A Convenient Synthetic Route to Insect Juvenile Hormone

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SINCE the elegant structural elucidation of the insect juvenile hormone (I) from *Hyalophora cecropia* by Roller, Dahm, Sweeley, and Trost,[1] several syntheses of this interesting compound have been reported.[2]

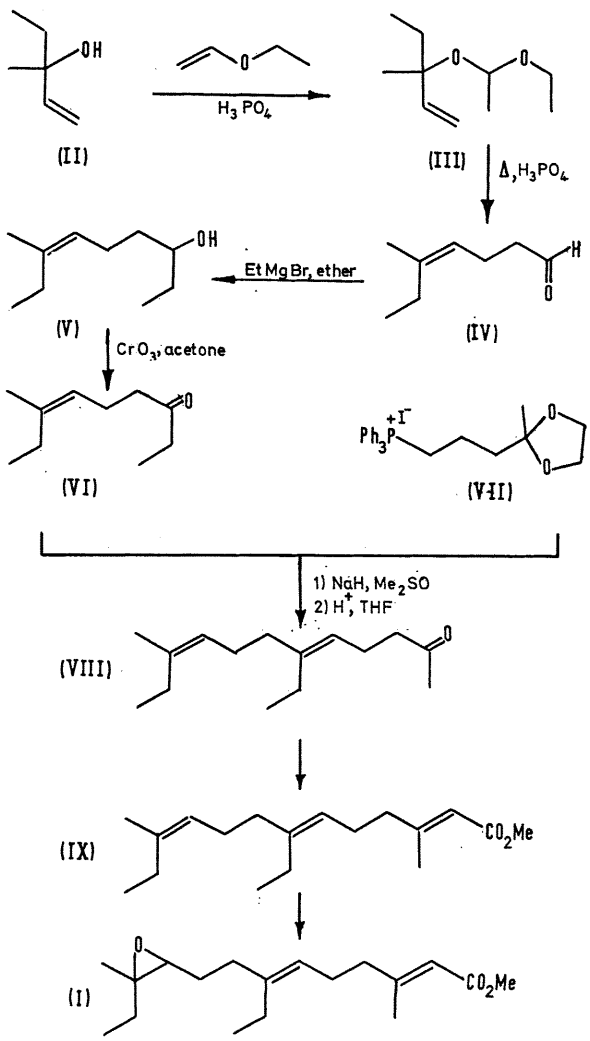
It is known that some isomers of the natural hormone (I) and of a synthetic precursor (IX) display relatively high levels of biological activity.[2a] We report here a short and efficient synthetic pathway to the several pure isomers of (IX) and (I).

Treatment of 3-methylpent-1-en-3-ol (II) in refluxing ethyl vinyl ether with a trace of H_3PO_4 gave the ketal (III) in 91% yield. Pyrolysis of (III) with a trace of H_3PO_4 gave in 54·5% yield a mixture of *cis*- and *trans*-5-methylhept-4-enal (IV).[3] Treatment of (IV) with EtMgBr in ether afforded a mixture of *cis*- and *trans*-alcohols (V) in 88% yield. Oxidation of (V) with an excess of Jones' reagent gave the corresponding ketones (VI) in 95% yield.

The salt (VII) was prepared quantitatively from 5-iodopentan-2-one by ketalization with ethylene glycol followed by treatment with triphenylphosphine. Wittig reaction of the ylide of (VII) with the ketones (VI) afforded, after acidic work-up and silica gel chromatography, in 84% yield the ketones (VIII). This mixture was shown by v.p.c. to comprise 15% *cis,cis*-, 23% *trans,cis*-, 25% *cis,trans*-, and 37% *trans,trans*-6-ethyl-10-methyldodeca-5,9-dien-2-one (VIII).

Preparative v.p.c. separation† of the *trans/cis*-mixture of alcohols (V) at 150° afforded in 3 : 2 ratio pure *trans*- and pure *cis*-(V). Repeating the synthesis employing pure *cis*-alcohol (V) gave a mixture of 40% *cis,cis*- and 60% *trans,cis*-(VIII) readily separable by preparative v.p.c.† at 160°. By parallel procedure the *trans*-alcohol (V) was utilized to prepare pure *trans,trans*- and pure *cis,trans*-(VIII).

The identity of the important *trans,cis*-(VIII) was indicated by the known preferred stereochemical courses of the reactions employed in generating each double bond and was fully supported by spectroscopic data. Conversion of this key intermediate into *trans,trans,cis*-(IX) and further elaboration to racemic juvenile hormone (I) was accomplished by known methods.[2a,b] The synthetic juvenile hormone (I) thus prepared showed identity in all



† All the synthetic compounds prepared in this work were fully characterized by mass spectrometry and n.m.r. and i.r. spectroscopy and displayed the expected characteristics. A Carbowax 20M column was used for the preparative v.p.c.

detail with the reported[2a,b] spectroscopic data, which allows its distinction from other isomers in the series.

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[1] H. Roller, K. H. Dahm, C. C. Sweeley, and B. M. Trost, *Angew. Chem. Internat. Edn.*, 1967, **6**, 179.

[2] (a) K. H. Dahm, B. M. Trost, and H. Roller, *J. Amer. Chem. Soc.*, 1967, **89**, 5292; K. H. Dahm, H. Roller, and B. M. Trost, *Life Sci.*, 1968, **7**, 129; (b) E. J. Corey, J. A. Katzenellenbogen, N. W. Gilman, S. A. Roman, and B. W. Erickson, *J. Amer. Chem. Soc.*, 1968, **90**, 5618; (c) R. Zurfluh, E. H. Wall, J. B. Siddall, and J. A. Edwards, *ibid.*, p. 6224; (d) W. S. Johnson, Tsung-Tsee Li, D. J. Faulkner, and S. F. Campbell, *ibid.*, p. 6225; (e) B. H. Braun, M. Jacobson, M. Schwarz, P. E. Sonnet, N. Wakabayashi, and R. M. Waters, *J. Econom. Entomol.*, 1968, **61**, 866.

[3] A similar preparation of other $\gamma\delta$-unsaturated aldehydes has been reported by G. Saucy and R. Marbet, *Helv. Chim. Acta*, 1967, **50**, 2099.