Geometrical Isomerization of 1,5-Dienes: Isomers of Gossyplure, the Pink Bollworm Sex Attractant

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ABSTRACT

The isomeric components of gossyplure, (Z,Z)- and (Z,E)-7,11-hexadecadien-1-ol acetates, were isomerized cleanly to the (E,E) and (E,Z) acetates by the method of Vedejs and Fuchs. This method is applicable to the double inversion of 1,5-dienes. Thus, geometrical isomers of some compounds of biological interest, such as the insect sex attractants, can be more readily obtained.

INTRODUCTION

The sex attractant of the pink bollworm moth, *Pectinophora gossypiella,* was identified as a mixture of (Z,Z)- and (Z,E)-7,11-hexadecadien-1-ol acetates [1] (2). Syntheses of these compounds produced materials contaminated with minor amounts of the other 2 geometrical isomers (3). We wished to synthesize the (E,E) and (E,Z) isomers to assess more accurately the isomer content of the pheromone of the female pink bollworm and the contents of synthetic preparations of the sex pheromone, and to study the chromatographic behavior of the set of 4 isomers. Moreover, the (Z,E) isomer has been identified as the sex pheromone of the angoumois grain moth, *Sitotroga cerealella* (4). The possibility that these or other 1,5-diene acetates may function as pheromones for other species of Lepidoptera encouraged us to develop a route that would provide samples of the (E,E) and (E,Z) isomers.

Recently, Vedejs and Fuchs (5) and Bridges and Whitham (6) independently developed related methods for olefin inversion proceeding from the epoxide of the olefin. The extension of the former method to the case of 1,5-diene double inversion is described here. Other rational methods of preparing the subject isomers failed to provide pure products. These are discussed briefly since they bear on an apparent necessity for the olefin inversion process in the case of the synthesis of the (E,E) isomers.

MATERIALS AND METHODS

Infrared (IR) spectra were obtained as 3% carbon tetrachloride solutions using a Perkin Elmer 457A Spectrophotometer. Nuclear magnetic resonance (NMR) spectra were obtained in carbon tetrachloride with a Varian T-60 spectrometer and chemical shifts reported in ppm downfield relative to tetramethylsilane as internal standard. Column chromatography was monitored by thin layer chromatography using plates from Brinkmann Instruments (Westbury, New York) precoated with 0.25 mm of Sil G-25 UV_{254}. Developing solvents were 15% ether: 85% petroleum ether for compounds [1] and [3], and 50% ether:50% petroleum ether for compound [2]. Gas chromatographic analyses were performed with a Perkin Elmer Model 3920 instrument with a Silar 10C capillary column (150 ft x 0.010 in.) operating at 150 C. Samples of acetates (2) were purchased from Farchan Chemical Co. (Willoughby, OH) and were of >95% purity.

EXPERIMENTAL PROCEDURES

(Z,E)-7,8:11,12-Diepoxy-1-hexadecyl Tetrahydropyranyl ether [2] and the (Z,Z)-Isomer

The acetate [1a] (5.60 g, 20 mmole) was added dropwise as a solution in anhydrous ether (20 ml) to a chilled (0-5 C) slurry of lithium aluminum hydride (0.76 g, 20 mmole) in ether (50 ml). After the addition was complete, the mixture was stirred for 15 min without any external cooling and for 15 min under gentle reflux. Excess reducing agent was decomposed with water, and the resulting mixture was suction filtered. Concentration of the filtrate yielded the crude alcohol (1b], which was added directly to dihydropyran (2.7 ml, 30 mmole) containing 2 drops of concd hydrochloric acid. The resulting solution stood for 2 hr and was then diluted with ether. The organic phase was washed successively with 1 N potassium hydroxide and water, then dried in magnesium sulfate and concentrated. Unreacted dihydropyran was removed by dissolving the crude diene ether [1c] in isooctane and concentrating again.

A solution of m-chloroperbenzoic acid (10.2 g, 50 mmole) in methylene chloride (80 ml) was chilled to 5 C, and a solution of crude [1c] in methylene chloride (20 ml) was added dropwise. The bath was removed, and the mixture was stirred overnight at room temperature. The reaction mixture was washed successively with 1 N potassium hydroxide and brine, dried in magnesium sulfate, and concentrated. The product was then chromatographed on silica gel (100 g) by using the following solvent sequence: petroleum ether (100 ml), 1:9 ether: petroleum ether (100 ml), 1:4 (300 ml), 3:7 (300 ml), and 2:3 (100 ml). The diepoxy ether [2] was obtained in the last 400 ml of eluant (3.8 g, 58% yield from [1a]): $n^{25}D$ 1.4657 cor; IR no characteristic bands; NMR 0.92 ppm (t, CH_3, $J=7\ H_z$), 2.53 and 2.75 (m, 4H, epoxide CH's), 3.2-4.0 (m, 4H, CH_2O's), 4.50 (bs, 1H, OCHO). Analysis calculated for $C_{21}H_{38}O_4$: C, 71,14; H, 10.80. Found: C, 70.94; H, 10.76.

