

STEREOSPECIFIC SYNTHESIS OF (Z,E)-9,11,13-TETRADECATRIEN-1-YL ACETATE AND ALDEHYDE
SEX PHEROMONE COMPONENTS OF STENOMA CECROPIA AND ECTOMYELOIS CERATONIAE

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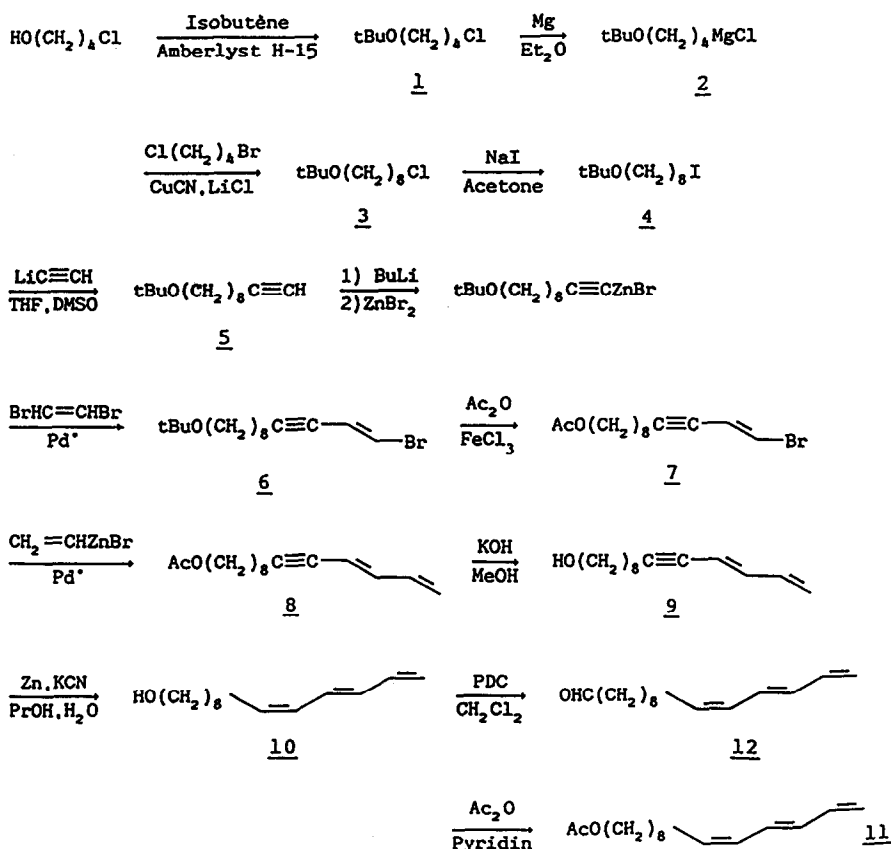
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Summary: a stereospecific synthesis of (Z,E)-9,11,13-tetradecatrien-1-yl acetate and aldehyde is described. The key steps are two sequential palladium-catalyzed cross-coupling reactions between adequate organo-zinc reagents and 1,2-dibromo ethylene with stereoselective semi-hydrogenation of a dienynic intermediate.

Ectomyelois ceratoniae (Lepidoptera, Pyralidae) is a widespread pyralid moth pest of nuts and fruits, including carobs and dates in North Africa and *Stenoma cecropia* (Lepidoptera, Stenomidae) is a defoliator of oil palm trees in South America. Several linear ethylenic compounds have been identified in the female sex pheromone gland extracts of these moths by gas liquid chromatography and mass spectroscopy. (Z,E)-9,11-tetradecadien-1-yl acetate and the corresponding aldehyde are the two main components found in the extract of *Stenoma cecropia* (1) and (Z,E) 9,11-tetradecadienal and (Z)-9-tetradecenal are the two minor components of the same one of *Ectomyelois ceratoniae* (2). Moreover, GC/MS data suggested also that minor components for *Stenoma cecropia* were linear conjugated triinsaturated C₁₄ acetate and aldehyde, with at least insaturations in 9 and 11 positions and that major component for *Ectomyelois ceratoniae* was the same C₁₄ aldehyde (m/z: 206 (M⁺, 6%); 79 (100%)). Our target was to confirm identification of this common C₁₄ product in both insects by total synthesis of the most putative isomer. Firstly, by analogy with precedent results on the processionary moth (3), (Z)-9,11-tetradecenyln-1-yl acetate and aldehyde were synthesized (4). Since their retention times were different with those of the natural products and their EAG responses for the two male species were very poor, enynic structures were excluded and corresponding trienic compounds, namely (Z,E)-9,11,13-tetradecatrien-1-yl acetate and aldehyde were considered. Herein is reported synthesis of these trienic products. Since a few years, several laboratories have been interested in synthesis of 1,3,5-undecatrienes (5-7) which are reported to exhibit odors highly appreciated in perfumery. These trienes are isolated from the essential oils of both Galbanum (*Ferula galbaniflua*) and an Hawaiian seaweed (*Dictyopteris*).

