Preparation of Pheromones by Simple Procedures

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Z. Naturforsch. **41c,** 555–558 (1986); received December 30, 1985/February 17, 1986

Pheromones, (*Z*)-11-Hexadecenol, (*Z*)-11-Hexadecenyl Acetate, (*Z*)-11-Hexadecenal, (*Z*)-13-Octadecenol, (*Z*)-13-Octadecenyl Acetate, (*Z*)-13-Octadecenal

(*Z*)-9-Tetradecenyl methanesulfonate derived from (*Z*)-9-tetradecenoic acid (myristoleic acid) of beef tallow served as starting material for the preparation of sets of alcohols, alkyl acetates, and aldehydes having 16 and 18 carbon atoms. These compounds are known to function as pheromones in various insect species. Chain elongation of (*Z*)-9-tetradecenyl methanesulfonate by malonic ester synthesis followed by esterification afforded the methyl ester of (*Z*)-11-hexadecenoic acid. This ester was converted to a set of pheromones having a C_{16}-chain with a (*Z*)-double bond in position 11. Chain elongation of (*Z*)-11-hexadecenyl methanesulfonate yielded the methyl ester of (*Z*)-13-octadecenoic acid which was used for the preparation of a set of pheromones having a C_{18}-chain with a (*Z*)-double bond in position 13. All the reaction steps involved provided excellent yields.

Introduction

The pheromones are of great current interest as a means of controlling insect pests [1–5]. These compounds include unsaturated alcohols, alkyl acetates, and aldehydes with chains of 14, 16 or 18 carbon atoms [1–7].

Pheromones have been prepared by Wittig synthesis, by metathesis, and by Kolbe electrolysis [2–7]. We have shown that (*Z*)-9-tetradecenoic acid (myristoleic acid), which can be isolated from the forerun of the distillation of the fatty acids derived from beef tallow, constitutes a highly suitable starting material for the semi-synthetic preparation of (*Z*)-9-tetradecenol, (*Z*)-9-tetradecenyl acetate, and (*Z*)-9-tetradecenal [8]. As an extension of this work, the present communication describes the semi-synthetic preparation of pheromones having chains of 16 and 18 carbon atoms with a (*Z*)-double bond in positions 11 and 13, respectively (Scheme 1).

Chain elongation of (*Z*)-9-tetradecenyl methanesulfonate by malonic ester synthesis followed by esterification leads to methyl (*Z*)-11-hexadecenoate from which three pheromones, (*Z*)-11-hexadecenol, (*Z*)-11-hexadecenyl acetate, and (*Z*)-11-hexadecenal are obtained by modification of the functional group. Similarly, chain elongation of (*Z*)-11-hexadecenyl methanesulfonate yields methyl (*Z*)-13-octadecenoate from which another three pheromones, (*Z*)-13-octadecenol, (*Z*)-13-octadecenyl acetate, and (*Z*)-13-octadecenal are derived.

The reactions involved in the semi-synthetic preparations of these six pheromones proceed in excellent yields; migration or (*Z*)/(*E*) isomerization of the (*Z*)-double bond does not occur.

Experimental

Analytical methods

The course of reactions and the purity of products were followed by thin-layer chromatography on Silica Gel G using mixtures of hexane with diethyl ether as solvents. Lipid fractions were detected by charring after spraying the plates with chromic-sulfuric acid solution.

Gas chromatography of methyl esters, alcohols, alkyl acetates, and aldehydes was carried out on a Perkin-Elmer F 7 Fractometer equipped with flame ionization detector and a column, 10 ft × ⅛″, packed with 10% EGSS-X on Gas-Chrom P, 100–120 mesh, at 175 °C. The flow rate of nitrogen was adjusted to yield optimum resolution. Peak areas were determined by triangulation. Capillary gas chromatography was carried out on a Perkin-Elmer F 22 instrument equipped with a flame ionization detector and coupled with an Autosampler AS 41 using a WCOT fused silica column, 50 m × 0.22 mm i.d., that was coated with a layer of Silar 5 CP, 0.21 μm. Nitrogen served as carrier gas; the temperature was programmed from 160 to 200 °C at a rate of 1 °C/min. Peak areas were calculated by a Perkin-Elmer PEP 2 integrator.

