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PHEROMONES OF INSECTS AND THEIR ANALOGS. LIII. SYNTHESIS OF FERRULACTONE I — A PHEROMONE OF *Cryptolestes ferrugineus*

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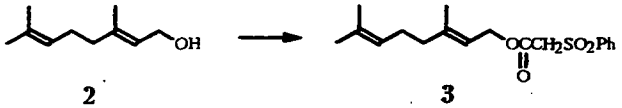
8-Acetoxy-3,7-dimethyl-1-(phenylsulfonylacetoxy)octa-2E,6E-diene has been synthesized, and its cyclization under the action of zerovalent palladium followed by desulfurization with the aid of sodium amalgam has led to ferrulactone I — one of the macrolide components of the aggregation pheromone of the rust-red grain beetle (Cryptolestes ferrugineus).

The aggregation pheromone of the rust-red grain beetle *Cryptolestes ferrugineus* is used to control the numbers of mature beetles in grain storehouses [1-2]. 4,8-Dimethyldeca-4E,8E-dien-10-olide (**1**) has been identified as the main component of the pheromone and has acquired the name ferrulactone I [3]. As a rule, macrolide (**1**) has been obtained by the cyclization of 10-hydroxy-4,8-dimethyldeca-4E,8E-dienoic acid [4-9], and the yields in this stage have been in the interval from 20 to 40%. The synthesis of ferrulactone I by the cyclization of 8-(bromoacetoxy)-2,6-dimethylocta-2E,6E-dienal has also been reported [10].

It appeared to us to be of interest to use for the synthesis of ferrulactone I (**1**) an approach described in the literature that is based on the cyclization under the action of zerovalent palladium of the phenylsulfonylacetates of alcohols containing an allylacetoxy group at the end of the carbon chain [11]. We have synthesized the 8-acetoxy-3,7-dimethyl-1-(phenylsulfonylacetoxy)octa-2E,6E-diene (**5**) required in this case from geraniol (**2**) in three stages. The interaction of geraniol with phenylsulfonylacetic acid in the presence of triphenylphosphine and diethyl azodicarboxylate in toluene gave the ester (**3**) in high yield. Its oxidation with *tert*-butyl hydroperoxide in the presence of SeO_2 in methylene chloride solution took place selectively, leading exclusively to 8-hydroxy-3,7-dimethyl-1-(phenylsulfonylacetoxy)octa-2E,6E-diene (**4**), although the oxidation of geraniol or its acetate under the same conditions gives as an impurity a product with a terminal oxo group [12]. As in the case of the allyl oxidation of the terminal methyl group of geranyl acetate [12], in the oxidation of the ester (**3**) it was the transoid methyl group that was attacked exclusively.

The *trans*- configuration of the Δ^6 bond in compound (**4**) was confirmed by the presence in its PMR spectrum of a single singlet of the H_2C^8 group, the position of which (δ 3.88 ppm) showed the (E) geometry of its terminal fragment [12]. The macrocyclization of the acetoxy derivative (**5**), obtained in the usual way from (**4**), was achieved in THF solution in the presence of Pd^0 generated from $(Ph_3P)_4Pd$ by the action of NaH. As a result, the macrolide (**6**) was synthesized with a yield of 37%. Elimination of the phenylsulfonyl group in the latter took place smoothly when it was treated with sodium amalgam. The overall yield of ferrulactone I in this five-stage synthesis amounted to 17%, calculated on the initial geraniol.



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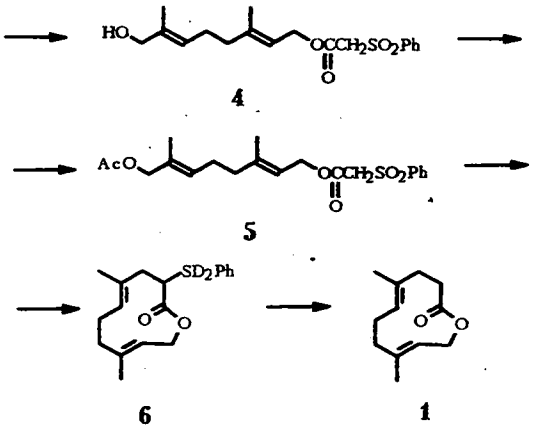

EXPERIMENTAL

IR spectra were taken on a UR-20 instrument in a thin layer. PMR spectra were measured relative to TMS on a Tesla BS-567 spectrometer, δ scale. GLC analysis was conducted on a Chrom-5 chromatograph, column length 1.2 m, stationary phase SE-30 (5%) on Chromaton N-AW-DMCS (0.6-0.20 mm), working temperature 50-300°C, carrier gas helium. The elementary analyses of the compounds obtained corresponded to the calculated figures.

