PHEROMONES OF INSECTS AND THEIR ANALOGS.

XXIX. METHYL-BRANCHED PHEROMONES FROM 4-METHYLTETRAHYDROPYRAN

4: SYNTHESIS OF (±)-15,19,23-TRIMETHYLHEPTATRIACONTANE – A PHEROMONE OF Glossina morsitans morsitans

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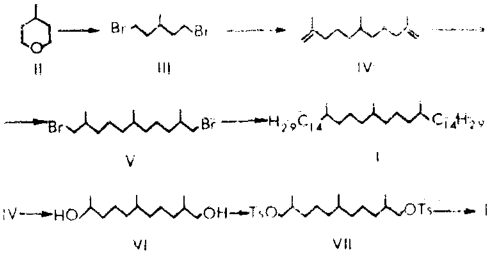
Racemic 15,19,23-trimethylheptatriacontane (the sex pheromone of the tsetse fly Glossina morsitans morsitans) has been synthesized from 1,5-dibromo-3-methylpentane, a product of the acid hydrolysis of 4-methyltetrahydropyran.

The synthesis of the (±)-diastereomeric 15,19,23-trimethylheptatriacontane (I) (a pheromone of the tsetse fly Glossina morsitans morsitans [1]) has been performed previously in 12 stages from geranyllinalool [2], an ester of 3-ketoglutaric acid [3], and methyl cyclopropyl ketone [4].

In the present communication the preparation of the long-chain hydrocarbon (I) of mixed acetogenin-isoprenoid nature by regioselective transformations of 1,5-dibromo-3-methylpentane (III), obtained by the acid cleavage of the readily available 4-methyltetrahydropyran (II) [5], is considered. The coupling of the dimagnesium derivative of the dibromide (III) with a twofold molar excess of methallyl chloride catalyzed by the complex of cuprous iodide with 2,2'-bipyridyl gave 2,6,10-trimethylundeca-1,10-diene (IV), which was transformed into the final product (I) in two stages. The hydroboration of the diene (IV) followed by treatment of the organoboron intermediate with bromine and sodium methanolate gave the dibromide (V) in good yield. The coupling of the latter with tridecylmagnesium bromide in the presence of cuprous iodide and 2,2'-bipyridyl led to the desired pheromone (I) with a yield of 34%, the yield of pheromone (I) calculated on the initial (II) being 10%. It must be mentioned that an alternative route from the diolefin (IV) to the pheromone (I) via the diol (VI) (obtained by the hydroboration reaction, followed by oxidation with hydrogen peroxide) and the tosylate (VII) gave an overall yield of the desired trimethyl-branched alkane only half as great.



EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer (in a film), and PMR spectra were recorded on a Tesla BS-467 instrument (working frequency 60 MHz) with CCl_4 or $(CD_3)_2CO$ as solvent and HMDS as internal standard. The mass spectra of compounds (I) and (IV) were measured on a MKh-1320 instrument with the aid of a direct-introduction system at a temperature of the ionization chamber of 110°C and an ionizing energy of 70 eV. GLC analysis was conducted on a Chrom-5 instrument with, as the stationary phase, the silicone liquid SE-30 (5%) on Chromaton N-AW-DMCS (0.16-0.20 mm) in a working temperature range of 50-300°C with helium as the carrier gas.

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1,5-Dibromo-3-methylpentane (III). A mixture of 25.0 g (0.25 mole) of 4-methyltetrahydropyran (II), 82 ml of 48% HBr, and 40 ml of 98% H_2SO_4 was boiled for 3 h, and the organic lower layer was separated off, washed successively with saturated solutions of $NaHCO_3$ and NaCl, dried with $MgSO_4$ and distilled. This gave 47.8 g (79%) of the dibromide (III), n_D^{22} 1.5060, mp 88-90°C (2 mm) [6]. IR spectrum (ν, cm^{-1}): 570, 650 (C–Br), 1390 (CH_3). PMR spectrum (60 MHz, CCl_4): 0.88 (d, 3H, J = 5.5 Hz, CH_3-3), 1.42–2.08 (m, 5H, H-2, H-3, H-4), 3.30 (t, 4H, J = 7 Hz, H-1, H-5).

