

PHEROMONES OF INSECTS AND THEIR ANALOGS.

XXI. SYNTHESIS OF ALK-8Z-EN-1-OLS AND THEIR ACETATES FROM A FUNCTIONALLY DIFFERENTIATED PRODUCT OF OZONOLYSIS OF CYCLOOCTENE

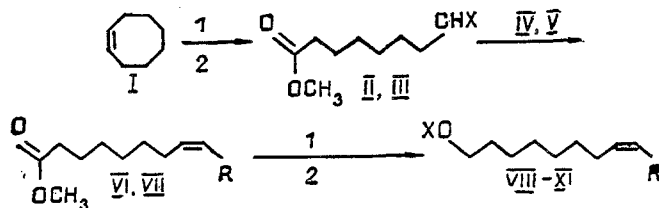
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Dodec-8Z-en-1-ol (VIII) and tetradec-8Z-en-1-ol (IX) and the corresponding acetates (X and IX) - components of the sex pheromones of many species of Lepidoptera - have been synthesized from cyclooctene (I) in three stages. The ozonolysis of (I) (-70°C , $\text{CH}_2\text{Cl}_2\text{-MeOH}$, NaHCO_3 ; -20°C , $\text{Ac}_2\text{O/Et}_3\text{N}$) led to methyl 8-oxooctanoate (II). The DNPH of (II), (III), mp $59\text{-}61^{\circ}\text{C}$. The coupling of (II) with $n\text{-C}_3\text{H}_7\text{CH=PPH}_3$ (IV) or with $n\text{-C}_5\text{H}_{11}\text{CH=PPH}_3$ (V) (-70°C , 2 h; 25°C , 15 h, Ar) gave the methyl esters of dodec-8Z-enoic (VI) and tetradec-8Z-enoic (VII) acids, respectively. The reduction of (VI) and (VII) [$(i\text{-Bu})_2\text{AlH}$, 0°C , 2 h; 25°C , 15 h] gave the corresponding alcohols (VIII) and (IX) by the acetylation ($\text{Ac}_2\text{O-Py}$, 25°C , 24 h) of which, (X) and (XI), were obtained. The yields (%): (II) 80, (VI) 45, (VII) 60, (VIII) 95, (IX) 90, (X) 75, (XI) 74. The IR and PMR spectra of compounds (II) and (VI-XI) are given.

The products of the ozonolysis of cycloolefins - bifunctional compounds with chemically nonequivalent end groups [1, 2] - are of interest for the synthesis of insect pheromones [3-5] and other biologically active substances [2, 6].

The ozonolysis of cyclooctene (I) under the conditions given in [1] led in high yield to methyl 8-oxooctanoate (II), which was used in the Wittig reaction with *n*-alkylidene-triphenylphosphoranes, opening up a simple route to insect pheromones having the structures of alk-8Z-en-1-ols and their acetates [7]. By using *n*-butylidene- and *n*-hexylidene-triphenylphosphoranes (IV and V, respectively), dodec-8Z-en-1-ol (VIII) and tetradec-8Z-en-1-ol (IX) and the corresponding acetates (X) and (XI) - components of the sex pheromones of many species of the Lepidoptera [7] - have been synthesized. For this purpose, the olefination products - the methyl esters of dodec-8Z-enoic and tetradec-8Z-enoic acids (VI and VII, respectively) - were reduced with the aid of diisobutylaluminum hydride, and the dodec-8Z-en-1-ol (VIII) and the tetradec-8Z-en-1-ol (IX) so obtained were acetylated. The yields of the desired pheromones (X) and (XI) calculated on the initial cycloalkene (I) were 29 and 36%, respectively.



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It must be mentioned that the olefination of the aldehydoester (II) by the phosphorane (V) led to the alkene (VII) exclusively with the (Z)-configuration, while when the yield (IV) was used the (Z)-alkene (VI) obtained contained about 3% of the (E)-isomer as impurity. The results of analysis by capillary GLC of the acetates (XI) and (X), respectively, led to the same conclusion concerning the stereochemistry of olefination. The configuration of the double bond in the alkene-1-ol (IX) was also confirmed by the value of the vicinal constant J for the olefinic H-8 and the H-9 protons in the PMR spectrum, which was 10.61 Hz and was characteristic for a (Z)-double bond [8]. The values of this constant and of others for the olefinic protons ($J_{H-8 H-7} = J_{H-9 H-10} = 7.38$ Hz and $J_{H-8 H-10} = J_{H-9 H-7} = -1.79$ Hz) and also the chemical shifts (δ , ppm) - 1.98 (H₂-10), 2.04 (H₂-7), and 5.36 (CH=CH) - were obtained by calculation of the six-spin system of the C-7-C-10 fragment of alcohol (IX) by the LAOCOON iteration program [9] with a mean square error of 0.173.

