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INSECT PHEROMONES AND THEIR ANALOGS.

L. A HIGHLY SPECIFIC SYNTHESIS OF (Z)-DISPARLURE — THE RACEMIC ANALOG OF THE SEX PHEROMONE OF *Porthetria dispar*

V. N. Odinokov, R. I. Galeeva, L. P. Botsman, and E. V. Gladysheva

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*A highly selective synthesis of 2-methyl-*cis*-7,8-epoxyoctadecane — the racemic analog of the sex pheromone of the gypsy moth* Porthetria dispar *L. — (Z)-disparlure — has been developed that is based on the functionally differentiated partial ozonization of cycloocta-1Z,5Z-diene.*

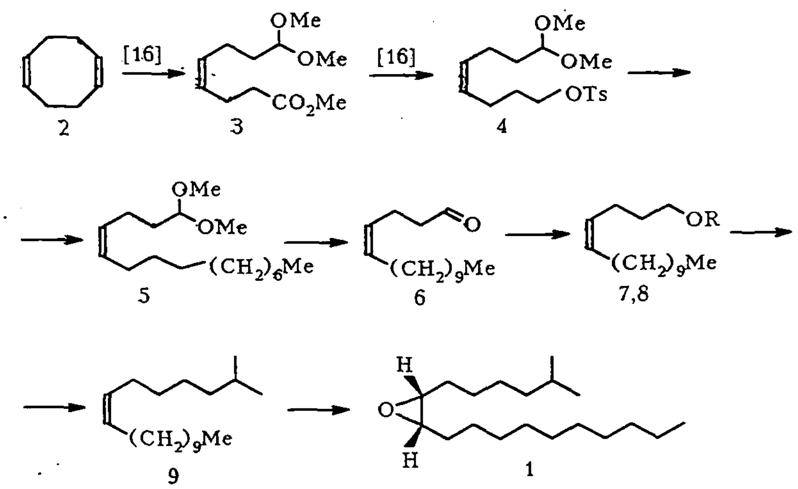
A whole series of syntheses is known [1-10] for the biologically active racemic analog of (Z)-disparlure — the sex pheromone of the gypsy moth *Porthetria dispar* L., which also exhibits attractant activity in relation to the black arches moth *Lymantria monarcha* Z. [11] and has the structure of 2-methyl-*cis*-7,8-epoxyoctadecane (1). We have reported a synthesis of the pheromone (1) based on the selective (at one multiple bond) ozonolysis of cyclooctadeca-1Z,5Z-diene (2) and a two-stage conversion of the peroxide product into oct-4Z-ene 1,8-dibromide and its subsequent selective coupling with heptyl- and isobutylmagnesium bromides [12, 13]. The yield of pheromone (1) in the synthesis described amounted to 25%, calculated on the initial butadiene dimer. The construction of the required carbon skeleton of the desired compound can be achieved with a higher selectivity from the product of the functionally differentiated partial ozonolysis of diene (2) when the peroxide product is subjected to hydrolytic cleavage to derivatives of a ω-oxocarboxylic acid [14]. We have synthesized a number of pheromones with an acetogenin structure in this way [15-21].

Using this approach, we have performed the synthesis of pheromone (1) with a substantially higher overall yield [about 60%, calculated on the initial butadiene dimer (2)] than in the earlier synthesis [13]. This is explained by the highly selective transformations to the final functional groups in the ozonolysis product — methyl 8,8-dimethoxyoct-4Z-enoate (3), the formation of which and its conversion into 1,1-dimethoxy-8-tosyloxyoct-4Z-ene (4) we have described previously [16]. The coupling of the tosylate (4) with heptylmagnesium bromide in the presence of Li_2CuCl_4 takes place smoothly with a high yield of the required product — 1,1-dimethoxypentadec-4Z-ene (5).