3,7-Dimethyl-1-(phenylsulfonylacetoxy)octa-2E,6E-diene (3). At 20-25°C, a solution of diethyl azodicarboxylate in 5 ml of dry toluene was added to a stirred solution of 1.31 g (5 mmole) of PPh_3, 0.77 g (5 mmole) of geraniol, and 1.4 g (7 mmole) of $PhSO_2CH_2COOH$ in 5 ml of dry toluene. The reaction mixture was stirred at room temperature for 12 h, the solvent was distilled off, and 10 ml of diethyl ether was added to the residue. The resulting precipitate was filtered off and was washed on the filter with ether. The filtrate was washed successively with saturated $NaHCO_3$ solution and H_2O, dried with $MgSO_4$, and evaporated. The residue was chromatographed (neutral Al_2O_3, hexane—ethyl acetate (2:3), iodine), giving 1.68 g (91.6%) of the ester (3). IR spectrum (ν_{max}, cm^{-1}): 820 (C=C), 1600 (Ar), 1740 (C=O). PMR spectrum (100 MHz, $CDCl_3$): 1.58 (9H, br.s, CH_3), 1.93 (4H, m, H-4, H-5), 4.1 (2H, s, CH_2-S), 4.47 (2H, d, J = 7 Hz, H-1), 5.05 (1H, t, J = 6 Hz, H-6), 5.28 (1H, t, J = 7 Hz, H-2), 7.57 and 7.87 (5H, m, Ar).

8-Hydroxy-3,7-dimethyl-1-(phenylsulfonylacetoxy)octa-2E,6E-diene (4). A solution of 0.32 g (2.9 mmole) of SeO_2 in 1.25 ml of abs. CH_2Cl_2 was treated with 1.0 ml (2.9 mmole) of a solution of *tert*-butyl hydroperoxide in CH_2Cl_2, the mixture was stirred at room temperature for 0.5 h, and was then cooled to 0°C, 0.5 g (1.4 mmole) of ester (3) in 0.5 ml of abs. CH_2Cl_2 was added, and stirring at 0°C was continued for 3 h. The reaction mixture was diluted with diethyl ether and was washed successively with 10% KOH solution and with saturated NaCl, dried with $MgSO_4$, and evaporated. Residue was chromatographed (SiO_2, ether), giving 0.43 g (81%) of compound (4). IR spectrum (ν_{max}, cm^{-1}): 1605 (Ar), 1725 (C=O), 3400 (OH). PMR spectrum (100 MHz, $CDCl_3$): 1.57 and 1.67 (6H, s, CH_3), 1.92-2.06 (4H, m, H-4, H-5), 3.88 (2H, s, H-8), 4.02 (2H, s, CH-S), 4.42 (2H, t, J = 7 Hz, H-1), 5.15 (1H, t, J = 6 Hz, H-6), 5.32 (1H, t, J = 7 Hz, H-2), 7.53-7.9 (5H, m, Ar).

8-Acetoxy-3,7-dimethyl-1-(phenylsulfonylacetoxy)octa-2E,6E-diene (5). With stirring, 0.96 ml of Ac_2O was added to a solution of 0.4 g (1.1 mmole) of compound (4) in 1.44 ml of dry pyridine. The reaction mixture was stirred for 24 h, diluted with diethyl ether, and washed successively with 1 N HCl, saturated NaCl solution, and H_2O, dried with $MgSO_4$, and evaporated. The residue was chromatographed (neutral Al_2O_3, hexane—ether (1:1); revealing agent anisaldehyde), giving 0.34 g (75.5%) of the acetate (5). IR spectrum (ν_{max}, cm^{-1}): 1610 (Ar), 1740, 1760 (C=O). PMR spectrum (100 MHz, $CDCl_3$): 1.6 (6H, br.s, CH_3), 2.06 (3H, s, CH_3CO), 2.15 (4H, m, H-4, H-5), 4.05 (2H, s, CH_2-S), 4.2 (2H, s, H-8), 4.42 (2H, d, J = 7 Hz, H-1), 5.15 (1H, t, J = 6 Hz, H-6), 5.32 (1H, t, J = 7 Hz, H-2), 7.5, 7.9 (5H, m, Ar).

4,8-Dimethyldeca-4E,8E-dien-10-olide (1). In portions, 0.13 g (5.4 mmole) of NaH was added to a stirred (Ar, 0°C) solution of 2.0 g (5 mmole) of the acetate (5) in 10 ml of abs. THF, the mixture was stirred at 0°C for 15 min and then at room temperature for 30 min, and 30 ml of abs. THF was added. The resulting mixture was added at 0°C to a solution of the catalyst* and 0.29 g of bisdiphenylphosphineethylene. The mixture was filtered through a layer of silica gel, which was

*Prepared by the addition of 0.2 ml of a 10% solution of Et_3N in hexane to a solution of 0.18 g of palladium acetylacetonate and 0.33 g of Ph_3P in 1.5 ml of abs. Et_2O and stirring the resulting mixture at 20°C for 3 h.

additionally washed with ether, the filtrate was evaporated, and the residue was chromatographed (neutral Al_2O_3, hexane—ethyl acetate (2:3; revealing agent iodine). This gave 0.6 g of compound (**6**). PMR spectrum (100 MHz, $CDCl_3$): 1.57 and 1.66 (6H, s, CH_3), 1.96 (4H, m, H-6, H-7), 3.91-4.12 (5H, m, H-2, H-3, H-10), 7.57 and 7.59 (5H, m, Ar).

A solution of 0.5 g of (**6**) in 30 ml of abs. EtOH at −20°C was treated with 0.15 ml of glacial AcOH and 0.44 g of granulated sodium amalgam, and the mixture was stirred at room temperature for 2.5 h, diluted with pentane, and filtered. The filtrate was washed successively with water and saturated solutions of $NaHCO_3$ and NH_4Cl, dried with $MgSO_4$, and evaporated, giving 0.30 g (82%) of the pheromone (**1**), its IR and PMR spectra being identical with those reported in [6].

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