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SYNTHESIS OF THE TWO ISOMERS OF THE POTENTIAL SEX PHEROMONE OF *THAUMETOPOEA PITYOCAMPA* (LEPIDOPTERA, NOTODONTIDAE) AND RELATED MODEL COMPOUNDS

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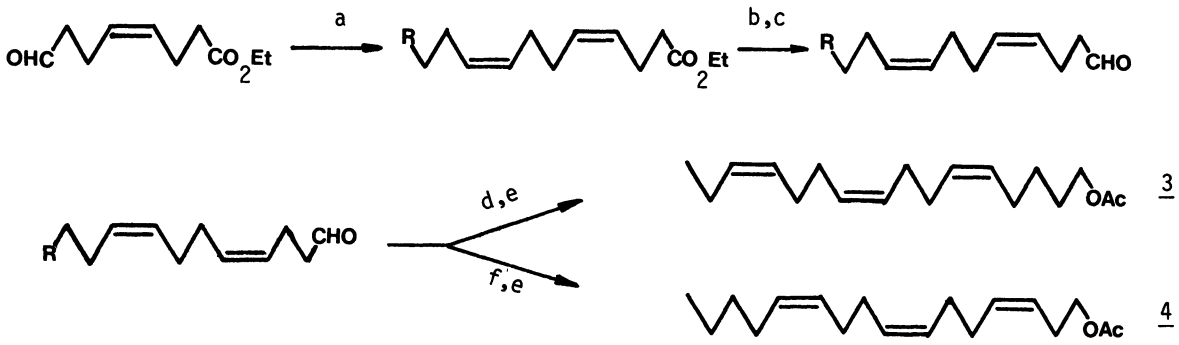
The synthesis of the major component of the sex pheromone secretion of the processionary moth, *Thaumetopoea pityocampa* (Denis and Schiff.) (Lepidoptera, Notodontidae), (Z)-13-hexadecen-11-ynyl acetate (1), the corresponding (E)-isomer (2) and the four structurally related model compounds (Z/E,Z,Z)-5,9,13-hexadecatrienyl acetate (3), (Z/E,Z,Z)-3,7,11-hexadecatrienyl acetate (4), (Z/E,E,Z)-7,9,13-hexadecatrienyl acetate (5) and (Z)-7-hexadecen-5-ynyl acetate (6) is described.

As we have mentioned in a previous communication[1], preliminary mass spectral data suggested a linear triunsaturated C_{16} acetate structure for the major component of the sex pheromone secretion of the processionary moth, *Thaumetopoea pityocampa*. To obtain gas chromatographic and mass spectral information about the nature of these unsaturations, we undertook the synthesis of several model compounds, previously unknown in the literature.

(Z/E,Z,Z)-5,9,13-hexadecatrienyl acetate (3) and (Z/E,Z,Z)-3,7,11-hexadecatrienyl acetate (4) were prepared by the sequence depicted in Scheme 1. Wittig condensation of ethyl (Z)-8-oxo-4-octenoate with n-propyl and n-pentyl triphenylphosphonium bromides (K-tBuO/THF, 30 min., 25ºC) afforded, respectively, the corresponding dienic esters in a 94:6 Z:E isomer ratio[2]. Reduction of these esters with LAH, followed by Collins oxidation of the resulting alcohols yielded the expected aldehydes which were condensed with the corresponding 5-hydroxypentyl and 3-hydroxypropyl triphenylphosphonium bromides to give, after acetylation, the desired 3 and 4 in a 1:1 Z:E isomer ratio at the new formed double bond[3,4] (δ_{CDCl_3} 5.35, t, HC=C).

