

SYNTHETIC PROOF OF THE STRUCTURE OF A PROPOSED CODLING MOTH SEX PHEROMONE

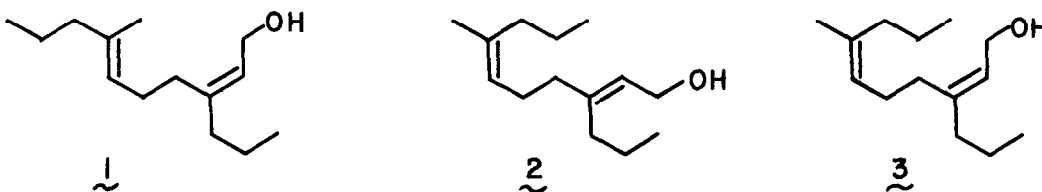
Manning P. Cooke Jr.

Department of Chemistry, Washington State University,

Pullman, Washington 99163

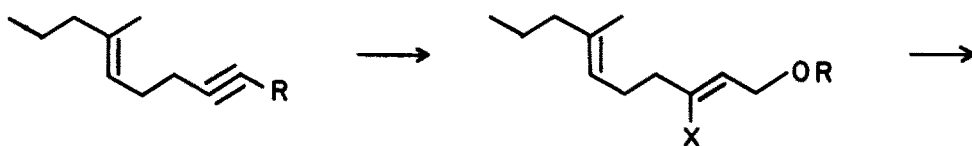
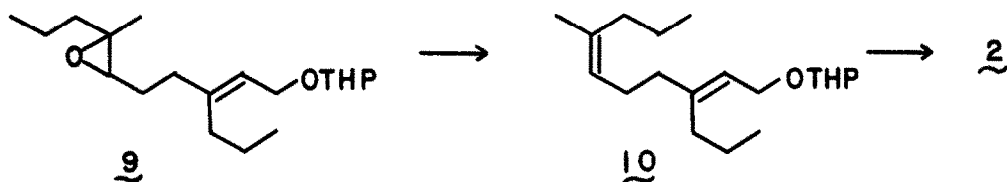
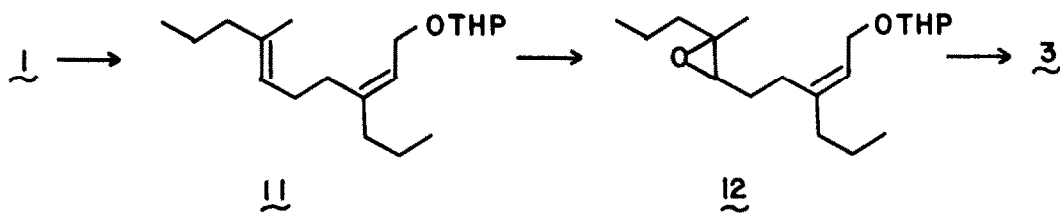
(Received in USA 19 March 1973; received in UK for publication 19 April 1973)

McDonough and coworkers¹ have recently isolated a stereoisomer of 7-methyl-3-propyl-2,6-decadien-1-ol from the Codling moth, *Laspeyresia pomonella* (L.) and proposed that it is a component of the sex pheromone.² The compound was thought to be the 2Z,6E isomer 1 based on nmr and glpc data. We have recently shown³ that this stereochemical assignment is incorrect insomuch as 1 prepared by a stereoselective synthesis is non-identical with the natural material. On the basis of spectral evidence and the original¹ glpc retention data⁴ we proposed that the natural product is likely the 2E,6Z isomer 2. We now wish to report the



stereoselective synthesis of 2 (Scheme 1) and syntheses of the remaining two stereoisomers, 3 and 7 (Schemes 1 and 2). The 2Z,6Z isomer 3 was found to be identical with the natural material.

