Samples for gel chromatography were taken directly from the reaction solutions. Gel chromatography was conducted on a column (1.1 × 40 cm) filled with Sephadex G-200. The solvent used was 0.5 M NaCl solution.

Optical densities were recorded on an SF-26 spectrophotometer at the wavelength λ_{max} = 280 nm.

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INSECT PHEROMONES AND THEIR ANALOGS.

XLVII. SYNTHESIS OF 11-OXODODECA-3,6-DIYNOIC ACID — THE ACYCLIC PRECURSOR OF A MACROLIDE COMPONENT OF PHEROMONES OF *Oryzaephilus mercator* AND *O. surinamensis*

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632.936.2

A new approach is proposed to the synthesis of 11-oxododeca-3,6-diynoic acid — the acyclic precursor of a macrolide component of pheromones of *Oryzaephilus mercator* and *O. surinamensis* — from the readily available tetrahydropyran or allylacetone via the intermediate 5-bromo-2,2-ethylenedioxypentane.

The synthesis of one of the macrolide components of the aggregation pheromones of the grain beetles *Oryzaephilus mercator* and *O. surinamensis* — dodeca-3Z,6Z-dien-11-olide (I) — requires 11-oxododeca-3,6-diynoic acid (II). It has been obtained previously from derivatives of but-3-yn-1-ol and hept-6-yn-2-ol [1, 2]. We have developed a new approach to the synthesis of the oxoacid (II) from tetrahydropyran (III) or allylacetone (IV), both readily available, the transformation of each of which leads to one and the same key synthon — 5-bromo-2,2-ethylenedioxypentane (V). (see scheme on next page).

The opening of the ring of (III) under the action of HBr and H_2SO_4 formed 1,5-dibromopentane (VI), which was selectively dehydrobrominated by heating in hexametapol, forming 1-bromopent-4-ene (VII) with moderate yield. The oxidation of the latter with molecular oxygen in the presence of $PdCl_2$—CuCl in aqueous THF gave 5-bromopentan-2-one (VIII), which was converted into its acetal (V).

The alternative pathway for the synthesis of compound (V), from the ketone (IV), includes the stage of ozonolysis of its ethylenedioxy derivatives (IX). The 2,2-ethylenedioxypentan-5-ol (X) so formed was smoothly converted into the desired bromide (V), the yield of which calculated on the initial (IV) was 63.4%. Since the overall yield (26.6%) of synthon (V)

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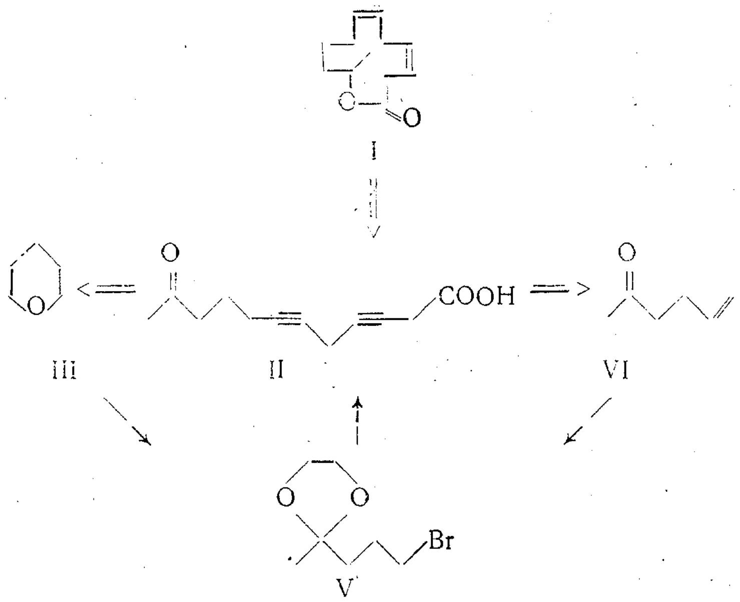
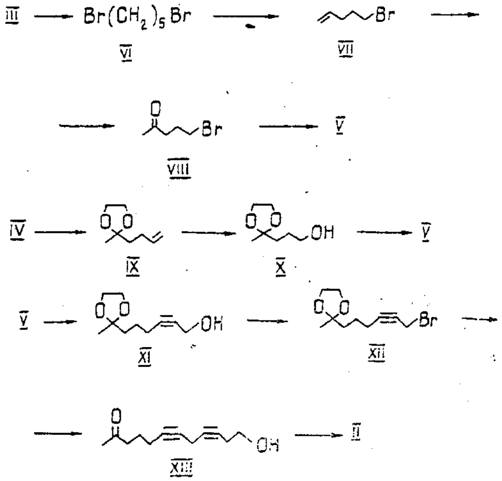