The need for regio and stereochemically pure compounds for biological tests is well-recognized. A number of stereoselective methods (6,7) for the obtention of these non-functionalized trienes have been described. In our case the approach which has given the best results was based upon a recent published method of Rossi (7) which involved two sequential palladium-catalyzed cross coupling reactions. A first coupling between a molar excess of commercially available (E)/(Z) 1,2-dibromoethylene and adequate alkynylzinc bromides led to (E)-1-bromo-1-en-3-yne derivatives with high stereoisomeric purity; (E)-1,2-dibromoethylene reacting preferentially when it is in blend with the (Z) stereoisomer. Intermediate bromoenynes were then coupled with vinylzinc bromide to afford the corresponding 1,(E)-3-dien-5-yne. The latter were then allowed to undergo a (Z) stereoselective reduction to give 1,(E)-3,(Z)-5-trienes. In all our syntheses, alcohols were first protected as t-butyl ethers because in a recent publication Alexakis et al.(8) have shown the great advantages of this protective group: preparation and reactivity of t-butoxy Grignard reagents were exactly as the non-functionalized ones. The synthesis of trienes is illustrated by the following scheme:



Chlorobutanol was protected as the t-butyl ether 1 by reaction with isobutene and an acid catalyst (Amberlyst H-15) in hexane (95%). The tert-butoxy Grignard reagent 2 was prepared in Et₂O in a good yield (88%) and its coupling with 1-bromo-4-chlorobutane under cuprous salts catalysis (CuCN, LiCl) in THF readily gave the chlorohydrin 3 (87%) which was converted into the iodide 4 (93%). Lithium acetylide (prepared from acetylene and n-BuLi) was alkylated with 4 to provide the tert-butoxyalkyne 5 in 89% yield. Alkynylzinc bromide (1 eq.) available via metalation of 5 was treated with (Z)/(E) (60/40) 1,2-dibromoethylene (5 eq.) and Pd(PPh₃)₄ (0.03 eq.) (16h) at r. t. to afford the (E) bromoenyne 6 in 50% yield with isomeric purity more than 99%. The t-butyl ether of 6 was easily cleaved into the corresponding acetate 7 with Ac₂O and FeCl₃ in Et₂O without isomerisation (92%). Alcohol should be deprotected here because trienic structures were unstable in presence of Lewis acid. Treatment of 7 (1eq.) with vinylzinc bromide (5eq.) under palladium catalyzed conditions (0.03 eq.) (12h) at r.t. led to the (E)-11,13-tetradecadien-9-yn-1-yl acetate 8 in 75% yield (96% isomeric purity). Saponification with KOH gave without isomerisation the corresponding alcohol 9 (98%). The triple bond of 9 was semi-hydrogenated according to Morris (9) (Zn, KCN, PrOH/H₂O, 24h, r.t., 90%) to furnish the (Z)-9,(E)-11,13-tetradecatrien-1-ol 10, which was either oxidized (PDC, CH₂Cl₂, 8h, r.t., 90% 12) or acetylated (Ac₂O, pyridin, 3h, r. t., 90% 11). The trienes 10, 11, 12 were obtained with isomeric purity of 98% (10). The stereochemistry of the double bonds has been ascertained by spectral properties (11) which were in good agreement with those previously reported in the literature (5,12).

In conclusion, this route allowed us to prepare trienic products with very high stereoisomeric purity. Mass spectrum and GC retention times of the synthetic samples were identical to those of the natural products. Moreover, these trienic structures were in agreement with a recent study of the sex pheromone components of *Ectomyelois ceratoniae* which has been reported while this manuscript was in preparation (12). Synthetic pheromone blends including this trienic compounds were shown to be attractive for males *Stenoma cecropia* during field testing in Columbia (1) and for *Ectomyelois ceratoniae* during field testing in Tunisia (2).

References and notes

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- (10) The stereoisomeric purity of the products was evaluated by gaz chromatographic analysis which were performed on a model 2900 Carlo Erba instrument equipped with fused silica capillary polar column (25m WCOT FFAP 0.32 id, 0.3 μ m phase, oven temp. 140°C; inj. temp. 225°C; FID temp. 250°C; H₂ carrier gas flow 25 ml/min, 1.2 b).
- (11) All NMR spectra were recorded in CDCl₃ on a Bruker AC 200 at 200 MHz

¹³C NMR (δ ppm):

<u>10</u>	137.2	133.2	132.9	128.6	128.4	116.6	62.4	
<u>11</u>	170.8	137.4	133.3	133.2	128.8	128.7	116.85	64.6
<u>12</u>	202.3	137.2	133.15	133.0	128.6	128.5	116.7	43.8

¹H NMR (δ ppm):

Data of the double bond system of alcohol 10, acetate 11, and aldehyde 12 are the same.

5.07(dd)H-14, 5.20(dd)H-14', 5.48(dt)H-9, 6.06(dd)H-10, 6.18(dd)H-12, 6.37(ddd)H-13, 6.46(dd)H-11, JH-9/H-10=11Hz, JH-8/H-9=7.5Hz, JH-10/H-11=11.5Hz, JH-11/H-12=15Hz, JH-12/H-13=11Hz, JH-13/H-14=10Hz, JH-13/H-14'=16.8Hz, JH-14/H-14'=2Hz.

10: 3.60(t)CH₂O; 11: 4.04(t)CH₂O; 12: 9.72(t, 1.75)CHO

Infrared spectra were obtained on a Perkin-Elmer 397 spectrometer

IR(neat) $\nu_{\text{cm}^{-1}}$:

10: 3340, 1620, 1570, 1455, 1000, 935, 895, 740, 720, 695.

11: 1745, 1235.

12: 2700, 1720.

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