EXPERIMENTAL

The IR spectra of the substances were obtained on a UR-20 instrument. PMR spectra were recorded on a Tesla BS-567 spectrometer (100 MHz) with CDCl₃ or (CD)₃CO [for compounds (X and XI)] as solvent and TMS as internal standard. ¹³C NMR spectra taken on a JEOL FX-90Q spectrometer (22.50 MHz) in CDCl₃. GLC analysis was carried out on a Chrom-5 instrument with a 3 × 1200 mm stainless steel column using as the stationary phase SE-30 (5%) or PEG-20M (15%) [for compounds (VIII and IX)] on the support Chromaton N-AW-DMCS, flame-ionization detector, carrier gas helium; for compounds (X and XI) a 0.2 × 55,000 mm glass capillary column was used with PEG-40M as the stationary phase. TLC analysis was conducted on Silufol 20 × 100 mm plates with fixed layer of SiO₂, the spots being revealed with iodine.

n-Butyl- and n-hexyltriphenylphosphonium bromides (IV and V, respectively), were obtained in accordance with [10].

Methyl 8-Oxo-octanoate (II). A mixture of ozone and oxygen at a rate of 30 liters/g (the productivity of ozonizer being 50 mmole of ozone/h) was bubbled through a solution of 4.4 g (40 mmole) of cyclooctene (I) in 48 ml of a mixture (5:1) of methylene chloride and methanol containing 3.36 g (40 mmole) of NaHCO₃ at -70°C until the ozone broke through (monitored by iodine-starch indicator paper). The reaction mixture was flushed with nitrogen and was treated at -20°C with a mixture of 4 ml of acetic anhydride and 10 ml of triethylamine. Then it was stirred for 3 h and left at 8°C for 15 h, after which it was evaporated and the residue was diluted with 300 ml of diethyl ether. The ethereal solution was washed with saturated solutions of NH₄Cl, NaHCO₃, and NaCl and was dried with MgSO₄ and evaporated, and the residue was distilled in vacuum. This gave 5.0 g (80%) of the aldehydoester (II) with bp 90-100°C (5 mm Hg) [11].

According to the results of GLC analysis the amount of the main substance in the product was not less than 90%. IR spectrum (ν , cm⁻¹): 1040, 1120, 1185, 1215, 1330, 1380, 1430, 1445, 1470, 1650, 1715, 1735, 2740. PMR spectrum (δ , ppm): 1.38 and 1.64 (8 H, m, CH₂), 2.35 (4 H, m, CH₂CO), 3.67 (3 H, s, CH₃COO), 9.76 (1 H, t, J = 1.8 Hz, CHO).

The 2,4-dinitrophenylhydrazone (III) of the aldehydoester (II) was obtained by the method of [12], with mp 59-61°C. The results of analysis (C, H, N) corresponded to the calculated figures.

Methyl Dodec-8Z-enoate (VI). At -30°C, 2.0 g (18.3 mmole) of tert-BuOK in 5 ml of absolute THF was added to a suspension of 7.3 g (18.3 mmole) of butyltriphenylphosphonium bromide in 40 ml of absolute THF, the mixture was stirred for 20 min (Ar) and was cooled to -78°C, and a solution of 2.0 g (11.6 mmole) of the aldehydoester (II) in 5 ml of absolute THF was added dropwise. The reaction mixture was stirred at -78°C for 2 h and was then warmed over 1.5 h to room temperature and was left for 15 h, after which it was diluted with 300 ml of n-pentane, filtered through a layer of SiO₂ (5 g), and evaporated. The residue was chromatographed [SiO₂, pentane-ether (7:1)] to give 1.1 g (45%) of the ester (III), R_f 0.65, n_D²⁵ 1.4535.

IR spectrum (ν , cm⁻¹): 720, 745, 890, 1035, 1090, 1130, 1180, 1210, 1265, 1380, 1660, 1740. PMR spectrum (δ , ppm): 0.89 (3 H, t, J = 7 Hz, CH₃), 1.26 and 1.32 (10 H, m, CH₂), 1.9 (4 H, m, CH₂C=C), 2.31 (2 H, t, J = 7.5 Hz, CH₂CO), 3.66 (3 H, s, OCH₃), 5.36 (2 H, m, CH=CH). ¹³C NMR spectrum (δ , ppm): 51.41 (CH₃O), 174.25 (C-1), 34.67 (C-2), 24.42 (C-3), 28.88 (C-4), 29.04 (C-5), 29.26 (C-6), 27.09 (C-7), 129.8 (C-8, C-9), 29.53 (C-10), 22.26 (C-11), 13.76 (C-12).

Methyl Tetradec-8Z-enoate (VII). As described in the preceding experiment, 1.67 g (60%) of the ester (IV) with R_f 0.65, n_D^{25} 1.4540, was obtained from 7.8 g (18.3 mmole) of hexyltriphenylphosphonium bromide, 2.0 g (18.3 mmole) of tert-BuOK, and 2.0 g (11.6 mmole) of the aldehydoester (II).

