INSECT PHERMONES AND THEIR ANALOGUES

XXXVIII. SYNTHESIS OF (±)-3-METHYLHENEICOSAN-2-ONE AND (±)-2-ACETOXY-3,7-DIMETHYLPENTADECANE USING THE REDUCTIVE β-VINYLATION OF α-OLEFINS

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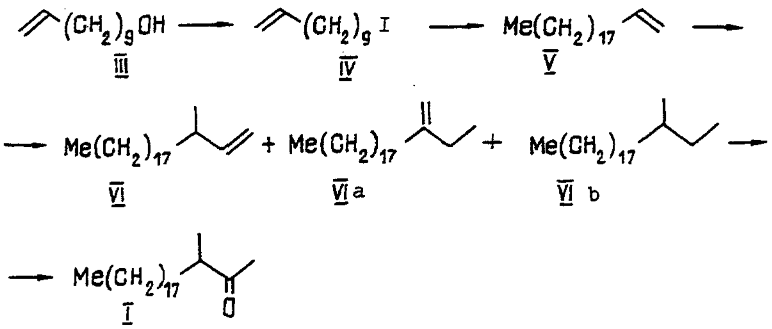
Schemes are proposed for the synthesis of (±)-3-methylheneicosan-2-one and (±)-2-acetoxy-3,7-dimethylpentadecane – racemic analogues of the sex pheromones of the common cockroach (Blatella germanica) and of plane sawflies of the genera Diprion and Neodiprion, respectively, using the reductive β-vinylation of α-olefins.

Syntheses have been described in the literature of racemic (±)-3-methylheneicosan-2-one (I) [1] and (±)-2-acetoxy-3,7-dimethylpentadecane (II) [2-9], which are analogues of sex pheromones of the common cockroach (Blatella germanica) and of plane sawflies of the genera Diprion and Neodiprion, respectively.

We propose a new rational approach to the synthesis of the above-mentioned acyclic methyl-branched pheromones which is based on the recently described [10, 11] reductive β-vinylation of α-olefins. The initial α-olefins for the realization of this approach – eicos-1-ene (V) and 6-methyltetradec-1-ene (IX) – were obtained, respectively, from undec-10-en-1-ol (III) via the intermediate iodide (IV) and 4-methyltetrahydropyran (VII) via the bromide (VIII) [9].



In the case of the vinylation of the olefin (V), the main reaction product was 3-methylheneicos-1-ene. In agreement with the literature [10, 11], it was contaminated with the isomeric alkene (VIa) and the saturated hydrocarbon (VIb), from which it was easily freed in the following stage – oxidation by oxygen over a palladium catalyst. Of the compounds (VI), (VIa), and (VIb) present in the mixture, only the alkene (VI) was oxidized, forming the corresponding ketone (I), which was readily isolated in the pure form with the aid of column chromatography. The yield of the attractant (I), calculated on the initial (III), was 33%. See scheme on following page.

Vinylation of the alkene (IX) gave a mixture of 3,7-dimetylpentadec-1-ene (X), its isomer (Xa), and the corresponding alkane (Xb), the oxidation of which ($O_2/PdCl_2$–CuCl) led to a mixture of 3,7-dimethylpentadecan-2-one (XI) and unchanged (Xa) (8%) and (Xb) (17%), from which the individual ketone (XI) was isolated with an overall yield in the two stages of 58%. The hydride reduction of ketone (XI) and subsequent acetylation led to pheromone

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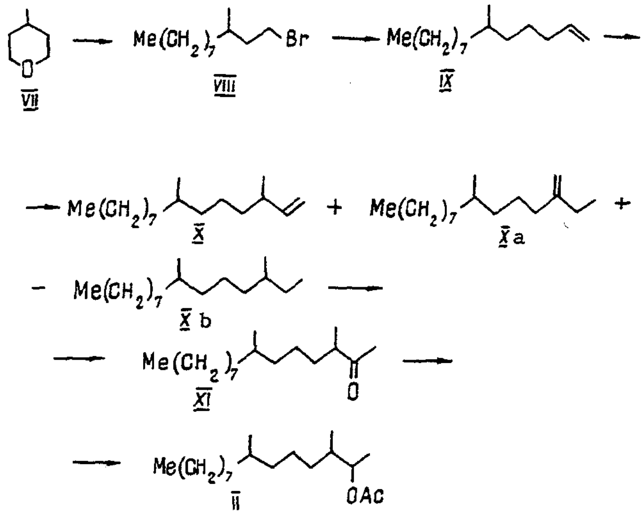

(II) with an overall yield of 13% calculated on the initial (VII) and with a ratio of the erythro- and threo- isomers of 1:1 (GLC results).