To complete the construction of the desired carbon skeleton we eliminated the acetal protection in (5) and converted the resulting aldehyde (6) by treatment with i-Bu_2AlH into pentadec-4Z-en-1-ol (7), which, in the form of the tosylate (8) was coupled with isobutylmagnesium bromide, giving, under mild conditions, a high yield of 2-methyloctadec-7-ene exclusively with the (Z)-configuration, confirmation of which was given by the positions of the signals of the vinyl and allyl carbon atoms in the ^{13}C NMR spectrum of the (Z)-alkene (9) (δ 129.2 and 27.25 ppm, respectively, while for its (E)- isomer the corresponding signals are found in the regions of δ 132.5 and 32.69 ppm [1]).

Signals in the regions of δ 55.97 ppm (C^7 and C^8) and 28.03 ppm (C^6 and C^9) for the epoxide (1) obtained by the interaction of the Z-alkene (9) with p-methoxycarbonylperbenzoic acid also unambiguously confirmed its assignment to the (Z)-series: the corresponding carbon atoms in the (E)- isomer of epoxide (9) resonate in the δ 57.55 and 32.20 ppm regions [1]. The stereochemical individuality of the synthesized pheromone (1) was confirmed by GLC in a capillary column.

Institute of Petroleum and Catalysis, Academy of Sciences of the Republic of Bashkortostan, 450075, Ufa, Prospekt Oktyabrya, 141. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 901-904, November-December, 1995. Original article submitted February 21, 1995.



R=H(7), Ts(8)

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer in a thin layer or in Nujol. PMR spectra were obtained on a Tesla BS-497 spectrometer (working frequency 100 MHz) with TMS as internal standard and $CDCl_3$ as solvent. ^{13}C NMR spectra were recorded on a JEOL-90Q instrument in the form 20% solutions in $CDCl_3$ with broad-band proton suppression in the monoresonance regime and partial retention of the Overhauser effect, using TMS as internal standard. GLC was conducted on a Chrom-5 instrument with 1,2,3-tris(β-cyanoethoxy)propane as the stationary phase in a column with dimensions of 0.25 mm × 50 m at a column temperature of 146°C, the carrier gas being helium. The elementary analyses of the compounds synthesized corresponded to the calculated figures.

1,1-Dimethoxypentadec-4Z-ene (5). To a solution of the Grignard reagent obtained from 4.82 g (0.2 g-atom) of magnesium turnings and 29.6 g (0.165 mole) of *n*-heptyl bromide in 170 ml of absolute THF (with iodine as initiator) was added (argon, −78°C) a mixture of 22.9 g (0.067 mole) of the tosylate (4) (obtained as in [6]), 80 ml of THF and 11 ml of a 0.5 M solution of Li_2CuCl_4 prepared by dissolving 4.25 g of LiCl and 6.70 g of $CuCl_2$ in 100 ml of ansolute THF. The reaction mixture was stirred for 2 h and was left at room temperature for 15 h. Then 200 ml of diethyl ether was added to it, and it was washed with saturated NH_4Cl solution and then with 10% $NaHCO_3$ solution, and was dried with Na_2SO_4 and evaporated. The residue was chromatographed (neutral Al_2O_3; pentane−ether (10:1)). This gave 15.3 g (85%) of the acetate (5), n_D^{20} 1.4629. IR spectrum (ν, cm^{-1}): 730 (C=C−H), 1070 (C−O), 1370, 1390, (CH_3). PMR spectrum (δ, ppm): 0.81 (t, 3H, J = 7 Hz, H-15), 1.2 (br.s, 18H, CH_2), 1.8-2.1 (m, 4H, H-3, H-6), 1.13 (s, 6H, OCH_3), 4.2 (t, 1H, J = 6 Hz, H-1), 5.23 (m, 2H, H-4, H-5).