2,6,10-Trimethylundecane-1,10-diene (IV). To a stirred suspension of 0.58 g ($3.07 \cdot 10^{-3}$ mole) of CuI in 35 ml of abs. THF was added 0.48 g ($3.07 \cdot 10^{-3}$ mole) of 2,2'-bipyridyl, the mixture was stirred for 0.5 h (20°C, Ar) and was then cooled to 2°C, and a solution of 6.13 g ($67.8 \cdot 10^{-3}$ mole) of methallyl chloride in 35 ml of abs. THF was added. The resulting mixture was stirred for 0.5 h and a solution of the Grignard reagent obtained from 1.62 g ($67.5 \cdot 10^{-3}$ g-atom) of Mg and 5.51 g ($22.6 \cdot 10^{-3}$ mole) of the dibromide (III) in 70 ml of abs. THF was added, and stirring was continued at 2°C for 2 h and at room temperature for 20 h; then 50 ml of saturated NH_4Cl solution was added and the resulting mixture was stirred at 10°C for 1 h and extracted with hexane (3 × 200 ml), and the extract was dried with $MgSO_4$ and evaporated. The residue was chromatographed (SiO_2, eluent – hexane). This gave 2.54 g (58%) of the diene (IV), bp 65°C (13 mm).

IR spectrum (ν, cm^{-1}): 900, 1650, 3080 ($C{=}CH_2$), 1385 (CH_3). PMR spectrum (60 MHz, CCl_4): 0.80 (d, 3H, J = 5 Hz, CH_3-6), 1.0–1.52 (m, 9H, H-4, H-5, H-6, H-7, H-8), 1.60 (s, 6H, CH_3-2, CH_3-10), 1.73–2.10 (m, 4H, H-3, H-9), 4.53 (s, 4H, H-1, H-11). Mass spectrum, m/z: 194 (M^+, 6.76) 179(5.00), 138(12), 123(25.88), 110(25.00), 109(70.58), 96(70.58), 95(26.47), 82(58.82), 81(52.94), 70(29.41), 69(94), 68(79), 55(100), 41(76.47). Found, %: C 86.45; H 13.45. $C_{14}H_{26}$. Calculated, %: C 86.51; H 13.49. M 194.35.

2,6,10-Trimethylundecane-1,11-diol (VI). Dropwise, 1.08 ml of boron trifluoride etherare in 23 ml of abs. THF was added to a suspension of 0.82 g ($4.2 \cdot 10^{-3}$ mole) of the olefin (IV) and 0.33 g ($8.7 \cdot 10^{-3}$ mole) of $NaBH_4$ in 61 ml of abs. THF (20-25°C, Ar) and the mixture was stirred for 1.5 h. Then 1.8 ml of water and, after 10 min, 1.9 ml of a 3 N solution of NaOH and 1.9 ml of 30% H_2O_2 were added, the reaction mixture was stirred and was left for 16 h, after which 300 ml of diethyl ether was added and it was washed with saturated NaCl solution, dried with Na_2SO_4 and evaporated. The residue was chromatographed (SiO_2, eluent – hexane–ethyl acetate (1:2)). This gave 0.72 g (74%) of the diol (VI). IR spectrum (ν, cm^{-1}): 1055 (C–O), 1385 (CH_3), 3350 (OH). PMR spectrum, [60 MHz, $(CD_3)_2CO$]: 0.79 (d, 9H, J = 6 Hz, CH_3-2, CH_3-6, CH_3-10), 1.0–1.6 (m, 15H, H-2, H-6, H-10, CH_2), 2.75 (s, 2H, OH), 3.26 (d, 4H, J = 5 Hz, H-1, H-11). Found, %: C 72.92; H 13.09. $C_{14}H_{30}O_2$. Calculated, %: C 72.98; H 13.13. M 230.98.

1,11-Ditosyloxy-2,6,10-trimethylundecane (VII). In portions, 0.44 g ($2.3 \cdot 10^{-3}$ mole) of p-toluenesulfonyl chloride was added to a solution of 0.24 g ($1.04 \cdot 10^{-3}$ mole) of the diol (VI) in 0.66 ml of dry pyridine cooled to 0°C, and the mixture was stirred for 0.5 h and was allowed to stand at the same temperature for 15 h, after which 100 ml of diethyl ether was added and it was washed successively with cooled 10% HCl and saturated solutions of $NaHCO_3$ and NaCl, dried with Na_2SO_4 and evaporated. This gave 0.46 g (82%) of the tosylate (VII). IR spectrum (ν, cm^{-1}): 1185, 1370 (SO_2), 1600 (Ar).

