INSPECT PHEROMONES AND THEIR ANALOGUES

XL1. SYNTHESIS OF FLUORINE-CONTAINING TETRA- AND HEXADEC-11E/Z-EN-1-OLS AND THE ACETATES CORRESPONDING TO THEM – ANALOGUES OF COMPONENTS OF INSECT PHEROMONES

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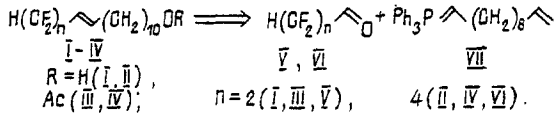
The synthesis of 13,13,14,14-tetrafluorotetradec-11E/Z-en-1-ol, and 13,13,14,14,15,15,16,16-octafluorohexadec-11E/Z-en-1-ol and their acetates – analogues of components of the pheromones of many insect species of the Lepidoptera order – has been achieved by the olefination of fluorinated aldehydes and the hydroboration of the fluorinated dienes obtained.

In recent years, interest has been shown in the synthesis of fluorine-containing analogues of insect pheromones [1-7]. In a preliminary communication [8] we have described the synthesis of a fluorinated analogue of the sex pheromone of the cabbage moth. We now give an expanded publication of the synthesis of 13,13,14,14-tetrafluorotetradec-11E/Z-en-1-ol (I) and 13,13,14,14,15,15,16,16-octafluorohexadec-11E/Z-en-1-ol (II) and the acetates (III) and (IV) corresponding to them. The nonfluorinated alcohols and acetates corresponding to the above-mentioned compounds are components of the pheromones of many insects of the order Lepidoptera [9 10].

The approach to the synthesis of fluorine-containing analogues of pheromones (I-IV) that we propose is based on the Wittig reaction of the readily accessible aldehydes (V) and (VI) with undecenylidenetriphenylphosphorane (VII).



The olefination of 2,2,3,3-tetrafluoropronalal (V) and 2,2,3,3,4,4,5,5-octafluoropentanal (VI) gave tetrafluorotetradeca-1,11-diene (VIII) and octafluorohexadeca-1,11-diene (IX), respectively, each in the form of mixtures of geometric isomers with respect to the Δ^{11} double bond. According to GLC analysis and ^1H, ^{13}C, and ^{19}F spectroscopies, the ratio of the 11E/11Z isomers was ≈53:47 in the case of the diene (VIII) and ≈70:30 for (IX). Which of the isomers was predominant in a mixture was judged from the ratio of the intensities of the signals of the vinyl protons at C-12 in the ^1H NMR spectra of the alkadienes (VIII) and (IX). For (VIII), these signals appeared in dtt form in the regions of δ 6.04 (Z-isomer) and 6.32 ppm (E-isomer), and for (IX) in the regions of 6.12 Z-isomer) and 6.40 ppm (E-isomer) [11]. The assignment of the isomers that was made agreed with the ^{13}C NMR spectra of the dienes (VIII) and (IX). In (IX) in the regions of 6.12 (Z-isomer) and 6.40 ppm (E-isomer) [11]. The assignment of the isomers that was made agreed with the ^{13}C NMR spectra of the dienes (VIII) and (IX). In the case of diene (IX) a substantially higher intensity of the signal of the C-10 allyl carbon atom at 32.04, corresponding to the e-configuration of the double bond than that of the signal in the δ 28.95 ppm region that is characteristic for the allyl carbon atom in Z-alkenes [12] was observed.

In the ^{19}F NMR spectrum of diene (VIII) the intensities of the signals of the F atoms at C-13 and C-14 in the −108.0 and −135.0 ppm regions, corresponding to the E-configuration, were somewhat greater than those of the corresponding signals at −113.0 and −134.6 ppm for the Z-siomer (VIII) [11].

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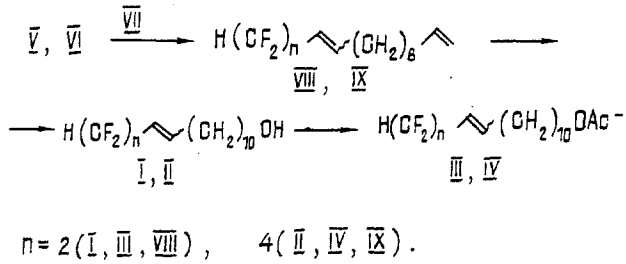

n = 2 (I, III, VIII), 4 (II, IV, IX).

