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A Male-Produced Pheromone of the Spined Citrus Bug

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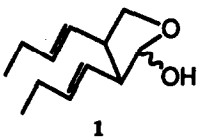
Abstract: An unusual hemiacetal, *cis*-3,4-bis[(E)-1-butenyl]tetrahydrofuran-2-ol, the major component of the dorsal abdominal glands of the title insect,was identified by spectral and chemical means, and the structure confirmed by synthesis.

The spined citrus bug, *Biprorulus bibax* Breddin (Hemiptera: Pentatomidae), is an Australian citrus pest of increasing importance[1]. The presence of sexual dimorphism in the dorsal abdominal glands (DAGs) of these bugs (the males have enlarged glands whereas those of the females are very small) suggested an analogy to certain predaceous pentatomids wherein a similar dimorphism was related to pheromone production by the male glands[2,3]. Because the availability of a pheromone could be useful for monitoring and control strategies, we have investigated the secretion of the male glands and here report its major components and the identification of the most abundant compound[4] as the previously unknown 12-carbon unsaturated hemiacetal **1**.



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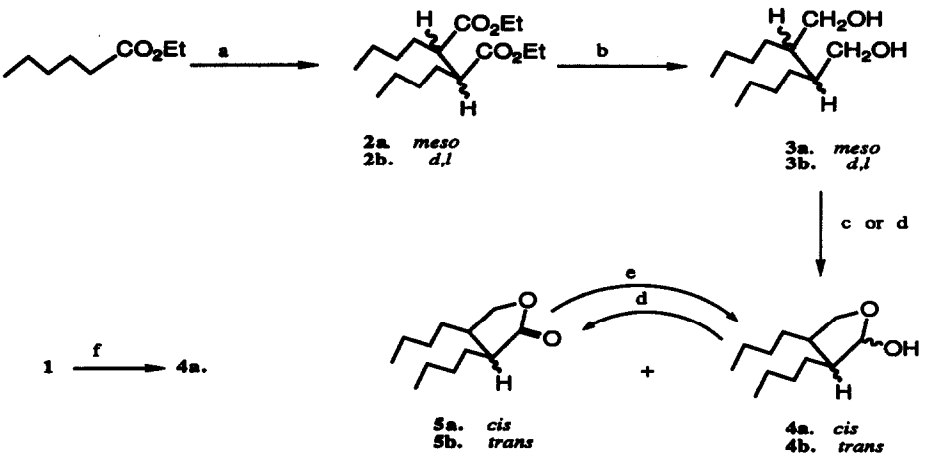
Using a dissecting microscope, DAGs from *ca.* 15 males were excised under water, blotted with tissue paper, and macerated with heptane in a small conical vial. The heptane solution was analyzed by gas chromatography-mass spectrometry (GC-MS). A high resolution MS of **1** established its empirical formula as $C_{12}H_{20}O_2$, and contained ions representing losses of H_2O and (H_2O+CO). Chemical ionization MS with ammonia and deuteroammonia as reagent gases, respectively, revealed the presence of a single exchangeable hydrogen. Preparative gas chromatography of most of the sample provided enough material (75 ug ?) for ^{1}H-NMR and the following experiments. Hydrogenation (PtO_2, 1 atm) resulted in uptake of two equivalents of hydrogen; thus the empirical formula of **1** required one ring or additional element of unsaturation. The hydrogenation product retained the exchangeable hydrogen and also displayed the losses of H_2O and (H_2O+CO) during electron ionization MS. Ozonolysis of **1** and derivatization with O-benzylhydroxylamine gave a single

product (observable by GC-MS) that was identified (by MS and retention time) as the O-benzyloxime of propanal.