Preparation of the (Z,Z)-diepoxy ether from (Z,Z)-7,11-hexadecadien-1-ol acetate was the same: $n^{25}D$ 1.4657; IR not materially different from that of [2]; NMR 0.92 ppm (t, CH_3 $J=7\ H_z$), 2.77 (m, 4H, epoxide CH's), 3.2-4.0 (m, 4H, CH_2O's), 4.48 (bs, 1H, OCHO). Analysis calculated for $C_{21}H_{38}O_4$: C, 71.14; H, 10.80. Found: C, 71.32; H, 10.90.

(E,Z)-7, 11-Hexadecadien-1-o1 Acetate [3a] and the (E,E)-Isomer.

The diepoxy ether [2] (1.42 g, 4.0 mmole) was added to a solution of lithium diphenylphosphide (8.0 mmole) that had been prepared under nitrogen by using diphenylphosphine and 2.0 M n-butyllithium in hexane brought together in dry tetrahydrofuran (10 ml). The resulting red solution was allowed to stand for 40 hr. Methyl iodide (0.8 ml, 12.0 mmole) was injected into the mixture, and after 0.5 hr the product was separated from the mixture by extraction into petroleum ether. The crude product was passed through a column of silica gel (20 g) by using 60 ml each of petroleum ether and 15% ether:petroleum ether. The isomerized diene ether [3c] so obtained was treated with acetyl chloride (0.5 ml, 7.0 mmole) in acetic acid (6

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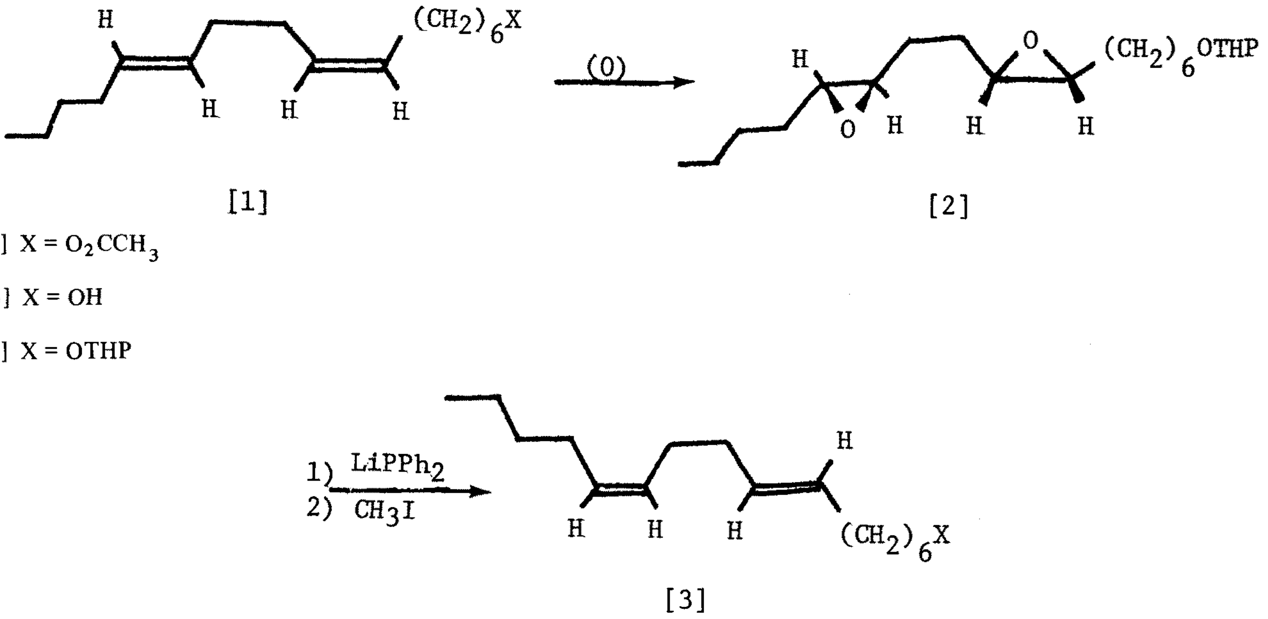
[1] Use of (Z) and (E) denotes *cis* and *trans*, respectively, as set forth by the International Union of Pure and Applied Chemists in "Tentative Rules for the Nomenclature of Organic Chemistry" (1).



