INSECT PHEROMONES AND THEIR ANALOGUES.
XVI. PRACTICAL SYNTHESIS OF HEXADEC-9Z-ENAL — A COMPONENT OF THE SEX PHEROMONE OF THE COTTON BOLLWORM *Heliothis armigera*

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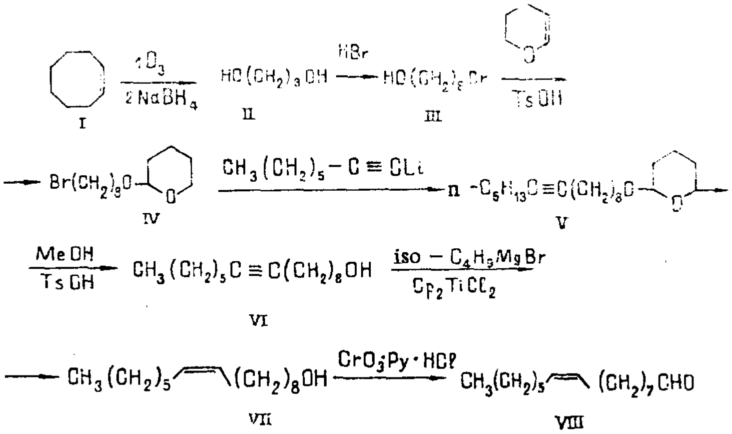
A synthesis of hexadec-9Z-enal — a component of the sex pheromone of the cotton bollworm *Heliothis armigera* (Hübner) — based on cyclooctene (I) is proposed. Through a solution of 22 g of (I), 250 ml of cyclohexane, and 40 ml of MeOH is passed (at 5°C) 0.2 M O_3/O_2, the solution is decanted off, and the precipitated ozonide is dissolved in 200 ml of MeOH and is reduced with 19 g of $NaBH_4$ (40°C) with the isolation, after the usual working up, of 23.4 g of octane-1,8-diol (II). From 0.5 mole of (II) and 0.6 mole of 45% HBr 8-bromooctan-1-ol (III) is obtained and this is converted into 1-(2-(THPL)oxy)-8-bromooctane (IV). The condensation of (IV) with oct-1-yne (Ar, $LiNH_2$, HMPTA, 10°C, 1 h, and then 55°C, 10 h) leads to 1-(2-THPL-oxy)hexadec-9-yne (V) the hydrolysis of which (MeOH, H_2O, p-TsOH, 20°C for 20 h) yields hexadec-9-yn-ol (VI). The reduction of (VI) (Et_2O, iso-BuMgBr, Cp_2TiCl_2, 0°C, 15 min, then 20°C, 1 h) yieldshexadec-9Z-en-1-ol (VII). The oxidation of (VII) ($PyHCrO_3^+$ Cl^-, CH_2Cl_2, 20°C, 2 h) gives hexadec-9Z-enal (VIII). Characteristics of the compounds (yield (%), $n_D^{20(25)}$: (II) — 80, mp 61-62°C; (III) — 75, 1.4807; (IV) — 99, —; (V) — 52, 1,4650; (VI) — 85, 1.4657; (VII) — 99, 1.4650; (VIII) — 98, 1.4600. Characteristics of the IR and PMR spectra of compounds (V-VII) are given.

The sex pheromone of the cotton bollworm *Heliothis armigera* Hübner contains hexadec-11Z- and -9Z-enals [1]. While a fairly large number of studies has been devoted to the synthesis of the first of the aldehydes mentioned [2, 3], there is only one communication on the synthesis of the second (via the carboxycupration of acetylene [4]). We have developed a convenient synthesis of hexadec-9Z-enal (VIII) from the readily available cyclooctene (I). The ozonolysis of this cyclene in cyclohexanol and methanol solution followed by sodium tetrahydroborate reduction gave a high yield of octane-1,8-diol (II), which was converted into 8-bromooctan-1-ol (III) and the latter into its tetrahydropyranyl ether (THPE) (IV). The coupling of the bromide (IV) with lithium oct-1-ynylide in hemametapol (HMPT) led to the THPE



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of hexadec-9-yn-1-ol (V), the hydrolysis of which in an acid medium gave the corresponding alcohol (VI). The conversion of the alkynol (VI) into hexadec-9Z-en-1ol (VII) was effected by reductive Grignardization with the aid of isobutylmagnesium bromide in the presence of dicyclopentadienyltitanium dichloride (Cp_2TiCl_2). The oxidation of the alk-Z-enol (VII) with pyridinium chlorochromate led to the desired alk-Z-enol (VIII). According to the results of analysis by capillary GLC, the pheromone (VIII) contained not less than 95% of the (Z)-isomer. The overall yield of compound (VIII) in the seven-stage synthesis amounted to 25.6%.