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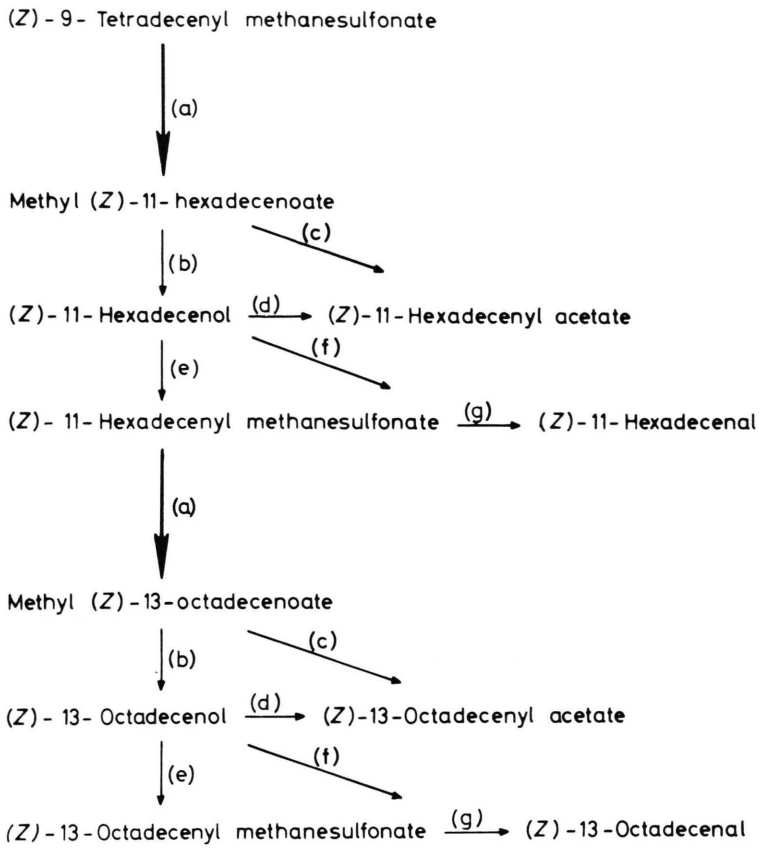
0341–0382/86/0500–0555 $ 01.30/0



Scheme 1. Preparation of some insect pheromones with 16 and 18 carbon atoms. (a) Chain elongation by malonic ester synthesis followed by esterification (~ 90% yield); (b) lithium aluminum hydride reduction (> 95% yield); (c) reaction with lithium aluminum hydride followed by acetylating decomposition of lithium-alumino complexes (> 95% yield); (d) acetylation with acetic anhydride (> 95% yield); (e) esterification with methanesulfonyl chloride (~ 80% yield); (f) oxidation with chromium trioxide-pyridine complex (~ 90% yield); (g) oxidation with dimethylsulfoxide (~ 70% yield).

Infrared spectra were taken on a Perkin-Elmer Infrared Spectrophotometer, Model 397, using carbon tetrachloride as solvent.

Melting points and critical solution temperatures with nitromethane, $CST_{(MeNO_2)}$, were determined on a Kofler heating stage under the microscope.

Syntheses

Chemicals and solvents were products of E. Merck AG, D-6100 Darmstadt.

As a rule, the various synthetic reactions were performed on a 0.01 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 in organic solvents.

The starting material, (*Z*)-9-tetradecenyl methanesulfonate, was synthesized from the constituent (*Z*)-9-tetradecenoic acid of beef tallow *via* the corresponding methyl ester and alcohol as described previously [8].

Methyl esters of elongated fatty acids were prepared in ~ 90% yield by the condensation of alkyl methanesulfonates with sodium diethyl malonate in xylene for 4 h at 110 °C followed by hydrolysis, decarboxylation and esterification [9]; methyl (*Z*)-11-hexadecenoate, m.p. −31 to −30 °C, $CST_{(MeNO_2)}$ 19 °C; methyl (*Z*)-13-octadecenoate, m.p. −13 to −12 °C, $CST_{(MeNO_2)}$ 41 °C.