The hydroboration of the dienes (VIII) and (IX) with the aid of 9-borobicyclo[3.3.1]-nonane (9-BBN) took place regioselectively with respect to the terminal double bond, and, after the oxidation of the organoboron intermediates the alcohols (I) and (II), respectively, were obtained. The acetylation of the latter gave the desired acetates (III) and (IV) in the form of mixtures of the E- and Z-isomers in the same ratio (GLC results) as that in which the geometrical isomers in the corresponding olefination products were present. With the aid of preparative HPLC it was possible to obtain from the (70:30) mixture of the E- and Z-isomers of (IV) a sample of the E-isomer containing 13% of the Z-isomer as impurity.

EXPERIMENTAL

IR spectra were taken on a UR-20 instrument (in films). PMR spectra were recorded on Tesla BS-567 (100 MHz) and Bruker AM-300 spectrometers in $CDCl_3$ with TMS as internal standard. ^{13}C NMR were taken on a Tesla BS-587A instrument (77 MHz) with $CDCl_3$ as solvent and CCl_3F as internal standard. GLC analysis was conducted on a Chrom-5 instrument with a flame-ionization detector, the stationary phase being SE-30 (5%) or FFAP (5%) on Chromaton N-Aw-MCS and the carrier gas He. Analysis of the stereoisomeric mixtures (I)–(IV), (VIII) and (IX) was carried out on a Shimadzu GC-9A instrument with a quartz capillary column (0.2 mm × 25 m). The preparative separation of the E/Z-isomers of (IV) by the HPLC method was performed on a Du Pont 8800 instrument with a Zorbax-NH_2 column, using refractometric detection, with hexane–ethyl acetate (320:7) as eluent. R_f values are given for a fixed layer of Silufol-brand SiO_2 (Czechoslovakia), the revealing agent being iodine. The analytical results (C, H, F) for the compounds synthesized corresponded to the calculated figures.

13,13,14,14-Tetrafluorotetradeca-1,11E/Z-diene (VIII). A suspension of 7.5 g ($15.2 \cdot 10^{-3}$ mole) of undecenyltriphenylphosphonium bromide in 60 ml of abs. THF was treated (–70°C, Ar) with 2.04 g ($18.24 \cdot 10^{-3}$ mole) of tert-BuOK. After 15 min, a solution of 2.5 g ($19.2 \cdot 10^{-3}$ mole) of the aldehyde (V) in 5 ml of abs. THF was added dropwise to the reaction mixture, and it was stirred at –70°C for 2 h and at room temperature for 1 h and was left to stand for 15 h. Then it was diluted with 1 liter of pentane, filtered, and evaporated. The residue (2.81 g) was chromatographed on SiO_2 in heptane, and the eluent was evaporated. This gave 1.7 g (42%) of the tetrafluorodecadiene (VIII), the ratio of E/Z-isomers being 53:47 (GLC). R_f 0.52, n_D^{20} 1.4141. IR spectrum, (ν, cm^{-1}): 718, 760 (HC=CH), 920, 980 ($HC=CH_2$), 1120, 1250 (C–F), 1642, 1670 (C=C), 3042 ($HC=CH_2$). ^1H NMR spectrum (δ, ppm): 1.30 (12H, br. s, H-4, H-5, H-6, H-7, H-8, H-9), 2.03-2.34 (4H, m, H-3, H-10), 4.90-5.05 (2H, m, H-1), 5.40-5.62 (1H, m, H-11), 5.69 (E) and 5.72 (Z) (1H, tt, $^3J_{H-F}$ 2.5 Hz, $^2J_{H-F}$, 54 Hz, H-14), 5.76-5.91 (1H, m, H-2), 6.04 (Z) and 6.32 (F) [1H, dtt, $^3J_{H-H}$ 12.0 (Z) and 16.0 Hz (E), H-12]. ^{13}C NMR spectrum (δ, ppm): 114.22 (t, C-1), 139.25 (d, C-2), 33.92 (t, C-3), 29.6 (t, C-4, C-5, C-6 and C-7), 29.5 (t, C-8), 29.2 (t, C-9), 28.3 (Z) and 32.22 (E) (t, C-10), 141.91 (Z) and 144.37 (E) [dt, $^3J_{C-F}$ 9.0 (Z) and 6.0 Hz (E), C-11], 117.56 (Z) and 116.75 (E) (dt, $^2J_{C-F}$ 23.0 Hz, C-12), 110.5 and 110.6 (tt, $^1J_{C=F}$ –248.0 Hz, $^2J_{C=F}$ 43.0 Hz, C-14). ^{10}F NMR spectrum (δ, ppm): –108.0 (E) and –113.0 (Z) (2F, F-13), –135.0 (E) and –134.6 (Z) (2F, d, $^2J_{F-H}$ 54.0 Hz, F-14).