from (III) was lower, the second of the routes to its formation that have been considered is preferable.

The transformation of compound (V) to conclude the synthesis of the keto acid (II) included its coupling with the lithium derivative of propargyl alcohol, with the formation of the known [2] 2,2-ethylenedioxy-oct-6-yn-8-ol (XI), which was smoothly converted into the corresponding bromoacetal (XII), and the latter was coupled with the tetrahydropyranyl (THPL) ether of but-3-yn-1-ol. Hydrolysis of the coupling product gave 12-hydroxydodeca-6,9-diyn-2-one (XIII), the Jones oxidation [1] of which led to the desired ketoacid (II). Since the yields in the last stages [the coupling of bromide (XII) and the oxidation of hydroxyketone (XIII)] were comparatively low, the overall yield of the ketoacid (II) calculated on the initial (III) was only 8.5%.



EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer (in a film). PMR spectra were recorded on a Tesla BS-567 instrument (working frequency 100 MHz; solvent $CDCl_3$). The ^{13}C NMR spectrum was obtained on a Jeol FX-90Q spectrometer (22.5 MHz, $CDCl_3$). Chemical shifts are given on the δ scale relative to TMS (internal standard). GLC analysis was conducted on a Chrom-5 instrument with the stationary phase SE-30 (5%) on Chromaton N-AW-DMCS (0.16-0.20 mm) at working temperatures of 50-300°C (for compounds (II), (V)-(VII), and (XI)]; and on a Chrom-41 instrument with the stationary phase Carbowax-6000 (5%) on Inerton Super (0.125-0.160 mm), working temperatures 50-170°C [for compounds (VIII)-(X), (XII), and (XIII)]; the carrier gas was helium. The results of the analysis of the compounds synthesized agreed with the calculated figures.

1.5-Dibromopentane(VI). To an ice-cooled mixture of 36 ml of 46% HBr (3.0 mole) and 148 g (80.6 ml) of conc. H_2SO_4 was added dropwise over 0.5 h, 43.0 g (0.5 mole) of tetrahydropyran (III). The solution was warmed to 20°C and was stirred for 1 h. Then the reaction mixture was boiled for 3 h and was cooled to room temperature, and, after the addition of 300 ml of H_2O, it was extracted with petroleum ether (3 × 300, ml). The extract was washed successively with saturated solutions, of $NaHCO_3$ and NaCl and was dried with Na_2SO_4 and evaporated. This gave 90.9 g (79%) of the dibromide (VI), n_D^{20} 1.5126 [3]. IR spectrum (ν_{max}, cm^{-1}): 640, 560 (C—Br).

1-Bromopent-4-ene (VII). With vigorous stirring, 15 ml of hexametapol was added dropwise over 5 min to 17.0 g ($73.9 \cdot 10^{-3}$ mole) of the dibromide (VI) at 195°C, and then the temperature of the reaction mixture was raised to 205°C, and after 5 min the reflux condenser was replaced by one for downward distillation and the product was distilled into a receiver cooled with solid CO_2. After redistillation, 4.84 g (44%) of the bromide (VII) was obtained, with bp 126°C, n_D^{20} 1.4640 (VIII) [4]. IR spectrum (ν_{max}, cm^{-1}): 1640, 990, 910 ($H_2C{=}CH$); 640, 560 (C—Br).