EXPERIMENTAL

IR spectra of thin layers of the substances were taken on a UR-20 spectrometer. The PMR spectra of solutions of the substance in $CDCl_3$ were measured relative to TMS on a Tesla BS-497 (100 MHz) instrument. GLC analysis was performed on a Chrom-4 instrument with the stationary phase SE-30 (15%) on Chromaton N-AW-DMCS (0.16-0.20 mm) at working temperatures of 50-300°C, using helium as the carrier gas. The stereochemical individuality of the final products was analyzed on a Chrom-5 instrument with 1,2,3-(β-cyanoethoxy)propane as stationary phase in a 0.25 mm × 50 m stainless-steel capillary column at a temperature of 170°C with helium as the carrier gas.

Octane-1,8-diol (II). At 5°C, a mixture of ozone and oxygen was passed at the rate of 25 liters/h through a solution of 22 g (0.2 mole) of cyclooctene (I) in 250 ml of cyclohexane containing 40 ml of methanol until 0.2 mole of ozone had been absorbed. The reaction mixture was purged with nitrogen, the solvent was decanted off, and the residual peroxide product of ozonolysis was dissolved in 200 ml of methanol; the solution was cooled to 15°C, and 19 g of $NaBH_4$ was added in portions of 15-20°C. The reaction mixture was stirred for 4 h and was allowed to stand for 15 h. Then with stirring, a mixture of 60 ml of water and 6 ml of CH_3COOH was gradually added to it and after 3 hours' stirring the solid matter was filtered off, the filtrate was evaporated, 200 ml of Et_2O was added to the residue, and the precipitate was filtered off and was washed with 500 ml of Et_2O. The ethereal solutions were combined and washed (3 × 50 ml) with saturated NaCl solution, dried with $MgSO_4$, and evaporated. This gave 23.4 g (80%) of the diol (II), mp 61-62°C.

8-Bromooctan-1-ol (III). A mixture of 73 g (0.5 mole) of the diol (II) and 100 g (0.6 mole) of 48% HBr was heated, and the mixture was worked up as described in [5]. This gave 78.8 g (75%) of compound (III) n_D^{20} 1.4807 (see [5]).

1-Bromo-8-(tetrahydropyran-2-yloxy)octane (IV). As described in [5], 36.5 g of the bromohydrin (III), 0.7 g of p-toluenesulfonic acid, and 27 ml of dry 2,3-dihydropyran gave 50 g (99%) of compound (IV) with R_f (SG, n-hexane—ether (8:1)) 0.36. The PMR spectrum was identical with that given in the literature [6].

1-(Tetrahydropyran-2-yloxy)hexadec-9-yne (V). With stirring at —30°C, 2.1 g of finely cut lithium and then 0.1 g of $FeCl_3$ were added to 200 ml of liquid ammonia (previously redistilled), after which the ammonia was allowed to evaporate off (under argon). Under argon, 200 ml of HMPTA was added to the $LiNH_2$ residue and the mixture was stirred at room temperature for 0.5 h, after which 33 g (0.3 mole) of oct-1-yne was slowly added, the mixture was stirred for another 1 h, and then it was cooled to 10°C and 29.3 g (0.1 mole) of the bromide (IV) was added gradually and the new mixture was kept at 10°C for 1 h and at room temperature for 15 h. It was then heated at 55°C for 10 h and was then cooled in the water bath with ice, after the addition of 100 ml of H_2O, it was extracted with Et_2O (3 × 500 ml), and the ethereal extract was washed with water (3 × 100 ml), dried with $MgSO_4$, and evaporated. The residue was chromatographed (SiO_2, $n\text{-}C_6H_{14}$—Et_2O (10:1)). This gave 16.75 g (52%) of compound (V) with n_D^{25} 1.4650. IR spectrum (ν, cm^{-1}): 720 m, 815 m, 880 m, 905 m, 1000 m, 1030 s, 1080 s, 1120 s, 1140 s, 1200 m, 1360 m, 1440 m, 1470 s. PMR spectrum (δ, ppm): 0.88 t (3H, CH_3, J = 7 Hz), 1.27-1.80 m (26H, CH_2), 2.13 t (4H, $CH_2C{\equiv}C$, J = 4 Hz), 3.32-3.87 m (4H, CH_2—O), 4.56 br.s (1H, OCH—O, $W_{h/2}$ = 10 Hz).

