INSECT PHEROMONES AND THEIR ANALOGS.

XIV. SYNTHESIS OF MUSCALURE – THE SEX PHEROMONE OF *Musca domestica*

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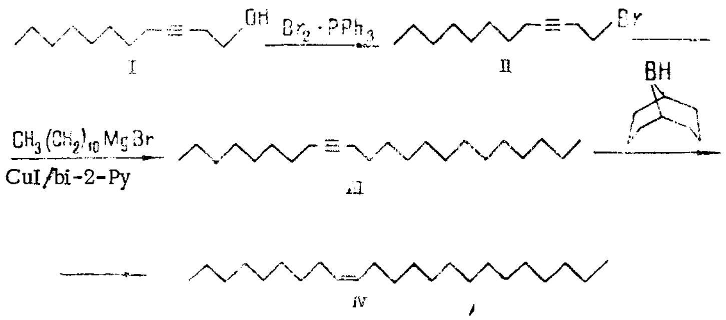
A new route to the synthesis of tricos-9Z-one – the sex pheromone of the house fly – has been developed.

Known schemes for the synthesis of tricos-9Z-ene – the sex pheromone of the house fly *Musca domestica* [1] – are based on the transformation of natural unsaturated acids [2-6], Wittig olefination [7], the disproportionation of olefins [8], Kolbe electrolysis [9], and the linkage of terminal alkynes with aklyl halides [10].

As the initial compound for the synthesis of tricos-9Z-ene (IV) we used dodec-3-yn-1-ol (I) – a readily accessible product of the β-hydroxyethylation of dec-1-yne with 2-chloroethyl vinyl ether (CEVE) [11]. The alkynol (I) was smoothly converted into 1-bromododec-3-yne (II), the combination of which with n-undecylmagnesium bromide gave tricos-9-yne (III); the reaction of (III) with 9-borabicyclo[3.3.1]nonane (9-BBN) then gave the desired alkene (IV) exclusively with the Z configuration, as was shown by the position of the single signal of the allyl carbon atoms (C^8 And C^{11}) in the 27.22 ppm region of the ^{13}C NMR spectrum [12].

The IR spectrum of compound (IV) lacked an absorption band in the 950-1000 cm^{-1} region [13], which also confirmed the stereochemical individuality of the desired product. Characteristic for the mass spectrum of the bromine derivative (II) was the presence of two molecular ions (M^+ 246 and 244) and of bromine-containing fragments with masses differing by two units (for example, 189, 197; 175, 173; 162, 160) [14]. Extremely characteristic was fragmentation at the C^2–C^3 bond with the equiprobable formation of a bromine-containing fragment (m/z 109 and 107) and of a fragment with m/z 137.



The total yield of muscalure (IV) calculated on the alkynol (I) was 58%.

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer (using films of the substances). PMR spectra were obtained on a Tesla BS-467 spectrometer with a working frequency of 60 MHz using $CDCl_3$ as solvent, and the chemical shifts are given in the δ scale reltive to the signal of TMS (internal standard). ^{13}C NMR spectra were recorded on a JEOL FX-90Q instrument in regimes with broad-band and partial suppression of proton interactions, with $CDCl_3$ as the solvent and TMS as internal standard. Mass spectra were measured on an MKh-1306 instrument at a tempera-

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ture of the ionization chamber of 150-170°C and with an ionizing energy of 70 eV. GLC analysis was performed in a Chrom-4 instrument [with the silicone fluid SE-30 (15%) on Chromaton N-AW-DMCS (0.16-0.20 mm) as the stationary phase at working temperatures of 50-300°C] or on a Chrom-5 instrument [with the polyethyleneglycol PEG-6000 (15%) on Chromaton N-AW (0.16-0.20 mm) as the stationary phase in a 1200 × 0.3 cm column at a working temperature of 170°C], the carrier gas being helium.