Alcohols were prepared in > 95% yield by the reaction of methyl esters with lithium aluminum hydride in boiling diethyl ether for 4 h followed by hydrolysis of the lithium alumino complexes with aqueous sulfuric acid [10]; (*Z*)-11-hexadecenol, m.p. −5 to −4 °C, $CST_{(MeNO_2)}$ 65.5 °C; (*Z*)-13-octadecenol, m.p. 11−12 °C, $CST_{(MeNO_2)}$ 74.5 °C.

Alkyl acetates were prepared in > 95% yield either by the reaction of methyl esters with lithium

aluminum hydride in boiling diethyl ether for 4 h followed by acetylating decomposition of the resulting lithium alumino complexes with acetic anhydride [11], or by the acetylation of alcohols with acetic anhydride/acetonitrile in the presence of Dowex 50 W − X 8 ion exchanger [12]; (*Z*)-11-hexadecenyl acetate, m.p. −33 °C, $CST_{(MeNO_2)}$ 24 °C; (*Z*)-13-octadecenyl acetate, m.p. −15 °C, $CST_{(MeNO_2)}$ 43.5 °C.

Alkyl methanesulfonates were prepared in ~ 80% yield by esterification of alcohols with methanesulfonyl chloride in pyridine for 1 h at 0 °C and another 5 h at room temperature [13]; (*Z*)-11-hexadecenyl methanesulfonate, m.p. 0−1 °C, $CST_{(MeNO_2)} < -50$ °C; (*Z*)-13-octadecenyl methanesulfonate, m.p. 8−9 °C, $CST_{(MeNO_2)} < -50$ °C.

Aldehydes were prepared either in ~ 90% yield by the oxidation of alcohols with chromium trioxide-pyridine complex in methylene chloride/pyridine for 1 h at room temperature [14], or in ~ 70% yield by the oxidation of alkyl methanesulfonates with dimethylsulfoxide for 10 min at 160 °C [15]; (*Z*)-11-hexadecenal, m.p. −7 to −9 °C, $CST_{(MeNO_2)}$ 3.5 °C; (*Z*)-13-octadecenal, m.p. < −25 °C, $CST_{(MeNO_2)}$ 24 °C.

Results and Discussion

Tallow and slaughtering wastes constitute abundant and inexpensive sources of (*Z*)-9-tetradecenoic acid (myristoleic acid) [8]. This fatty acid can be used as starting material for the facile preparation of a series of nine pheromones in high yields. These include three pheromones having a chain of 14 carbon atoms with a (*Z*)-double bond in position 9, as described previously [8], three having a chain of 16 carbon atoms with a double bond in position 11, and three having a chain of 18 carbon atoms with a double bond in position 13. Thin-layer chromatography and gas chromatography on a packed column show that the compounds prepared are about 98.5% pure. Capillary gas chromatography, however, proves the presence of a total of 1.5 to 3.5% positional isomers in the starting material as well as the various pheromones; (*E*)-isomers are not present.

The alcohols, alkyl acetates, and aldehydes prepared are potentially useful in combatting insect pests without causing environmental pollution. Thus, (*Z*)-11-hexadecenol is part of the pheromones in the clover cutworm, *Scotogramma trifolii* [16], (*Z*)-11-hexadecenyl acetate is a major pheromone constituent in the bertha armyworm, *Mamestra configurata* [17], and (*Z*)-11-hexadecenal is part of the pheromones produced by the tobacco budworm, *Heliothis virescèns* [18]. (*Z*)-13-Octadecenol enhances the activity of pheromones in the African rice borer, *Chilo zacconius* [19] and, together with (*Z*)-13-octadecenyl acetate, it is a sex attractant in the sugarcane borer, *Chilo sacchariphagus* [20], whereas (*Z*)-13-octadecenal is a component of a mixture of pheromones in the striped rice borer, *Chilo suppressalis* [21].