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer (in a film), and PMR spectra on a Tesla BS-567 instrument (working frequency 100 MHz) with $CDCl_3$ as solvent: chemical shifts are given on the δ scale relative to TMS (internal standard). GLC analysis for compound (II) was conducted on a Shimadzu instrument with the stationary phase PEG-20M in a 0.2 mm × 25 m glass capillary column at a working temperature of 170°C, and for the other compounds on a Chrom-5 instrument with, as the stationary phase, the silicone liquid SE-30 (5%) on Chromaton N-AW-DMCS (0.16-20 mm) at a working temperature of 50-300°C, the carrier gas being helium. The elementary analyses of the compounds synthesized corresponded to the calculated figures.

1-Iodoundec-10-ene (IV). At 0°C, 5.46 g ($28.7 \cdot 10^{-3}$ mole) of TsCl was added in portions to a solution of 3.5 g ($20.6 \cdot 10^{-3}$ mole) of undec-10-en-1-ol (III) in 8.4 ml of dry pyridine; the mixture was kept at the same temperature for 12 h and, after the addition of 0.3 liter of diethyl ether, it was washed successively with 10% HCl and with saturated solutions of $NaHCO_3$ and NaCl, and was dried with $MgSO_4$, and evaporated. The residue (5.92 g) was dissolved in 44 ml of abs. acetone, and 5.05 g ($33.7 \cdot 10^{-3}$ mole) of NaI was added; the mixture was boiled for 1.5 h, and was left in the dark at 20°C for 48 h and evaporated, after which the residue was treated with 30 ml of water that had been cooled to 0°C, and was extracted with diethyl ether (3 × 100 ml); the extract was washed successively with saturated solutions of $Na_2S_2O_3$ and NaCl, dried with $MgSO_4$, and evaporated. The residue was chromatographed (SiO_2, hexane), giving 4.5 g (78%) of the iodide (IV), n_D^{23} 1.4969, cf. [12]. IR spectrum (ν, cm^{-1}): 925, 1010, 1650, 3090 ($CH{=}CH_2$). PMR spectrum (100 MHz, $CDCl_3$): 1.1-1.6 (m, 12H, CH_2), 1.7-2.16 (m, 4H, H-2, H-9), 3.18 (t, 2H, J = 7 Hz, H-1), 4.85-5.1 (m, 2H, H-11), 5.6-6.0 (m, 1H, H-10).

Eicos-1-ene (V). To a stirred suspension of 0.54 g ($2.83\ 10^{-3}$ mole) of CuI in 27 ml of abs. THF was added 0.43 g ($2.83 \cdot 10^{-3}$ mole) of 2,2'-bipyridyl, and the mixture was stirred at 20°C under argon for 0.5 h and was then cooled to 2°C, and to it were added a solution of 3.75 g ($13.4 \cdot 10^{-3}$ mole) of the iodide (IV) in 27 ml of abs. THF and, after 10 minutes stirring, the Grignard reagent prepared from 0.81 g ($33.8 \cdot 10^{-3}$ g-atom) of magnesium, and 6.42 g ($31.0 \cdot 10^{-3}$ mole) of n-nonyl bromide in 36 ml of abs. THF. The reaction mixture was stirred at 2°C for 2 h and at 20°C for 12 h and, after the addition of 50 ml of a saturated solution of NH_4Cl that had been cooled to 0°C, it was extracted with diethyl ether (3 × 100 ml), and the extract was washed successively with saturated solutions of $Na_2S_2O_3$ and NaCl, dried with $MgSO_4$, and evaporated. The residue was distilled, to give 2.66 g (71%) of compound (V), bp 150-151°C (1.5 mm), mp 27-29°C, cf. [13]. IR spectrum (ν, cm^{-1}): 920, 1000, 1654, 3080 ($CH{=}CH_2$).