Pentadec-4Z-enal (6). A mixture of 14.5 g (0.05 mole) of the acetal (5), 150 ml of acetone, and 30 ml of 5% HCl was stirred at room temperature for 6 h, and, after the addition of 20 ml of diethyl ether, it was washed with 10% $NaHCO_3$ solution and dried with Na_2SO_4. After evaporation, 11.8 g (98%) of the aldehyde (6) was obtained, with n_D^{20} 1.4620. IR spectrum (ν, cm^{-1}): 735 (C=C−H), 1730 (C=O), 2730 (O=C−H). PMR spectrum (δ, ppm): 0.80-1.06 (m, 3H, H-15), 1.2 (br.s, 16H, CH_2), 1.80-2.08 (m, 4H, H-3, H-6), 2.35 (br.s, 2H, H-2), 5.30 (m, 2H, H-4, H-5), 9.58 (br.s, 1H, H-1).

Pentadec-4Z-en-1-ol (7). A mixture of 26.5 ml (0.117 mole) of a 73% toluene solution of diisobutylaluminum hydride and 25 ml of diethyl ether was added dropwise (argon, −10°C) to a solution of 11.5 g (0.051 mole) of the aldehyde (6) in 250 ml of absolute diethyl ether; the mixture was stirred at −10°C for 1.5 h and then 30 ml of water was slowly added and it was allowed to warm to room temperature, stirred for 3 h, and left for 15 h. The reaction mixture was filtered, the residue was washed with ether (4 × 50 ml), and the combined filtrates were dried with Na_2SO_4. Evaporation yielded 10.9 g (95%) of the alcohol (7), n_D^{20} 1.4473. IR spectrum (ν, cm^{-1}): 735 (C=C−H), 1065 (C−O), 3350 (OH). PMR spectrum (δ, ppm): 0.8 (t, J = 7 Hz, 3H, H-15), 1.18 (br.s, 18H, CH_2), 1.8-2.13 (m, 4H, H-3−H-6), 3.48 (t, J = 6 Hz, 2H, H-1), 3.85 (s, 1H, OH), 5.3 (m, 2H, H-4, H-5).

1-Tosyloxypentadec-4Z-ene (8). At −10°C, 9.3 g (0.049 mole) of TsCl was gradually added to a solution of 10.0 g (0.044 mole) of the alcohol (7) in 14.2 ml of absolute pyridine, and the reaction mixture was left for 15 h at the same temperature. Then it was poured into ice water and extracted with diethyl ether (4 × 100 ml). The etheral solution was washed with 5% HCl and then with 10% $NaHCO_3$ solution and was dried with Na_2SO_4. Evaporation gave 16.6 g (99%) of the tosylate (8). IR spectrum (ν, cm^{-1}): 750, 820, 845, 935, 980 ($C=C-H$, $C_{Ar}-H$), 1105, 1180, 1195 ($C-O$, CH_3), 1600 (Ar). PMR spectrum (δ, ppm): 0.78 (t, J = 7 Hz, 3H, H-15), 1.14 (br.s, 18H, CH_2), 1.8-2.1 (m, 4H, H-3, H-6), 2.32 (s, 3H, CH_3-Ar), 3.89 (t, J = 6 Hz, 2H, H-1), 5.25 (m, 2H, H-4, H-5), 7.23 (d, J = 8 Hz, 2H, H−Ar), 7.67 (d, J = 8 Hz, 2H, H−Ar).

2-Methyloctadec-7Z-ene (9). We followed the procedure described above in the synthesis of compound (5): from 15.0 g (0.039 mole) of the tosylate (8) in 50 ml of absolute THF, a solution of the Grignard reagent obtained from 13.1 g (0.096 mole) of isobutyl bromide and 2.8 g (0.12 g-atom) of magnesium turnings in 100 ml of absolute THF), and 6.4 ml of a 0.5 M solution of Li_2CuCl_4 in THF we obtained 9.8 g (95%) of the alkene (9), n_D^{20} 1.4429. Its IR and ^1H and ^{13}C NMR spectra were identical with those given in [1].

(Z)-2-Methyl-7,8-epoxyoctadecane (1) was obtained with a yield of 98% by the epoxidation of the (Z)-alkene (9) as described previously; its spectral characteristics coincided completely with those given in [1].

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