1,11-Dibromo-2,6,10-trimethylundecane (V). A solution of 0.93 g ($4.8 \cdot 10^{-3}$ mole) of the diene (IV) in 4 ml of abs. THF (0°C, Ar) was treated dropwise with 12 ml of a 1.19 M solution of diborane in THF, the mixture was stirred (0°C, 0.5 h; 20°C, 0.5 h) and, after the addition of 0.1 ml of MeOH, it was cooled to –15°C and 0.66 ml ($12.8 \cdot 10^{-3}$ mole) of bromine was added dropwise and this was followed, at 5°C, by a solution of sodium methanolate obtained from 0.95 g ($41.3 \cdot 10^{-3}$ g-atom) of sodium in 10 ml of abs. MeOH; the reaction mixture was heated to 25°C and was stirred for 0.5 h, after which 20 ml of hexane and 2 ml of saturated K_2CO_3 solution were added. After extraction with hexane (3 × 30 ml), the combined extract was washed with saturated NaCl solution, dried with $MgSO_4$ and evaportated. The residue was chromatographed (SiO_2, eluent – hexane). This gave 1.11 g (65%) of the bromide (V). IR spectrum (ν, cm^{-1}): 650 (C–Br) 1380 (CH_3). PMR spectrum, (60 MHz, CCl_4): 0.79 (d, 3H, J = 5 Hz, CH_3-6), 0.93 (d, 6H, J = 6 Hz, CH_3-2, CH_3-10), 1.06–1.5 (m, 15H, CH_2, H-2, H-6, H-10), 3.23 (d, 4H, J = 5 Hz, H-1, H-11). Found, %: C 47.11; H 7.87; Br 44.65. $C_{14}H_{28}Br_2$. Calculated, %: C 47.21; H 7.92; Br 44.87. M. 356.18.

15,19,23-Trimethylheptatriacontane (I). a) A stirred solution of 0.32 g ($1.68 \cdot 10^{-3}$ mole) of CuI in 14 ml of abs. THF was treated with 0.26 g ($1.68 \cdot 10^{-3}$ mole) of 2,2'-bipyridyl and the mixture was stirred (20°C, Ar) and was then cooled to 2°C and 1.4 g ($3.93 \cdot 10^{-3}$ mole) of the dibromide (V) in 14 ml of abs. THF was added. The mixture was stirred for 0.5 h, and the Grignard reagent obtained from 0.49 g ($20.5 \cdot 10^{-3}$ g-atom) of Mg and 4.14 g ($15.7 \cdot 10^{-3}$ mole) of n-tridecyl bromide in 42 ml of abs. THF was added; the reaction mixture was stirred at 2°C for 2 h, and at room temperature for 20 h, and, after the addition of 15 ml of saturated NH_4Cl solution, it was stirred at 10°C for 1 h and was extracted with hexane (3 × 150 ml), and the extract was dried and evaporated. The residue was chromatographed (Al_2O_3, eluent – hexane) and was then subjected to vacuum at 180°C (0.5 mm). This gave 0.75 g (34%) of the alkane (I), n_D^{20} 1.4576 [2], its mass spectrum being identical with that described in [4].

b) A solution of the Grignard reagent obtained from 0.11 g ($4.36 \cdot 10^{-3}$ g-atom) of Mg and 1.13 g ($4.3 \cdot 10^{-3}$ mole) of n-tridecylbromide in 8 ml of absolute diethyl ether was added dropwise, to a solution of 0.46 g ($0.87 \cdot 10^{-3}$ mole) of the tosylate (VII) in 1 ml of absolute diethyl ether and this was followed by 0.04 g ($0.22 \cdot 10^{-3}$ mole) of CuI, and the mixture was stirred for 1 h, after which it was heated to room temperature over 2 h and was allowed to stand for 15 h; then 5 ml of saturated NH_4Cl solution was added, the product was extracted with hexane (3 × 30 ml), and the extract was dried with $MgSO_4$ and evaporated. The residue was chromatographed (Al_2O_3, eluent-hexane), was then subjected to vacuum at 180°C (0.5 mm). The residue, 0.093 g (19%) of compound (I), identical with that obtained in experiment a.

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