13,13,14,14,15,15,16,16-Octafluorohexadeca-1,11E/Z-diene (IX). As described in the preceding experiment, 3.63 g ($7.35 \cdot 10^{-3}$ mole) of undecenyltriphenylphosphonium bromide, 0.95 g ($8.61 \cdot 10^{-3}$ mole) of tert-BuOK, and 1.38 g ($6 \cdot 10^{-3}$ mole) of the aldehyde (VI) gave 0.7 g (45%) of the octafluorodecadiene (IX) with a ratio of the E/Z-isomers of 70:30 (GLC), R_f 0.6, n_D^{20} 1.3961. IR spectrum (ν, cm^{-1}): 750, 770 (HC=CH), 930, 985 ($HC=CH_2$), 1125, 1255 (C–F), 1650, 1675 (C=C), 3090 ($HC=CH_2$). ^1H NMR spectrum (δ, ppm): 1.30 (12H, m, H-4, H-5, H-6, H-7, H-8 and H-9); 2.00-2.34 (4H, m, H-3, H-10), 4.93-5.10 (2H, m, H-1), 5.44-5.60 (1H, m, H-11), 6.04 (Z) and 6.05 (E) (1H, tt, $^3J_{H-F}$ 5.6 Hz, $^2J_{H-F}$ 52.1 Hz, H-16), 6.07-6.17 (1H, m, H-2), 6.12 (Z) and 6.40 (E) [1H, dtt, $^4J_{H-F}$ 2.40 (Z) and 2.41 Hz (E), $^3J_{H-F}$ 7.9 (Z) and

7.1 Hz (E), $^3J_{H-H}$ 12.1 (Z) and 15.7 Hz (E), H-12]. ^{13}C NMR spectrum (δ, ppm): 114.17 (t, C-1), 139.92 (d, C-2), 33.82 (t, C-3), 28.63, 28.95, 29.10, 29.14, 29.32 and 29.38 (t, C-4, C-5, C-6, C-7, C-8, C-9), 28.02 (Z) and 32.04 (E) (t, C-10), 143.18 (Z) and 145.61 (E) (dt, $^3J_{C-F}$ 6.0 (Z) and 9.0 Hz (E), C-11), 116, 00 (Z) and 116.83 (E) (dt, $^2J_{C-F}$ 23.0 Hz, C-13, C-14, C-15, C-16).

