INSECT PHEROMONES AND THEIR ANALOGUES

XXXII. CHIRAL PHEROMONES BASED ON (S)-(+)-3,7-DIMETHYLOCTA-1,6-DIENE. 1. SYNTHESIS OF (4R,8RS)-4,8-DIMETHYLDECANAL

V. N. Odinokov, G. Yu. Ishmuratov, R. Ya. Kharisov,
M. P. Yakovleva, R. M. Sultanov, E. P. Serebryakov,
U. M. Dzhemilev, and G. A. Tolstikov

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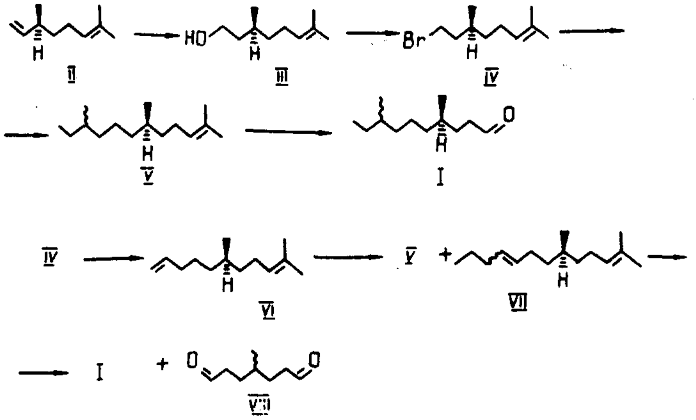
The synthesis of optically active (4R,8RS)-4,8-dimethyldecanal — the aggregation pheromone of the flour beetles Tribolium confusum and T. castaneum — has been effected. The starting compound was the readily available enantiomerically enriched (S)-(+)-3,7-dimethylocta-1,6-diene with an optical purity of ~50%.

A number of syntheses are known [1-7] of optically active stereoisomers of the aggregation pheromone of the confused flour beetle (Tribolium confusum) and of the rust-red flour beetle (T. castaneum), which has been identified as 4,8-dimethyldecanal [8, 9].

We have proposed a new route for transformations of the readily available (S)-(+)-3,7-dimethylocta-1,6-diene (II) [10] that leads to the optically active 4,8-dimethyldecanal (I) in the form of a mixture of (4R,8RS)-diastereomers. The four-stage synthesis of the desired pheromone (I) included the following reactions. Under the action of triisobutylaluminum (TIBA) the initial diene (II) was selectively hydroaluminated at the vinyl group, and, after oxidation, the organoaluminum intermediate gave β-(−)-citronellol (III) with a yield of more than 60%. The bromide (IV) obtained from the alcohol (III) was coupled with the Grignard reagent from 2-methylbutyl bromide, which led with a yield of 65% to (6R,10RS)-2,6,10-trimethyldodec-2-ene (V), the ozonolysis of which gave the desired pheromone (I), the overall yield of (I) calculated on the initial (II), being 30%.

We have now found an alternative route for the conversion of bromide (IV) consisting in the coupling of the corresponding Grignard reagent with allyl bromide giving with a yield of more than 80% the diene (VI), which was subject to the carbomagnesiation reaction. On catalysis by dicyclopentadienylzirconium dichloride (Cp_2ArCl_2) this reaction took place regioselectively and gave, with a yield of more than 90%, compound (V) contaminated with 5% of a diene the structure of which, according to [11] corresponded to (6R)-2,6-dimethyltrideca-2,9-diene (VII). Exhaustive ozonolysis of the mixture of (V) and (VII) gave the desired aldehyde (I) containing as impurity the dialdehyde (VIII), which was eliminated by chromatography. This two-stage conversion of the bromide (IV) gave a higher yield of compound (V), and the overall yield of the pheromone (I) calculated on the diene (II) rose to 34%.



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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, solvent CCl_4), chemical shifts being given on the δ scale relative to the signal of HMDS (internal standard). GLC analysis was conducted on a Chrom-5 chromatograph with the mobile phase FFAP (5%) on Chromaton N-AW-DMCS (0.16-0.20 mm) at a working temperature of 50-200°C [for compounds (I), (II), and (V)-(VIII)]; and on a Chrom-41 instrument with Carbowax-6000 (5%) on Inerton Super (0.125-1.160 mm) at a working temperature of 50-170°C [for compounds (III) and (IV)]; the carrier gas was helium. The $[\alpha]_D$ values were determined in $CHCl_3$ on a Perkin–Elmer 141 polarimeter. The results of the analysis of the compounds that had been synthesized corresponded to the calculated figures.

