A new synthesis of (Z, E)-undec-5-enoic acids, the sex pheromone of the varied carpet beetle *Anthrenus verbasci*

V. I. Bykov,^{a*} A. R. Goletiani,^b T. A. Butenko,^a and E. Sh. Finkelshtein^a

 ^aA. V. Topchiev Institute of Petrochemical Synthesis, Russian Academy of Sciences, 29 Leninsky prosp., 117912 Moscow, Russian Federation. Fax: +7 (095) 230 2224, E-mail: bykov@ips.ac.ru
^bIv. Dzhavakhishvili Tbilisi State University, 1 prosp. I Chavchavadze, 380028 Tbilisi, Georgia. Fax: +7 (883 2) 22 1103

A new synthesis of (Z,E)-undec-5-enoic acids with the natural isomer composition Z/E = 85: 15, the sex pheromone of the varied carpet beetle *Anthrenus verbasci* was developed based on co-metathesis of cycloocta-1,5-diene and ethylene.

Key words: olefin metathesis; pheromones; 1,5-cyclooctadiene, ethylene, undec-5-enoic acids, varied carpet beetle.

The varied carpet beetle *Anthrenus verbasci* is a highly dangerous pest damaging stuffed insects and animals in entomological and zoological museums.¹ The sex pheromone (SF) of this insect is a mixture of (*Z*, *E*)-undec-5-enoic acids **6** in the ratio Z/E = 85:15. Its synthetic analog with the stereoisomer ratio Z/E = 75:25 was obtained using the Wittig reaction.² Later, Harada and Mori attained a stereoisomer ratio, Z/E = 82:18, closer to the natural one, by performing the Wittig reaction with 2-hydroxytetrahydropyran.³

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Previously, we synthesized the (Z)-5- (Z)-7-monoenoic components⁴ of the lepidopterous SF and also (Z)-tricos-9-ene (the SF of the house fly *Musca domestica*) and (Z)-7,8-epoxy-2-methyloctadecane (the SF of gypsy moth *Limantrya dispar*).⁵ As the key reaction, we used the (Z)-stereoselective co-metathesis of cycloocta-1,5-diene (1) with ethylene (2) (Scheme 1). In the presence of MoCl₅/SiO₂—SnMe₄ under mild conditions^{5,6} and with incomplete conversion of 1 (23–87%), (Z)-deca-1,5,9-triene (92–68%) is formed as the major product, together with an *E*-stereoisomer impurity (0.3-1.2%).^{4,5}

In this study, in order to prepare the exact replica of the pheromone of varied carpet beetle *Anthrenus verbasci*, we used both stereoselective and nonstereoselective versions of the co-metathesis between 1 and 2.

The ratio of geometric isomers in deca-1,5,9-triene **3** formed upon metathesis with almost complete conversion of **1** was found to approach the thermodynamically equilibrium value (Z/E = 16:84). At a temperature of 20 °C and an ethylene pressure of 10 atm, the degree of conversion of **1** is 99.5% after 48 h and the ratio of the triene isomers Z/E = 21:79. At a lower degree of conversion (80%), this ratio is 99:1. Thus, using triene samples obtained with different degrees of conversions of **1**, it is possible to obtain a mixture with the composition Z/E = 85:15. Mixing of two triene samples with Z/E 99:1 and 21:79 (10 and 2.18 g, respectively) gave sample **3** with Z/E = 85:15, required for the synthesis of an exact replica of the natural pheromone (Scheme 1). It is note-



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worthy that this isomer ratio did not change throughout the subsequent steps of the synthesis.

Triene **3** was subjected to partial regioselective hydroboration-iodination⁷ using 9-BBN as the hydroborating agent. (Z,E)-Undeca-1,5-diene (**5**) was prepared by crosscoupling of (Z,E)-10-iododeca-1,5-diene (**4**) with lithium dimethylcuprate.⁸ Hydroboration—oxidation⁹ of diene **5** furnished (Z,E)-undec-5-en-1-ol (**6**) in a high yield; this was oxidized to aldehyde¹⁰ and then to (Z,E)-undec-5enoic acid (**7**). Note that the Moffatt oxidation,¹⁰ which we have used earlier to prepare unsaturated aldehydes, gives nearly quantitative product yields.¹¹ Further oxidation of the product with 30% hydrogen peroxide in the same reaction vessel for 48 h gave acid **7** in 50% yield.