Dodec-3-yn-1-ol (I). At −30°C, 100 ml of absolute diglym, 0.32 g of iron acetylacetonate, and then, dropwise over 0.5 h, a solution of 16 g (0.15 mole) of CEVE in 200 ml of absolute diethyl ether were added to a suspension of lithium decynide obtained from 3.45 g (0.15 mole) of lithium amide and 21 g (0.15 mole) of dec-1-yne in 500 ml of dry liquid ammonia. The temperature of the reaction mixture was raised to 30° over 5 h and it was stirred in an atmosphere of Ar for 15 h, after which 100 ml of water and then, over 0.5 h, 100 ml of 10% HCl were added. The resulting mixture was stirred at 30°C for 2 h and then 1 liter of diethyl ether was added and the organic layer was separated off, washed with saturated NaCl, dried with Na_2SO_4, and evaporated, and the residue was distilled, giving 17.5 g (64%) of the alcohol (I) with bp 108-110°C (1 mm), n_D^{20} 1.4593 [15]. IR spectrum (ν, cm^{-1}): 1050 s; 1380 w; 1470 m; 2242 w; 2380 w; 3400 br.s. PMR spectrum (ppm): t 0.88 (3 H, CH_3, J = 7 Hz); b.r.s. 1.3 (12 H, CH_2); m 1.97-2.35 (2 H, $C^5H_2C{\equiv}C$); t 2.37 (2 H, $C^2H_2C{\equiv}C$, J = 6 Hz); br.s. 2.65 (1 H, OH); t 3.65 (2 H, CH_2O, J = 6 Hz). Mass spectrum[m/z (1, %)]: M+ 182 (0.6), 180 (0.4), 153 (0.7), 151 (0.6), 149 (0.7), 139 (1.6), 123 (1.1), 111 (1.3), 109 (1.1), 108 (0.6), 107 (1.4), 97 (18.5), 84 (11.8), 81 (11.0), 55 (15.1), 44 (100.0).

1-Bromododec-3-yne (II). A solution of 0.82 ml (16 mmole) of bromine in 20 ml of absolute CCl_4 was added dropwise to a solution of 4.19 mg (16 mmole) of triphenylphosphine in 80 ml of absolute CCl_4 (Ar, 15°C), and the mixture was stirred at 20°C for 0.5 h, after which a solution of 2.9 g (16 mmole) of the alcohol (I) in 2.3 ml of triethylamine was added at 15°C, the mixture was stirred at 20°C for 12 h, and 200 ml of pentane was added and, after filtration, the filtrate was evaporated in vacuum. The residue was chromatographed (SiO_2, n-pentane), giving 3.2 g (82%) of the bromide (II), n_D^{20} 1.4796. IR spectrum (ν, cm^{-1}): 575 w; 645 s; 1215 m; 1275 m; 1340 w; 1380 w; 1470 s; 2240 w; 2378 m.

PMR spectrum (ppm): t 0.88 (3 H, CH_3, J = 7 Hz); br.s. 1.3 (12 H, CH_2); m 1.92-2.33 (2 H, $C^5H_2C{\equiv}C$); t 2.73 (2 H, $C^2H_2C{\equiv}C$, J = 6.5 Hz); t 3.42 (2 H, CH_2Br, J = 6.5 Hz). Mass spectrum [m/z (I, %)]: M+ 246 (1.8) and 244 (1.4), 189 (13.6), 187 (13.6), 175 (4.9), 173 (5.1), 162 (16.4), 160 (16.9), 137 (16.7), 123 (11.5), 121 (7.7), 109 (17.7), 107 (51.3), 91 (19.7), 82 (19.2), 81 (18.7), 80 (16.9), 67 (24.9), 57 (65.4), 44 (100.0). Found, %: C 58.71; H 8.59; Br 32.46. $C_{12}H_{21}Br$. Calculated, %: C 58.80; H 8.57; Br 32.63.