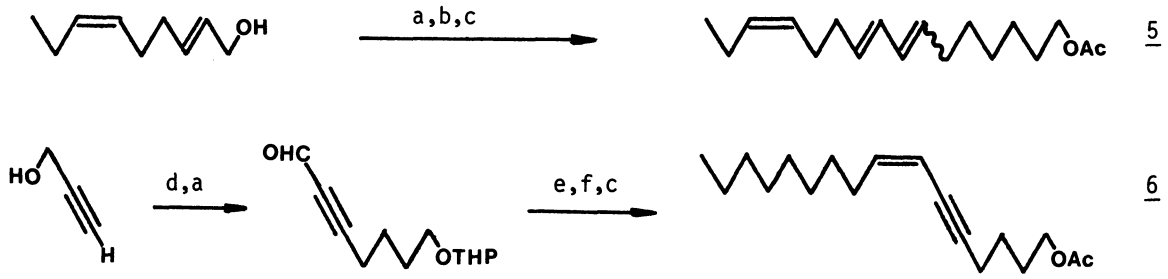
The GC retention times of the triunsaturated acetates 3 and 4 on polar and apolar columns were shorter than that exhibited by the natural product. Since it is known that conjugated dienes show longer retention times than unconjugated isomers[5], some kind of interaction between the double bonds in the active compound was inferred. Therefore, (Z/E,E,Z)-7,9,13-hexadecatrienyl acetate (5) and (Z)-7-hexadecen-5-ynyl acetate (6) were synthesized as outlined in Scheme 2.

Scheme 1



a: $Ph_3P^+(CH_2)_3R\ Br^-$, K-tBuO/THF R=H 64%, R=Et 45%; b: LAH/Et_2O 97%; c: CrO_3/Py 90%; d: $Ph_3P^+(CH_2)_5OH\ Br^-$, BuLi/THF 69%; e: Ac_2O/Py 95%; f: $Ph_3P^+(CH_2)_3OH\ Br^-$, BuLi/THF 45%.

Scheme 2



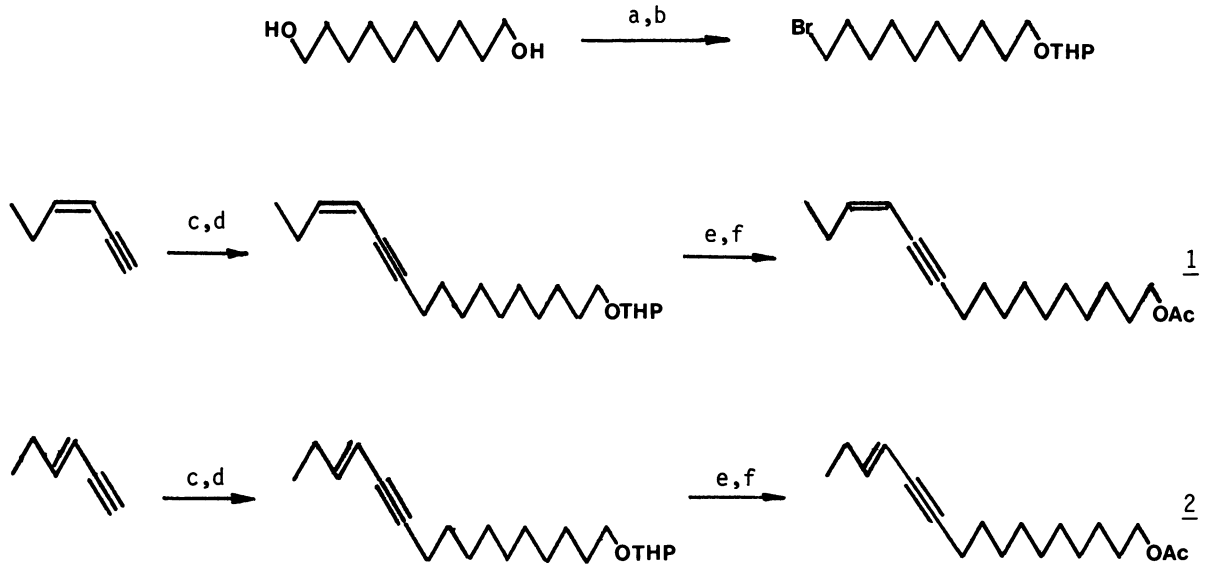
a: MnO_2/C_5H_{12} 67%; b: $Ph_3P^+(CH_2)_7OH\ Br^-$, BuLi/THF 20%; c: Ac_2O/Py 77%; d: $LiNH_2/NH_3/Cl(CH_2)_4OTHP$ 66%; e: $Ph_3P^+(CH_2)_8CH_3\ Br^-$, K-tBuO/THF 44%; f: p-TsOH/MeOH 94%.