Thus, we proposed a new, convenient synthesis of the sex pheromone of the varied carpet beetle *Anthrenus verbasci* through co-metathesis of readily available cyclo-octadiene and ethylene.

Experimental

The purity of solvents, starting compounds, and reaction products was checked and the reactions were monitored by GLC using a LKhM-8MD chromatograph with a flame ionization detector (a 50 m × 0.2 mm quartz capillary column) with the SKTFP or SE-30 stationary phases and H₂ as the carrier gas. The analyses were carried out with linear temperature programming (12 °C min⁻¹) from 35 °C to a temperature 100 °C below the boiling point of the compound. ¹H and ¹³C NMR spectra were recorded on a Bruker MSL-300 spectrometer in CDCl₃ relative to Me₄Si. IR spectra were measured on a Specord IR-75 instrument in thin films. Mass spectra (EI) were run on a Finigan MAT 95 XL mass spectrometer at 70 eV. The stereoisomer composition was determined by GLC and ¹H NMR and ¹³C NMR spectroscopy. All reactions were carried out under high-purity argon; the solvents were distilled from LiAlH₄ under argon.

(Z,E)-Deca-1,5,9-triene (3). The catalyst⁶ MoCl₅/SiO₂ (50 g, 12.5 mmol of Mo) and cycloocta-1,5-diene 1 (Fluka, 135 g, 1.25 mol) were charged into a steel autoclave equipped with a stirrer, a manometer, and a sampling device, and the pressure of ethylene 2 was brought to 10 atm. A solution of Me₄Sn (Fluka, 5.34 g, 30 mmol) in toluene (93 mL) saturated with ethylene at 12 atm was added from a special vessel. After 48 h (20 °C), the reaction mixture was separated from the catalyst and fractionated to give 46 g of triene 3 (Z/E = 21:79), yield 27%, b.p. 170 °C (760 Torr), n_D^{20} 1.4487. Purity 99.0%. MS, m/z (I_{rel} (%)): 136 [M]⁺ (3), 41 [M - 95]⁺ (100). ¹H NMR (CDCl₃), δ: 2.15 (m, 8 H, CH₂-CH=); 4.90 (m, 4 H, $CH_2=CH-$; 5.39 (t, 0.42 H, Z-CH=CH-, J = 6.0 Hz); 5.42 (m, 1.58 H, *E*-C<u>H</u>=C<u>H</u>-); 5.80 (m, 2 H, -C<u>H</u>=CH₂). ¹³C NMR (CDCl₃), δ : 27.0 (<u>C</u>H₂-CH=CH); 34.0 $(CH_2=CH-\underline{C}H_2)$; 114.8 ($\underline{C}H_2=CH$); 129.6 and 130.2 $(\underline{C}H=\underline{C}H);$ 138.5 $(CH_2=\underline{C}H).$ IR, $v/cm^{-1}:$ 730 (Z-H-C=C-H); 950 (E-H-C=C-H); 1640 (C=C).

(*Z*,*E*)-10-Iododeca-1,5-diene (4). Triene 3, Z/E = 85:15 (12.18 g, 89.6 mmol) was added at 6 °C to a suspension of dimeric 9-BBN (10.9 g, 44.7 mmol) in THF (40 mL), and the

mixture was stirred until the precipitate dissolved. Then the mixture was allowed to warm to room temperature and stirred for 1 h. The mixture was then cooled to -20 °C, solutions of MeONa (4.8 g, 89.6 mmol) in MeOH (50 mL) and I₂ (22.7 g, 89.6 mmol) in THF (80 mL) were successively added dropwise. After removal of the solvents, the residue was extracted with hexane and the extract was washed with water and dried with MgSO₄. The removal of hexane and distillation *in vacuo* gave 8.3 g (35%) (*E*,*Z*-10-iododeca-1,5-diene, b.p. 125 °C (15 Torr). ¹H NMR (CDCl₃), δ : 1.30–2.20 (m, 10 H, CH₂); 3.18 (t, 2 H, CH₂–I, *J* = 7.4 Hz); 4.9 (m, 2 H, CH₂=CH–); 5.40 (t, 1.7 H, *Z*-CH=CH–, *J* = 6.0 Hz); 5.42 (m, 0.3 H, *E*-CH=CH–); 5.80 (m, 1 H, –CH=CH₂).

