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PHEROMONES OF INSECTS AND THEIR ANALOGS.

XX. METHYL-BRANCHED PHEROMONES BASED ON 4-METHYLTETRAHYDROPYRAN.

I. SYNTHESIS OF RACEMIC 4,8-DIMETHYLDECANAL - THE PHEROMONE OF THE FLOUR BEETLES *Tribolium confusum* AND *Tribolium castaneum*

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A synthesis is proposed of 4,8-dimethyldecanal (VIII) - a pheromone of the flour beetles *Tribolium confusum* and *T. castaneum*. By heating 71.2 g of 4-methyltetrahydropyran (I), 83.2 g of AcBr and 1.57 g of ZnCl₂ (45°C), then 120°C, 2 h), 1-acetoxy-5-bromo-3-methylpentane (II) was obtained. The hydrolysis of 19.8 g of (II) (MeOH-H₂O, TsOH, 20°C, 15 h) gave 5-bromo-3-methylpentan-1-ol (III). From 18.1 g of (III) and 38.9 ml of 2,3-dihydropyran (Et₂O, TsOH, 20°C, 20 h) was obtained the 2-THPL ester of (III), (IV), which was converted into 3-methyloct-7-en-1-ol (V) by the treatment of the corresponding Grignard reagent with allyl bromide (THF, CuI-bi-2-pyridyl, 2°C, 4 h, Ar). The interaction of 1.42 g of (V) with Et₃Al (hexane, 20°C, Cp₂ZrCl₂, Ar) gave 3,7-dimethylnonan-1-ol (VI), boiling which with 48% HBr in the presence of concentrated H₂SO₄ gave 1-bromo-3,7-dimethylnonane (VII) which was then converted into the desired (VIII) by the reaction of the corresponding Grignard reagent with DMFA (0-2°C, 1 h; 20°C, 2 h; Ar). The characteristics of the compounds - yield (%), n_D²⁰ (°C): (I), 79, 1.4340 (22); (III) 89, 1.4660 (23); (IV), 82, 1.4739 (23); (V), 85, -; (VI), 90, 1.4483 (20); (VII), 88, 1.4409 (22); (VIII), 88, 1.4589 (22). Details of the IR and PMR spectra of compounds (II)-(VII) are given.

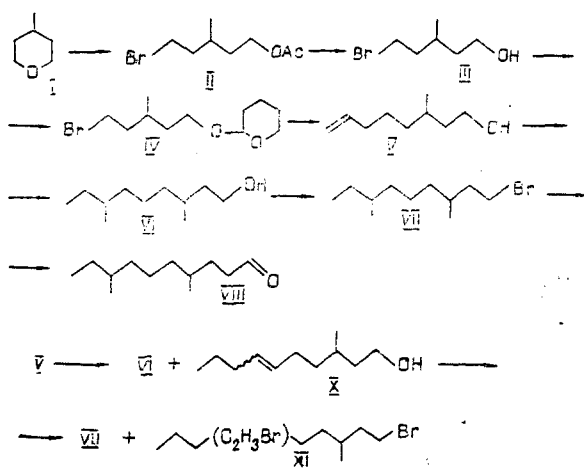
Racemic 4,8-dimethyldecanal, which possesses attractant activity in relation to the flour beetles *Tribolium confusum* and *T. castaneum* [1] has been obtained previously from citronellal [2, 3], methyl cyclopropyl ketone [4], and the cyclic dimer of isoprene [5].

Broad possibilities for the synthesis of methyl-branched pheromones are opened up by the use of synthons of α,ω-bifunctional 3-methylpentanes - products of the cleavage of the readily available 4-methyltetrahydropyran (I) [6]. Thus, the reactions of compound (I) with acetyl bromide in the presence of zinc chloride led to 1-acetoxy-5-bromo-3-methylpentane (II), which was converted into 1-bromo-3-methyl-5-(tetrahydropyran-2-yl)pentane (IV) via the bromohydrin (III). The 1,5-dimethyl-branched carbon skeleton of the desired pheromone was constructed by the carboalumination of the terminally unsaturated alcohol (V) obtained by the coupling of the bromide (IV) with allyl bromide by means of the Grignard reaction. The carboalumination reaction catalyzed by dicyclopentadienylzirconium

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dichloride (Cp_2ZrCl_2) took place regiospecifically and gave a high yield of 3,7-dimethylnonan-1-ol (VI), exclusively. The Grignard coupling of the bromohydrin (IV) with 2-methylbutyl bromide (IX) led to the alcohol (VI) by a shorter route but with a yield not exceeding 45%, while in the two-stage transformation described its yield amounted to 79%. The bromination of the dihydrohomocitronellol (VI) gave the corresponding bromide (VII), the magnesiation of which and interaction with dimethylformamide led to the desired 4,8-dimethyldecanal (VIII). The overall yield of the pheromone (VIII) in the seven-stage synthesis amounted to 34%, calculated on the initial methyltetrahydropyran (I).

