Polyunsaturated Pheromones: Semi-Synthesis of (*Z,Z*)-6,9-Alkadienes and (*Z,Z,Z*)-3,6,9-Alkatrienes from Naturally Occurring Fatty Acids

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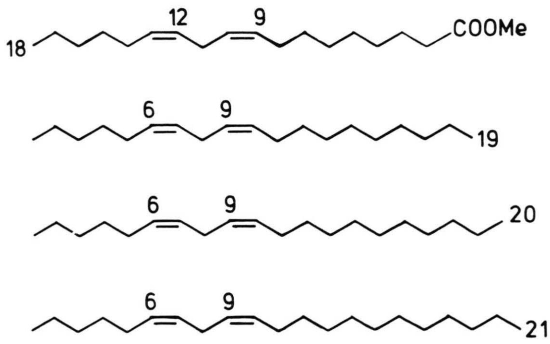
Pheromones, (*Z,Z*)-6,9-Nonadecadiene, (*Z,Z*)-6,9-Icosadiene, (*Z,Z*)-6,9-Henicosadiene, (*Z,Z,Z*)-3,6,9-Nonadecatriene, (*Z,Z,Z*)-3,6,9-Icosatriene, (*Z,Z,Z*)-3,6,9-Henicosatriene

Chain elongation of the methyl esters of linoleic and linolenic acids by one, two, or three methylene groups followed by elimination of the functional groups leads to (*Z,Z*)-6,9-alkadienes and (*Z,Z,Z*)-3,6,9-alkatrienes that function as pheromones in various insects. All of the simple reactions involved proceed in excellent yield, they do not require expensive reagents, high pressure or high temperature. The route of synthesis is applicable on a large scale. Rigorous analyses prove the purity of the hydrocarbons prepared.

Introduction

The constituent fatty acids of lipids in plant and animal tissues include polyunsaturated species that are characterized by a methylene-interrupted system of double bonds [1, 2]. The same structural feature is found in some insect pheromones [3, 4]. It is, therefore, tempting to use naturally occurring fatty acids as abundant starting material for the preparation of such "chemical messengers" (Scheme 1).



Scheme 1. Methyl linoleate and (*Z,Z*)-6,9-alkadienes derived therefrom.

The present communication describes the semi-synthesis of polyunsaturated hydrocarbons that function as pheromones in various insects. Methyl linoleate and methyl linolenate, *i.e.* the methyl esters of (*Z,Z*)-9,12-octadecadienoic and (*Z,Z,Z*)-9,12,15-octadecatrienoic acids, are converted *via* the alcohols, methanesulfonates, and cyanides to methyl esters of fatty acids with a chain length of 19 carbon atoms. Following the same route, further chain elongation leads to the methyl esters of fatty acids with 20 and 21 carbon atoms. The reaction of methanesulfonates with lithiumaluminumhydride affords the desired hydrocarbons (Scheme 2).

Obviously, methanesulfonates play a pivotal role as intermediates in the sequence of reactions that lead from fatty acids to hydrocarbons having one, two, or three methylene groups more than the starting material.

In contrast to total syntheses [3, 4], the fairly simple procedures described do not require expensive reagents, they save both time and energy. Relatively large amounts of polyunsaturated hydrocarbons can be produced in high yields by workers who need not be experts in organic synthesis. The application of these pheromones should contribute to the control of insect pests without leading to environmental pollution.