13,13,14,14-Tetrafluorotetradec-11E/Z-en-1-ol (I). A solution of 0.7 g ($5.64 \cdot 10^{-3}$ mole) of 9-BBN in 11 ml of abs. THF was added dropwise to a solution of 1 g ($3.76 \cdot 10^{-3}$ mole) of the diene (VIII) in 12 ml of abs. THF at 0°C, and then the temperature was raised to that of the room and the reaction mixture was stirred for 5 h. then it was cooled to 0°C and was treated with a mixture of 3.32 ml of 3 N NaOH and 3.32 ml of 28% H_2O_2, allowed to stand at room temperature for 1 h, added to a cooled saturated solution of $Na_2S_2O_3$, and extracted with CH_2Cl_2. The extract was dried with Na_2SO_4, and evaporated. The residue (1.25 g) was chromatographed on SiO_2. Elution with hexane–diethyl ether (15:1) gave 0.5 g (50%) of the initial (VIII). Elution with hexane–diethyl ether (7:1) gave 0.25 g (47%) of the alcohol (I) (E/Z = 53:47, according to GLC). IR spectrum, (ν, cm^{-1}): 750, 995 (CH=CH), 1130 (C–F), 1680 (C=C), 3400 (OH). ^1H NMR spectrum (δ, ppm): 1.2-1.6 (16H, m, H-2, H-3, H-4, H-5, H-6, H-7, H-8, and H-9), 2.10-2.35 (2H, m, H-10), 3.57 (2H, t, $^3J_{H-H}$ 6.5 Hz, H-1), 5.35-5.60 (1H, m, H-11), 5.69 (Z) and 5.86 (E) [1H, tt, $^3J_{H-F}$ 2.5 Hz, $^2J_{H-F}$ 54.0 Hz, H-14), 6.01 (Z) and 6.27 (E) [1H, dtt, $^4J_{H-F}$ 2.2 (Z) and 2.4 Hz, (E), $^3J_{H-F}$ 8.0 (Z) and 6.8 Hz (E), $^3J_{H-H}$ 12.0 (Z) and 16.0 Hz (E), H-12]. ^{13}C NMR spectrum (δ, ppm): 62.80 (t, C-1), 32.77 (t, C-2), 33.92 (t, C-3), 29.60 (t, C-4, C-5, C-6 and C-7), 29.50 (t, C-8), 29.20 (t, C-9), 28.30 (Z) and 32.10 (E) (t, C-10), 141.81 (Z) and 144.00 (E) (dt $^3J_{C-F}$ 9 (Z) and 6 Hz (E), C-11), 117.50 (E) and 116.40 (Z) (dt, $^2J_{C-F}$ 23.8 Hz, C-12), 110.50 (tt, $^1J_{C-F}$ −248.0 Hz, $^2J_{C-F}$ 43.0 Hz, C-13), 110.5 (tt, $^1J_{C-F}$ −248.0 Hz, $^2J_{C-F}$ 43.0 Hz, C-14).

13,13,14,14,15,15,16,16-Octafluorohexadec-11E/Z-en-1-ol (II). As described in the preceding experiment, 1.02 g ($2.78 \cdot 10^{-3}$ mole) of the diene (IX) and 0.35 g ($2.78 \cdot 10^{-3}$ mole) of 9-BBN gave 0.5 g (50%) of the initial diene (IX) and 0.26 g (48%) of the alcohol (II) (E/Z = 70:30, according to GLC). IR spectrum (ν, cm^{-1}): 730, 980, (HC=CH), 1140 (C–F), 1680 (C=C), 3400 (OH). ^1H NMR (δ, ppm): 1.28 (14H, br. s, H-3, H-4, H-5, H-6, H-7, H-8 and H-9), 1.50-1.65 (2H, m, H-2), 1.77-1.90 (1H, m, OH), 2.15-2.37 (2H, m, H-10), 3.64 (2H, t, $^3J_{H-H}$ 6.6 Hz, H-1), 5.40-5.65 (1H, m, H-11), 5.95-6.10 (1H, m, H-16), 6.30-6.65 (1H, m, H-12).

