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# Microscale, Random Reduction: Application to the Characterization of (3*E*,8*Z*,11*Z*)-3,8,11-Tetradecatrienyl Acetate, a New Lepidopteran Sex Pheromone*

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**Abstract**: The major sex attractant released by *Scrobipalpuloides absoluta*, a devastating tomato pest, was identified as (3*E*,8*Z*,11*Z*)-3,8,11-tetradecatrienyl acetate by a novel strategy involving the random reduction of double bonds. The technique is applicable to double bond localization of polyunsaturated compounds available even in nanogram quantities. The triene ester was synthesized by a stereospecific procedure and shown to be highly attractive to conspecific males and identical to the natural substance.

Over 400 compounds, most of which are straight-chain unsaturated hydrocarbons, acetates, aldehydes, or alcohols, have been characterized as sex pheromones of moths.[4,5] Although the structures of these molecules are rather simple, their characterization is not always easy since often only nanogram amounts of material, usually as a complex mixture, are available for structure elucidation. The characterization of polyunsaturated compounds is particularly challenging since there is no single, reliable technique for determining the location and configuration of double bonds. Only about ten pheromones bearing three or more double bonds have been fully characterized.[5] *Scrobipalpuloides absoluta* Meyrick (Lepidoptera: Gelechiidae: Gelechiinae) is one of the most devastating pests on tomato in Brazil and many other South American countries. Since females of *S. absoluta* release a potent sex pheromone attractive to conspecific males,[6] we undertook the characterization and synthesis of this pheromone, which should be a powerful element in designing an integrated pest management (IPM) program for combating this pest.

A preliminary examination of hexane extracts made from excised pheromone-producing glands of females that were actively attracting conspecific males, using capillary GC-MS, showed the presence of two significant chromatographic peaks in the region where lepidopteran pheromones usually appear. The mass spectrum corresponding to the major peak (90%) showed a base peak at *m/z* 43 indicating that this component is an acetate; the ion produced by loss of acetic acid ($M^+$-60) at *m/z* 190 indicated that the compound is a tetradecatrienyl acetate. A comparison of the integrated GC peak area of this component with that of an external standard showed the amount of this constituent obtainable from each female gland to be about 1-5 ng.

An attractive strategy to locate the position and configuration of the three double bonds in this compound might be to carry out a partial reduction of the material (by the diimide procedure[7,8]) in the hope

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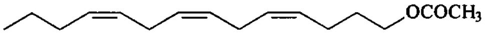
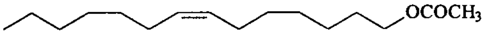
* Dedicated to Professor Hans Jürgen Bestmann on the occasion of his 70th birthday.

of obtaining a product mixture containing all possible monoene acetates, since excellent techniques are available for the determination of the position of a double bond in monoenes.[9-11] The exact conditions required to carry out this two-step procedure using less than 100 ng of the starting material were worked out using (4*Z*,7*Z*,10*Z*)-4,7,10-tetradecatrienyl acetate[12] **1**, as a model. The three expected tetradecenyl acetates (**2**-**4**) were readily characterized by GC/MS by comparing retention times and mass spectra of the products with those obtained from authentic standards. The identifications were further confirmed by converting the tetradecenyl acetates to their dimethyl disulfide derivatives and recording the mass spectra of the adducts.[9,10]



**1**

**2**



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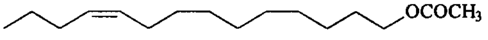
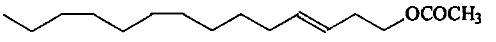