3-Methylheneicosan-2-one (I). The mixture obtained by the successive addition of 0.684 g ($6.0 \cdot 10^{-3}$ mole) of $AlEt_3$ and 1.4 g ($5.0 \cdot 10^{-3}$ mole) of the alkene (V) to 0.0262 g ($0.1 \cdot 10^{-3}$ mole) of Cp_2ZrCl_2 was stirred udner argon at room temperature for 10 h and was then cooled to −5°C and was treated with a mixture of 1.38 g ($18.0\cdot10^{-3}$ mole) of allyl chloride and the catalyst prepared by mixing 0.0643 g ($0.25\cdot10^{-3}$ mole) of $Ni(acac)_2$, 0.262 g ($1.0\cdot10^{-3}$ mole) of PPh_3, and 0.284 g ($2.0\cdot10^{-3}$ mole) of $i\text{-}Bu_2AlH$ in 1 ml of hexane; the resulting mixture was heated to room temperature, and was stirred for 10 h (the reaction was accompanied by the evolution of propene); then, at 0°C, 5 ml of 5% HCl was added, the products were extracted with pentane (3 × 50 ml), and the extract was washed with saturated NaCl solution, dried with $MgSO_4$, and evaporated. The residue (1.5 g, containing 76% of the alkene (VI), GLC results) was added dropwise to a catalytic mixture prepared by the addition of 0.99 g ($10.0\cdot10^{-3}$ mole) of CuCl to a suspension of 0.177 g ($1.0\cdot10^{-3}$ mole) of $PdCl_2$ in 90 ml of THF and 10 ml of water at 60°C and then, with stirring, oxygen was bubbled through the reaction mixture at the rate of 5 liters/h for 5 min. Stirring was continued under the conditions for the preparation of the catalytic mixture (60°C, O_2) for another 6 h, and then the reaction mixture was filtered, and the filtrate was diluted with 200 ml of chloroform and was washed successively with 5% HCl (3 × 10 ml) and saturated NaCl solution, dried with $MgSO_4$, and evaporated. Chromatography of the residue on SiO_2 with gradient elution from hexane to hexane–diethyl ether (from 100:0 to 90:10) gave 0.96 g (59%) of the attractant (I), mp 34.0-35.0°C, cf. [1], its IR and PMR spectra being identical with those given in [14].

6-Methyltetradec-1-ene (IX). A stirred suspension of 1.20 g ($6.64\cdot10^{-3}$ mole) of CuI in 32 ml of abs. THF was treated with 0.96 g ($6.64\cdot10^{-3}$ mole) of 2,2'-bipyridyl, and the mixture was stirred at 20°C under argon for 0.5 h, after which it was cooled to 2°C and a solution of 3.87 g ($32\cdot10^{-3}$ mole) of allyl bromide in 32 ml of abs. THF and, after 10 minutes of stirring, the Grignard reagent obtained from 0.43 g ($18\cdot10^{-3}$ g-atom) of magnesium and 3.0 g ($12.0\cdot10^{-3}$ mole) of the bromide (VIII) (obtained from 4-methyltetrahydropyran (VII) as described in [9]) in 29 ml of abs. THF were added. The reaction mixture was stirred at 0°C for 2 h and at 20°C for 12 h, and, after the addition of 20 ml of cooled saturated NH_4Cl solution, it was extracted with pentane (3 × 100 ml), and the extract was washed with saturated NaCl solution, dried with $MgSO_4$, and evaporated. The residue was distilled, giving 2.0 g (79%) of compound (IX), n_D^{25} 1.4450, bp 130-131°C (15 mm). IR spectrum, (ν, cm^{-1}): 925, 1010, 1650, 3090 ($CH{=}CH_2$), 1390 (CH_3). PMR spectrum (100 MHz, $CDCl_3$): 0.76-0.98 (m, 6H, CH_3-6, H-14), 1.05-1.58 (m, 19H, CH_2, H-6), 2.0 (t, 2H, J = 6.5 Hz, H-3), 4.84-5.14 (m, 2H, H-1), 5.62-6.06 (m, 1H, H-2).

3,7-Dimethylpentadecan-2-one (XI). The mixture obtained by the successive addition of 0.684 g ($6.0\cdot10^{-3}$ mole) of $AlEt_3$ and 1.05 g ($5.0\cdot10^{-3}$ mole) of the alkene (IX) to 0.0262 g ($0.1\cdot10^{-3}$ mole) of Cp_2ZrCl_2 was stirred under argon at room temperature for 10 h and was then treated as described for the ketone (I). This gave 1.15 g of an intermediate product containing, according to GLC analysis, 75% of the alkene (X); its oxidation under the conditions described for the preparation of ketone (I) gave 0.73 g (58%) of ketone (XI), n_D^{22} 1.4542. IR spectrum, ν, (cm^{-1}): 1390 (CH_3), 1720 ($C{=}O$). PMR spectrum (100 MHz, $CDCl_3$): 0.76-0.99 (m, 6H, CH_3-7, H-15), 1.08 (d, 3H, J = 7 Hz, CH_3-3), 1.15-1.65 (m, 21H, CH_2, H-7), 2.13 (s, 3H, H-1), 2.46 (m, 1H, H-3).