Likewise, Wittig reaction of (E,Z)-2,6-nonadienal with 7-hydroxyheptyl triphenylphosphonium bromide under the same conditions indicated above, followed by acetylation, gave the triunsaturated acetate 5 with a 1:1 isomer ratio at C-7[3,4] (δ_{CDCl_3}: 5.7, m, HC=CH-CH=CH; 5.3, t, CH_2-CH=CH-CH_2). On the other hand, alkylation of propargylic alcohol with 4-tetrahydropyranyloxy-1-chlorobutane and oxidation of the resulting alcohol afforded the expected aldehyde which was subjected to a Wittig reaction with nonyl triphenylphosphonium bromide, under the above reaction conditions, to yield, after acetylation, the enyne acetate 6 (Z:E 94:6)[2,4] (δ_{CDCl_3}: 5.85, dt J=11 Hz, CH_2-CH=C; 5.45, d J=11 Hz, C=CH-C≡C).

Whereas the GC retention time of 5 was still shorter than that of the natural

product, that of 6 was very similar, suggesting the presence on an enyne functionality in the active compound. In fact, when enough amount of natural pheromone secretion was available for FT-NMR analysis, the structure of (Z)-13-hexadecen-11-ynyl acetate (1) could be assigned to the putative pheromone.[1] The structure elucidation was confirmed by comparison with authentic samples of 1 prepared by two independent routes. We describe herein one of them, the short and efficient sequence depicted in Scheme 3,[7,8] and the other one will be described elsewhere.[9]

Scheme 3



a: HBr 48%/C_7H_{16} 70%; b: DHP/H^+ 75%; c: BuLi/THF/HMPT; d: $Br(CH_2)_{10}OTHP$ 98%; e: p-TsOH/MeOH 94%; f: Ac_2O/Py 83%.

The required 3-hexen-1-yne[10] was obtained as a 60:40 Z:E isomer mixture by dehydration of hex-1-yn-4-ol through the corresponding tosylate.[11,12] Separation of this mixture into the corresponding pure Z and E isomers was easily accomplished by spinning band distillation at atmospheric pressure. Condensation of the lithium salt of the Z isomer with 10-tetrahydropyranyloxy-1-bromodecane[13] in HMPT at room temperature gave the expected tetrahydropyranyl derivative of (Z)-13-hexadecen-11-ynol in nearly quantitative yield (98%). Acid hydrolysis of the crude, followed by acetylation, afforded the desired (Z)-13-hexadecen-11-ynyl acetate (1) in 83% yield. (δ_{CDCl_3} 5.45, d J=10,5 Hz, C=C<u>H</u>-C≡C; 5.85, dt J=10,5 Hz and J'=7,5 Hz, CH_2<u>CH</u>=C; 4.1, t J=7 Hz, <u>CH_2</u>OAc; 2.35, t J=7 Hz, C≡C-<u>CH_2</u>; 2.3, q J=7,5 Hz, <u>CH_2</u>C=C; 2.1, s, <u>CH_3</u>CO; 1.3, complex absorption, <u>CH_2</u> sat.; 1.0, t J=7,5 Hz, <u>CH_3</u>CH_2).[4]

The E isomer 2 was obtained from the E enyne in comparable yields for each step.

(δ_{CDCl_3} 5.5, d J=16 Hz, C=CH-C≡C; 6.1, dt J=16 Hz and J'=6,5 Hz, $CH_2\underline{CH}$=C; 4.1, t J=7 Hz, $\underline{CH_2}$OAc; 2.3, t^3J=7 Hz, C≡C-$\underline{CH_2}$; 2.1, q J=7,5 Hz, $\underline{CH_2}$C=C; 2.1, s, $\underline{CH_3}$CO; 1.3, complex absorption, $\underline{CH_2}$ sat.; 1.0, t J=7,5 Hz, $\underline{CH_3}CH_2$).[4]

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