All of the compounds described in the present communication have been obtained previously by numerous syntheses employing products of ozonolysis and other fragments of various unsaturated fatty acids as building blocks. These syntheses invariably lead to mixtures of geometrical isomers which have to be resolved by chromatography. In contrast, we have prepared several pheromones from a single compound, myristoleic acid, simply by chain elongation and modification of its functional group, thus preserving the (*Z*)-double bond. This route of synthesis "mimics" biosynthetic pathways that lead from fatty acids to pheromones [22].

In view of the abundance of beef tallow, the starting material, and because of the ease of the reactions employed, our semi-synthetic approach is applicable to the production of pheromones in less developed countries. Moreover, this approach is certainly more economical than rather sophisticated routes of synthesis.

Acknowledgement

The authors are grateful Ms Gisela Werner for carrying out analyses by capillary gas chromatography.

[1] M. C. Birch (ed.), Pheromones, North-Holland Publishing Company, Amsterdam and London 1974.
[2] J. M. Brand, J. Chr. Young, and R. M. Silverstein, in: Progress in the Chemistry of Organic Natural Products, **Vol. 37,** pp. 1–190 (W. Herz, H. Grisebach, and G. W. Kirby, eds.), Springer Verlag, Wien 1979.
[3] H. J. Bestmann and O. Vostrowsky, in: Chemie der Pflanzenschutz- und Schädlingsbekämpfungsmittel, **Bd. 6,** S. 29–164 (R. Wegler, Hrsg.), Springer Verlag, Berlin, Heidelberg, New York 1981.
[4] B. A. Bierl-Leonhardt and M. Beroza (eds.), Insect Pheromones Technology: Chemistry and Applications, ACS Symposium Series 190, American Chemical Society, Washington, D.C. 1982.
[5] H. E. Hummel and T. A. Miller (eds.), Techniques in Pheromone Research, Springer Verlag, New York, Berlin, Heidelberg, Tokyo 1984.
[6] H. J. Bestmann and O. Vostrowsky, Chem. Phys. Lipids **24,** 335 (1979).
[7] K. Mori, in: The Total Synthesis of Natural Products, **Vol. 4,** pp. 1–183 (J. ApSimon, ed.), John Wiley-Interscience, New York 1981.
[8] N. A. El-Rabbat and H. K. Mangold, Z. Naturforsch. **35c,** 982 (1980).
[9] F. Spener and H. K. Mangold, Chem. Phys. Lipids **11,** 215 (1973).
[10] R. F. Nystrom and W. G. Brown, J. Amer. Chem. Soc. **69,** 1197 (1947).
[11] L. A. Horrocks and D. G. Cornwell, J. Lipid Res. **3,** 165 (1962).
[12] N. Totani and T. Muramatsu, Chem. Phys. Lipids **29,** 375 (1981).
[13] W. J. Baumann and H. K. Mangold, J. Org. Chem. **29,** 3055 (1964).
[14] A. J. Valicenti and R. T. Holman, Chem. Phys. Lipids **17,** 389 (1976).
[15] V. Mahadevan, F. Phillips, and W. O. Lundberg, Lipids **1,** 183 (1966).
[16] D. L. Struble and G. E. Swailes, Environ. Entomol. **4,** 632 (1975).
[17] M. D. Chisholm, W. F. Steck, A. P. Arthur, and E. W. Underhill, Can. Entomol. **107,** 355 (1975).
[18] W. L. Roelofs, A. S. Hill, R. T. Cardé, and T. C. Baker, Life Sci. **14,** 1555 (1974).
[19] P. Zagatti, G. A. Bosson, J. Etienne, J. Berniere, C. Descoins, and M. Gallois, C. R. Seances Acad. Sci., Ser. 3, **296,** 85 (1983).
[20] B. F. Nesbitt, P. S. Beevor, D. R. Hall, R. Lester, and J. R. Williams, J. Chem. Ecol. **6,** 385 (1980).
[21] B. F. Nesbitt, P. S. Beevor, D. R. Hall, R. Lester, and V. A. Dyck, J. Insect Physiol. **21,** 1883 (1975).
[22] L. B. Bjostad and W. L. Roelofs, J. Biol. Chem. **256,** 7936 (1981).