The intermediate (E)-6-methyl-5-nonen-1-yne (4) previously employed³ in the synthesis of 1 served as a precursor for both isomers possessing the 2E configuration (2 and 7) (Scheme 1). Treatment of 4 with butyllithium in THF followed by paraformaldehyde⁵ gave the propargyl alcohol 5⁶ (bulb-to-bulb distillation, $T_{\text{bath}} 160^\circ$, 3 mm) in 78% yield. Reduction of 5 with lithium aluminum hydride in the presence of sodium ethoxide followed by iodination of the intermediate vinyl aluminum species by the method of Corey⁷ gave iodo-alcohol 6 in 75% yield

Scheme 14 (R = H)5 (R = CH₂OH)6 (X = I, R = H)7 (X = Pr, R = H)8 (X = Pr, R = THP)9102Scheme 2111123

after preparative tlc purification (silica gel, methylene chloride). The stereochemical configuration of **6** follows from the known stereospecificity of this method.⁷ Propylation of **6** with di-*n*-propylcopper lithium gave after preparative tlc purification dienol **7** free of any detectable amounts of 2Z isomer. Since it had been previously deduced³ from the C-7 methyl proton resonance in **1** that the natural product must possess a 6Z configuration, it was necessary to invert the configuration of the C-6 double bond in **7**. This was readily accomplished by the method of Vedejs.⁸ Conversion of **7** into the THP ether **8** (dihydropyran, TsOH, 100% crude yield) followed by selective terminal epoxidation⁹ of crude **8** with *m*-chloroperbenzoic acid in CH₂Cl₂ at 0° gave epoxide **9** in 71% overall yield from **7** after purification by preparative tlc (silica gel pH 7 buffered, 9:1 methylene chloride:ethyl acetate). Treatment of epoxide **9** with lithium diphenylphosphide in THF (3 hr at 48°) followed by treatment with methyl iodide gave THP-diene **10**. Removal of the tetrahydropyranyl ether group by hydrolysis of **10** in a 1:1 mixture of acetic acid-water (45°, 1 hr) gave after purification by preparative tlc **2** (bulb-to-bulb distillation, T_{bath} 160°, 2 mm) in 81% yield from **9**. Despite the spectral similarities of **2** with the natural product, glpc analysis¹⁰ showed **2** to be non-identical with the natural material leaving the 2Z,6Z isomer **3** as the remaining possibility.

The 2Z,6Z isomer **3** was readily prepared as shown in Scheme 2 by subjecting the previously synthesized³ 2Z,6E isomer **1** to the terminal olefin inversion scheme employed above. Thus selective epoxidation of the THP ether **11** with *m*-chloroperbenzoic acid gave epoxide **12** which after treatment with lithium diphenylphosphide and methyl iodide followed by hydrolysis of the tetrahydropyranyl ether group gave **3** which was purified by preparative tlc followed by bulb-to-bulb distillation (T_{bath} 160°, 2 mm) (53% overall yield from **1**). Glpc showed the inversion to be highly stereoselective¹¹ demonstrating the utility of this method in the synthesis of terpenoid compounds when coupled with regioselective epoxidation.

Glpc analysis¹⁰ of **3** as well as spectral analysis showed this isomer to be identical to the natural material from the Codling moth. Thus the structure of the proposed pheromone is proved to be (2Z,6Z)-7-methyl-3-propyl-2,6-decadien-1-ol (**3**).

Acknowledgment. The author thanks Washington State University for its support through a grant-in-aid.

REFERENCES

1. L. M. McDonough, D. A. George, B. A. Butt, J. M. Ruth and K. R. Hill, Science, **177**, 177 (1972).
2. There is now reason to believe that this compound is not a true component of the sex pheromone; see footnote 2, reference 3.
3. M. P. Cooke, Jr., Tetrahedron Lett., in press (1973).
4. It now appears that the relative retention time data upon which this prediction was based is in error. Dr. McDonough has kindly informed us that at least one of the four major peaks in his synthetic mixture does not correspond to one of the four isomers now available through stereoselective synthesis.
5. A. Schaap, L. Brandsma and J. F. Arens, Rec. Trav. Chim., **84**, 1200 (1965).
6. The ir and nmr spectra were in agreement with the assigned structures of all compounds reported. Satisfactory elemental analyses were obtained for all purified intermediates.
7. E. J. Corey, J. A. Katzenellenbogen and G. H. Posner, J. Amer. Chem. Soc., **89**, 4245 (1967).
8. E. Vedejs and P. L. Fuch, J. Amer. Chem. Soc., **95**, 822 (1973).
9. E. E. van Tamelen and T. J. Curphey, Tetrahedron Lett., 121 (1962); E. E. van Tamelen and K. B. Sharpless, ibid., 2655 (1967).
10. We thank Dr. McDonough for making the gas chromatographic comparisons with the natural material.
11. Glpc analysis indicated the presence of a small amount (<6%) of the 6E isomer which likely arose from the inversion of the small amount (~7%) of 6Z isomer present in starting material ⁴.