IR spectrum (ν , cm^{-1}): 720, 745, 865, 895, 1005, 1040, 1100, 1130, 1180, 1215, 1260, 1370, 1445, 1470, 1660, 1745. PMR spectrum (δ , ppm): 0.89 (3 H, t, $J = 6$ Hz, CH_3), 1.39 (14 H, m, CH_2), 2.01 (4 H, m, $\text{CH}_2\text{C}=\text{C}$), 2.31 (2 H, t, $J = 7.5$ Hz, CH_2CO), 3.66 (3 H, s, OCH_3), 5.34 (2 H, m, $\text{CH}=\text{CH}$). ^{13}C NMR spectrum (δ , ppm): 51.42 (CH_3O), 174.25 (C-1), 34.13 (C-2), 24.98 (C-3), 28.93, 29.09, 29.47 (C-4-C-6, C-11), 27.14 (C-7, C-10), 129.65 and 130.09 (C-8, C-9), 31.53 (C-12), 22.59 (C-13), 14.09 (C-14). The results of analysis (C, H, C=C, OCH_3) corresponded to the calculated figures.

Dodec-8Z-en-1-ol (VIII). With stirring (-10°C , Ar) a mixture of 2.4 ml of a 73% toluene solution of $(\text{iso-C}_4\text{H}_9)_2\text{AlH}$ and 3 ml of absolute diethyl ether was added slowly, dropwise, to a solution of 0.85 g (4.0 mmole) of the ester (VI) in 15 ml of absolute diethyl ether, the mixture was stirred at 0°C for 2 h and was then gradually warmed to room temperature, and it was left for 15 h. After this, with stirring, 2.5 ml of water was added dropwise at 0°C , the reaction mixture was warmed to room temperature and was stirred for 1 h, and the precipitate was filtered off and was carefully washed with diethyl ether-benzene (8:1). The filtrate was dried with MgSO_4 and evaporated (in vacuum) to give 0.7 g (95%) of the alcohol (VIII).

IR spectrum (ν , cm^{-1}): 710, 740, 1060, 1085, 1130, 1380, 1470, 1660, 3020, 3350, and (OH). PMR spectrum (δ , ppm): 0.89 (3 H, t, $J = 7$ Hz, CH_3), 1.32 (12 H, m, CH_2), 2.04 (4 H, m, $\text{CH}_2\text{C}=\text{C}$), 2.24 (1 H, s, OH), 3.62 (2 H, t, $J = 6.3$ Hz, CH_2O), 5.36 (2 H, m, $\text{CH}=\text{CH}$).

Tetradec-8Z-en-1-ol (IX). As described in the preceding experiment, 1.44 g (6.0 mmole) of the ester (VII) and 3.6 ml of a 73% toluene solution of $(\text{iso-C}_4\text{H}_9)_2\text{AlH}$ gave 1.15 g (90%) of the alcohol (IX). IR spectrum (ν , cm^{-1}): 710, 745, 1065, 1130, 1390, 1470, 1660, 3015, 3350 (OH). PMR spectrum (δ , ppm): 0.89 (3 H, t, $J = 6.3$ Hz, CH_3), 1.32 (16 H, m, CH_2), 1.92 (2 H, m, H_2-10), 2.04 (2 H, m, H_2-7), 3.62 (3 H, t, $J = 6.3$ Hz, CH_2O), 5.36 (2 H, dtt, $J_{\text{H}-8 \text{ H}-9} = 10.61$ Hz, $J_{\text{H}-7 \text{ H}-8} = 7.38$ Hz, $H_{\text{H}-7 \text{ H}-9} = -1.79$ Hz, $\text{CH}=\text{CH}$).

Dodec-8Z-en-1-yl Acetate (X). A solution of 0.5 g (2.7 mmole) of the alcohol (VIII) in 6.75 ml of a 2:3 mixture of acetic anhydride and pyridine was kept at room temperature for 24 h, and then 150 ml of diethyl ether was added to the reaction mixture and it was washed successively with saturated solutions of NH_4Cl , Na_2CO_3 , and NaCl , and was dried with MgSO_4 and evaporated. The residue was chromatographed (Al_2O_3 , neutral, Brockmann activity grade II; pentane-ether (20:1), and 0.45 g (75%) of the acetate (X) was obtained with R_f 0.45. The IR and PMR spectrum were identical with those given previously [13].

Tetradec-8Z-en-1-yl Acetate (XI). As described in the preceding experiment, 0.87 g (4.1 mmole) of the alcohol (IX) and 10.25 ml of a 2:3 mixture of acetic anhydride and pyridine gave 0.77 g (74%) of the acetate (XI) with R_f 0.45. The IR and PMR spectra were identical with those given previously [13].

SUMMARY

Alk-8Z-en-1-ols and their acetates - components of the sex pheromones of many species of insects of the order Lepidoptera - have been synthesized by the functionally differentiated ozonolysis of cyclooctene and Wittig coupling.

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