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단 신

집파리 성 페로몬인 (Z)-9-트리코센의 효과적인 합성

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A Convenient Synthesis of (Z)-9-Tricosene (Muscalure), the Housefly Sex Pheromone

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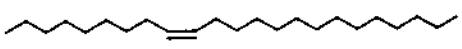
(Z)-9-Tricosene (*Fig.* 1), muscalure, is a hydrocarbon sex pheromone isolated from the cuticule and feces of the sexually mature female houseflies, **Musca domestica** L. in 1971 by Carlson *et al.*[1].

This sex attractant was found to be active by field tests[2]. It was reported that in the fields, this compound **1** may act as an aggregation pheromone[3] luring both male and female flies, rather than as a sex attractant for males only. (Z)-9-Tricosene(**1**) which has been synthesized was commercialized as Muscamone® fly attractant to enhance the effectiveness of a sugar-base fly bait containing insecticides[4]. Several syntheses[5] have been reported in the literature. Owing to the commercial importance of muscalure in pest control, an economical synthesis of the compound **1** is still desirable. The synthesis of muscalure by the coupling of erucylmethanesulfonate or erucyl bromide with MeMgCl is known[6]. However, economical production of the compound **1** by this method is hindered by the limted commercial availability of erucyl alcohol[7] and methanesulfonly chloride.



(Z)-9-Tricosene

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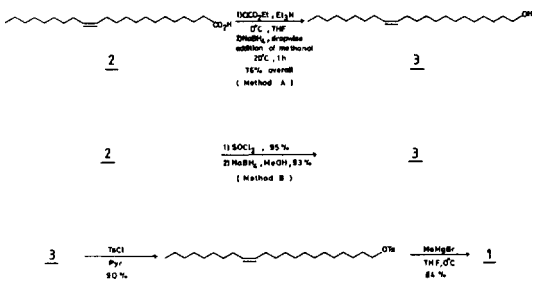
Fig. 1.

Here we wish to report a convenient synthesis of muscalure **1** which involves an economical synthesis of erucyl alcohol and the coupling of methylmagnesiumbromide with erucyltoluenesulfonate instead of erucylmethanesulfonate. Readily available and inexpensive starting material erucic acid (**2**) having a double bond in the correct position, serves nicely as the C_{22} component. Erucic acid (**2**) was easily converted into erucyl alcohol (**3**). Erucic acid anhydride prepared in situ from erucic acid (**2**) and ethyl chloroformate (1 equiv.) in THF in the presence of triethylamine (1 equiv.) was reduced[8] by sodium borohydride (3 equiv.) with dropwise addition of methanol to give erucyl alcohol (**3**) in 76% yield after separation by preparative thin layer chromatography (*Scheme* 1, Method A). Alternatively, erucic acid chloride from erucic acid and thionyl chloride was reduced with sodium borohydride (3 equiv.) in THF

with dropwise addition of methanol to give erucyl alcohol (3) in 93% yield (*Scheme* 1, Method B). Conversion of erucyl alcohol (3) into its tosylate 4 was carried out with *p*-toluenesulfonyl chloride and pyridine. Coupling



Scheme 1

of erucyl *p*-toluenesulfonate with methylmagnesiumbromide in dry THF in the presence of a catalytic amount of Li_2CuCl_4[9] afforded (Z)-9-tricosene (1) in 84% yield (*Scheme* 1). The (Z)-9-tricosene (1) thus obtained was identical in all respect (TLC, IR, ^{1}H-NMR) with the authentic compound purchased from Aldrich Chem. Co.

The above synthetic procedure described is considered to be convenient and economical for large scale production.

Infrared spectra were recorded with Shimadzu IR-400 Spectrophotometer. ^{1}H-NMR were taken on a BRUKER WP 80 SY, 80 MHz Spectrometer, using tetramethylsilane as an internal reference. All chemicals and solvents were analytical grade.

Erucyl alcohol (3).