If at the stage of converting the olefin (V) into the homoterpene alcohol (VI) carbocationic aluminination was replaced by a carbomagnesiation reaction, then, under similar conditions, together with the main product (VI) an unsaturated compound was formed which (see [7]) was assigned the structure of 3-methyldec-6-en-1-ol (X). Treatment of the mixture of alcohols (VI/X, 95:5) with hydrobromic acid in the presence of concentrated H_2SO_4 gave a mixture of the bromide (VII) and the dibromide (XI) which were readily separated chromatographically. The bromide (XI) is obviously formed as the result of the hydrobromination of the double bond and the substitutive bromination of the hydroxy group in the unsaturated alcohol (X).



EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer (in a film). The PMR spectra of compounds (II-IV) were obtained on a Tesla BS-467 instrument in CCl_4 at a working frequency of 60 MHz, and those of compounds (V-VIII) on a Tesla BS-567 instrument in CDCl_3 at a working frequency of 100 MHz with TMS as the internal standard. GLC analysis was performed on a Chrom-5 instrument with a silicone liquid SE-30 (5%) as the stationary phase on Chromaton N-AW-DMCS (0.16-0.20 mm) at working temperatures of 50-300°C with helium as the carrier gas.

1-Acetoxy-5-bromo-3-methylpentane (II). With stirring at room temperature, 83.2 g (0.676 mole) of acetyl bromide was added dropwise to a mixture of 71.2 g (0.71 mole) of 4-methyltetrahydropyran (I) and 1.57 g of ZnCl_2 , whereupon the temperature rose spontaneously to 45°C. The reaction mixture was then heated to 120°C, kept there for 2 h, cooled to 20°C, diluted with 1 liter of diethyl ether, washed successively with saturated solutions of NaHCO_3 and NaCl , dried with MgSO_4 , and evaporated. After distillation, 134.4 g (89%) of the acetate (II) was obtained: n_D^{23} 1.4660, bp 70-71°C (2 mm Hg). IR spectrum (ν , cm^{-1}): 570, 610, 645 (C-Br), 1245 (C-O-C), 1740 (C=O). PMR spectrum (60 MHz, CCl_4): 0.88 (d, 3 H, J = 5 Hz, CH_3 -3), 1.3-1.8 (m, 5 H, H-2, H-3, H-4), 1.87 (s, 3 H, AcO-1), 3.32 (t, 2 H, J = 7 Hz, H-5), 3.97 (t, 2 H, J = 6.5 Hz, H-1).

The results of the analysis of (II) ($\text{C}_8\text{H}_{15}\text{BrO}_2$) corresponded to the calculated figures.

5-Bromo-3-methylpentan-1-ol (III). A solution of 19.8 g (0.0887 mole) of compound (II) in 200 ml of methanol was treated with 1 ml of water and 1.98 g (0.0115 mole) of p -TsOH, and the reaction mixture was boiled for 0.5 h, after which it was stirred at room temperature for 15 h and was then evaporated; the residue was dissolved in 500 ml of diethyl ether and the solution was washed successively with saturated NaHCO_3 and NaCl .

solutions, dried with Na_2SO_4 , and evaporated. This gave 13.2 g (82%) of the alcohol (III), n_D^{23} 1.4739 [8]. IR spectrum (ν , cm^{-1}): 570, 650 (C-Br), 1060 (C-O), 3350 (O-H). PMR spectrum (60 MHz, CCl_4): 0.87 (d, 3 H, $J = 5$ Hz, CH_3 -3), 1.2-2.0 (m, 5 H, H-2, H-3, H-4), 3.33 (t, 2 H, $J = 7$ Hz, H-5), 3.55 (t, 2 H, $J = 6.5$ Hz, H-1), 4.56 (br.s, 1 H, OH).