5-Bromopentan-2-one (VIII). To a suspension of 3.50 g ($19.8 \cdot 10^{-3}$ mole) of $PdCl_2$ in 400 ml of THF and 40 ml of H_2O heated to 60°C was added 19.60 g ($198 \cdot 10^{-3}$ mole) of CuCl. Oxygen was passed through the reaction mixture with stirring at the rate of 5 liters/h for 5 min. Then 29.50 g ($198 \cdot 10^{-3}$ mole) of the bromide (VII) was added, and the bubbling of O_2 was continued at 60°C for 6 h, after which the reaction mixture was filtered, and the filtrate was diluted with 440 ml of $CHCl_3$, washed with 5% HCl (3 × 100 ml) and then with H_2O (to pH 7), dried with $MgSO_4$, and evaporated. This gave 21.27 g (65%) of the ketone (VIII), n_D^{20} 1.4982. Its IR and PMR spectra were identical with those given in the literature [5].

2,2-Ethylenedioxyhex-5-ene (IX). A mixture of 50.00 g ($510 \cdot 10^{-3}$ mole) of allylacetone (IV), 38.00 g ($613 \cdot 10^{-3}$ mole) of ethylene glycol, 2.74 g ($10.9 \cdot 10^{-3}$ mole) of pyridinium tosylate, and 340 ml of benzene was boiled for 28 h with the elimination of water (9.2 ml or $519 \cdot 10^{-3}$ mole). The benzene was distilled off from the reaction mixture, 400 ml of Et_2O was added to the residue, and the resulting solution was washed successively with saturated solutions of $NaHCO_3$ and of NaCl, and was dried with Na_2SO_4 and evaporated. This gave 65.30 g (90%) of the acetal (IX), n_D^{20} 1.4305. Its IR and PMR spectra were identical with those given in the literature [6].

2,2-Ethylenedioxypentan-5-ol (X). A mixture of ozone and oxygen (productivity of the ozonizer 0.1 mole of O_3/h) was bubbled through a solution of 14.20 g ($100 \cdot 10^{-3}$ mole) of the alkene (IX) in 150 ml of MeOH at 5°C until 0.1 mole of O_3 had been absorbed. The reaction mixture was purged with argon, and 6.42 g ($169 \cdot 10^{-3}$ mole) of $NaBH_4$ was added in portions, the temperature not being allowed to rise above 20°C. The mixture was stirred for 5 h and was left overnight, and it was then evaporated under vacuum. The residue was diluted with 300 ml of Et_2O and was washed with saturated NaCl solution, dried with Na_2SO_4, and evaporated. This gave 12.80 g (88%) of the hydroxyacetal (X) n_D^{22} 1.4397. Its IR and PMR spectra were identical with those given in the literature [7].

5-Bromo-2,2-ethylenedioxypentane (V). a. A mixture of 21.09 g ($128.0 \cdot 10^{-3}$ mole) of the bromoketone (VIII), 9.52 g ($153 \cdot 10^{-3}$ mole) of ethylene glycol, 0.58 g ($2.3 \cdot 10^{-3}$ mole) of pyridinium tosylate, and 72 ml of benzene was boiled for 32 h with a Dean—Stark trap, 2.3 ml of water (or $128 \cdot 10^{-3}$ mole) being taken off, and then the benzene was distilled off, the residue was taken up in 200 ml of Et_2O, and the resulting solution was washed with saturated solutions of $NAHCO_3$ NaCl dried with Na_2SO_4, and evaporated. This gave 24.04 g (90%) on the bromide (V), nD^{20} 1.4733. IR spectrum (ν_{max}, cm^{-1}) 1195, 1170. 1120, 1070, 1040 (O—C—O); 640, 540 (C—Br). The PMR spectrum was identical with that given in the literature [8].