**4**

Once the optimal conditions for the necessary micromanipulations were established, the natural pheromone extract was subjected to a partial diimide reduction.[13] GC-MS analysis of the resulting product mixture showed the presence of three tetradecenyl acetates along with doubly unsaturated and saturated acetates. In order to identify these three tetradecenyl acetates precisely, we measured the mass spectra as well as the GC retention times of all 23 possible tetradecenyl acetates on two different GC stationary phases (DBWax, and DB-23), and compared these data to those obtained for the three tetradecenyl acetates that resulted from partial reduction of the natural pheromone. In this way, two of the monoenes derived from the natural pheromone were identified unambiguously as (*E*)-3-tetradecenyl acetate (**5**) and (*Z*)-8-tetradecenyl acetate (**6**). However, retention data alone could not establish the identity of the third isomer, since the retention times of (*Z*)-11-tetradecenyl acetate (**7**) and 13-tetradecenyl acetate were very similar on both GC phases. To establish the identity of the third tetradecenyl acetate, the mixture was converted into a mixture of the corresponding dimethyl disulfide (DMDS) adducts.[9-11] GC-MS analysis of this mixture showed the expected presence of DMDS adduct of an 8-tetradecenyl acetate *m/z* (%), 348 ($M^+$, 10), 217 (40), 131 (23), and that of an 11-tetradecenyl acetate. *m/z* (%), 348 ($M^+$, 15), 259 (95), 89 (38).[14] The retention times of these two adducts on a DB-1 capillary column were identical to those obtained from the DMDS derivatives of authentic (*Z*)-8-tetradecenyl acetates (**6**) and (*Z*)-11-tetradecenyl acetate (**7**). Based on these results, the triply unsaturated compound was identified as (3*E*,8*Z*,11*Z*)-3,8,11-tetradecatrienyl acetate **8**.



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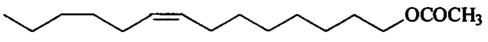
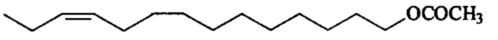
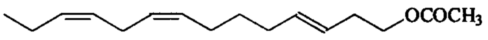


**6**

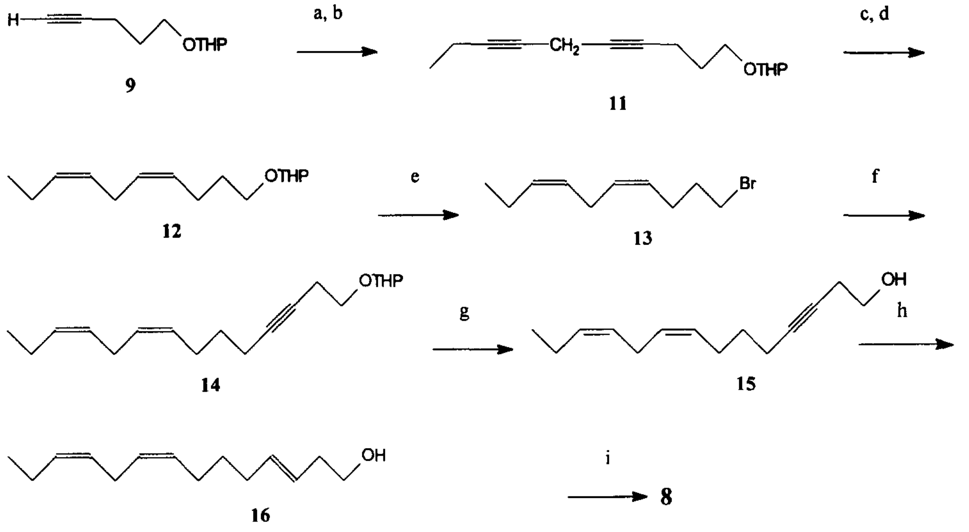


**7**



**8**

This structure and stereochemistry were confirmed by synthesis, as outlined in Scheme 1. The protected pentynol **9** was converted to an acetylenic Grignard which carried out a Cu(I)-catalyzed nucleophilic displacement on the propargylic tosylate **10**, giving diyne **11** in quantitative yield. This diyne **11** was hydroborated with dicyclohexylborane, obtained from borane-methylsulfide complex and cyclohexene.