(3S)-3,7-Dimethyloct-6-en-1-ol (III). At 80°C (Ar) 20.0 g of redistilled technical dihydromyrcene, containing, according to GLC, ~70% of (S)-(±)-3,7-dimethylocta-1,6-diene (II) with an optical purity of ~50% [8, 9], was added dropwise to 9.8 ml of a 88% solution ($33.8 \cdot 10^{-3}$ mole) of TIBA. The reaction mixture was heated to 100°C and was stirred for 5 h; then it was cooled to 0°C and was diluted with 75 ml of absolute diethyl ether, and dry air was passed through it at the rate of 3 liters/h (0-20°C, 1 h) followed by oxygen (20°C, 1 h; 30-40°C, 3 h). After this, the reaction mixture was cooled to 0°C, 28 ml of 10% H_2SO_4 was added dropwise, and, after one hour's stirring at room temperature, the products were extracted with diethyl ether (3 × 200 ml), and the combined extract was washed successively with saturated solutions of $NaHCO_3$ and NaCl and was dried with Na_2SO_4 and evaporated. The residue was distilled under vacuum to give 9.81 g (62%) of the alcohol (III) with a purity, according to GLC, of not less than 92%, n_D^{23} 1.4510, bp 102-103°C (8 mm), $[\alpha]_D^{23}$ −2.57° (c 8.5; $CHCl_3$), its IR and PMR spectra being identical with those described previously [12].

(3S)-1-Bromo-3,7-dimethyloct-6-ene (IV). Under argon at −15°C, 1.0 ml ($10.5 \cdot 10^{-3}$ mole) of phosphorus tribromide was added dropwise to a solution of 4.9 g ($31.4 \cdot 10^{-3}$ mole) of the alcohol (III) and 0.45 ml ($5.5 \cdot 10^{-3}$ mole) of pyridine in 30 ml of absolute ether, and then 100 ml of diethyl ether was added and the mixture was poured into 40 ml of ice water and extracted with diethyl ether (3 × 100 ml); the combined extracts were washed successively with saturated solutions of $NaHCO_3$ and NaCl, dried with $MgSO_4$, and evaporated. The residue was chromatographed (SiO_2, hexane) to give 6.32 g (92%) of the bromide (IV) with a purity, according to GLC, of not less than 93%, n_D^{23} 1.4738, $[\alpha]_D^{23}$ +3.22° (c 3.0; $CHCl_3$), its IR and PMR spectra being identical with those described previously [13].

(6R)-2,6-Dimethylundeca-2,10-diene (VI). A solution of 0.4 g ($2.6 \cdot 10^{-3}$ mole) of 2,2'-bipyridyl in 12 ml of absolute THF was added to a stirred suspension of 0.5 g ($2.6 \cdot 10^{-3}$ mole) of CuI in 12 ml of absolute THF, and then the mixture was cooled to 2°C and a solution of 3.35 g ($27.7 \cdot 10^{-3}$ mole) of allyl bromide in 24 ml of absolute THF, was added, followed after 10 minutes' stirring, by a solution of the Grignard reagent obtained from 0.56 g ($23.3 \cdot 10^{-3}$ g-atom) of Mg and 4.0 g ($18.3 \cdot 10^{-3}$ mole) of the bromide (IV) in 70 ml of absolute THF; after being stirred at 2°C for 4 h the reaction mixture was treated with 21 ml of a saturated solution of NH_4Cl, stirred at 10°C for 1 h, and extracted with diethyl ether, and the extract was washed with saturated NaCl solution, dried with $MgSO_4$, and evaporated. The residue was chromatographed (SiO_2, hexane) to give 2.73 g (83%) of the diene (VI) with a purity of 98% according to GLC, n_D^{23} 1.4445, $[\alpha]_D^{17}$ +0.45° (c 24.5; $CHCl_3$). IR spectrum (ν, cm^{-1}): 850, 920, 1010, 3030, 3085 (C=C–H), 1385 (CH_3), 1665, 1675 (C=C). PMR spectrum (δ, ppm, CCl_4): 0.83 (d, 3H, J = 5.5 Hz, CH_3-6), 1.0-1.47 (m, 7H, H-5, H-6, H-7, H-8), 1.55 and 1.62 (s, 6H, CH_3-2, H-1), 1.93-2.17 (m, 4H, H-4, H-9), 4.67-5.17 (m, 3H, H-3, H-11), 5.4-5.96 (m, 1H, H-10).