Mehtod A: To a stirred solution of erucic acid (2) (0.50g, 1.50mmol) in dry THF (10.0m*l*) was added triethylamine (0.21m*l*, 1.50mmol) followed by ethyl chloroformate (0.14m*l*, 1.50 mmol) in dry THF (13.0m*l*) drop by drop for 30min at 0°C. After an additional 30 min at the same temperature, the mixture was filtered with suction. To the filtrate was added sodium borohydride (0.17g, 4.50mmol) in one portion and then methanol (3.00m*l*) was added dropwise for 1h at room temperature. After the reaction mixture was quenched with 6N hydrochloric acid (7.0m*l*), the solvents were evaporated at reduced pressure. The reaction mixture was extracted with ether, washed with saturated $NaHCO_3$ solution, brine and water. The organic layer was dried over anhydrous magnesium sulfate. The crude product was separated by column chromatography (silica gel, eluent= CH_2Cl_2, Rf=0.40) to give erucyl alcohol (3) (0.36g, 76%). IR(neat); 3600~3100, 2900, 1460, 1380, 1050, 720cm^{-1}; ^{1}H-NMR($CDCl_3$); δ0.89(*t*, 3H), 1.09~1.54(*m*, 32H), 1.81~2.20 (*m*, 4H), 3.63(*t*, 2H), 5.36(*t*, 2H).

Method B; To a stirred solution of erucic acid (2) (1.00g, 3.00mmol) in dry heptane (10.0 m*l*) was added thionyl chloride (0.43g, 3.60 mmol). The reaction mixture was stirred at reflux for 12h. After evaporation of the solvent, the crude product was distilled on Kugelrohr to give erucyl chloride (1.02g, 95%). To a stirred solution of erucyl chloride (0.20g, 0.56 mmol) in dry THF (3.00m*l*) was added $NaBH_4$ (0.06g, 1.68mmol) in one portion and then methanol (1.00m*l*) was added dropwise for 1h at room temperature. After an additional stirring for 1h, the reaction mixture was quenched with 1N HCl solution (3.0m*l*). After evaporation of the solvents, the reaction mixture was extracted with ether, washed with saturated sodium bicarbonate solution, brine and water. The organic layer was dried over anhydrous magnesium sulfate. Concentration in vacuo gave pure erucyl alcohol (3) (0.17g, 93%).

Erucyl *p*-toluenesulfonate (4).

To a stirred solution of erucyl alcohol (3) (0.35g, 1.1mmol) in dry CH_2Cl_2(8.0m*l*) and dry pyridine (2.0m*l*) at 0°C under nitrogen atmosphere was added *p*-toluenesulfonyl chloride

(0.28g, 1.47mmol) in dry CH_2Cl_2 by drop by drop. The reaction mixture was stirred overnight at 0°C. The solution was evaporated under reduced pressure and the residue was extracted with ether, washed with 10% cupric sulfate, saturated sodium bicarbonate solution and then brine. The organic layer was dried over anhydrous sodium sulfate to give erucyl *p*-toluenesulfonate(4) (0.46g, 90%), TLC: Rf =0.69(CH_2Cl_2); IR(neat): 1650, 1600, 1470, 1370, 1180, 670cm^{-1}; ^{1}H-NMR($CDCl_3$): δ0.89 (*t*, 3H), 1.05~1.75(*m*, 32H), 1.82~2.22(*m*, 4H), 2.45(*s*, 3H), 4.03(*t*, 2H), 5.35(*t*, 2H), 7.32(*m*, 2H), 7.80(*m*, 2H).

(Z)-9-Tricosene (1).

To a stirred solution of erucyl *p*-toluenesulfonate(4) (0.10g, 0.21mmol) in dry THF (0.21m*l*) was added Li_2CuCl_4(0.002g, 0.01mmol) and then methylmagnesiumbromide (1.0M in THF, 0.32m*l*, 0.32mmol). The reaction mixture was stirred at room temperature for 1h. The reaction mixture was quenched with saturated NH_4Cl solution and evaporated under reduced pressure. The crude product was extracted with ether, washed with brine and water. The organic layer was dried over anhydrous magnesium sulfate to afford pure (Z)-9-tricosene (1) (0.57g, 84%). TLC: Rf= 0.84(EtOAc: hexane=3 : 2). IR(neat): 3030, 1650, 1470, 1380, 730cm^{-1}; ^{1}H-NMR($CDCl_3$): δ0.89(*t*, 6H), 1.11~1.65(*m*, 34H), 1.82~2.23(*m*, 4H), 5.34(*t*, 2H).

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