INSECT PHEROMONES AND THEIR ANALOGUES

XXX. SYNTHESIS OF OCTA-2E,6E-DIENE-1,8-DIOL DIISOVALERATE – THE SEX PHEROMONE OF Agriotes tauricus

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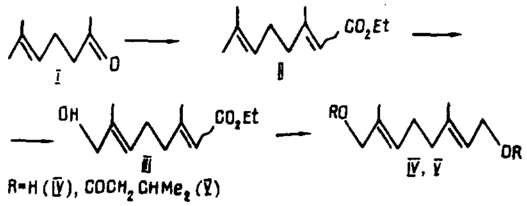
The synthesis has been effected of octa-2E,6E-diene-1,8-diol diisovalerate – the sex pheromone of the Crimean click beetle Agriotes tauricus – by the carboxymethylenation of the readily available 6-methylhept-5-en-2-one, the allyl oxidation of a terminal methyl group, reduction of the ester fraction, and interaction of the diol so obtained with isovaleryl chloride. The required pheromone can also be obtained from available cyclic oligomers of isoprene.

Octa-2E,6E-diene-1,8-diol diisovalerate, which has been identified as the sex pheromone of the Crimean clock beetle Agriotes tauricus [1], has previously been synthesized by the allyl oxidation of geraniol isovalerate with a yield of 30%, the amount of desired pheromone in the product being 73% [2].

We have effected the synthesis of this pheromone (V) from 6-methylhept-5-en-2-one (I) or the cyclodimers of isoprene (VI) and (VII). The carboxymethylation of ketone (I) by the action of ethyl trimethylsilylacetate led with a yield of 87% to the α,β-unsaturated ester (II) in the form of a mixture of E- and Z-isomers in a ratio of 60:40 (according to GLC and ^{1}H NMR). The allyl oxidation of the ester (II) with a mixture of tert-butyl hydroperoxide and selenium dioxide under conditions differing from those described in [3] (change of solvent, lowering of the reaction temperature) led with a yield of 65% to the alcohol (III) – the product of the selective oxidation of the transoid terminal methyl group in compound (II).

Reduction of the dienic ester (III) with the aid of lithium tert-butoxyhydroaluminate took place smoothly with the formation of the diol (IV), which was converted into the final product (V) by treatment with isovaleryl chloride in the presence of triethylamine. According to GLC, the ratio of (V) and its 2E,6E- and 2Z,6E-isomer was 88:12, i.e., there had been an enrichment of the final product with the (E)-Δ^2 isomer – obviously at thestage of the reduction of the ester (III) with the complex lithium hydride reagent. The desired 2E,6E-isomer (V) was isolated with the aid of HPLC. The yield of the pheromone (V) calculated on the initial methylheptenone was 37%.



It is possible to arrive at the dienic ester (II) from the readily available products of the cyclooligomerization of isoprene (VI) and (VII) [4], the exhaustive ozonolysis of which gives 1,1-dimethoxypentan-4-one (VIII) [5]. Carboxymethylenation of the latter, acid hydrolysis of the acetal (IX) and Wittig olefination of the aldehyde (X) led to the ester (II) with a yield of 58% calculated on the (VIII).

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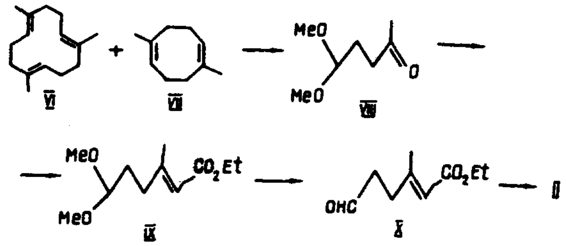

EXPERIMENTAL

IR spectra of the substances were taken on a UR-20 instrument in a thin layer, and PMR spectra were obtained on a Tesla BS-576 (100 MHz) instrument in $CDCl_3$ solution relative to TMS. Analysis by the GLC method was conducted on a Chrom-5 chromatograph with a column 1200-mm long, SE-30 as the stationary phase, and helium as the carrier gas at a working temperature of 50-300°C (12°C/min). Preparative separation was achieved on a Du Pont Zorbax Sil instrument (column 21.5 × 2500 mm).