Hexadec-9-yn-1-ol (VI). A solution of 16.6 g of the ether (V) in 200 ml of MeOH and 20 ml of H_2O was treated with 4 g of p-TsOH, and the mixture was stirred for 18 h, after which the solvent was distilled off, the residue was treated with 1 liter of Et_2O, and the ethereal solution was washed with 100 ml of saturated $NaHCO_3$, dried with $MgSO_4$, and evaporated. The residue was chromatographed (SiO_2, $n\text{-}C_6H_{14}$—Et_2O 3:1). This gave 10.5 g (85%) of the alkyne (VI), n_D^{20} 1.4657. IR spectrum (ν, cm^{-1}): 710 m, 1050 s, 1330 m, 1380 m, 1450 s, 3400 br.s. PMR spectrum (δ, ppm): 0.89 t (3H, CH_3, J = 7 Hz), 1.27-1.54 m (20H, CH_2), 1.78 br.s (1H, OH, $W_{h/2}$ = 12 Hz), 2.14 t, (4H, $CH_2C{\equiv}C$, J = 4 Hz), 3.63 t (2H, CH_2—O, J = 6 Hz).

Hexadec-9Z-en-1-ol (VII). At 0°C, 300 ml of a 1.5 N solution of iso-BuMgBr was added to a solution of 16.8 g of the alkyne (VI) in 200 ml of absolute Et_2O, the mixture stirred for 15 min and was then heated to room temperature and 1 g of Cp_2TiCl_2 was added: The reaction mixture was stirred vigorously for 3 h and was then cooled to 0°C and 100 ml of a saturated solution of NH_4Cl was gradually added and then 300 ml of 10% HCl, and the mixture was extracted with diethyl ether (3 × 500 ml). The ethereal extract was washed successively with saturated solutions (100 ml each) of NaCl and $NaHCO_3$ and then with NaCl again (2 × 100 ml) and was dried with $MgSO_4$ and evaporated. This gave 16.75 g (99%) of the alk-Z-enol (VII) with n_D^{25} 1.4650. IR spectrum (ν, cm^{-1}): 710 m, 1035 s, 1380 s, 1460 m, 3400 br.s. PMR spectrum (δ, ppm): 0.89 t (3H, CH_3, J = 7 Hz), 1.28-1.57 m (2 OH, CH_2), 2.05 m (4H, $CCH_2{=}C$), 3.64 t (2H, $CH_2{-}O$, J = 6 Hz), 5.36 t (2H, HC=CH, J = 5 Hz).

Hexadec-9Z-enal (VIII). At room temperature, a solution of 16.7 g of the alkenol (VII) in 40 ml of anhydrous CH_2Cl_2 was added to a suspension of 22.4 g of pyridinium chlorochromate in 120 ml of anhydrous CH_2Cl_2, and the mixture was stirred for 2 h, after which 200 ml of Et_2O was added and the solution was decanted off and filtered through a layer of SiO_2 (20 g) on a porous glass filter and was evaporated. This gave 16.3 g (98%) of the aldehyde (VIII) with n_D^{25} 1.4600. IR spectrum (ν, cm^{-1}): 710 m, 1090 m, 1130 m, 1380 m, 1455 m-s, 1720 s, 2730 m. PMR spectrum (δ, ppm): 0.89 t (3H, CH_3, J = 7 Hz), 1.27 m (18H, CH_2), 1.99-2.04 m (4H, $CH_2C{=}C$), 2.35-2.42 m (2H, CH_2CO), 5.35 t (2H, HC=CH, J = 5 Hz), 9.77 t (1H, HC=O, J = 1.5 Hz).

SUMMARY

Hexadec-9Z-enal — a component of the sex pheromone of the cotton bollworm *Heliothis armigera* Hübner — has been synthesized from cyclooctene. The conversion of an acetylenic alcohol into an alkenic alcohol with the (Z)-configuration was effected with the aid of the reductive Grignardization reaction.

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