(Z,E)-Undeca-1,5-diene (5). A suspension of CuBr (5.2 g, 36 mmol) and LiCl (3.12 g, 72 mmol) in THF (120 mL) was stirred at ~20 °C until a homogeneous solution formed. This solution was cooled to -70 °C, and methyllithium (1.6 g, 72 mmol) was added. After stirring for 1 h, (Z,E)-10-iododeca-1,5-diene (4) (7.9 g, 30 mmol) was added. The mixture was heated to ~20 °C, stirred for 2 h, and hydrolyzed with 30 mL of 5% aqueous HCl. The organic layer was separated, neutralized with K₂CO₃, washed with water, and dried with MgSO₄. The removal of the solvents and vacuum distillation gave 3.04 g (67%) (Z,E)-undeca-1,5-diene (5), b.p. 188 °C (760 Torr), $n_{\rm D}^{20}$ 1.4383, impurity content ~2%. MS, m/z ($I_{\rm rel}$ (%)): 152 [M] (2), 124 [M - 28] (4), 110 [M - 42] (12), 96 (14), 81 (44), 67 (64), 55 (78), 41 (100). ¹H NMR (CDCl₃), δ: 0.85 (m, 3 H, CH₃-CH₂); 1.29 (m, 6 H, CH₂-CH₂); 2.15 (m, 6 H, CH_2 -CH=); 4.90 (m, 2 H, CH_2 =CH-); 5.39 (t, 1.7 H, Z-CH=CH-, J = 6.0 Hz); 5.41 (m, 0.3 H, E-CH=CH); 5.80 $(m, 1 H, CH = CH_2).$

(Z,E)-Undec-5-en-1-ol (6). Diene 4 (3.04 g, 20 mmol) was added at 12 °C to a stirred suspension of dimeric 9-BBN (2.44 g, 10 mmol) in anhydrous THF (20 mL). The mixture was stirred at 12 °C for 1 h and at 25 °C for 1 h and cooled to 6 °C. Methanol (30 mL), 3 M NaOH (5 mL), and 30% H₂O₂ (20 mL) were added at such a rate that the temperature did not exceed 20 °C. The volatile components were distilled in vacuo and the residue was extracted with hexane. The extract was washed with water, dried with MgSO₄, concentrated, and distilled to give 3.1 g (91%) of (Z, E)-undec-5-en-1-ol, b.p. 108 °C (12 Torr), $n_{\rm D}^{20}$ 1.4526, impurity content ~1%. ¹H NMR (CDCl₃), δ : 0.90 (br.s, 3 H, CH_3 -CH₂); 1.31 (br.s, 8 H, CH_2 -CH₂); 1.51 (m, 2 H, $-CH_2-CH_2-O$; 1.99 (br.s, 4 H, ($CH_2-CH=CH$); 2.24 (br.s, OH); 3.52 (m, 2 H, $-CH_2-O$); 5.29 (br.s, 2 H, -CH=CH-). ¹³C NMR (CDCl₃), δ: 13.9 (<u>C</u>H₃-CH₂); 22.9, 26.6, 29.3, 29.9, 30.3, 31.8, 32.6 (7 CH₂); 62.4 (CH₂-O); 129.9 (Z-CH=CH); 130.1 (E-CH=CH).

(*Z*,*E*)-Undec-5-enoic acid (7). Pyridinium trifluoroacetate (0.5 g) in 10 mL of DMSO was added to a mixture of (*Z*,*E*)-undec-5-en-1-ol (6) (3.1 g, 18.2 mmol), DMSO (1.6 g, 20.5 mmol), and DCC (4.2 g, 20.6 mmol) in toluene (30 mL), and the mixture was stirred for 4 h. A 30% solution of H₂O₂ (40 mL) was added, the reaction mixture was stirred at room temperature for 48 h, and 40 mL of H₂O was added. The organic layer was separated and the aqueous layer was extracted with hexane. Drying (MgSO₄), removal of the solvents, and distillation *in vacuo* gave 1.9 g (50%) of (*Z*,*E*)-undec-5-enoic acid (7), b.p. 138 °C (2 Torr), n_D^{20} 1.4502, impurity content about 5%. ¹H NMR (CDCl₃), δ : 0.89 (m, 3 H, CH₃-CH₂); 1.34 (m, 6 H,

 CH_2-CH_2); 1.82–2.11 (m, 6 H, $-CH_2-$); 2.31 (t, 2 H, $CH_2-COOH, J = 7.0 \text{ Hz}$); 5.29 (br.s, 2 H, -CH=CH-); 11.1 (br.s, 1 H, O<u>H</u>).

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