Ethyl 3,7-Dimethylocta-2E/2Z-dienoate (II). a. To a solution of 6.82 ml of freshly redistilled diisopropylamine in 120 ml of absolute THF (−20°C, Ar) was added, dropwise, 12.4 ml of a 4.0 M solution of n-butyllithium in hexane, the mixture was kept at −20°C for 0.5 h, and it was then cooled to −70°C and a solution of 8.21 g of ethyl trimethylsilylacetate in 15 ml of absolute THF was added. The resulting mixture was kept at −70°C for 40 min, and a solution of 5 g of the methylheptenone (I) in 15 ml of absolute THF was added; the reaction mixture was stirred at −70°C for 1 h and then the temperature was gradually raised to 20°C and was kept there for 1 h, after which 80 ml of saturated NH_4Cl solution was added. The organic layer was separated off, and the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with saturated NaCl and were dried with $MgSO_4$.

Evaporation of the solvent yielded 6.8 g (78%) of compound (II), bp 68-70°C (1 mm Hg), n_D^{20} 1.4799, IR spectrum (ν, cm^{-1}): 870 m, 1075 s, 1160 s, 1380 m, 1650 s, 1710 s. PMR spectrum (100 MHz, $CDCl_3$): 1.28 (3H, t, CH_3, J = 7 Hz), 1.64 and 1.7 (6H, s, CH_3-7), 1.75 (Z) and 2.08 (E) (3H, d, CH_3-3, J = 1.5 Hz), 2.5-2.76 (4H, m, H-4, H-5), 4.15 (2H, q, CH_2O, J = 7 Hz), 5.1 (1H, t, H-6, J = 5 Hz), 5.67 (1H, s, H-2). Mass spectrum, m/z (%): 196 [(M^+, 20)], 168 [$(M - CO)^+$, 7.14], 151 [$(M - OC_2H_5)^+$, 16.29], 137(100), 123 [$(M - CO_2C_2H_5)$, 8.5], 111(57), 95(90), 69(15.11), 56(31). Found, %: C 73.21; H 10.14; C=C 24.31. $C_{12}H_{20}O_2$. Calculated, %: C 73.43; H 10.27; C=C 24.45.

b. A mixture of 2.25 g of the acetal (IX), 105 ml of acetone, 2.5 ml of water, and 0.68 g of pyridinium tosylate was boiled for 2 h. The acetone was distilled off in vacuum, the residue was dissolved in diethyl ether, and the solution was washed successively with $NaHCO_3$, NaCl, 1 N HCl, and NaCl solutions, and was dried with $MgSO_4$ and evaporated. This gave 1.33 g of ethyl 3-methyl-6-oxohex-2E/Z-enoate (X) [IR spectrum (ν_{max}^{KBr}, cm^{-1}): 875, 1655 (C=C); 1150, 1720, 2725 (CHO, $CO_2C_2H_5$). PMR spectrum (100 MHz, $CDCl_3$): 1.27 (3H, t, CH_3, J = 7 Hz), 1.82 (Z) and 2.2 (E) (3H, s, CH_3-3), 1.91 (2H, H-5), 4.12 (2H, q, CH_2O, J = 7 Hz), 5.76 (1H, s, H-2), 9.8 (1H, s, CHO)].

A suspension of 2.25 g of isopropyltriphenylphosphonium bromide in 22 ml of absolute THF was treated dropwise (Ar, −78°C) with 5.1 ml of 1.05 M solution of butyllithium in hexane, the mixture was kept until the dark red coloration of the ylide had become established (1 h), and 1.1 g of compound (X) in 5 ml of absolute THF was added. The resulting mixture was stirred at −78°C for another 1 h and was left to stand for 12 h. Then 300 ml of pentane was added to it and it was filtered through a layer of silica gel and evaporated. This gave 0.91 g (72%) of compound (II), identical with that obtained in experiment a.

