig. 1.

We disconnected the target compound into three fragments (C₅+C₅+C₆) and the

* Part II, see Lit.¹⁾

** (6*E*, 11*Z*)-6, 11-Hexadecadienal is electroantennographically more active than (6*Z*, 11*Z*)-isomer toward the antenna of male eri-silk moths¹⁾; the latter was, however, selected for this work as it was considered to be more easily prepared.

synthons were coupled to each other by means of the Wittig reaction under *Z*-selective conditions (silazide method).⁴⁾ Thus we have reached the dienol compound **7** directly after the second Wittig reaction by using an unprotected hydroxy-phosphonium compound as the C₆-component.

C₅+C₅-component **4** was prepared according to the Lit.^{5,6)} : **1** was condensed with **2** by using the *Z*-selective Wittig reaction⁴⁾ to give **3**. An oily product **3** was purified either by the preparative tlc (in the case of small scale) or by the SiO₂-column chromatography (in the case of large scale). It was then converted to **4** by means of Corey's oxidation method.⁷⁾

5 was obtained by the usual method from 1,6-hexanediol, while **6** was prepared by treating **5** with triphenyl phosphine at 90–100°C under nitrogen without any solvent. The reaction product was solid, owing to its highly hygroscopic nature, however, this solid matter **6** was directly condensed with **4** again under *Z*-selective reaction conditions. The product obtained after purification by preparative tlc was spectroscopically assigned as **7** (14%). **7** was then oxidized with pyridinium chlorochromate⁷⁾ to give the target compound **8**. The structure of this product was established spectroscopically after purification using preparative tlc (yield, 55%).

The synthesized product **8** was assayed on the male eri-silk moths. As expected, it showed the pheromonally stimulating action and the response pattern was identical with that by the pheromone extract itself from the female eri-silk moths. The activity of this product was then determined by using the conventional wing fluttering test using 20 specimens of the male eri-silk moth.⁸⁾ The positive response in the individual test was estimated when the animal started to vibrate his wings characteristically within about 20 sec after the test glass rod was put in front of the antenna, and the test solution was decided as positive when more than half of the test insects responded positively to it. The experiment was several times replicated and the minimum concentration of the product **8** was elucidated to be 100 μg/ml (n-hexane). In this test such animals that were sensitive up to 10⁻³ F. E. (female equivalent) were used.

EXPERIMENTAL PROCEDURES

¹H-NMR-spectra : Hitachi R-24 (60MHz), TMS as standard. — Mass spectrum: Shimadzu GCMS-7000 (70ev). — IR-spectra : spectrophotometer Hitachi EPI-52. — GLC : Hitachi 063, FID-detector, column 1m × 3mm ID and, unless otherwise described, OV-17(5%). — tlc : hexane/ethyl-methyl ketone (4:1 vol.) was thoroughly used as developing solvent including preparative tlc. The spot was visualized by spraying with 10% H₂SO₄.

1. (*Z*)-5-decen-1-al (**4**): According to the procedure in the Lit.⁷⁾ **3**^{5,6)} was oxidized

with pyridinium chlorochromate. An oil, bp₉86–92°(64%). Lit.⁵⁾ bp₁₄ 100–120° (53%), Lit.⁶⁾ bp₁₀ 89–91° (70%). tlc : *Rf*=0.89. GLC(100°) : *t_R*=2.0 min, a single peak. IR(film) : $\frac{\text{cm}^{-1}}{\text{max}}$ 3000(CH=) 2700(CHO) 1730(HC=O) and no absorption at 960. NMR(CDCl₃): δ 0.90(3H, t, *J*=5Hz, CH₃) 1.05–1.7 (6H, m, -CH₂- × 3) 1.7–2.2 (4H, m, CH₂-CH=CHCH₂) 2.45 (2H, d-t, CH₂-CHO) 5.1–5.6 (2H, m, CH=CH) 9.65 (1H, t, *J*=5Hz, CHO).