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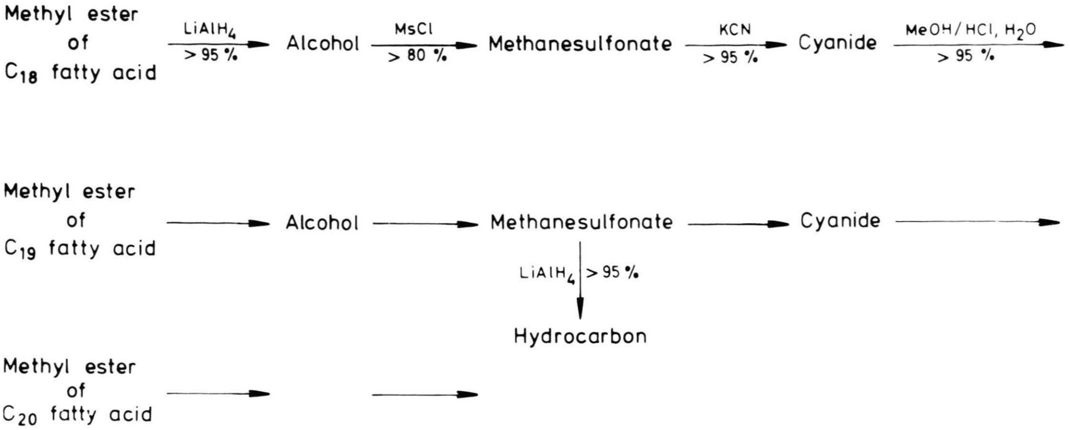

Scheme 2. Preparation of hydrocarbons from the methyl esters of fatty acids.

Experimental

Analytical methods

The course of reactions was followed by adsorption thin-layer chromatography on Silica Gel H (E. Merck, D-6100 Darmstadt) using hexane-diethyl ether, 90:10, as developing solvent. Lipid fractions were detected by exposing the chromatograms to iodine vapors.

The purity of the final products, hydrocarbons, was assessed by chromatographic, spectroscopic and thermoanalytical methods. Adsorption chromatography was carried out on thin layers of Silica Gel H and argentation chromatography on thin layers of Silica Gel H containing 10% silver nitrate; hexane-diethyl ether, 90:10 and 80:20, served as developing solvents. Lipid fractions were detected by charring after spraying the chromatograms with sulfuric acid-water, 50:50. Gas chromatography was carried out both on a Carlo Erba Fractovap 4160 instrument (Carlo Erba Instruments, D-6238 Hofheim) that was equipped with a fused silica capillary, 30 m × 0.33 mm i.d., coated with DB-5, film thickness 0.20 μm (ict, D-6230 Frankfurt 80) and on a Varian Model 3700 instrument (Varian, D-6100 Darmstadt), with a fused silica capillary, 30 m × 0.32 mm i.d., coated with DB-210, film thickness 0.50 μm (ict). The flow rate of hydrogen, the carrier gas, was adjusted to yield optimum resolution; the column temperature was 120 °C or 140 °C. Peak areas were calculated by a Merck-Hitachi Chromato-Integrator D-2000 (E. Merck).

Infrared spectra were taken on a Perkin-Elmer Spectral Photometer 257 (Perkin-Elmer Bodenseewerk, D-7770 Überlingen) using carbon tetrachloride as solvent. Ultraviolet spectra were recorded on a Pye Unicam SP 8-200 UV-VIS spectrophotometer (Pye Unicam, Cambridge CB1 2PX) in ethanol solution.

Critical solution temperatures with nitromethane (Fluka AG, CH-9470 Buchs), $CST_{(MeNO_2)}$, were determined on a Kofler heating stage under the microscope [5].

Syntheses

All reagents, adsorbents, and solvents were products of E. Merck. Methyl linoleate and methyl linolenate, products of Nu-Check-Prep Inc., Elysian MN 56028, had been prepared from safflor *(Carthamus tinctorius)* and perilla *(Perilla frutescens)* seed oils, respectively.

The syntheses were performed on a 30 g (0.1 mol) scale. All procedures were carried out under purified nitrogen in freshly distilled solvents; oxygen-free water was used for washing solutions of the reaction products.

Alcohols were obtained in > 95% yield by the reduction of methyl esters with lithiumaluminumhydride in diethylether for 4 h at 35 °C followed by hydrolysis of the lithiumalumino complexes with aqueous sulfuric acid [6].

Methanesulfonates were prepared in > 80% yield by esterification of alcohols with methanesulfonyl chloride, either in pyridine for 1 h at 0 °C and another 5 h at room temperature [7], or in hexane-triethylamine for 0.5 h at 0 °C [8].

Cyanides were obtained in > 95% yield by the reaction of methanesulfonates with potassium cyanide in dimethylsulfoxide for 1 h at 80 °C [9].