Tricos-9-yne (III). To 0.39 g (2.05 mmole) of CuI in 10 ml of absolute THF was added 0.33 g (2.05 mmole) of bi-2-pyridyl, and the mixture was stirred at 20°C (Ar) for 0.5 h and was then cooled to 2°C and to it were added first a solution of 2.6 g (10.5 mmole) of the bromide (II) in 10 ml of absolute THF, after which it was stirred for 10 min, and then the Grignard reagent obtained from 0.6 g (0.25 g-atom) of magnesium and 3.53 g (15 mmole) of undecyl bromide in 20 ml of absolute THF. The reaction mixture was stirred at 2°C for 2 h and at room temperature for 12 h and, after the addition of 10 ml of 10% HCl, it was kept at 20°C for 2 h and then 500 ml of diethyl ether was added. The organic layer was separated off and was washed successively with 10% $NaHCO_3$ (to pH 8) and with saturated NaCl (to pH 7), dried with Na_2SO_4, and evaporated. The residue was distilled in vacuum, giving 2.5 g (74%) of the alkyne (III) with bp 169-170°C (0.5 mm), n_D^{20} 1.4545 [10].

PMR spectrum (ppm): 0.87 (6 h, CH_3, J = 7 Hz); br.s. 1.27 (34 h, CH_2); m 1.92-2.33 (4 H, $CH_2C{\equiv}C$). Mass spectrum [m/z (I, %)]: M^+ 320 (1.2), 277 (0.5), 264 (0.7), 263 (0.6), 250 (0.5); 240 (0.6), 226 (0.6), 208 (1.2), 207 (1.3), 194 (2.7), 193 (2.0), 180 (1.2), 179 (1.0), 166 (1.2), 165 (1.2), 152 (2.1), 151 (1.6), 138 (3.8), 137 (5.2), 124 (6.1), 123 (6.8), 111 (7.3), 110 (7.0), 109 (19.5), 97 (15.7), 96 (22.9), 95 (32.9), 83 (20.0), 82 (24.3), 81 (32.7), 69 (25.7), 68 (23.0), 67 (78.6), 57 (57.1), 56 (17.9), 55 (78.6), 54 (18.6), 43 (100.0), 41 (100.0).

Tricos-9Z-ene (IV). At 0-2°C (Ar), 5.5 ml (2.75 mmole) of a 0.5 M solution of 9-BBM [16] in absolute THF was added to a solution of 0.8 g (2.5 mmole) of the tricosyne (III). The reaction mixture was kept at 0°C for 24 h and then 3 ml of glacial AcOH was added and it was boiled for 5 h. Then it was cooled to 20°C and was treated with 250 ml of diethyl ether, washed with 15 ml of 6 M NaOH and then with 20 ml of saturated NaCl, dried with $MgSO_4$, and evaporated. Chromatography of the residue (Al_2O_3, with pentane as eluent) gave 0.76 g (95%) of the alkene (IV) with mp 27-28°C [10].

^{13}C NMR spectrum (δ, ppm): C^1 (C^{23}) 14.11; C^2 (C^{22}) 22.69; C^3 (C^{21}) 39.92; C^4 (C^5, C^6, C^7, C^{12}, C^{13}, C^{14}, C^{15}, C^{16}, C^{17}, C^{18}, C^{19}, C^{20}) 29.34; 29.39; 29.56; 29.69; 29.78; C^8 (C^{11}) 27.22; C^9 (C^{10}) 129.88. Mass spectrum, [m/z (I, %)]: M+ 322 (1.9), 294 (0.3), 252 (1.1), 220 (1.9), 183 (1.3), 182 (1.4), 181 (1.0), 169 (1.5), 168 (1.2), 167 (1.2), 155 (1.7), 154 (2.0), 153 (1.9), 141 (2.0), 140 (2.2), 139 (3.0), 125 (6.3), 111 (14.9), 97 (1.5), 83 (23.7), 71 (31.2), 69 (32.2), 57 (78.0), 55 (80.5), 43 (97.6), 41 (100.0).

SUMMARY

A new route to the synthesis of tricos-9Z-ene – the sex pheromone of the house fly Musca domestica – has been developed from dodec-3-yn-1-ol, the product of the β-hydroxyethylation of dec-1-yne with 2-chloroethyl vinyl ether, using stereospecific reduction of the acetylene fragment with 9-borabicyclo[3.3.1]nonane.

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