(6R,10RS)-2,6,10-Trimethyldodec-2-ene (V). a. At −10°C (Ar), 0.49 ml of a 0.1 M solution of Li_2CuCl_4 and a solution of the Grignard reagent obtained from 0.45 g ($18.9 \cdot 10^{-3}$ g-atom) of Mg and 2.37 g ($15.7 \cdot 10^{-3}$ mole) of 2-methylbutyl bromide in 29 ml of absolute THF were added to a solution of 2.3 g ($10.6 \cdot 10^{-3}$ mole) of the bromide (IV) in 5 ml of absolute THF; the mixture was stirred (−10°C, 1 h; 20°C, 15 h), and then 15 ml of saturated NH_4Cl solution was added at 5°C; stirring was continued at the same temperature for 1 h, the products were extracted with diethyl ether (3 × 100 ml), and the extract was dried with $MgSO_4$ and evaporated.

The residue was chromatographed (SiO_2, hexane) to give 1.45 g (65%) of compound (V) with a purity, according to GLC, of 96%, n_D^{23} 1.4430 [14]. IR spectrum (ν, cm^{-1}): 840

(C≡C–H), 1380 (CH_3), 1670 (C=C). PMR spectrum (δ, ppm, CCl_4): 0.7-0.95 (m, 9H, CH_3-6, CH_3-10, H-12), 1.0-1.37 (m, H-5, H-6, H-7, H-8, H-9, H-10, H-11), 1.5 and 1.58 (s, 6H, CH_3-2, H-1), 1.73-2.06 (m, 2H, H-4), 4.95 (t, 1H, J = 6.5 Hz, H-3).

b. At 20°C (Ar) , 0.062 g ($2.14 \cdot 10^{-4}$ mole) of Cp_2ZrCl_2 was added to 21.4 ml of a 1.5 M solution of diethylmagnesium obtained according to [15], the mixture was stirred for 10 min and was then cooled to 0°C, and 2.7 g ($15 \cdot 10^{-3}$ mole) of the diene (VI) was added dropwise; after this, the temperature was raised to 25°C over 0.5 h and the mixture was stirred at this temperature for 1.5 h and was then cooled to 0°C, 11 ml of 5% HCl was added, the products were extracted with diethyl ether (3 × 100 ml), and the extract was washed with saturated $NaHCO_3$ solution, dried with $MgSO_4$, and evaporated. The residue was chromatographed (SiO_2, hexane) to give 3.03 g of a mixture of (V) and (VII) (95:5 according to GLC). The yield of (V) was 91%.

(4R,8RS)-4,8-Dimethyldecanal (I). a. At −60°C a mixture of ozone and oxygen (2% of O_3 by weight) was passed at the rate of 5 liters/h through a solution of 0.67 g ($3.2 \cdot 10^{-3}$ mole) of the olefin (V) in 2.8 ml of absolute CH_2Cl_2 containing 0.27 ml of absolute MeOH until $3.5 \cdot 10^{-3}$ mole of ozone had been absorbed. The reaction mixture was purged with argon, and, at the same temperature, 2.06 ml ($64 \cdot 10^{-3}$ mole) of dimethyl sulfide was added, and, after further stirring (−60°C, 1 h; −15°C, 1 h; 0°C, 1 h; 20°C, 12 h) the mixture was diluted with 100 ml of diethyl ether and was washed with water (2 × 5 ml), dried with $MgSO_4$, and evaporated. Chromatography of the residue [SiO_2, hexane–diethyl ether (9:1)] gave 0.48 g (81%) of the aldehyde (I) with a purity according to GLC of not less than 96%, n_D^{23} 1.4344, $[\alpha]_D^{23}$ −0.5° (c 4.5; EtOH). Its IR and PMR spectra were identical with those described previously [7].

b. The mixture of (V) and (VII) (0.71 g) was ozonized and the products were worked up as in the preceding experiment. After chromatography [SiO_2, hexane–diethyl ether (9:1)] 0.46 g (79%) of the pheromone (I) was obtained with a purity of 98%, identical with the compound (I) obtained in experiment a.

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