Methyl esters of elongated fatty acids were prepared in > 95% yield by treating cyanides with methanol-hydrogen chloride for 2 h at < 20 °C followed by hydrolysis of the resulting imino ethers with conc. hydrochloric acid for 2 h at < 20 °C [9].

Hydrocarbons were obtained in > 95% yield by the reaction of methanesulfonates with lithiumaluminumhydride for 4 h at 35 °C [10].

The following three pheromones were prepared using methyl linoleate as starting material: (*Z,Z*)-6,9-nonadecadiene, $CST_{(MeNO_2)}$ 135 °C; (*Z,Z*)-6,9-icosadiene, $CST_{(MeNO_2)}$ 139.5 °C; (*Z,Z*)-6,9-henicosadiene, $CST_{(MeNO_2)}$ 144 °C. Another three pheromones were obtained from methyl linolenate: (*Z,Z,Z*)-3,6,9-nonadecatriene, $CST_{(MeNO_2)}$ 121 °C; (*Z,Z,Z*)-3,6,9-icosatriene, $CST_{(MeNO_2)}$ 127.5 °C; (*Z,Z,Z*)-3,6,9-henicosatriene, $CST_{(MeNO_2)}$ 132.5 °C.

Results and Discussion

The lipids and their constituent fatty acids are abundant natural products whose utilization for the semi-synthesis of biologically active compounds of considerable value is far from being fully exploited.

The present communication demonstrates that pheromones having 19, 20, and 21 carbon atoms can be prepared in high yields from the methyl esters of naturally occurring polyunsaturated fatty acids with a chain of 18 carbon atoms. Methyl linolenate, for example, serves as starting material for the semi-synthesis of (*Z,Z*)-6,9-nonadecadiene, a component of the pheromone complex of the moth *Alsophila quadripunctata* [11], as well as homologous hydrocarbons with 20 and 21 carbon atoms. Methyl linolenate is used for the preparation of (*Z,Z,Z*)-3,6,9-nonadecatriene, a sex attractant of the giant looper, *Boarmia selenaria* [12], and homologous hydrocarbons that serve as pheromones in other insect species.

Chromatographic and spectroscopic techniques prove that the hydrocarbons we prepared are free of other classes of compounds. Argentation chromatography, gas chromatography, and infrared spectroscopy, however, show the presence of between 1.5 and 5% of configurational isomers in the diunsaturated hydrocarbons and up to 10% in the triunsaturated ones. Conjugated systems of double bonds, which would be apparent in the ultraviolet spectra, are not found.

The very low melting points of the polyunsaturated hydrocarbons are of little value as physical constants. In contrast, the CST-values of these as well as other pheromones prove to be most useful for their characterization. The $CST_{(MeNO_2)}$-values of the (*Z,Z*)-6,9-alkadienes and (*Z,Z,Z*)-3,6,9-alkatrienes with 19, 20, and 21 carbon atoms increase with increasing chain length. Obviously, the $CST_{(MeNO_2)}$-values of hydrocarbons having the same chain length decrease with increasing number of (*Z*)-double bonds in a linear fashion. The positions of the double bonds, however, have hardly any effect [5].

In carrying out the sequence of reactions delineated in Scheme 2, it is not necessary to isolate the intermediate alcohols. The reduction of methyl esters to alcohols and the esterification of the latter can even be combined in a one-pot procedure by reacting the lithiumalumino complexes with methanesulfonic anhydride. Moreover, neither the cyanides formed by the reaction of methanesulfonates with potassium cyanide, nor the imino ethers derived therefrom need be isolated. Instead, the methanesulfonates are converted in a one-pot procedure to methyl esters of fatty acids having one methylene group more than the starting material. Malonic ester synthesis, which is frequently employed for chain elongation of methanesulfonates by two methylene groups, cannot be recommended as this reaction leads to as much as 10% conjugated polyenes.

At present, the high price of unsaturated fatty acids impedes their use as starting material for the preparation of pheromones on an industrial scale. It can be expected, however, that as a consequence of current interest in the exploitation of renewable resources large amounts of these natural products will become available in high purity and at reasonable prices.

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