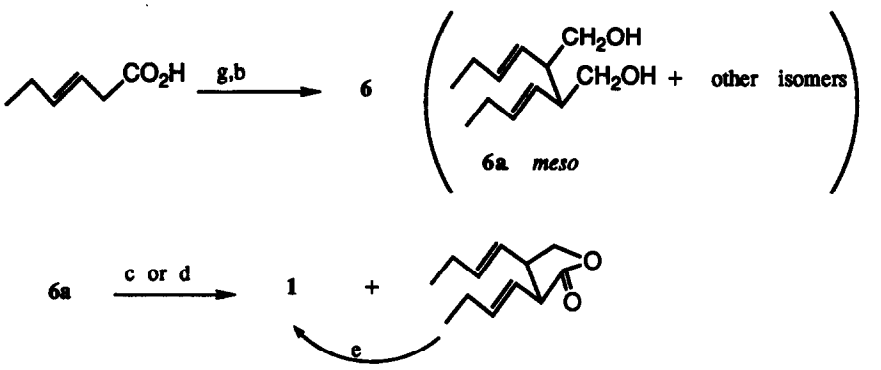
A gas phase infrared spectrum (GC-FTIR) contained bands at 3644, 1737, and 968 cm^{-1}, suggesting OH, carbonyl, and E-olefin; thus the MS and IR data seemed consistent with a hydroxy aldehyde. The ^{1}H-NMR spectrum (C_6D_6; **1** was rather unstable in $CDCl_3$)[5],however, showed no sign of a strongly deshielded signal representing an aldehyde CHO, but did contain what seemed to be a broadened singlet (∂ 5.25) within the complex olefinic region and too many moderately deshielded signals to be explained by a carboxylic acid or a hydroxy ketone. Also puzzling in the ^{1}H-NMR spectrum were several well defined multiplets that were too small (*ca.* 0.25 H each) to relate to the stronger signals or to be consistent with the apparent high purity of the sample as judged by GC. Although the sample was too small for ^{13}C or COSY experiments, some tentative connectivities could be deduced from decoupling, and it was possible to postulate a tetrahydrofuran-2-ol substituted in the 3- and 4-positions with 1-butenyl groups. This general structure would also explain the unequal sets of ^{1}H-NMR signals if the cyclic hemiacetal existed as an equilibrium mixture of the two anomers.

This conclusion was supported by synthesis of hydrogenation product (**4a**) (Scheme 1). Coupling of ethyl hexanoate with LDA followed by cupric bromide[6] produced the *meso* and *d,l*-succinates **2a** and **2b** which were separated by flash chromatography. Each succinate was reduced with LAH to the corresponding diol, **3a** and **3b**, and each diol was shaken with activated manganese dioxide in benzene. The reactions, monitored by GC, proceeded in two stages, with lactol (**4a** or **4b**) formation preceeding a slower conversion to lactones **5a** or **5b**. (For preparative purposes it was more convenient to oxidize the diols directly to the lactones **5a** or **5b** with pyridinium chlorochromate, then reduce to **4a** or **4b** with diisobutylaluminum hydride). The *cis*-3,4-dibutyllactol **4a**, from the *meso*-diester and diol, was found to be identical to the hydrogenation product of **1**[7,8].



Scheme 1. a. 1) LDA 2) $CuBr_2$, -70°. b. $LiAlH_4$ c. MnO_2 / C_6H_6
d. PCC / CH_2Cl_2 e. DIBAL-H / toluene f. H_2, Pt

The GC-FTIR band at 968 cm^{-1} strongly indicated a E-double bond, but under the conditions a Z-double bond might not have been detected by IR, and the olefinic region of the ^{1}H-NMR spectrum was too complex for definitive geometry assignments; thus whether **1** possessed two E-double bonds or one (E) and one (Z) was uncertain. This was resolved by preparing a sample of racemic **1** by a route analogous to (but much less practical than) the preparation of **4a**. Oxidative coupling of (E)-3-hexenoic acid (dianion preparation with LDA followed by 1/2 equivalent of I_2)[9] gave a complex mixture (olefin location and geometry can both be altered by the conditions) that was reduced without separation to a mixture of diols **6**. Flash chromatography on silica gel (30-40% ethyl acetate in hexanes) yielded a fraction containing the E,E-*meso*-diol **6a** and an isomer in which one double bond had evidently been inverted. Preparative RP-HPLC (250 x 20 mm ODS column eluted with 32% acetonitrile in water) was required to obtain pure **6a**; **6a**, by virtue of its symmetry, provided a simpler ^{1}H-NMR spectrum[10] from which the E,E-geometry assignment could confidently be made. Conversion of **6a** to racemic **1** (Scheme 2) was parallel to the **2a-4a** conversion above and confirmed the E,E geometry in **1**. The **1** thus prepared was identical by GC-MS, ^{1}H-NMR, and GC-retention time to the material isolated from *B. bibax*. GC Comparison of the synthetic and natural products on a chiral Cyclodex B™ column (J&W Scientific) clearly showed the insect-derived compound to be a single enantiomer; syntheses of both enantiomers have been initiated in another laboratory, and assignment of the absolute configuration of **1** will await the outcome of those experiments.