13,13,14,14-Tetrafluorotetradec-11E/Z-en-1-yl Acetate (III). With stirring, 0.1 g ($0.35 \cdot 10^{-3}$ mole) of the alcohol (I) was treated with 1.5 ml of a mixture (2:3) of Ac_2O and Py at room temperature. The reaction mixture was kept for 30 h, diluted with 25 ml of Et_2O, and washed successively with 5% HCl and with saturated solutions of $NaHCO_3$ and NaCl, and it was dried with $MgSO_4$ and evaporated. The residue was chromatographed on SiO_2 [eluent: pentane–ether (15:1)] and gave 0.12 g (95%) of the acetate (III) with, according to GLC, a ratio of the E/Z-isomers of 53:47, R_f 0.52, n_D^{20} 1.4209. IR spectrum (ν, cm^{-1}): 1120, 1160 (C–F), 1660 (C=C), 1240, 1730 (OAc). ^1H NMR spectrum (δ, ppm): 1.25-1.70 (16H, m, H-2, H-3, H-4, H-5, H-6, H-7, H-8 and H-9), 2.02 (3H, s, CH_3CO), 2.15-2.35 (2H, m, H-10), 4.04 (2H, t, $^3J_{H-H}$ 6.7 Hz, H-1), 5.38-5.62 (1H, m, H-11), 5.73 (E) and 5.90 (Z) (1H, tt, $^3J_{H-F}$ 2.5 Hz, $^2J_{H-F}$ 54.0 Hz, H-14), 6.05 (Z) and 6.32 (E) [1H, dtt, $^4J_{H-F}$ 2.1 (Z) and 2.4 Hz (E), $^3J_{H-F}$ 7.9 Hz (Z) and 7.0 Hz (E), H-12]. ^{13}C NMR spectrum (δ, ppm): 21.00 (q, CH_3CO), 171.23 (s, CH_2CO), 64.68 (t, C-1), 32.11 (t, C-2), 28.17-29.49 (t, C-3, C-4, C-5, C-7, C-8 and C-9), 28.95 (Z) and 32.1 (E) (t, C-10), 141.97 (Z) and 144.50 (E) (dt, $^3J_{C-F}$ 9.1 Hz, C-12), 110.6 (tt, $^1J_{C-F}$ −250.0 Hz, $^2J_{C-F}$ 42.5 Hz, C-13), 110.6 (tt, $^1J_{C-F}$ −250.0 Hz, $^2J_{C-F}$ 43.0 Hz, C-14).

13,13,14,14,15,15,16,16-Octafluorohexadec-11E/Z-en-1-yl Acetate (IV). As described in the preceding experiment, 0.13 g ($0.34 \cdot 10^{-3}$ mole) of the alcohol (II) and 1 ml of a mixture (2:3) of Ac_2O and Py gave 0.12 g (86%) of the acetate (IV), with a ratio of the E/Z-isomers of 70:30 (GLC), R_f 0.43, n_D^{20} 14.117. The preparative HPLC of this product yielded a mixture of the E/Z-isomers in a ratio of 87:13 (GLC), n_D^{20} 1.4249. IR spectrum (ν, cm^{-1}): 1140, 1180 (C–F), 1670 (C=C), 1260, 1745 (OAc). ^1H NMR spectrum (δ, ppm): 1.29 (14H, br. s H-3, H-4, H-5, H-6, H-7, H-8 and H-9), 1.50-1.58 (2H, m, H-2), 2.03 (3H, CH_3CO), 2.10-2.26 (2H, m, H-10), 4.05 (2H, t, $^3J_{H-H}$ 7.0 Hz, H-1), 5.35-5.65 (1H, m, H-11), 6.30 (Z) and 6.40

(E) [1H, dtt, $^4J_{H-F}$ 2.1 (Z) and 2.4 Hz (E), $^3J_{H-F}$ 1.9 (Z) and 7.0 Hz (E), $^3J_{H-H}$ 16.0 (E) and 12.0 Hz (Z), H-12], 6.05 (1H, tt, $^3J_{H-F}$ 2.5 Hz, $^{-3}J_{H-F}$ 51.0 Hz, H-16), ^{13}C NMR spectrum (δ, ppm): 20.95 (q, CH_3CO), 171.17 (s, CH_3CO), 64.65 (t, C-1), 29.95 (t, C-2), 28.62, 28.69, 28.96, 29.13, 29.32, 24.46 (t, C-4, C-5, C-6, C-7, C-8 and C-9), 28.04 (Z) and 32.03 (E) (t, C-10), 143.1 (Z) and 145.5 (E) [dt, $^3J_{C-F}$ 9.0 (Z) and 6.0 Hz (E), C-11], 117.2 (Z) and 116.1 (E) (dt, $^2J_{C-F}$ 24.0 Hz C-12), 110.0-118.0 (m, C-13, C-14, C-15), 108.2 (tt, $^1J_{C-F}$ −250.0 Hz, $^2J_{C-F}$ 43.0 Hz, C-16). ^{19}F NMR spectrum (δ, ppm): −107.21 (E) and −111.72 (Z) (2F, m, F-13), −126.47 (2F, m, F-14), −130.50 (2F, m, F-15), −137.69 (2F, d $^2J_{H-F}$ 51.0 Hz, F-16).

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