b. The alcohol (X) (12.6 g; $86.3 \cdot 10^{-3}$ mole) was added dropwise to a solution of 19.6 g ($103 \cdot 10^{-3}$ mole) of TsCl in 66 ml of Py. The mixture was left overnight, and then it was poured into 120 ml of ice water and was extracted with Et_2O (3 × 100 ml). The extract was washed successively with saturated solutions of $CuSO_4$, $NaHCO_3$, and NaCl, dried with Na_2SO_4, and evaporated. This gave 25.2 g of tosylate, a solution of which in 260 ml of dry DMFA was treated with 54.2 g ($526.2 \cdot 10^{-3}$ mole) of NaBr; the mixture was stirred at 65°C for 2 h, cooled, treated with 500 ml of hexane, washed with H_2O (3 × 100 ml), dried with Na_2SO_4, and evaporated. This gave 14.4 g (80%) of the bromide (V), identical with that obtained in the preceding experiment.

2,2-Ethylenedioxy-8-hydroxyoct-6-yne (XI). In an atmosphere of Ar, 0.1 g of $FeCl_3$ and 1.19 g ($170 \cdot 10^{-3}$ gram-atom) of Li were added to 130 ml of liquid NH_3. The mixture was stirred until the blue color had disappeared (about 0.5 h) and then, at −37°C, 4.29 g ($76.6 \cdot 10^{-3}$ mole) of propargyl alcohol was added dropwise and, after another three hours' stirring, a solution of 9.10 g ($43.5 \cdot 10^{-3}$ mole) of the bromide (V) in 64 ml of abs. Et_2O, also dropwise. The reaction mixture was stirred at −37°C for 4 h and was left overnight at room temperature. The NH_3 was evaporated off, and 175 ml of H_2O was slowly added to the residue. The organic layer was separated off, the aqueous layer was extracted with Et_2O (3 × 20 ml), and the combined organic layers were washed with H_2O dried with Na_2SO_4, and evaporated. This gave 6.49 g (81%) of the hydroxyacetate (XI), n_D^{20} 1.4722. IR spectrum (ν_{max}, cm^{-1}): 3700-3200 (O—H), 2230 (C≡C), 1140, 1120, 1080, 1060, 1040, 1035 (C—O). PMR spectrum (100 MHz, $CDCl_3$): 1.32 (s, 3H, H-1), 1.40-1.80 (m, 4H, H-3, H-4), 2.16-2.28 (m, 2H, H-5), 2.40 (br.s, 1H, OH), 3.94 (br.s, 4H, OCH_2CH_2O), 4.24 (s, 2H, H-8).

2,2-Ethylenedioxy-8-bromooct-6-yne (XII). At −5 to 0°C, 6.33 g ($33.2 \cdot 10^{-3}$ mole) of TsCl in portions and then, keeping the temperature at about 0°C, 15.38 g ($274.6 \cdot 10^{-3}$ mole) of powdered KOH were added to a stirred solution of 5.05 g ($27.4 \cdot 10^{-3}$ mole) of the alcohol (XI) in 55 ml of abs. Et_2O. The reaction mixture was stirred at 0°C for 0.5 h, and then 150 ml of ice-cold H_2O was added. The organic layer was separated off and the aqueous layer was extracted with Et_2O (2 × 100 ml). The combined organic layers were washed with NaCl solution, dried with Na_2SO_4, and evaporated, and the residue was kept in vacuum at room temperature for 2 h. This gave 9.21 g of a tosylate, a solution of which in 87 ml of dry DMFA was treated with 17.61 g ($171 \cdot 10^{-3}$ mole) of NaBr,and the resulting reaction mixture was stirred at 65°C for 2 h, treated with 40 ml of H_2O, and extracted with hexane (3 × 170 ml). The extract was washed with H_2O (3 × 50 ml), dried with Na_2SO_4, and evaporated. This gave 5.76 g (85%) of the bromide (XII), n_D^{19} 1.4970. IR spectrum (ν_{max}, cm^{-1}): 2220 (C≡C); 1460, 1380, 1168, 1132, 1112, 1084, 1064 (O—C—O); 608, 564 (C—Br). The PMR spectrum was identical with that given in the literature [2].