Scheme 2. g. 2 LDA then 1/2 I_2, -70° b. $LiAlH_4$ c. MnO_2 / C_6H6
d. PCC / CH_2Cl2 e. DIBAL-H

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2. James, D. G., and Warren, G. N. *J. Aust. Entomol. Soc.* **1989**, 28, 75-76.
3. Aldrich, J. A., Kochansky, J. P., and Abrams, C. B., *Environ. Entomol.* **1984**, 13, 1031-1036.
4. The gland extract also contained smaller amounts of linalool, nerolidol, and two isomers of farnesol, identified by comparison of their mass spectra to those in the data system library.
5. **1**, ^{1}H-NMR (300 MHz, C_6D_6, major anomer): δ 0.82-0.95 (6H, overlapping t's, CH_3, 1.8-2.0 (4H, m, CH_2), 2,79 (1 H, dd, J=7.2 & 7.5 Hz, H-3), 3.2-3.35 (1 H, m, H-4), 3.69 (1H, dd (apparent t), J=8 & 8 Hz, H-5a), 4.13 (1H, dd (apparent t), J=7.8 & 8.1 Hz, H-5b), 5.25 (1H, br. s, H-2), 5.2-5.52 (4H, m, olefinic). Mass spectrum , EI (m/z, %): 178 (3), 150 (8), 121 (55), 108(10), 107 (48), 105 (5), 98 (15), 95 (9), 94 (29), 93 (56), 91 (20), 83 (15), 82 (10), 81 (37), 80 (6), 79 (100), 55 (18), 69 (13), 67 (24), 65 (6), 57 (9), 55 (38), 53 (11).
6. Rathke, M. W., and Lindert, A. *J. Am. Chem. Soc.*, **1971**, 93, 4605-4606.
7. Initial assignments of *meso* vs. *d,l* -stereochemistry were made on the basis of gas chromatographic considerations (Sniegoski, P. J., *J Org. Chem.*, **1971**, 36, 2200-2201). Strong support for the assignments was realized when the solutions of the saturated lactols **4a** and **4b** used for recording ^{1}H-NMR spectra were reexamined by gas chromatography after several weeks. Spectra had been recorded in both $CDCl_3$ and C_6D_6, and the latter solutions contained unchanged samples. In contrast, in the $CDCl_3$, invariably contaminated with traces of DCl, considerable isomerization of the *cis*-3,4-dialkyl lactol **4a** to the *trans* -isomer **4b** had occurred (presumably via enolization of the open-chain hydroxy aldehyde in equilibrium with the cyclic hemiacetal) whereas little or no isomerization of **4b** to **4a** was detected. This assignment of *cis*-stereochemistry in **4a** translates to the *meso* assignment for its precursors **2a** and **3a**.
8. **4a** Mass spectrum, EI (m/z, %): 182, M-H_2O (0.3), 154, M-H_2O-CO (10), 125 (10), 112 (6), 111 (13), 98 (10), 97 (29), 85 (6), 84 (17), 83 (5), 82 (12), 81 (5), 71 (10), 70 (34), 69 (65), 67 (12), 57 (40), 56 (81), 55 (100). ^{1}H-NMR (C_6D_6) (major anomer) δ 0.78-0.93 (6H, m, CH_3), 1.0-1.4 (m, 12 H, CH_2), 2.14-2.27 (1H, m, H-3), 2.27-2.50 (1H, m, H-4), 3.59 (1H, m, H-5), 3.96-4.12 (1H, m, H-5), 5.63 (1H, d, J=2.1 Hz, H-2).
9. Belletire, J. L., Spletzer, E. G., and Pinhas, A. R. *Tetrahedron Lett.* **1984**, 25, 5969-5972.
10. **6a**. ^{1}H-NMR (C_6D_6) δ 0.85 (6 H, t, J=7.3 Hz), 1.86 (4H, m), 2.0-2.15 (2H, m), 3.29 (2H, dd, J=10.5 and 6.6), 3.60 (2H, dd, J=10.5 and 4.2), 5.14 (2H, dd, J=15.1 and 8.7 Hz), 5.41 (2H, d, J=15.3 Hz). Mass spectrum, EI (m/z, %): 168 (1), 150 (2), 121 (2), 107 (7), 98 (31), 95 (5), 93 (8), 91 (9), 83 (17), 82 (98), 81 (94), 79 (29), 77 (12), 70 (6), 69 (36), 67 (72), 57 (38), 55 (100), 53 (15).

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