1-Bromo-3-methyl-5-(tetrahydropyran-2-yloxy)pentane (IV). At a temperature of 10-15°C, 38.9 ml (32.7 g; 0.389 mole) of 2,3-dihydropyran was added to a solution of 18.1 g (0.1 mole) of compound (III) and 0.2 g of TsOH in 290 ml of absolute diethyl ether, and the mixture was warmed to room temperature and was stirred for 20 h, after which 200 ml of diethyl ether was added and it was washed successively with saturated solutions of NaHCO_3 and NaCl and was dried with NaSO_4 and evaporated. After chromatography of the residue [SiO_2 , hexane-ethyl acetate (10:1)], 22.5 g (85%) of compound (IV) was obtained. IR spectrum (ν , cm^{-1}): 570, 650 (C-Br); 1040, 1080, 1130 (acetal). PMR spectrum (60 MHz, CCl_4): 0.87 (d, 3 H, $J = 5.5$ Hz, CH_3 -3), 1.2-2.0 (m, 11 H, CH, CH_2), 3.16-3.93 (m, 6 H, CH_2O , CH_2Br), 4.4 (br.s, 1 H, OCHO).

3-Methyloct-7-en-1-ol (V). A solution of 3.29 g (0.0207 mole) of bi-2-pyridyl in 60 ml of absolute THF was added to a stirred suspension of 3.93 g (0.0207 mole) of CuI in 60 ml of absolute THF and the mixture was stirred for 0.5 h (20°C, Ar) and was then cooled to 2°C, after which a solution of 23.73 g (0.196 mole) of allyl bromide in 100 ml of absolute THF was added, followed after another 10 minutes' stirring by a solution of the Grignard reagent obtained from 3.13 g (0.13 g-atom) of Mg and 26.5 g (0.1 mole) of the bromohydrin (IV) in 140 ml of absolute THF; the reaction mixture was stirred at 2°C for 4 h, and then 120 ml of saturated NH_4Cl solution was added and after being stirred at 10°C for 1 h, the resulting mixture was extracted with diethyl ether (3 \times 300 ml). The extract was evaporated, the residue was dissolved in a mixture of 300 ml of MeOH, 120 ml of H_2O , and 3 g of TsOH, the solution was stirred at room temperature for 15 h and was then evaporated and the residue was extracted with diethyl ether (4 \times 300 ml), the extract then being washed successively with saturated solutions of NaHCO_3 and NaCl, dried with Na_2SO_4 , and evaporated. The residue was chromatographed [SiO_2 , hexane-diethyl ether (7:3)], giving 12.8 g (90%) of the alkenol (V), n_D^{20} 1.4483. IR spectrum (ν , cm^{-1}): 910, 1000 (C-H), 1065 (C-O), 1380, 1460 (CH_3), 1645 (C=C), 3200-3600 (O-H). PMR spectrum (100 MHz, CDCl_3): 0.88 (d, 3 H, $J = 7$ Hz, CH_3 -3), 1.10-1.63 (m, 7 H, H-2, H-3, H-4, H-5), 1.86-2.12 (m, 2 H, H-6), 2.27 (s, 1 H, OH), 3.60 (t, 2 H, $J = 7$ Hz, H-1), 4.76-5.02 (m, 2 H, H-8), 5.50-5.90 (m, 1 H, H-7).

The results of the analysis of compound (V) ($\text{C}_9\text{H}_{18}\text{O}$) corresponded to the calculated figures.

3,7-Dimethylnonan-1-ol (VI). A. in an atmosphere of argon at 20°C, 1.42 g (0.010 mole) of the alcohol (V) in 2 ml of absolute hexane was added to a solution of 3.5 ml of an 85% hexane solution (0.022 mole) of triethylaluminum and 0.15 g (0.0005 mole) of $\text{Cp}_2\text{-ZrCl}_2$ in 5 ml of absolute hexane, the mixture was stirred for 1 h and was then cooled to -5°C, and, after the addition of 5 ml of 5% HCl, it was extracted with diethyl ether (3 \times 100 ml) and the extract was washed with the saturated solution of NaHCO_3 , dried with Na_2SO_4 , and evaporated. The residue was chromatographed [SiO_2 , hexane-diethyl ether (7:3)] and gave 1.51 g (88%) of alcohol (VI) with n_D^{22} 1.4409 [3]. IR spectrum (ν , cm^{-1}): 1070 (C-O), 1380, 1462 (CH_3), 3200-3600 (O-H). PMR spectrum (100 MHz, CDCl_3): 0.72-1.00 (m, 9 H, CH_3 -3, CH_3 -7, H-9), 1.05-1.66 (m, 12 H, CH, CH_2), 2.05 (s, 1 H, OH), 3.68 (t, 2 H, $J = 6.5$ Hz, H-1).