12-Hydroxydodeca-6,9-diyn-2-one (XIII). A solution of EtMgBr obtained from 0.26 g ($10.8 \cdot 10^{-3}$ g-atom) of Mg and 1.40 g ($12.8 \cdot 10^{-3}$ mole) of EtBr in 7.7 ml of abs. THF was added dropwise to a solution of the THPL ether of but-3-yn-1-ol (1.70 g; $11.0 \cdot 10^{-3}$ mole) in 60 ml of abs. THF (25-30°C, Ar), the mixture was stirred for 2 h, and, at room temperature, 1.20 g ($1.21 \cdot 10^{-3}$ mole) of CuCl was added to it. It was then stirred for another 0.5 h and was cooled to 0°C and 2.05 g ($8.3 \cdot 10^{-3}$ mole) of the bromide (XII) in 22 ml of hexametapol was added, and, after being stirred at 20°C for 2.5 h, the resulting mixture was left overnight. Then it was cooled to 0°C and, after the addition of 100 ml of saturated NH_4Cl solution, it was extracted with Et_2O (3 × 100 ml), and the extract was washed successively with saturated solutions of NH_4Cl and NaCl and was evaporated. The residue (5.69 g) was dissolved in 20 ml of MeOH, 0.40 g of TsOH and 1.5 ml of H_2O were added, the mixture was stirred for 24 h, the MeOH was evaporated off, the residue was dissolved in 100 ml of Et_2O, and the solution was washed successively with saturated solutions of $NaHCO_3$ and NaCl and it was dried with Na_2SO_4 and evaporated. The residue was chromatographed (SiO_2, 50 g, hexane—Et_2O, from 2:8 to 1:1), to give 0.91 g (57%) of compound (XIII), n_D^{19} 1.4922. IR spectrum (ν_{max}, cm^{-1}): 3550-3350(O—H), 2240 (C≡C), 1720 (C=O), 1060 (C—O). PMR spectrum (100 MHz, $CDCl_3$): 1.64—1.98 (m, 2H, H-4), 2.17 (s, 3H, H-1), 2.32—2.88 (m, 4H, H-3, H-5, H-11), 3.13 (t, 2H, J = 2.0 Hz, H-8), 3.72 (t, 2H, J = 6.0 Hz, H-12), ^{13}C NMR: (22.5 MHz, $CDCl_3$); 9.75 (C-8), 18.15 (C-11), 22.65 (C-5), 23.17 (C-4), 30.09 (C-1), 42.43 (C-3), 61.16 (C-12), 75.13, 77.22, 77.46, 79.70 (C-10, C-7, C-6, C-9 coincides with the signal from $CHCl_3$), 208.75 (C-2).

11-Oxododeca-3,6-diynoic Acid (II). A solution of 0.24 g ($1.25 \cdot 10^{-3}$ mole) of the hydroxyketone (XIII) in 15 ml of acetone was added dropwise over 4 h to a solution of 0.78 g ($7.8 \cdot 10^{-3}$ mole) of CrO_3 in 8 ml of 3.5 M H_2SO_4 at −5°C. The reaction mixture was heated to 20° over 0.5 h, and, after the addition of 25 ml of H_2O, it was extracted with Et_2O (4 × 15 ml). The extract was washed with saturated NaCl solution (3 × 20 ml), dried with $MgSO_4$, and evaporated (in vacuum). The residue was chromatographed (SiO_2, 5 g, hexane—AcOEt—AcOH (75:75:1), giving 0.10 g (38%) of the hydroxyacid (II). Its IR and PMR spectra were identical with those given in the literature [1].

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