2. *6-Bromohexanol* (**5**): According to a related procedure in Lit.⁶⁾ **5** was prepared from **1**, 6-hexanediol. An oil, bp₁₀110–116°(71%). (Lit.¹⁰⁾ bp₅105–106°(81%). Lit.⁵⁾ bp₁₄ 111–118° (72%). tlc : *Rf*=0.32. IR(film : $\frac{\text{cm}^{-1}}{\text{max}}$ 3300(OH). NMR(CCl₄) : δ 1.2–1.8 (4H, m, -CH₂- × 2) 1.8–2.35 (4H, m, -CH₂- × 2) 3.33 (2H, t, *J*=7Hz, CH₂Br) 3.48 (2H, t, *J*=6Hz, CH₂-OH) 4.0 (1H, s, OH).

3. *6-Hydroxyhexyl triphenylphosphonium bromide* (**6**):**5** and triphenyl phosphine (1 eq) were heated under nitrogen for 24h (bath temp. 90–100°). The reaction mixture (a hard mass) was recrystallized from chloroform and benzene. The crystals were hygroscopic in the atmosphere. It was then heated in ether under reflux for 15h. The solid matter (88%) was fully dried in a desiccator and used directly in the next reaction. NMR(CDCl₃): δ 2.9 (1H, s, OH) 3.0–4.0 (4H, m, CH₂-OH, CH₂-PPh₃) 7.7(15H, s, PPh₃). Found:C, 65.02;H, 6.37. Calcd. for C₂₄H₂₉OPBr (444.4):C, 64.87;H, 6.58%.

4. (*6Z, 11Z*)-*6, 11-Hexadecadien-1-ol* (**7**): According to the procedure in Lit.⁴⁾, to the solution of sodium bis(trimethylsilyl) amide (1.5 eq) in Na-dry THF was added **6** (4.00g, 9.0m mole) with stirring under argon to give the corresponding ylid. After further stirring for 1/4h the solution was chilled in dry-ice/methanol mixture (–50°) and **4** (1.39g, 1eq) was added under argon. The stirring was continued overnight. The reaction mixture was concentrated *in vacuo*, the residue was stirred with n-hexane and allowed to stand in an ice-box overnight. The precipitate was filtered off, the filtrate was washed successively with 2N HCl aq, sat. NaHCO₃ aq and 10% NaHSO₃ aq, dried over Na₂SO₄ and evaporated *in vacuo*. The residue was purified by preparative tlc. **7** was obtained as an oil (0.30g, 14%). tlc:*Rf*=0.55. GLC(160°) :*t_R*=4.7min, a single peak. IR(film): $\frac{\text{cm}^{-1}}{\text{max}}$ 3350 (OH) 3000 (CH=) 800 (C=C) and no absorption at 960. NMR(CCl₄): δ 0.9 (3H, t, *J*=6Hz, CH₃) 1.06–1.67 (12H, m, -CH₂- × 6) 1.67–2.25 (8H, m, CH₂-CH=CH-CH₂ × 2) 2.35 (1H, s, OH) 3.5 (2H, t, *J*=6Hz, CH₂-OH) 5.27(4H, t, *J*=4.6Hz, CH=CH × 2).

5. (*6Z, 11Z*)-*6, 11-Hexadecadien-1-al* (**8**): In the same manner as described in 1, **7** was oxidized with pyridinium chlorochromate. The product was purified by means of preparative tlc. An oil (55%). tlc : *Rf*=0.90 GLC (160°) : *t_R*=3.6min,

accompanied with one small impure peak in the range apart from the main peak. IR(film) : cm^{-1} $\frac{\text{max}}$ 3000(CH=) 2700(CHO) 1730(C=O). No absorption at 960. NMR(CCl_4) : δ 0.9 (3H, t, $J=6\text{Hz}$, CH_3) 1.0–1.6 (8H, m, $\text{CH}_2\text{-CH=CH-CH}_2 \times 2$) 2.15–2.55 (2H, m, $\text{CH}_2\text{-CHO}$) 5.31 (4H, t, $J=5\text{Hz}$, $\text{CH=CH} \times 2$) 9.67(1H, t, $J=1.6\text{Hz}$, CHO). MS : m/Z 236(M^+ , 8%).