B. To 10 ml of a 1.5 M solution of diethylmagnesium, obtained in accordance with [9] in absolute diethyl ether, was added (20°C, argon) 0.029 g (0.0001 mole) of Cp_2ZrCl_2 and the mixture was stirred for 10 min and was then cooled to 0°C, after which 1.0 g (0.007 mole) of the alcohol (V) was added dropwise, and the temperature was raised to 25°C over 0.5 h; the mixture was stirred at this temperature for 1.5 h and was then cooled to 0°C and, after the addition of 5 ml of 5% HCl, it was extracted with diethyl ether (3 \times 100 ml), and the extract was washed with saturated NaHCO_3 solution, dried with Na_2SO_4 , and evaporated. The residue was chromatographed [SiO_2 , hexane-diethyl ether (7:3)], giving 1.15 g of a mixture (95:5 according to the results of GLC analysis) of the alcohols (VI) and (X).

C. A solution of 0.58 g (0.00272 mole) of bi-2-pyridyl in 10 ml of absolute THF was added to a stirred suspension of 0.71 g (0.00272 mole) of CuI in 10 ml of absolute THF (20°C, argon, and the mixture was stirred for 0.5 h and was then cooled to 2°C; a solution

of 4.12 g (0.0273 mole) of 2-methylbutyl bromide (IX) in 20 ml of absolute THF was added and the mixture was stirred for 10 min, after which the Grignard reagent obtained from 0.68 g (0.0283 g-atom) of Mg and 4.83 g (0.0182 mole) of the bromohydrin derivative (IV) in 40 ml of absolute THF were added. The reaction mixture was stirred at 2°C for 4 h, and then 30 ml of saturated NH_4Cl solution was added and after it had been stirred at 10°C for 1 h the mixture was extracted with diethyl ether (3 × 100 ml) and the extract was evaporated. The residue was dissolved in 43 ml of methanol, 8 ml of H_2O and 0.43 g of TsOH were added, and the mixture was stirred at room temperature for 15 h and was then evaporated. The residue was extracted with diethyl ether (3 × 80 ml), and the extract was washed with saturated NaHCO_3 solution, dried with Na_2SO_4 , and evaporated. The residue was chromatographed [SiO_2 , hexane-diethyl ether (7:3)] to give 1.41 g (45%) of the alcohol (VI) identical with that obtained in experiment A.

1-Bromo-3,7-dimethylnonane (VII). A. A mixture of 0.55 g (0.0032 mole) of the alcohol (VI), 0.76 ml of 48% HBr and 0.18 ml of concentrated H_2SO_4 was boiled for 6 h and was then cooled to room temperature, diluted with 10 ml of water, and extracted with hexane (3 × 100 ml), after which the extract was washed successively with saturated NaHCO_3 and NaCl solutions and was dried with MgSO_4 and evaporated. The residue was chromatographed (SiO_2 , 10 g, hexane) to give 0.66 g (88%) of the bromide (VII). n_D^{22} 1.4589 [10]. IR spectrum (ν , cm^{-1}): 575, 655 (C-Br); 1385, 1470 (CH_3). PMR spectrum (100 MHz, CDCl_3): 0.72-0.98 (m, 9 H, CH_3 -3, CH_3 -7, H-9), 1.05-1.40 (m, 10 H, CH_2), 1.46-1.75 (m, 2 H, CH), 3.42 (t, 2 H, J = 6 Hz, H-1).

B. Under the conditions of the preceding experiments, 0.58 g of a mixture (95:5) of the alcohols (VI) and (X), 0.76 ml of 48% HBr, and 0.18 ml of concentrated H_2SO_4 yielded 0.74 g of a mixture of the bromide (VII) and the dibromide (XI). After chromatography (SiO_2 , 50 g, hexane), 0.64 g (85%) of compound (VII) identical with that obtained in the preceding experiment was isolated.

4,8-Dimethyldecanal (VIII). At 0-2°C (argon) over 1 h, the Grignard reagent prepared from 0.16 g (0.0067 g-atom) of Mg and 0.72 g (0.00306 mole) of the bromide (VII) in 6 ml of absolute THF was added to a solution of 0.24 g of DMFA in 2 ml of absolute THF, and then the mixture was heated to room temperature and was stirred for 2 h and, after the addition of 5 ml of 10% HCl, it was extracted with diethyl ether (3 × 50 ml) and the extract was dried with MgSO_4 and evaporated. The residue was chromatographed [SiO_2 , hexane-diethyl ether (8:2)], giving 0.44 g (79%) of the aldehyde (VIII) with n_D^{22} 1.4340 [5].

SUMMARY

Racemic 4,8-dimethyldecanal - an attractant of the flour beetles *Tribolium confusum* and *Tribolium castaneum* - has been synthesized from the bifunctional product of the cleavage of 4-methyltetrahydropyran.

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