[1a] X = O_2CCH_3

[1b] X = OH

[1c] X = OTHP

SCHEME 1. Isomerization of 1,5-dienes.

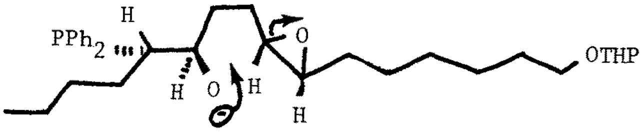
ml) for 16 hr at 40 C. The crude product was isolated in the usual manner and purified by passage through silica gel (20 g), eluting with 60 ml of each of the same 2 solvents employed in purifying [3c]. The (E,Z) acetate [3a] was thereby obtained, 0.65 g (58% yield from [2]): $n^{25}D$ 1.4564 cor; IR 1735 (C=O), 965 (E C=C) cm^{-1}; NMR 0.89 ppm (t, CH_3, J=7 H_z), 1.95 (s, 3H, CH_3C=O), 3.97 (bt, 2H, CH_2O), 5.3 (m, 4H, vinyl H). Analysis calculated for $C_{18}H_{32}O_2$: C, 77.09; H, 11.50. Found: C, 76.99; H, 11.51.

(E,E)-7,11-hexadecadien-1-ol acetate was obtained from the (Z,Z)-diepoxyether in the same manner: $n^{25}D$ 1.4559 cor, IR same as [3a] but with a stronger 965 cm^{-1} band for E double bond; NMR essentially same as [3a]. Analysis calculated for $C_{18}H_{32}O_2$: C, 77.09; H, 11.50. Found: C, 76.94; H, 11.55.

The relative retention times for the 4 geometrical isomers of 7,11-hexadecadien-1-ol acetate on the capillary gas liquid chromatograph (GLC) column/temperature described previously were (E,E) 1.0, (Z,E) 1.06, (E,Z) 1.08, and (Z,Z) 1.14.

DISCUSSION

A rational preparation of the *trans* double bonds of the 2 isomers involves sodium-liquid ammonia reduction of an acetylenic linkage. Thus the (E,Z) and (E,E) isomers could be obtained by reducing a 1,5-enyne or diyne, respectively. We found, however, that a clean reduction product could not be obtained in this manner. Despite considerable variation in reaction conditions (solvent, temperature, proton source), the desired reduction product was invariably accompanied by overreduction and underreduction products, and by compounds so similar in gas chromatographic retention time that they were probably positional, rather than geometrical isomers. For example, after acetolysis, reduction of 7,11-hexadecadiyn-1-yl tetrahydropyranyl ether with excess sodium in liquid ammonia containing t-butanol provided a mixture of acetates assessed by GLC areas as 72% (E,E)-diene, 5% each of 2 materials of shorter retention time (which mass spectral, IR, and hydrogenation data indicated were cyclic acetates), and 18% of other dienes. Clearly the proximity of the centers of unsaturation provided pathways for the formation of other compounds. Although an extension of our reported synthesis of the (Z,E) compound would yield the (E,Z) isomer (3), failure of sodium-ammonia reduction of the diyne and commercial availability of the two pink bollworm borne isomers caused us to examine olefin inversion as a means to the (E,Z) and (E,E) isomers.



SCHEME 2. Possible side reaction.

The synthetic sequence for the conversion of the (Z,E) to the E,Z) compound is outlined in Scheme 1. Absolute configurations are not implied, only relative geometries of the double bonds and epoxide rings. The sequence involving double inversion of (Z,Z) to (E,E) is completely analogous. Vedejs and Fuchs (5) noted that ester carbonyl could be attacked by diphenylphosphide anion; hence, the acetates were first converted to tetrahydropyranyl ethers (OTHP). Excess m-chloroperbenzoic acid converted the diene ethers to the corresponding diepoxides, which were purified by column chromatography, thereby removing any unreacted or monoepoxidized materials.

Treatment of the diepoxide ethers, e.g. [2], with lithium diphenylphosphide presumably generated a mixture of bis-diphenylphosphine dioxides by cleavage of both epoxide rings. It was at this stage that the proximity of the double bonds could have caused undesirable side reactions (Scheme 2). After 40 hr at room temperature, the red color of the phosphide anion had materially lightened. After reaction with methyl iodide and purification of the products by column chromatography, the diene ethers [3c] were obtained in good yield. Acetolysis and assessment of isomer content indicated complete inversion of both double bonds. Although a thorough search for products other than the diene ethers was not made, the major course of events was, in fact, sequential opening of each of the 2 epoxide rings of the diepoxy ethers [2]. Thus, the method of Vedejs and Fuchs for olefin inversion is indeed useful in isomerizing 1,5-dienes with great selectivity.

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