Acknowledgements

We are indebted to thank Prof. H.J. Bestmann (Erlangen University) and Dr. D.R. Hall (London, Tropical Products Institute) for their kind information about the antennographical studies and the related experimental procedures. These experiments were performed partially with financial help from the Science Promoting Association of Nagano Prefecture. For the measuring of mass spectrum we are also thankful to Dr. D. Karasawa (Shinshu University, Dept. of Agricultural Chemistry).

REFERENCES

1. H.J. Bestmann, private communication. cf. Part. II.I. Tomida, Y. Kato and H. kayahara, *J. Fac. Agric. Shinshu Univ.*, **20**, 133 (1983).
2. J. Kochansky, J. Tette, E.F. Taschenberg, R.T. Carde, K.E. Kaissling and W.L. Loeloffs, *J. Insect Physiol.*, **21**, 1977 (1975).
3. H.J. Bestmann and O.Vostrowsky, *Chem. Phys. Lipids.*, **24**, 335 (1979).
4. H.J. Bestmann, W. Stransky and O.Vostrowsky, *Chem. Ber.*, **109**, 1694 (1976).
5. K.H. Koschatzky, "Doctoral Thesis" (Erlangen, 1979).
6. H.J. Bestmann and K. Li, *Tetrahedron Lett.*, 4941 (1981).
7. E.J. Corey and J.W. Suggs, *Tetrahedron Lett.*, 2647 (1975).
8. I. Tomida and S. Ishii, *App. Ent. Zool.*, **3**, 103 (1968).
9. Org. Synth., Coll. Vol. III, p.446.
10. F. Degering and L.G. Eoatright, *J. Amer. Chem. Soc.*, **72**, 5137 (1950).

摘 要

エリ蚕雌フェロモンに関する研究 III
 (6*Z*, 11*Z*)-6, 11-ヘキサデカジエナールの合成と、
 それのエリ蚕蛾雄に対するフェロモンミックス
 としての活性度

富田一郎・高木一全・加藤喜章・茅原 紘

信州大学農学部 生物化学研究室

標題の化合物は、サク蚕の一種 *Anthereae polyphemus* の雌から得られるフェロモン成分の1つである (6*Z*, 11*Z*)-6, 11-ヘキサデカジエナールとともに、エリ蚕 *Philosamia cynthia ricini* の雄蛾に対して電磁触角的に活性を示す物質である。我々は標題の化合物をエリ蚕の性フェロモンの研究のモデル化合物の1つとして合成を試みた。すなわち、ペンチルトリフェニルホスホニウムブロマイドからシラジド法で得られるイリドに対し、5-ヒドロキシペンタナールを*Z*選択的ウィティヒ反応の条件で縮合し、(Z)-5-デセン-1-オールを得、これを酸化して相当するアルデヒドにした。一方、6-ブロモヘキサノールから6-ヒドロキシヘキシル トリフェニルホスホニウムブロマイドとし、これを上記で得たアルデヒドと再び*Z*選択的ウィティヒ反応で縮合し、(6*Z*, 11*Z*)-6-11-ヘキサデカジエノールに一挙に導き、更に酸化して相当するアルデヒド、すなわち目的物に導いた。このものはガスクロマトグラフ的には少量の不純ピークを伴うが、主ピークに関しては*Z*, *Z*の単一幾何異性体と結論された。このものはエリ蚕の雄蛾に対して、天然のフェロモン抽出物と全く同様の反応パターンを惹き起した。そして、従来の羽搏きテスト法では100 $\mu\text{g}/\text{ml}$ の低濃度までの活性度を示した。なお、このとき使用したエリ蚕雄蛾は雌浸漬抽出液を 10^{-3} 濃度まで希釈しても、それに対し感応するものであった。