Scheme 1. a) EtMgBr / THF; b) $CH_3$ -$CH_2$-C ≡ C-$CH_2$-OTs (**10**)/Cu(I)Br.$Me_2S$, -20 °C - 0 °C; c) $Cy_2BH$, 4.4 eq.; d) $CH_3CO_2H$; e) $PPh_3$ / $Br_2$ 1.5 eq, $CH_2Cl_2$ ; f) Li—≡—⁄⁀OTHP , DMPU / THF 0 °C; g) Dowex / MeOH; h) $LiAlH_4$ / diglyme, 120-140 °C; i) $Ac_2O$ / pyridine.

Protonolysis of the resultant *bis*-vinylborane with acetic acid gave the THP protected alcohol **12**. This protected alcohol was converted directly into bromide **13** in 32% overall yield (based on **9**), by treating with triphenylphosphine dibromide. The bromide **13** was treated with the lithium salt of 2-(3-butynyloxy)tetrahydro-2*H*-pyran in a mixture of THF/N,N'-dimethylpropyleneurea (DMPU) to yield dieneyne **7** in 82% yield. The deprotection of **14** to give the alcohol **15** was accomplished by stirring with Dowex 50W-X8 in methanol. The alcohol **15** was reduced with $LiAlH_4$ in dry diglyme for 2-5 hrs. The resulting trienol **16** was then acetylated to the desired product, (3*E*,8*Z*,11*Z*)-3,8,11-tetradecatrien-1-yl acetate (**8**), in 7% overall yield and 97% purity (GC on SE-54 and Carbowax capillary columns). Both the mass spectrum and gas chromatographic retention times of the synthetic product were congruent with those of the natural pheromone.

In wind-tunnel bioassays, *S. absoluta* males showed induced wing beating, oriented flight, and landing on the source of the synthetic pheromone when tested by depositing a 100 ng sample on a rubber septum. The wind-tunnel results were similar to those observed with males responding to virgin females. Finally, the synthetic pheromone was tested in the field using traps (n = 20) baited with 1 , 10 , and 100 μg of **1**, which caught on average 535, 945 and 1276 males (per night, per trap), respectively. Traps (n = 20) each baited with three virgin females caught an average of 280 males (per night, per trap). These results show clearly that the synthetic pheromone is attractive to *S. absoluta* males.

Tetradecatrienyl acetate **8** is closely related to only a few known lepidopteran pheromones.[4,5] Although the ω-3, ω-6 structural moiety is found in many pheromonal polyunsaturated hydrocarbons, and in related epoxides, this moiety is rare among acetate ester sex pheromones.[4,5] A somewhat related compound, (4*E*,7*Z*,10*Z*)-4,7,10-tridecatrienyl acetate, together with the corresponding diene, (4*E*,7*Z*)-4,7-tridecadienyl acetate, has been characterized as the sex attractant of another gelechiid, *Phthorimaea operculella.*[15] Interestingly, our traps baited with female *S. absoluta* also attracted a few *P. operculella* males.

In summary, we have developed a new approach to determining the structure of polyene pheromones. This technique has been applied successfully to the characterization of the major component of the *S. absoluta* female sex pheromone (**8**). We have also completed a convenient stereospecific synthesis of this triene acetate. The high biological activity of the synthetic pheromone suggests that it will prove useful in monitoring pest populations in the field, and that it may also be useful in mating disruption.

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13. An ethanol extract containing 125 female sex glands was concentrated to a few microlitres and mixed with a solution of hydrazine (10 μl, 10% in ethanol) and $H_2O_2$ (10 μl, 0.6 % in ethanol). The mixture was heated at 60 °C for 2.5 hr and allowed to cool to room temperature. It was acidified with dil. HCl and extracted with hexane (3 x 15 μl). The combined hexane layers were reduced to 2-3 μl and reconstituted to 10 μl with hexane. One μl of this extract, together with hexadecane and tetracosane as internal standards, was analyzed by GC-MS. The rest of the mixture was derivatized with DMDS.[9]
14. The presence of a peak corresponding to a DMDS adduct of a 3-tetradecenyl acetate could not be established. A competitive derivatization reaction conducted with synthetic 3-, 8-, and 11-tetradecenyl acetates showed that the 3-isomer is the most difficult to derivatize.
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