2-Acetoxy-3,7-dimethylpentadecane (II). At 0-5°C, 0.038 g ($1.0\cdot10^{-3}$ mole) of $NaBH_4$ was added to a solution of 0.252 g ($1.0\cdot10^{-3}$ mole) of ketone (XI) in 5 ml of ethanol, and the mixture was gradually heated to room temperature and was stirred for 8 h, and then, after the addition of 5 ml of 5% HCl, it was stirred for another 2 h and was evaporated and extracted with diethyl ether (3 × 50 ml), and the extract was dried with Na_2SO_4 and evaporated. The residue was treated with 1.5 ml of a mixture (2:3) of acetic anhydride and pyridine and the reaction mixture was kept at room temperature for 24 h, diluted with 80 ml of methylene chloride, washed successively with 10% HCl and with saturated solutions of $NaHCO_3$ and NaCl, dried with [illegible]SO_4, and evaporated. The residue was chromatographed (SiO_2; hexane–diethyl ether (9:1), giving 0.24 g (82%) of the acetate (II) (ratio of erythro- and threo- isomers 1:1 according to the results of capillary GLC), n_D^{20} 1.4402, cf. [7]; its IR and PMR spectra were identical with those given in [3].

LITERATURE CITED

1. T. Sato, R. Nishida, Y. Kuwahara, H. Fukami, and S. Ishii, Agric. Biol. Chem., 40, No. 2, 391 (1976).
2. R. Baker, P. M. Winton, and R. W. Turner, Tetrahedron Lett. 21, No. 12, 1175 (1980).
3. V. N. Odinokov, V. R. Akhmetova, G. Yu. Ishmuratov, L. P. Botsman, and G. A. Tolstikov, Zh. Org. Khim., 22, No. 5, 953 (1986).

4. K. Mori, S. Masuda, and M. Matsui, Agric. Biol. Chem., 42, No. 5, 1015 (1978).
5. P. Place, M. -L. Roumestant, and J. Gore, J. Org. Chem., 43, No. 5, 1001 (1978).
6. Y. Magnusson, Tetrahedron, 34, No. 9, 1385 (1978).
7. É. P. Serebryakov and G. D. Gamalevich, Izv. Akad. Nauk SSR, Ser. Khim., No. 1, 114 (1987).
8. P. J. Kocienski and J. M. Ansell, J. Org. Chem., 42, No. 6, 1102 (1977).
9. V. N. Odinokov, G. Yu. Ishmuratov, R. Ya. Kharisov, and G. A. Tolstikov, Khim. Prir. Soedin., No. 4, 573 (1989).
10. U. M. Dzhemilev, A. G. Ibragimov, A. P. Zolotarev, R. R. Muslukhov, and G. A. Tolstikov, Izv. Akad. Nauk, Ser. Khim., No. 1, 207 (1989).
11. U. M. Dzhemilev, A. G. Ibragimov, A. P. Zolotarev, R. R. Muslukhov, and G. A. Tolstikov, Izv. Akad. Nauk, Ser. Khim. (1992).
12. C. Kaiser and F. Pueschel, Chem. Ber., 97, No. 10, 2926 (1964); Chem. Abstr., 61, No. 12, 14517 (1964).
13. C. Niemann and C. D. Wagner, J. Org. Chem., 7, 227 (1942).
14. Nguen Kong Khao, M. V. Mavrov, and É. P. Serebryakov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 3, 690 (1988).

INSECT PHEROMONES AND THEIR ANALOGUES

XLII. SYNTHESIS OF 2,6-DIMETHYLOCT-1-YL FORMATE – A MIMIC OF THE AGGREGATION PHEROMONE OF FLOUR BEETLES

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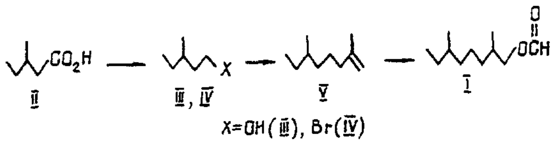
2-6-Dimethyloctan-1-ol, the formate of which is a mimic of the aggregation pheromone of the flour beetles Tribolium confusum and T. castaneum, has been synthesized by the hydroboration of 2,6-diemthyloct-1-ene, obtained from β-methylvaleric acid.

The aggregation pheromone of the flour beetles Tribolium confusum and T. castaneum, which has been identified as 4,8-dimethyldecanal [1], is deactivated under the conditions of use, being oxidized in the air. A stable analogue of the pheromone has been found – 2,6-dimethyloct-1-yl formate (I) – for which a five-stage synthesis based on the condensation of methyl sodiomalonate with the difficultly accessible 4-methylhex-3E-en-1-yl bromide has been proposed [2].

We have developed a more rational route for the synthesis of the formate (I) from the available β-methylvaleric acid (II). Its reductioin to 3-methylpentan-1-ol with the aid of lithium tetrahydroaluminate took place with a high yield, as also did the following oeprations for obtaining the bromide (IV), which are described in [3]. Condensation of the bromide (IV) with methallyl chloride completed the construction of the carbon skeleton, and hydroboration of 2,6-dimethyloct-1-ene (V) so obtained, with oxidation of the organoboron intermediate by alkaline H_2O_2 and treatment with formic acid, led to the desired formate (I), the overall yield of which amounted to 54%, calculated on the initial acid (II).



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