Octa-2E/6E-diene-1,8-diol Diisovalerate (V). To a stirred suspension of 0.8 g (7.2 mmoles) of SeO_2 in 1 ml of methylene chloride was added 11.8 ml of a solution of tert-butyl hydroperoxide in methylene chloride (2.6 mmoles of t-BuOOH in 1 ml of solution) and stirring was continued for another 1 h. The reaction mixture was cooled to 0°C, and a solution of 1.87 g (9 mmoles) of compound (II) in 0.5 ml of methylene chloride was added in drops. Stirring at 0°C was continued for 3 h, and then 30 ml of diethyl ether was added. The organic layer was separated off and washed with saturated NaCl solution and dried with $MgSO_4$. The solvent was evaporated off, and the residue was chromatographed on silica gel [with hexane—

ether (30:70) as eluent]. This gave 2.1 g (65%) of ethyl 8-hydroxy-3,7-dimethylocta-2E/-Z,6-dienoate (III) [IR spectrum (ν_{max}^{KBr}, cm^{-1}): 1050, 3400 (OH); 1260, 1720 (CO_2Et); 1655 (C=C)].

With stirring, a suspension of lithium tert-butylhydroaluminate (obtained from 0.5 g of $LiAlH_4$ and 0.13 ml of tert-butyl alcohol in 25 ml of absolute diethyl ether) was added dropwise (3.5 h, 0°C, Ar) to a solution of 2.0 g of the hydroxy ester (III) in 20 ml of absolute diethyl ether, and then 26 ml of water was added and the resulting precipitate was filtered off and washed on the filter with water and then with ether.

The combined etheral solution was washed with saturated NaCl solution, dried with $MgSO_4$, and evaporated. This gave 1.24 g (77.5%) of the 2,6-dimethylocta-2E/Z,6-dienediol (IV) [IR spectrum (ν_{max}^{KBr}, cm^{-1}): 1030, 2380 (OH). PMR spectrum (100 MHz, $CDCl_3$): 1.67 (6H, s, CH_3), 3.98 (2H, s, H-8), 4.14 (2H, d, H-1, J = 6.5 Hz)].

At 25°C, 2.68 ml of isovaleryl chloride was added dropwise to a stirred solution of 1.2 g of the diol (IV) and 1.84 ml of triethylamine in 40 ml of absolute THF, and the reaction mixture was stirred for another 2 h and was left overnight. Then it was diluted with 40 ml of diethyl ether and stirred for 30 min, and the resulting precipitate was filtered off and was washed on the filter with 50 ml of diethyl ether. The combined filtrates were washed successively with saturated solutions of $NaHCO_3$ and NaCl, dried with $MgSO_4$, and evaporated. The residue (2.1 g) was chromatographed on Al_2O_3 [eluent: hexane–ether (60:40)] to give 2.03 g (85%) of the diisovalerate, with, according to GLC, a ratio of the 2E,6E- and 2Z,6E-isomers of 88:12. Using HPLC, 1.62 g of the 2E,6E-isomer (V) was isolated, with n_D^{20} 1.4714 (compare [2]).

Ethyl 6,6-Dimethoxy-3-methylhex-2E/Z-enoate (IX). Under the conditions described for compound (II) in experiment a, 3.15 g of the keto acetal (VIII) and 4.38 g of ethyl trimethylsilylacetate gave 4.46 g (95%) of the ethyl ester (IX), bp 90°C (1 mm), n_D^{20} 1.4540. IR spectrum (ν_{max}^{KBr}, cm^{-1}): 860, 1650 (C=C); 1080 (OCH_3); 1250, 1750 (CO_2Et). PMR spectrum (100 MHz, $CDCl_3$): 1.25 (3H, t, CH_3, J = 7 Hz), 1.87 (Z) and 2.15 (E) (3H, s, CH_3-3), 2.6 (2H, m, CH_2-3), 3.47 (6H, s, OCH_3), 4.13 (2H, q, CH_2O, J = 7 Hz), 5.65 (1H, s, H-2). Mass spectrum, m/z (T): 216 [(M^+, 0.06)], 215(1.9), 185 [$(M - OCH_3)^+$, 5.3], 187(7), 152 [$(M - 2CH_3OH)^+$, 17], 139(14), 111(19), 79(63), 61(100). Found, %: C 61.09; H 9.31; C=C 11.06. $C_{11}H_{20}O_4$. Calculated, %: C 61.11; H 9.25; C=C 11.11.

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